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The 3rd International Electronic Conference on Biomolecules

23–25 April 2024 | Online

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The 3rd International Electronic Conference on Biomolecules

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23–25 April 2024 | Online

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Welcome from the Chair

Dear Colleagues,

It is with great enthusiasm that we announce the **3rd International Electronic Conference on Biomolecules (IECBM2024)**. The conference is organized by the MDPI open-access journal *Biomolecules* (ISSN: 2218-273X, Impact Factor 5.5), and will be held **online** from **23 to 25 April 2024**.

This conference will provide leading scientists working in the field with an online platform on which to share their latest research and engage in exciting discussions. The main topics and sessions of the conference are:

1. Biomolecular Structures and Functions;

2. Molecular Mechanisms in Cellular Processes;

3. Biomolecular Interactions and Networks;

4. Biomaterials Design and Characterization;

5. Biocatalysis and Enzyme Engineering;

6. Bioinformatics and Computational Biology.

This is an excellent opportunity for biomolecular researchers and scientists to interact with each other, communicate with their colleagues, learn from each other, share ideas and results, help solve problems, and suggest alternative options for a better future. As well as the energetic and dynamic nature of the virtual international conference, another advantage is that you do not need to travel anywhere to attend the conference. You can take advantage of the above opportunities from wherever you live.

Under the virtual conference settings, there are additional advantages: (1) engagement tools that keep energy levels high, (2) participants are given a voice, (3) far stronger attention is received while one is talking, (4) Q&A through "Chat" is also possible if you do not wish to raise your question verbally, (5) polls, (6) feedback through Chat, (7) use of symbols under "Reactions" function to show your voice, appreciation, or a request, (8) greater reach with remote audiences, and (9) the ability to deliver live and pre-recorded presentations simultaneously.

All accepted abstracts will be available online in Open Access form on Sciforum.net during and after the conference.

Prof. Dr. Vladimir N. Uversky
Conference Chair
Department of Molecular Medicine, University of South Florida, USA

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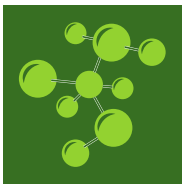

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Biomolecules (ISSN 2218-273X) is an international, peer-reviewed open access journal whose scope lays in the intersection between chemistry, biology, molecular medicine and material sciences. The journal has a strong focus on structures and functions of bioactive and biogenic substances, molecular mechanisms with biological and medical implications as well as biomaterials and their applications. Biomolecules publishes Articles, Reviews, Communications and Editorials. Basic research, in vitro and in vivo investigations and pre-clinical studies are welcome. Since our aim is to encourage scientists to publish their experimental and theoretical results in as much detail as possible, there is no upper limit on the length of papers. The full experimental details must be provided such that the results can be reproduced.

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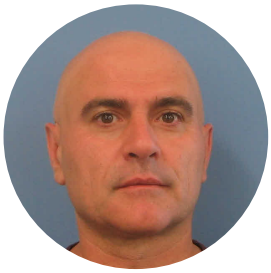

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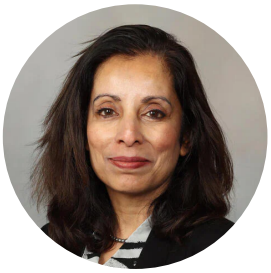

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Medway School of Pharmacy, Universities of Kent and Greenwich, UK

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School of Medicine,
Cardiff University, UK

Prof. Dr. Andrey P. Anisimov
Laboratory for Plague Microbiology, Especially Dangerous Infections Department, State Research Center for Applied Microbiology and Biotechnology, Russia

Prof. Dr. Undurti N. Das
UND Life Sciences, USA, Department of Medicine, Omega Hospitals, India, Department of Biotechnology, Indian Institute of Technology, India

Prof. Dr. Haiteng Deng
School of Life Sciences, Tsinghua University, China

Dr. Travis Beddoe
Centre for Livestock Interactions with Pathogens (CLiP), Department of Animal, Plant and Soil Sciences, AgriBio, Centre for AgriBiosciences, 5 Ring Road, La Trobe University, Australia

Dr. Frederick H. Silver
Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, Rutgers, the State University of New Jersey, USA

Dr. Guang Yu Deng
School of Materials & Engineering, University of Shanghai for Science and Technology, China

Speakers

Keynote Speakers

Prof. Dr. Jürg Bähler
Department of Genetics, Evolution & Environment and Institute of Healthy Ageing, University College London, UK

Dr. Frederick H. Silver
Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, Rutgers, the State University of New Jersey, USA

Prof. Dr. Salvador Ventura
Institute of Biotechnology and Biomedicine, Autonomous University of Barcelona, Spain, Department of Biochemistry and Molecular Biology, Autonomous University of Barcelona, Spain

Prof. Dr. Anna Rita Franco Migliaccio
Unit of Microscopic and Ultrastructural Anatomy, University Campus Bio-Medico, Italy, Altius Institute for Biomedical Sciences, USA

Prof. Dr. Zhanhui Wang
National Key Laboratory of Veterinary Public Health and Safety, Beijing Key Laboratory of Detection Technology for Animal-Derived Food, College of Veterinary Medicine, China Agricultural University, China

Prof. Dr. Umesh Desai
Department of Medicinal Chemistry, Virginia Commonwealth University, USA, Drug Discovery and Development, Institute for Structural Biology, Virginia Commonwealth University, USA

Dr. Benoit Coulombe
Translational Proteomics Research Unit, IRCM, Canada, Department of Biochemistry and Molecular Medicine, University of Montreal, Canada

Dr. Marc Maresca
CNRS, Aix-Marseille University, Centrale Marseille, iSm2, Marseille, France

Dr. Ping K. Yip
Blizard Institute, Queen Mary University of London, UK

Dr. Xuexian Yang
Department of Molecular Genetics and Microbiology, School of Medicine, University of New Mexico, USA

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Department of Chemistry, State University of New York, USA

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Institut de Chimie et Biochimie Moléculaire et Supramoléculaire, France

Prof. Dr. Anna Mitraki
Department of Materials Science and Technology, University of Crete, Greece, Institute of Electronic Structure and Laser (I.E.S.L.), Foundation for Research and Technology—Hellas (FO.R.T.H.), Vassilika Vouton, Greece

Dr. Irina Nesmelova
University of North Carolina at Charlotte, USA

Program at a Glance

The 3rd International Electronic Conference on Biomolecules
23–25 Apr 2024, Online

DAY 1 Morning	DAY 2 Morning	DAY 3 Morning
Session 1. Biomolecular Structures and Functions **Session 3.** Biomolecular Interactions and Networks	**Session 2.** Molecular Mechanisms in Cellular Processes	**Poster Session**
DAY 1 Afternoon	**DAY 2 Afternoon**	**DAY 3 Afternoon**
Session 4. Biomaterials Design and Characterization	**Session 6.** Bioinformatics and Computational Biology	**Session 5.** Biocatalysis and Enzyme Engineering

IECBM 2024 Program

23rd April 2024 (Tuesday)
Session 1. Biomolecular Structures and Functions
Session 3. Biomolecular Interactions and Networks

Time: 9:00 (CEST, Basel) | 03:00 (EDT, New York) | 15:00 (CST Asia, Beijing)

Time in CEST	Speaker	Title
09:00–09:10	**Dr. Luigi Vitagliano** **Prof. Dr. María S. García Gutiérrez** Session Chairs of S1	**Welcome from the session chair**
09:10–09:30	**Prof. Dr. Salvador Ventura** Keynote Speaker	A Structure-Based Approach to Tackle Protein Aggregation in Parkinson's Disease
09:30–09:50	**Dr. Marc Maresca** Keynote Speaker	Studying the multi-activity of Anti-Microbial Peptides (AMPs): case study of the Temporins SH family
09:50–10:10	**Dr. Ping K. Yip** Keynote Speaker	Using living patients' brain tissue to study severe traumatic brain injury
10:10–10:25	**Daniela Valeria Miniero** Selected Speaker	The role of the charged residues in the C-gate of the yeast mitochondrial NAD+ transporter Ndt1p
10:25–10:40	**Dr. Androulla Miliotou** Selected Speaker	Genetic Insights into E-Cadherin Modulation: Exploring the Benefits of Synthetic Acetyl Hexapeptide-1 in Wound Healing and Anti-Aging for Dermo-cosmetics
10:40–10:55	**Franklin Chamorro** Selected Speaker	Maximizing Bioactive Compound Extraction: How do Factors Influence the Performance of the Microwave-Assisted Technique?
10:55–11:00	**Prof. Dr. Piero Crespo** Session Chair of S3	**Welcome from the session chair**
11:00–11:20	**Dr. Xuexian Yang** Keynote Speaker	The Extracellular Signal-Mediated Activation of IRE1 Promotes TH17 Responses
11:20–11:40	**Prof. Dr. Fadi Bou-Abdallah** Keynote Speaker	Human heteropolymer ferritin derived from a novel plasmid design: subunit composition, thermostability and physiological significance
11:40–15:55	**Max Myakishev-Rempel** Selected Speaker	Molecular structure considerations for the possibility of sequence-dependent DNA resonances

23rd April 2024 (Tuesday)
Session 4. Biomaterials Design and Characterization

Time: 15:00 (CEST, Basel) | 09:00 (EDT, New York) | 21:00 (CST Asia, Beijing)

Time in CEST	Speaker	Title
15:00–15:10	**Dr. Martin Muschol** Session Chair	**Welcome from the session chair**
15:10–15:40		Self-assembly of Macroscopic Biomaterials from Individual Amyloid Fibrils
15:40–16:10	**Prof. Dr. Zhanhui Wang** Keynote Speaker	Production and In Vitro Affinity Maturation of Broad-Specific Quinolones Nanobody
16:10–16:40	**Prof. Dr. Anna Mitraki** Keynote Speaker	Self-assembling protein and peptide folds as scaffolds for biomaterials design
16:40–17:00	**Dr. Joel Giron Hernandez** Invited Speaker	From cocoa waste to sustainable bioink: valorising pectin for circular economy-driven tissue engineering
17:00–17:20	**Marcin Wekwejt** Selected Speaker	p(HEMA)-enhanced magnesium phosphate cement: pioneering advances in dual-setting bone cements
17:20–17:40	**Priyanka Meena** Selected Speaker	Development of pH-sensitive xanthan gum-based hydrogel as a vehicle for delivering a hydrophobic drug
17:40–18:00	**Raphael Oladokun** Selected Speaker	COMSOL multiphysics computational studies of dielectrophoresis-based characterization and separation of tenogenically differentiating mesenchymal stem cells

24th April 2024 (Wednesday)
Session 2. Molecular Mechanisms in Cellular Processes

Time: 10:00 (CEST, Basel) | 04:00 (EDT, New York) | 16:00 (CST Asia, Beijing)

Time in CEST	Speaker	Title
10:00–10:10	**Prof. Dr. Jürg Bähler** Session Chair	**Welcome from the session chair**
10:10–10:30		Functional characterization of a long non-coding RNA that affects cellular ageing
10:30–10:50	**Prof. Dr. Anna Rita Franco Migliaccio** Keynote Speaker	A drugable interaction between malignant megakaryocytes and neutrophils driven by the CXCL8/P-selectin axes as a driver for myelofibrosis
10:50–11:10	**Dr. Vincenzo Brancaleone** Keynote Speaker	Novel molecular mechanisms regulating the interplay between NO and H2S in hyperglycemia
11:10–11:30	**Dr. Vadim Sumbayev** Keynote Speaker	Tim-3-galecting-9 pathway as a crucial component of cancer immune evasion biochemical machinery and immune surveillance
11:30–11:50	**Dr. Laurent Soulere** Keynote Speaker	Inhibition of FtsZ with synthetic 2,6-difluorobenzamide derivatives: A comprehensive study
11:50–12:10	**Dr. Irina Nesmelova** Keynote Speaker	Effect of chemokine heterodimerization on CXCL12-mediated cell response.
12:10–12:25	**Yannan Yu** Selected Speaker	Exploring the Role of N-WASP in Breast Cancer Metastasis Through Mass Spectrometry and Potential Signalling Pathway Analysis

24th April 2024 (Wednesday)
Session 6. Bioinformatics and Computational Biology

Time: 15:00 (CEST, Basel) | 09:00 (EDT, New York) | 21:00 (CST Asia, Beijing)

Time in CEST	Speaker	Title
15:00–15:10	**Dr. Thomas R. Caulfield** Session Chair	**Welcome from the session chair**
15:10–15:40	**Prof. Dr. Umesh Desai** Keynote Speaker	Combinatorial Virtual Library Screening Algorithm in Discovering Highly Selective Glycosaminoglycan Sequences
15:40–16:10	**Prof. Dr. Mire Zloh** Keynote Speaker	Putative Epigenetic Targets of Cannabis Sativa for the Treatment of Multiple Sclerosis: A Network Pharmacology and Molecular Docking Approaches
16:10–16:40	**Prof. Dr. Sanjoy Bhattacharya** Keynote Speaker	Comparable Omics, the need for standardization, concepts of normalization and normativity
16:40–16:55	**Wei Yao** Selected Speaker	The Application of Machine Learning in CYP450s Specificity Prediction

25th April 2024 (Thursday)
Poster Session

09:00–11:00 (CEST, Basel) | 03:00–05:00 (EDT, New York) | 15:00–17:00 (CST Asia, Beijing)

CEST (Central European Summer Time - UTC+2)	EDT (Eastern Daylight Time - UTC-4)	CST Asia (China Standard Time - UTC+8)	Speaker	Title
09:00–11:00	03:00–05:00	15:00–17:00	Poster Session	The Poster Sessions will take place in Zoom break-out rooms. The list of names and titles of the posters will be found here.

25th April 2024 (Thursday)
Session 5. Biocatalysis and Enzyme Engineering

Time: 16:00 (CEST, Basel) | 10:00 (EDT, New York) | 22:00 (CST Asia, Beijing)

Time in CEST	Speaker	Title
16:00–16:10	**Dr. Tzanko I. Doukov** Session Chair	**Welcome from the session chair**
16:10–16:40	**Prof. Dr. Tae Seok Moon** Keynote Speaker	Systems and synthetic biology: constructing smart and programmable microbes to address global problems
16:40–17:10	**Dr. Frederick H. Silver** Keynote Speaker	Use of Vibrational OCT to Study Skin Cancers
17:10–17:40	**Dr. Benoit Coulombe** Keynote Speaker	The PAQosome, a unique HSP90 co-chaperone for protein complex assembly and maturation; implication in disease
17:40–18:00	**SHAKEEL ANSARI** Selected Speaker	The stabilization and utility of β galactosidase immobilized on thiolated silica nanoparticles
18:00–18:15	**Sumit Kumar** Selected Speaker	Repurposing halophilic α-amylase for future biotechnological applications

Poster List

Poster Session	
Name	**Title**
Boryana Nikolova-Mladenova	Design and bioactivity evaluation of chloro-substituted hydrazones
Goran Slivšek	The Evaluation of the Antibacterial Efficacy and Drug Safety of Thymoquinone against Acinetobacter baumannii: Utilising Bioinformatics and Cheminformatics Methods in Microbiology
Fabiola Gutiérrez	Assessing the bio-functional properties of TiO 2/Antibiotic electrophoretic deposits on segmented polyurethane-coated metallic surfaces
Ahmed Fatimi	Pulegone Application Trends: Exploration of Uses Based on Leading Patent Applicants
Balbina Makurat-Kasprolewicz	Production of Bioactive Coatings on Titanium Implants Using a Micro-Arc Oxidation Process Assisted with Ultrasound
Piotr Rusin	The role of glutathione in the symplast and apoplast in the PVYNTN interplay with a potato host with different resistance levels to the virus
Patryk Drejka	Antibacterial properties of dental copolymers modified with monomers possessing quaternary ammonium groups
Miruna Stan	Simulation on the interaction between FITC functionalized gold nanoparticles and lipid bilayers
Pengren Zou	Sources, biosynthesis pathways, bioavailability, bioactivity, and pharmacology of dihydrodaidzein
Quanyong Wu	Differences in the degradation and utilization of low-esterification pectin by different intestinal bacteria
Viktor Filatov	Towards skin longevity: the development of a novel plant-based combination with a potent stimulation of collagen I synthesis in vitro
Olena Aliyeva	HIF-1α as a potential target for pharmacologic correction after prenatal hypoxia
Sylwia Grabska-Zielińska	The comparison of physicochemical properties of chitosan/silk fibroin/collagen-based materials cross-linked with chemical agents
Ana Olívia Serra Jorge	Selenium Confers Protection against Methylmercury in the Human Body: a Comprehensive Review of Biomolecular Interactions
Chloe Kam	Multilayer immunohistochemical analysis of brain tissue in severe traumatic brain injury
Ezenwalie Ifechukwudelu Ezenwalie	Integrated Analysis of Glioblastoma: Unravelling Molecular Signatures Across Diverse Datasets for Enhanced Diagnosis
Camila F. Secco Bastos	Phlorotannins as bioactive agents from brown algae: chemical characterization and extraction methods
María Carpena	Insights into the Toxicity and Molecular Mechanisms of Aflatoxin B1 and Ochratoxin A in Herbal Products
María Carpena	Exploring Algal Metabolism: Insights from Metabolomics and Computational Approaches
Pauline Donn	Recent advances in understanding keys factors influencing Pressurized Liquid Extraction of Secondary Metabolites: A comprehensive review
Savanah Senn	Draft Transcriptomic Resources for the California Native Plant Trichostema lanatum from the Angeles National Forest

Poster Session	
Name	**Title**
Magdalena Górecka	Novel Bio-Cement for Regenerative Medicine: Magnesium Phosphate with Polyvinyl Alcohol Enhancement
Wanning Ma	Comparison of the immunomodulatory bioactivity of three dietary fibers on cyclophosphamide (CTX)-induced immunosuppression
Paula Barciela Álvarez	Bromophenols in red algae: exploring the chemistry and uncovering biological benefits of these unknown compounds
Boya Ouyang	Fermentation characteristics of exogenous lactic acid bacteria in tartary buckwheat sourdough and changes in the bread quality of frozen dough
Katarzyna Sala	Eco-Friendly Synthesized Silver-Nanoparticle-Modified PVA/PEG Hydrogels
Magdalena Bańkosz	Innovative Hydrogels with Silver Nanoparticles: Synthesis and Applications
Maryia Khamenka	Advancements in Injectable Biocements: The Role of Gellan Hydrogel in Magnesium Phosphate Bone Cement
Artem Sinolits	Study of carbon nanotube–bovine serum albumin interaction using the tritium radiotracer technique and supercomputer simulation
Ekaterina Litus	S100A8 interaction with amyloid β peptide suppresses its fibrillation
Nesteve John Agosto	The Evaluation of Citrus bergamia Phytochemicals as Potential Cholesterol-Lowering Agents against HMG-CoA Reductase: An In Silico Molecular Docking Study
Ayyagari Ramlal	In silico analyses of strawberry and soybean bioactive compounds' inhibitory effects against angiotensin-converting enzyme (ACE)
Anastasia Micha	Cationic Linear Scorpion peptide Mucroporin displays antimicrobial activity against Neisseria Subflava
Himanshu Prasad	Functional and Structural Annotation of Uncharacterized Lysine Methyltransferase proteins in Candida auris
Khushboo Choudhury	Computational drug repositioning of mast cell stabilizers against human Protease-Activated Receptor 2 (PAR2) involved in Rheumatoid Arthritis

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Abstracts

Session 1. Biomolecular Structures and Functions

sciforum-086244: *Suillus mediterraneensis* from the Algerian Coastline: Morphological Recognition and Mycochemical Profiling

Mimoune Souna [1], Choukri Tefiani [2], Salim Habi [3] and Abdelmalek Chaalel [4]

[1] Faculty of Natural and Life Sciences, Earth and Universe Sciences, University of Abou Bekr Belkaïd, Tlemcen, Algeria
[2] Laboratory of Functional Agrosystems & Technologies of Agronomic Sectors, Faculty of Natural and Life Sciences, Earth and Universe Sciences, University of Abou Bekr Belkaïd, Tlemcen, Algeria
[3] Laboratory of Physiology, Physiopathology and Biochemistry of Nutrition, Department of Biology, Faculty of Natural and Life Sciences, Earth and Universe Sciences, University of Abou Bekr Belkaïd, Tlemcen 13000, Algeria
[4] Laboratory of Beneficial Microorganisms, Functional Food and Health, Faculty of Natural Sciences and Life, Abdelhamid Ibn Badis University of Mostaganem, Mostaganem 27000, Algeria

Suillus mediterraneensis is an ectomycorrhizal mushroom of two-needle pines. The purpose of the present study is to initially determine the morphological characterization of the species and, thereafter, the mycochemical investigation of the hydro-methanolic extract in order to identify the main chemical classes of their composition in terms of secondary metabolites using simple and rapidly recognized methods and techniques. This survey is being carried out in the coastal region of Ghazaouet within the wilaya of Tlemcen. The morphological determination of the mushroom is based on a range of macroscopic features, including the cap (by its shape, size, color, and surface or its cuticle), the hymenophore, the hymenium (tubes: their color, their shape, and the way they are attached), the stipe (thickness and shape), and the flesh. Furthermore, microscopic examination, either fresh or with reagents, especially Melzer's reagent, is needed to determine the shape, ornamentation, and size of the spores. The macro-chemical reaction of the different parts can be useful. This identification allows us to determine the species *S. mediterraneensis*, the family of Suillaceae, under *Pinus halepensis* with the presence of granules on the stipe. The results of the mycochemical screening carried out on the extract showed the presence of substances belonging to the classes of active compounds that include flavonoids, tannins, alkaloids, free quinones, reducing compounds, and coumarins. Anthraquinones, terpenoids, and saponins are absent. These preliminary results encourage the characterization of other molecules, and further studies are needed to evaluate their biological activities.

sciforum-089175: A Combined Experimental/Computational Structural Characterization of All Members of the KCTD Protein Family

Nicole Balasco [1], Luciana Esposito [2], Giovanni Smaldone [3], Alessia Ruggiero [2], Rita Berisio [2] and Luigi Vitagliano [2]

[1] Institute of Molecular Biology and Pathology CNR c/o Department of Chemistry, Sapienza University of Rome, 00185 Rome, Italy
[2] Institute of Biostructures and Bioimaging, CNR, 80131 Naples, Italy
[3] IRCCS SYNLAB SDN, 80143 Naples, Italy

Introduction

KCTD proteins represent an emerging class of proteins involved in fundamental physio-pathological pathways and pathological states, including neurological and neurodevelopmental processes, cancer, and genetic diseases [1–3]. In the past decade, we have conducted extensive biochemical/biophysical characterizations of these proteins [4–6]. However, the lack of structural data prevented a full understanding of their activities at the atomic level.

Methods

Here, by combining experimental (X-ray crystallography) and computational (molecular modeling/dynamics and structure prediction), we have extensively characterized the structural properties of all members of the KCTD family.

Results

Taking advantage of the recent advent of effective predictive approaches based on machine learning techniques (AlphaFold), we recently performed a detailed structural characterization of all members of the KCTD family. First, we demonstrated that the vast majority of these proteins share a structurally similar C-terminal domain despite the absence of sequence similarities. We generated a novel and comprehensive structure-based pseudo-phylogenetic tree that unraveled previously undetected similarities among the family [7]. A comprehensive analysis of the structural states of functional oligomers of all members of the family led us to identify reliable three-dimensional models [8]. Finally, we applied this approach to explore, at the atomic level, the Cul3 recognition of all KCTDs [9].

Conclusions

Recently developed methodologies for protein structure prediction have made it possible to perform analyses on entire protein families. By combining experimental structural characterizations with effective predictions, we were able to gain insights into the structure of some KCTDs that will hold important implications for their biological function.

References

1. Teng, X.; Aouacheria, A.; Lionnard, L.; Metz, K.A.; Soane, L.; Kamiya, A.; Hardwick, J.M. KCTD: A new gene family involved in neurodevelopmental and neuropsychiatric disorders. *CNS Neurosci. Ther.* **2019**, *25*, 887–902.
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sciforum-089314: Antibacterial Effect of *Cymbopogon citratus* Essential Oil against Gram Positive Bacterial Strains

Dicla Aline Semedo da Veiga [1], Bernardina De Paixão Santos [1], Francisco Sérgio da Silva Sousa [1], Everton Vieira da Silva [2] and Sávio Benvindo Ferreira [3]

[1] Academic Unit of Life (UACV), Teacher Training Center (CFP), Federal University of Campina Grande (UFCG), Cajazeiras, PB, Brazil
[2] Academic Unit of Exact and Natural Sciences (UACEN), Teacher Training Center (CFP), Federal University of Campina Grande (UFCG), Cajazeiras, PB, Brazil
[3] Federal University of Campina Grande, Cajazeiras, PB, Brazil

Cymbopogon citratus, popularly known as "lemongrass" is a herbaceous species originating from India, belonging to the Poaceae family, to which it is acclimatized in several typical regions of Brazil. *C. citratus* is one of the best-known medicinal plants in traditional medicine, as it is known for its diverse activities, including antibacterial, anticonvulsant and antimalarial. In this sense, with the spread and bacterial resistance, the search for antimicrobials based on natural compounds has intensified. Address and evaluate the possible antibacterial activities of *Cymbopogon citratus* in comparison with gram-positive microorganisms reported in the literature. This is a literature review, in which the Health Sciences Descriptors (DeCS) "*Cymbopogon citratus*", "Antibacterial Activity" and Essential Oil" were used to search the MedLine and LILACS databases, accessed through the Library Virtual Health System (VHL), with the screening of relevant data, according to the established theme, the final sample was composed of 14 studies, without temporal delimitation. It was observed that the antibacterial activity of essential oils based on *C. citratus* overlaps the number of studies with extracts. Of the bacteria evaluated, *C. citratus* demonstrated antibacterial activity against all bacteria tested, in which the following halos and Minimum Inhibitory Concentration were determined: *Bacillus subtilis* (2 mg/mL), *Listeria monocytogenes* (0.33 mg/mL–1.56 mg/mL), *Staphylococcus saprophyticus* (21 mg/mL) and S*treptococcus mutans* (0.25 mg/mL). The antibacterial activity of *C. citratus* was high compared to *S. aureus* in all studies evaluated. The results obtained were dose dependent, ranging from 50 to 0.1 mg/mL. With the evaluation of different studies, the activity of essential oils may vary depending on: the composition, location, climatic conditions and the technique for extracting and using the oil and the method used to evaluate its antimicrobial activity.

sciforum-089004: Molecular Structure Considerations for the Possibility of Sequence-Dependent DNA Resonances

Ivan Savelev [1], Alexandre Vetcher [2], Nelli Zyryanova [3], Richard A. Miller [4] and Max Myakishev-Rempel [1]

[1] DNA Resonance Research Foundation, San Diego, CA, USA
[2] Deputy Director of IBCTNT at RUDN
[3] DNA Resonance Research Foundation, San Diego, CA, USA
[4] OAK, Inc., Grants Pass, OR, USA

For years, the mechanisms of non-chemical and non-contact communication between cells and organisms have not been studied to the same extent as those associated with the chemical mediators. The novel molecular structure considerations for the possibility of DNA sequence-dependent electromagnetic resonances (DNASDEMRs) are proposed. It is hypothesized that the resonant vibrations naturally occur in the clouds of delocalized electrons and protons in a stack of DNA bases and that some DNA sequence repeats, abundant in the genome, serve as universal resonators, which bidirectionally connect the chromatin structure. The existence of a DNA resonance code is proposed as an algorithm for the transformation of the genomic sequence into the organism's structure, and an initial model of sequence-specific electromagnetic resonances in DNA was proposed to explain some reported observations. The DNA interaction with a weak electromagnetic field due to DNASDEMR can play a role in non-contact communication between cells as well as in the development of certain non-communicable diseases (NCDs). Our additions to the original concept of DNA resonance give extra reasons to link the organism-level consideration to the molecular consideration through the idea of field coordination and adjustment. This allows us to explain the soft coordination of all molecular events in the body through non-contact communication. Solving this issue will bring medical technologies to a fundamentally new level.

sciforum-089014: The Impact of Fatty Acid Compounds in a Sacha Inchi Oil Supplement on Rats

Tepparit Samrit and Pornanan Kueakhai

Faculty of Allied Health Sciences, Burapha University, Chonburi, Thailand

Dietary oils are important sources of macronutrients and micronutrients, which can affect health. Sacha inchi oil (SIO), a type of edible oil extracted from *Plukenetia volubilis*, a plant native to tropical regions, is reported to be rich in omega-3 fatty acids. Previous studies have shown that omega-3 fatty acids are essential, offering numerous health benefits, including improvements in metabolic syndrome, cardiovascular disease, and gut microbiota. Typically, omega-3 sources are animal-based, especially fish oil and cod liver oil. SIO presents an interesting plant-based source of essential fatty acids. However, the compounds and effects of SIO on health and safety are not yet clear. In this study, the effects of SIO were studied both in vitro and in vivo. In vitro, we investigated the chemical compounds by evaluating the fatty acid and antioxidant content. In the in vivo study, the oil supplements were administered orally to male Sprague-Dawley rats continuously for 12 weeks. The effects were also evaluated through measurements of the body composition, fatty acid profile, liver enzymes, and morphology and lipid content of organs; the histology of the organs was assessed using H&E and Oil Red O staining. SIO has a high content of omega-3 fatty acids and significant antioxidant capacity. The rats treated with SIO for 12 weeks showed no increased risk of fatty liver or toxicity in any organs. These results indicate that SIO has high levels of alpha-linolenic acid (omega-3) fatty acids and antioxidant compounds, without altering body composition or serum parameters. Furthermore, SIO did not result in any adverse effects in the rats. These results confirm that SIO is a safe and effective source of omega-3, offering benefits for health.

sciforum-089280: Yeast Approach in Amyloidogenic Proteins Study

Andrew Zelinsky [1], Marina Ryabinina [1], Yury Chernoff [2] and Alexandr Rubel [1]

[1] Laboratory of Amyloid Biology, St. Petersburg State University, 199034 St. Petersburg, Russia
[2] School of Biological Sciences, Georgia Institute of Technology, Atlanta, GA 30332-2000, USA

Self-reproducing protein aggregates of a fibrillar nature (amyloids) are associated with a number of animal and human diseases. Some amyloids (prions) possess infectious properties as they can be transmitted between tissues, organs, and even organisms. However, there are examples of prions and amyloids that have normal biological functions [1]. The number of proteins capable of forming functional and pathological amyloids is constantly expanding. For example, some bioinformatics algorithms predict that over a hundred human proteins may have the ability to form amyloids.

In our study, we applied the ArchCandy algorithm to identify human proteins with amyloidogenic properties. This algorithm is capable of identifying the potential formation of β-arches (structures specific to amyloid proteins). By applying an in silico approach, we selected nine proteins that demonstrated amyloidogenic potential and experimentally validated these predictions. To evaluate the amyloidogenic potential of proteins, we employed an original yeast test system that we developed [2]. This system enables us to assess amyloidogenicity of individual proteins as well as to conduct large-scale screenings of amyloidogenic proteins using a genetic analysis. Using this test system, we demonstrated that six out of the nine predicted amyloidogenic proteins were prone to amyloid formation. Among the proteins that demonstrated amyloidogenic properties, there were proteins involved in chromatin remodeling, transcription regulation, and oncogenesis. For several potentially amyloidogenic proteins identified in the yeast model, their amyloid properties were confirmed both in vitro and in a human cell culture.

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sciforum-087113: A Novel Facile Non-Invasive Method for Diagnosis of Onchocerca Volvulus Antigen in Human Urine

Lum Abienwi Ambe [1,2], Elizabeth Limunga Mbolle [1], Mbah Clarisse [2] and Faustin Kamena [1]

[1] Laboratory for Molecular Parasitology, Department of Microbiology and Parasitology, University of Buea, Buea P.O. Box 63, Cameroon
[2] Institute of Medical Research and Medicinal Plants Studies (IMPM), Centre for Research on Health and Priority Pathologies, Yaoundé P.O. Box 13033, Cameroon

Introduction

Human onchocerciasis affects an estimated 21 million people, with 99% of cases reported in 31 sub-Saharan countries (WHO, 2020a). The Expanded Special Program for Elimination of Neglected Tropical Diseases (ESPEN) has as objective to eliminate onchocerciasis with other Neglected Tropical Diseases (NTDs) by 2030. But one problem faced by the control programs is the absence of an antigen based diagnostic test to determine an active infection with *Onchocerca volvulus*. Onchocerciasis diagnosis is hampered by the lack of early, sensitive and objective laboratory tests.

Methods

We mined for *O. volvulus* proteins in patient urine and assessed the suitability of one of the proteins as antigenic diagnostic marker for human onchocerciasis. We describe a facile method for the diagnosis of the filarial *Onchocerca volvulus* based on specific detection of the antigen which has been shown to be components of extracellular secretory proteins in human urine. Dot blot filtration assays allow for the filtration and concentration of proteins from human urine.

Results

Standard antibody techniques using an antibody raised against this antigen allowed for the detection of as little as fmol of the protein in urine. Most importantly, using urine samples from endemic areas, we were able to distinguish filariasis patients from control individuals not affected with any form of filariasis. Using urine samples from other endemic parasitic diseases, our test showed an overall sensitivity of 80% and specificity of 90%. These findings provide the proof of principle for developing a cheap highly sensitive and specific tests for filarial diseases

Conclusions

Development of a more efficient diagnostic test for human onchocerciasis will serve control programs to map for the disease and follow up treatment, especially as onchocerciasis and other NTDs are programed for elimination by 2030 by WHO.

sciforum-086260: Agmatine Attenuates Attention Deficit Hyperactivity Disorder Using Exposure of 6-OHDA in Mice

Aman B. Upaganlawar

SNJB's Shriman Sureshdada Jain College of Pharmacy, Neminagar, Chandwad, Nashik, India

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that affects both children and adults and is characterized by persistent patterns of inattention, hyperactivity, and impulsivity. During adolescence, the prefrontal cortex develops connectivity with other brain regions to engage executive functions and impulsive behavior. Thus, injecting 6-hydroxydopamine, a neurotoxin, results in lesioning of dopaminergic neurons, which results in motor and cognitive impairments, similar to ADHD in humans. This study was planned to investigate the effect of agmatine, a primary amino compound and a member of guanidines, on 6-OHDA-induced ADHD-like behavior in mice.

Methods

Animals administered with 6-OHDA on PND 5 exhibited the major ADHD-like symptoms, i.e., hyperactivity in an open-field test and attention deficit and impulsivity in an object-based attention task. Further, the model revealed discrete co-existing symptoms, i.e., memory deficits, anxiety-related compulsive-like behavior, and depressive and anti-social behavior, in a three-chamber social interaction task.

Result

In the present study, 6-OHDA-induced ADHD-like behavior was significantly attenuated by agmatine (20, 40, and 80 mg/kg, i.p.), L-Arginine (60 mg/kg, i.p.), and aminoguanidine (50 mg/kg, i.p.). Additionally, agmatine reduces elevated oxidative stress parameters and improves the reduced dopamine level in the 6-OHDA mouse brain.

Conclusions

These findings suggest that agmatine can be a potential therapeutic target for behavioral alteration associated with ADHD.

sciforum-089251: Analysis of the Amyloid-like Properties of COL2A1 Protein

Aleksandra Brukkel [1], Andrey Zelinsky [2], Marina Ryabinina [2] and Aleksandr Anatolevich Rubel [2]

[1] SCAMT, ITMO University, 191002 Saint-Petersburg, Russia
[2] Laboratory of Amyloid Biology, Saint-Petersburg State University, 199034 Saint-Petersburg, Russia

Amyloids are proteins which exist in the form of insoluble aggregates and possess a characteristic cross-beta structure. The formation of amyloid aggregates can be seen during several pathological processes in humans, including neurodegenerative diseases, diabetes, and systemic amyloidoses. Despite their infamous association with the previously mentioned conditions, amyloids can also serve a functional role in biological systems. For example, Pmel17, which is involved in melanin polymerization in mammalian cells, resembles an amyloid structure, and some peptide hormones are also known to be stored in amyloid form in secretory granules of the endocrine system. Thus, studying amyloids as functional proteins may aid in both determining targets for the treatment of pathological conditions and in understanding their unique role in the organism. The analysis of amyloid-like properties requires a comprehensive approach using bioinformatic prediction, which can later be verified using bacterial and yeast systems as well as various biochemical tests. The object of this study is the protein COL2A1, better known as type II collagen. This type of collagen forms the basis of cartilage tissue and its mutant form can cause diseases known as collagenopathies. This protein possesses some distinctive features characteristic of amyloids. These features include Congo red staining and a tendency to form fibrillar structures. In addition, the possibility of it forming amyloid structures was predicted for the third isoform of type II collagen via the ArchCandy program. In this work, we present data on the investigation of COL2A1's amyloid properties in a C-DAG system and a yeast model. Currently, additional studies are being conducted to obtain the protein in a bacterial system to assess its biochemical properties.

sciforum-087286: Anti-Filarial Efficacy of *Ocimum sanctum*: Implications in Drug Targeting and Designing

Anchal Singh, Ayushi Mishra, Vipin Kumar and Sunil Kumar

Department of Biochemistry, Institute of Science, Banaras Hindu University, Varanasi 221005, U.P., India

Introduction

Apart from lacking macrofilaricidal activity, the anti-filarial drugs DEC, albendazole and ivermectin are also often associated with several severe side-effects. Therefore, macrofilaricidal drugs which are non-toxic and have minimal side effects are needed as better treatment options.

Methods

An ethanol extract of *Ocimum sanctum* (EOS) leaves was prepared and its anti-filarial activity was investigated by a combined biochemical and proteomics approach. Equal size and number of adult *Setaria cervi* worms were exposed to EOS following which the anti-oxidant activities were estimated and proteomic profile was studied by two-dimensional electrophoresis. The differentially expressed proteins were subjected to drug docking against EOS bioactive compounds.

Results

The EOS significantly reduced the viability of adult female *Setaria cervi* after 6 hr of incubation at 37 °C. An increase in lipid peroxidation (51.92%), protein carbonylation (48.99%), and NADPH oxidase (88.88%) activity and a decrease in the glutathione (GSH) (−39.23%), glutathione reductase (GR) (−60.17%), and glutathione S- transferase (GST) (−50.48%) activity were observed after EOS treatment. There were alterations in the proteomic profile of EOS-treated *S. cervi* at 250 μg/mL concentration in comparison to the control group of *S. cervi,* and 2D gel electrophoresis revealed 20 downregulated and 11 upregulated protein spots in the treated parasites. Further, in drug docking analysis, EOS bioactive compounds eugenol, kaempferol, luteolin, rutin and rosmarinic acid showed high binding affinity with the major differentially expressed proteins.

Conclusions

Herein, we report for the first time that the anti-filarial activity of EOS is largely mediated by its impact on the anti-oxidant, energy metabolism and stress response systems of the filarial parasites.

sciforum-089271: Antibacterial Action of *Lippia origanoides* Essential Oil

Francisco Sérgio da Silva Sousa [1], Dicla Aline Semedo da Veiga [1], Bernardina De Paixão Santos [1], Rafaelle Cavalcanti de Lira [1] and Sávio Benvindo Ferreira [2]

[1] Academic Unit of Life (UACV), Teacher Training Center (CFP), Federal University of Campina Grande (UFCG), Cajazeiras, PB, Brazil
[2] Federal University of Campina Grande, Cajazeiras, PB, Brazil

Bacterial resistance to antibiotics makes infections increasingly difficult to fight. In this context, the antimicrobial capacity of *Lippia origanoides* proved to be a relevant alternative. The purpose of this review is to evaluate the antibacterial activity of this essential oil against bacterial strains. This is a narrative review of the literature using the following guiding question: "Does *Lippia origanoides* essential oil have antimicrobial activity against bacterial strains?". The descriptors "*Lippia origanoides*" and "Antimicrobial activity" were applied to the PubMed, Virtual Health Library (VHL) and Embase databases. The inclusion criteria were as follows: contain, whether in the title, abstract or body of the text, a relationship with the antibacterial activity of *L. origanoides*, and the possibility of accessing the full article. A total of 62 articles were found and 19 studies were chosen. A total of 13 bacteria were analyzed in the tests and the Minimum Inhibitory Concentration (MIC) was as follows: *Bacillus cereus* (0.62 μL/mL), *Bacillus subtilis* (1.25 μL/mL), *Staphylococcus aureus* (1.25–60 μL/mL), *Chromobacterium violaceum* (0.37 μL/mL), *Escherichia coli* (0.15–60 μL/mL), *Pseudomonas aeruginosa* (240 μL/mL), *Salmonella cholerasuis* (30 μL/mL), *Salmonella thypimurium* (1.25 μL/mL) and *Vibrio parahaemolyticus* (0.313 μL/mL). In *Bifidobacterium* breve and *Lactobacillus acidophilus*, the Minimum Bactericidal Concentration (MBC) was, respectively, 50 μL/mL and 3.135 μL/mL. In *Staphylococcus epidermidis* and *Salmonella enteritidis*, there was only MIC_{50} (concentration to inhibit 50% of the sample), specifically, 0.37–3.0 μL/mL and 0.37 μL/mL. In total, 27.3% of articles evaluated the antibiofilm capacity of *L. origanoides*, and the inhibition of biofilm formation reached more than 70% in *E. coli* and *S. aureus*. *Lippia origanoides* essential oil revealed antimicrobial activity in all studies. Ultimately, *P. aeruginosa* proved to be a strain that still requires further experimentation.

sciforum-087154: Application of In Silico Computational Biology Strategies and Gene Expression Analysis to Demonstrate Mechanism of Oral Cancer Cell Death by a Natural Peptide

Dominic Augustine

Department of Oral Pathology & Microbiology, Faculty of Dental Sciences, MS Ramaiah University of Applied Sciences, Bengaluru, India

Introduction

This research work is designed to identify biomolecules from Earthworm Coelomic Fluid (ECF) of *Eudrilus Eugeniae* (EE) that can inhibit cancer cellproliferation. This study aims to construct a homology model of the 18 kDa protein from the ECF of EE (18-ECFP) with molecular dynamics simulation (MDS) to enable its molecular docking with pro-apoptotic caspase receptors with a determination of binding energy scores. This study also evaluates the anti-cancer potential of 18-ECFP on SCC-9 cells in vitro by wet lab techniques.

Methods

Following SDS-PAGE and MALDI-TOF/MS-MS sequencing, the 18 kDa protein was subjected to Nano-LCMS-based AA sequencing. Due to the unavailability of a 3D structure in Protein Data Bank (PDB), it had to be modelled via energy-based methods using Prime module—Schrödinger. The MDS of the protein was analyzed followed by Protein–Protein Docking (PPD) using Schrödinger 2020 software. The op 5 poses exhibiting a high PIPER score were subjected to energy calculations**.** The 18-ECFP was also evaluated by RT-PCR, Western blot and Q-PCR techniques on SCC-9 cells in vitro to further establish its anti-cancer potential.

Results

The homology model of the 18-ECFP was constructed with Schrödinger software with stable molecular dynamics. PPD demonstrated binding affinity of 18-ECFP with the pro-apoptotic genes Caspase-3 and Caspase-8. The MM-GBSA revealed satisfactory binding energy scores. Gene expression studies revealed an upregulation of the apoptotic genes Caspase-3 and Caspase-8 induced by the 18-ECFP, validating the in silico findings.

Conclusions

This is the first report of a homology model with MDS of an anti-cancer protein from an earthworm source docked to human caspase receptors with a determination of binding energy values supported by validation through multiple in vitro gene expression techniques. The current study has provided valuable insights pertaining to the molecular structure of the novel anti-cancer protein of ECF. The findings may contribute to the development of naturally available drugs to combat cancer.

sciforum-085176: Bioactive Polysaccharides Promote Gut Immunity via Different Ways

Xincheng Wu and Shaoping Nie

State Key Laboratory of Food Science and Technology, China–Canada Joint Lab of Food Science and Technology (Nanchang), Key Laboratory of Bioactive Polysaccharides in Jiangxi Province, Nanchang University, 235 Nanjing East Road, Nanchang 330047, China

Numerous kinds of bioactive polysaccharides are identified as having intestinal immunomodulatory activity; however, the ways in which the different polysaccharides work differ. Therefore, we selected nine representative bioactive polysaccharides, including xanthan gum, inulin, guar gum, arabinogalactan, carrageenan, glucomannan, araboxylan, xylan, and fucoidan, and compared their intestinal immunomodulatory mechanisms. A cyclophosphamide (CTX)-induced immunosuppressed model was used in this experiment, the expression of CD4+ and CD8+ T cells in the ileum was detected by immunohistochemical staining, the relative expression levels of RORγt and T-bet in the ileum were determined by real-time quantitative PCR, the secretion of ileal cytokines TNF-α, IFN-γ, IL-17, and IL-22 was detected by ELISA kit, and the levels of SCFAs in the cecum contents were determined by gas chromatography, combined with UPLC-QTOF/MS for metabolomics analysis of colon contents, and 16S rRNA sequencing of gut microbes. The effects of these polysaccharides on the number of T cells in the intestinal mucosa, expression of transcription factors and inflammatory factors, intestinal metabolome and gut microbiota were compared and discussed. The results revealed that the nine polysaccharides promote intestinal immunity in different ways. In detail, guar gum, inulin and glucomannan better alleviated immune suppression in intestinal mucosal T cells. Inulin improved the intestinal microenvironment by significantly upregulating the abundance of *Lactobacillus* and *Monoglobus* and promoted short chain fatty acid (SCFA) production. Fucoidan and carrageenan promoted the colonization of the beneficial bacteria *Rikenella* and *Roseburia*. In addition, fucoidan, inulin and carrageenan inhibited the colonization of harmful bacteria *Helicobacter*, upregulated the abundance of *Clostridia_UCG-014* and alleviated the accumulation of amino acids, bile acids and indoles in the large intestine. In conclusion, our study uncovered the different intestinal immunomodulatory mechanisms of the different polysaccharides and provided a guideline for the development of superior intestinal immunomodulatory polysaccharides.

sciforum-089308: Bromophenols in Red Algae: Exploring the Chemistry and Uncovering Biological Benefits of These Unknown Compounds

P. Barciela [1], M. Carpena [2], A. Perez-Vazquez [1], A. Silva [1,3], A. O. S. Jorge [4,5] and M. A. Prieto [1,6]

1 Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Faculty of Science, Universidade de Vigo, E32004 Ourense, Spain
2 Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Faculty of Science, Universidade de Vigo, E32004 Ourense, Spain
3 REQUIMTE/LAQV, Instituto Superior de Engenharia do Porto, Instituto Politécnico do Porto, Rua Dr António Bernardino de Almeida 431, 4200-072 Porto, Portugal
4 REQUIMTE/LAQV, Department of Chemical Sciences, Faculty of Pharmacy, University of Porto, R. Jorge Viterbo Ferreira 228, 4050-313 Porto, Portugal
5 Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Faculty of Science, Universidade de Vigo, E32004 Ourense, Spain
6 Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal

Bromophenols, which belong to the family of phenolic compounds, are halogenated secondary metabolites characterized by the incorporation of bromine atoms into the phenol ring structure, resulting in unique chemical properties. These compounds, synthesized as secondary metabolites by algae, exhibit different isomeric forms due to bromine substitution at different positions within the phenol ring, showing variability among species. Bromine substitution not only confers specific chemical properties but also plays an important role in the ecological functions of bromophenols by inducing increased lipophilicity, which affects solubility and reactivity, an adaptive response to external conditions. Certain genera of red algae, such as *Gracilaria* and *Rhodomela*, have been identified as important sources of bromophenols. Research on bromophenols involves extraction, commonly using solvents such as methanol or methanol-dichloromethane, and identification and structural elucidation using advanced analytical techniques such as mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy for the precise determination of structure and configuration. Bromophenols display diverse biological activities, highlighting antimicrobial, antidiabetic, antiviral and antioxidant properties, which are closely related to their specific chemical structure. The importance of understanding the chemical group of bromophenols is underlined by their role in chemical defense mechanisms, contributing to potential biotechnological applications and broader contributions to the marine ecosystem [1–6]. Therefore, this study is aimed to review the chemical characteristics and biological properties of bromophenols in red algae.

sciforum-088987: Cathepsin B-Induced Degradation of Lysozyme Amyloid Fibrils

Maksim I. Sulatsky [1], Olga V. Stepanenko [2], Olesya V. Stepanenko [2], Ekaterina V. Mikhailova [2] and Anna I. Sulatskaya [2]

[1] Laboratory of Cell Morphology, Institute of Cytology of the Russian Academy of Sciences, 4 Tikhoretsky ave., 194064 St. Petersburg, Russia
[2] Laboratory of Structural Dynamics, Stability and Folding of Proteins, Institute of Cytology of the Russian Academy of Sciences, 4 Tikhoretsky ave., 194064 St. Petersburg, Russia

Diseases associated with the accumulation of ordered protein aggregates, amyloid fibrils, once thought to be rare, are predicted to soon become epidemics. However, there are still no effective drugs without serious side effects for the degradation of amyloid plaques, which is currently considered a promising therapeutic strategy. We tested the proteolytic enzyme cathepsin B, involved in the cellular immune response, as a potential amyloid-degrading agent.

Our investigation focused on model lysozyme amyloid fibrils that accumulate in systemic non-neuropathic hereditary amyloidosis. Various microscopic, biochemical, and spectroscopic approaches were used to study the properties of amyloids and their degradation products. We showed that cathepsin B-mediated proteolysis of amyloid-forming proteins led to fibril fragmentation. In some amyloid fragments, the loss of an ordered structure was also observed. The identified effects can be attributed to the disruption of intra- and intermolecular hydrogen bonds in the fibril core. At the same time, with the stepwise addition of cathepsin B (as opposed to a one-step enzyme addition at the same concentration), we observed a lower number of "fluffed" fragments, although the efficiency of amyloid degradation remained practically unchanged. Cathepsin B deactivation did not lead to fibril reassembly (as is the case with other amyloid-degrading factors) for at least 5 days. Despite the observed cathepsin B-induced degradation of amyloids, cell viability was not increased in its presence, indicating an equally high cytotoxicity of intact amyloids and of their degradation products.

The results of our study show that the visible destruction of amyloid fibrils does not always lead to a decrease in their cytotoxicity. However, the transformation of amyloids into smaller and less stable aggregates with an altered structure (as effected by cathepsin B) is an important step in the development of effective and safe anti-amyloid agents.

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sciforum-087229: Cationic Linear Scorpion Peptide Mucroporin Displays Antimicrobial Activity against Neisseria Subflava

Anastasia Micha, Yiannis Sarigiannis, Tolis Panayi and Christos Petrou

Department of Health Sciences (Pharmacy Program), University of Nicosia, CY-2417 Nicosia, Cyprus

The emergence of antibiotic resistance makes the development of a new generation of powerful antimicrobials able to kill super bugs more essential than ever. Linear scorpion venom peptides are a small group of venom peptides that display antimicrobial, anticancer, and anti-inflammatory activities, although, in many cases, they exhibit strong hemolytic activity hinderingtheir further development.

Here, we present an improved synthesis of Mucroporin, a linear scorpion peptide of 17 amino acids, isolated from the Chinese Scorpion Lychas Mucronatus. The synthesis was conducted on a Microwave Peptide Synthesizer (Biotage Initiator+) by using an ultra-fast method at elevated temperature, 90 °C, avoiding some common steps in the conventional methods and reducing the total synthesis time by 40% and the total waste by 50% without affecting the purity of the crude peptide, which was calculated to 90%, making the final purification easier than ever. The synthesis was performed by using N-butyl-2-pyrrolidone (NBP), a green alternative to DMF solvent, which is under restriction for use in therapeutic peptides as ofDecember 2023 in EU.

Mucroporin was tested for its antimicrobial activity against gram-positive and gram-negative bacterial strains (Escherichia coli, Staphylococcus epidermidis, Neisseria subflava and Streptococcus pneumoniae Strain) by the serial dilution method in liquid cultures of bacteria with a cell density of ~2×10^5 CFU/mL in different concentrations and incubated for 24 h, and then the optical density was measured at 600 nm. Ampicillin was used as a positive control at a concentration of 100 μg/mL. The peptide completely inhibited the growth of Staphylococcus epidermidis and Streptococcus pneumoniae, as expected from earlier studies. Of particular interest is the inhibitory activity of Neisseria subflava at a final concentration of 120 μg/mL.

This is the first time that mucroporin has ever been reported to be effective against gram-negative strains; therefore, its activity against Neisseria subflava is of particular interest.

sciforum-084611: Chitosan-Based Biomaterial Drug Delivery System: An Overview

Rajakarthikeyan U., Thamizhselvan S. and Emmanuel A.

Ug Student, Bachelor of Pharmacy, Shri Venkateshwara College of Pharmacy, Ariyur, Pondicherry, India

Chitosan (CS) derivatives are extensively employed in a range of biomedical applications due to their special qualities, which include biocompatibility, mucoadhesion, non-toxicity, and the ability to form gels. They are also promising prospects for the development of films, tablets, and systems based on nanotechnology and could be scaled up commercially and industrially. Only systems requiring a higher solubility and drug release rate can employ CS due to its poor solubility at physiological pH (>6.0). A further drawback of CS is its high degree of swelling and water adsorption in aquatic environments, which might cause quick drug release. Through the chemical modification of one amino group and two hydroxyl groups on the CS chains, the carboxymethyl moieties will alter the properties of the CS. At various pH values, the water solubility of carboxymethyl chitosan (CMC) is determined by the degree of carboxymethylation. CMC derivatives have the ability to interact with cells to promote wound healing, tissue regeneration, and cell growth. Because of their antimicrobial, emulsion stabilising, and moisture absorption/retention qualities, they are also utilised in the production of cosmetics. Current CMC derivatives with biological activity, i.e., antibacterial, anticancer, antitumor, antioxidant, and antifungal, in areas like wound healing, tissue engineering, drug/enzyme delivery, bioimaging, and cosmetics will be the main topics of this presentation.

sciforum-086564: Classical and Non-Classical Compound Combinations for Treatment of Prostate Cancer Cell Line PC3

Lidiya Petrova [1], Diana Zasheva [2], Nikolay Gergov [3], Els Van Damme [4], Tsvetelina Oreshkova [5], Vanya Bogoeva [3] and Teodora Aleksandrova [6]

[1] Department of Biology, Medical University—Pleven, 5800 Pleven, Bulgaria
[2] Institute of Biology and Immunology of Reproduction, Bulgarian Academy of Sciences, 1000 Sofia, Bulgaria
[3] Institute of Molecular Biology "Acad. Rumen Tzanev", Bulgarian Academy of Sciences, 1000 Sofia, Bulgaria
[4] Department Biotechnology, Ghent University, Proeftuinstraat 86, 9000 Gent, Belgium
[5] Institute of Biology and Immunology of Reproduction, Bulgarian Academy of Sciences, 1000 Sofia, Bulgaria
[6] Department of Chemistry and Biochemistry, Faculty of Pharmacy, Medical University, Pleven, Bulgaria

Prostate cancer is one of the leading causes of death among men. Our study focuses on seeking new compounds and combinations to diminish the severe side effects of classical anticancer drugs for treating this type of cancer. In this study, we investigated and compared the classical anticancer drugs and non-classical compounds docetaxel, Au porphyrin, and the plant lectin jacalin, and in different combinations on the prostate cancer cell line PC3.

Jacalin, isolated from jackfruit seeds by affinity chromatography on immobilized galactose, specifically recognizes the tumor-associated Thomsen–Friedenreich antigen. The present investigation shows the interaction of jacalin with Au porphyrin, registering conformational changes within the protein due to the binding. From the titration curve, the affinity of 1.8 ± 0.39 μM for the jacalin–Au porphyrin complex was calculated.

In vitro experiments with PC3 cells treated with docetaxel or Au porphyrin indicated a decrease in cell viability, compared with the jacalin–Au porphyrin complex, as registered by viability assays.

The IC_{50} for Au porphyrin and for docetaxel were studied and indicated that the calculated IC_{50} for docetaxel was 8 orders of magnitude higher than that for Au porphyrin.

Our results demonstrate the effects of three compounds as well as the effects of their combinations upon treatment of PC3 cells. Molecular mechanisms will be studied in future experiments.

Keywords: Au porphyrin; jacalin; docetaxel; prostate cancer; PC3; apoptosis

sciforum-085240: Comparison of the Immunomodulatory Bioactivity of Three Dietary Fibers on Cyclophosphamide (CTX)-Induced Immunosuppression

Wanning Ma

Ph.D., Department of Analytical Chemistry and Food Science, Faculty of Science, Nutrition Food Group, University of Vigo, Vigo, Spain

Enhancing immunity is essential for the maintenance and restoration of body homeostasis, facing the pandemic of coronavirus disease 2019 (COVID-19), and combatting the effects of an unbalanced lifestyle [1]. Previous research has proven that dietary fibers have multiple bioactivities, indicating their great potential in functional food development [2,3].

In this study, the immunomodulatory activity of three dietary fibers on cyclophosphamide (CTX)-induced immunosuppression are investigated from the perspective of humoral immunity. We compared the changes in mouse body weight, thymus or spleen index, IgM secretion and metabolism in serum, splenic cytokine TNF-α secretion, splenic mRNA expression of GATA-3 and T-bet detected by quantitative real-time PCR (RT-PCR), and the percentage of $CD3^+$ cells in splenic lymphocytes using flow cytometry. The results show that all three dietary fibers improved the status of immunosuppressed mice by recovering body weight and relative organ weight as well as increasing the secretion of serum IgM and splenic cytokine TNF-α. Among the three dietary fibers, apple pectin mostly enhanced T-bet levels, regulating the balance of Th1/Th2 cells [3]. In addition, the percentage of $CD3^+$ cells in splenic lymphocytes improved significantly after treatment with inulin and guar gum. Our research compared the immunomodulatory bioactivity of three different dietary fibers in a CTX-induced immunosuppressed mice model, providing evidence for the bioactivity potential of dietary fibers and a view of integrated immunometabolic responses.

sciforum-087899: Complex DNA Nanomachines for the Ultrasensitive Detection of Ribonucleic Acids

Margarita Kuzina, Victoria Khorolskaya and Maria Rubel

ITMO University, 197101 Saint-Petersburg, Russia

Background

DNA nanomachines were developed as highly accurate alternatives to costly and unreliable methods used for measuring gene expression levels. However, despite their potential, DNA nanomachines also come with several limitations. One major drawback is their tendency to interact with various biological molecules, which can compromise their functionality. Additionally, background noise often hampers their performance, leading to reduced sensitivity and less precise results.

Goal

The goal of our work was to create DNA nanomachines for the highly sensitive detection of RNA extracted from cell culture that can be used for assessing mRNA concentrations without amplification.

Methods

DNA nanomachines were partially preassembled to add more auxiliary structures and additional quenchers were added to the structure to decrease the background noise and increase the dynamic diapason and limit of detection. The pre-assembly was performed with the gradual cooling of samples after a short boiling period. The resulted structures were visualized via PAGE gel. Samples were incubated at 55 °C and different times of exposure were analyzed. The DNA nanomachines were characterized based on limits of detection and their activity was based on total RNA extracted from cell culture.

Results

The results of the optimization experiments showed that incorporating a specific amount of DNA nanomachine with quenchers effectively reduced the background noise and fluorescence, therefore leading to more accurate evaluation. The limit of detection experiments revealed that these engineered structures were capable of detecting their target at concentrations as small as picomolar. Notably, the machines equipped with quenchers exhibited even greater sensitivity, further enhancing their performance.

Conclusions

The optimization experiments conducted on DNA nanomachines have unequivocally demonstrated that their sensitivity can be significantly enhanced through the incorporation of new designs and additional elements. This breakthrough paves the way for the potential utilization of these advanced constructions as highly efficient point-of-care diagnostics in the future.

sciforum-089289: Design and Bioactivity Evaluation of Chloro-Substituted Hydrazones

Boryana Nikolova-Mladenova

Department of Chemistry, Faculty of Pharmacy, Medical University of Sofia, Sofia 1000, Bulgaria

Aroylhydrazones, created by combining aromatic aldehydes and hydrazides, have numerous biological effects such as analgesic, anti-inflammatory, anticancer, antimicrobial, and antibacterial. The current study reports how the presence of a chlorine atom in hydrazone molecules affects their lipophilicity and molecular characteristics.

Methods

A series of novel chloro-substituted salicylaldehyde benzoylhydrazone derivatives was created by inserting the Cl atom in the aldehyde and hydrazide moiety and changing the substituent positions. To select the lead chloro-hydrazones with suitable pharmacological properties, the molecular and bioactivity scores of the proposed compounds were evaluated using a group contribution approach.

Results

Including a chlorine atom in the salicylaldehyde or hydrazide moiety raises the value of log P. Despite minor variances, all chloro-substituted salicylaldehyde benzoyl hydrazone derivatives show acceptable lipophilicity, with log P values up to 4.51. Cl-hydrazones have a TPSA of less than 140 Å², indicating high permeability to the cellular plasma membrane. Bioactivity scores indicate biological activity against GPCR ligands, ion channel modulators, kinase inhibitors, nuclear receptor ligands, protease inhibitors, and other enzyme targets.

Conclusions

The results revealed that all compounds are potential candidates for future drug discovery studies.

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sciforum-089333: Design, Development, and Method Evaluation of Aptamer-Based Diagnostics for the Detection of Multidrug-Resistant Bacteria

N. Jaya Lakshmi and Hariprasad P.

Centre for Rural Development and Technology, Indian Institute of Technology, New Delhi, India

Bacterial multidrug resistance poses a growing hazard to public health worldwide. *Pseudomonas aeruginosa* is a ubiquitous bacterial species that has been identified as the second most critical pathogen on the list of drug-resistant bacteria posing a huge threat to human health. *P. aeruginosa* is an opportunistic Gram-negative bacterium that rapidly produces multiple virulence factors that promote adhesion, host cell penetration, and pathogenicity. It possesses inherent resistance to multiple classes of antibiotics, evading antibiotic treatment by triggering the persister phenotype. Traditional approaches for detecting pathogens in laboratory and clinical settings primarily involve microbiological, nucleic acid-based, immunological, and sequencing techniques, among others. These procedures are time-consuming, necessitate advanced laboratory equipment and skilled staff, and incur large setup costs, rendering them unsuitable for on-the-spot detection of bacterial infections in settings with limited resources. Aptasensors utilize nucleic acid aptamers as bio-receptors to detect pathogens. They circumvent the existing limitations of conventional detection systems due to their sensitivity, versatility for modification, cost-efficiency, and ability to enable real-time detection. So far, as per the literature, three aptamers have been developed against *P. aeruginosa* using whole bacterial cells but with unreported binding sites. This study aims to identify highly specific aptamers that can bind specifically to *P. aeruginosa* using whole-bacterium SELEX at any stage of growth with an extensive study of binding site interaction and identification. The objective is to develop an aptamer-based kit enabling rapid point-of-care detection of *P. aeruginosa* in clinical and environmental samples.

sciforum-086308: Differences in the Degradation and Utilization of Low-Esterification Pectin by Different Intestinal Bacteria

Quanyong Wu

University of Vigo, Vigo, Spain

The gel of low-esterification pectin has no special requirements for soluble solids and is often used as a thickening agent, gelling agent and stabilizer in food. Pectin is difficult to digest and absorb when ingested by the human body. It is mainly fermented and utilized by the intestinal flora at the end of the intestine to produce active substances such as short-chain fatty acids. Therefore, pectin may be able to regulate the composition of intestinal flora and affect human health. The intestinal flora is diverse, and there may be a preference for the utilization of low-ester pectin. This study selected three different human intestinal bacteria, including five strains of Bacteroides xylanolyticus, two strains of Enterococcus faecium and two strains of Bifidobacterium longum, to explore their differences in the degradation and utilization of low-esterification pectin. The culture medium was prepared using low-ester pectin L102 as the sole carbon source. Through the growth pattern, pH value, sugar content and short-chain fatty acid changes of each strain in the pectin culture medium, the degradation effect of the different intestinal bacteria on low-esterification pectin was elucidated. The results showed that Bifidobacterium longum had a weak ability to degrade low-ester pectin and poor growth. Both Bacteroides xylanolyticum and Enterococcus faecium can degrade low-esterification pectin and grow well, among which Bacteroides xylanolyticum Bt-17 and Enterococcus faecium ET-2 are the best. The difference is that Bacteroides xylanolyticum Bt-17 degrades low-esterification pectin to mainly produce acetic acid and propionic acid, while Enterococcus faecium ET-2 degrades low-esterification pectin to mainly produce acetic acid. The research results provide a theoretical basis for the selective interaction between low-ester pectin and the intestinal flora and provide a strategy for selectively regulating the composition of the intestinal flora.

sciforum-088998: Existence of Brain Metabolites, Betaine and DMG as Acetylcholinesterase Inhibitors: A Novel Strategy for the Therapeutic Intervention of Dementia

Kritika Kumari and Laishram Rajendrakumar Singh

Dr. B. R. Ambedkar Center for Biomedical Research, University of Delhi, Delhi 110007, India

Introduction

Methylamines (MAs) are important brain metabolites that are known to exhibit neuroprotective effects. However, their role in the cholinergic system has been less explored. In the present study, we have investigated the effect of 4 MAs (sarcosine; dimethylglycine, DMG; betaine and trimethylamine N-oxide, TMAO) on the structure and function integrity of acetylcholinesterase (AChE), an important enzyme of the cholinergic system responsible for the hydrolysis of the neurotransmitter, acetylcholine (ACh) to choline and acetate.

Methods

The findings were generated from the systematic functional activity assay of AChE in the presence of MAs and further characterization using in silico, biophysical, and cellular approaches.

Results

We discovered that betaine and DMG are competitive inhibitors of AChE and could also reverse the cytotoxic effect of Aβ in cells which is a key characteristic of AChE inhibitors. We also observed that betaine and DMG enhance the efficacy of donepezil, rivastigmine, and galantamine which are currently used drugs for the treatment of dementia.

Conclusions

As Betaine and DMG are FDA-approved supplements, the results implicate that they could be employed independently for the treatment of dementia. The use of AChE inhibitors is not sufficient to control different symptoms of dementia as the pathophysiology of Dementia is multifactorial. Therefore, the use of combinatorial therapy of AChE inhibitors and Betaine/DMG mixtures would be a newer approach.

sciforum-086666: Fermentation Characteristics of Exogenous Lactic Acid Bacteria in Tartary Buckwheat Sourdough and Changes in the Bread Quality of Frozen Dough

Boya Ouyang

Nutrition and Bromatology Group, Department of Analytical and Food Chemistry, Faculty of Sciences, University of Vigo, 32004 Ourense, Spain

Tartary buckwheat is one of the world's minor cereal crops; it contains all 18 essential amino acids. Frozen baked goods made from raw materials such as tartary buckwheat have attracted increasing attention. Due to the strong carbohydrate metabolism function of Lactobacillus plantarum (Lp), the fermentation ability of Lactobacillus fermentum (Lf), and the ability of Weissella confuse (Wc) to produce a large amount of extracellular polysaccharides (EPSs) with certain anti-freeze properties during fermentation, the mixed fermentation of sourdough prepared by these strains will have a higher improvement effect on product quality. In this study, using HPLC, SDS-PAGE, and other methods, the growth of exogenous lactic acid bacteria in sourdough, major metabolic products (such as organic acids and sugars), and protein distribution, among other things, were investigated. The sourdough was then applied to produce frozen dough bread, and the quality characteristics of the bread products were characterized. The results showed that with the Lf + Wc mixed strain, the bacterial count reached 9.18 (lg(CFU/g)) (based on the mass of sourdough) after 12 h of fermentation, with a large amount of fructose (11.82 mmol/kg) and EPS (3.132 g/kg) produced. Compared with other groups, it had a moderate acid production rate, lower proteinase activity, and a slower protein degradation rate. Furthermore, when the Lf + Wc group was applied to frozen dough bread, the degree of quality decline after 13 weeks of frozen storage was smaller, with a baking loss rate decreasing by only 5.3%. In addition, the GC-MS spectrometry analysis of flavor components found that after 13 weeks of frozen storage, there was an increase in eight volatile compounds (Lf + Wc frozen dough bread). In conclusion, Lf and Wc have good synergistic effects, with a fast sugar metabolism rate and the ability to produce a large amount of EPSs with anti-freeze properties, which also explains why the final frozen dough product has the best anti-freeze performance.

sciforum-087072: Genetic Insights into E-Cadherin Modulation: Exploring the Benefits of Synthetic Acetyl Hexapeptide-1 in Wound Healing and Anti-Aging for Dermo-Cosmetics

Nikoleta Topouzidou, Christos Petrou, Androulla N. Miliotou and Yiannis Sarigiannis

Department of Health Sciences, School of Life and Health Sciences, University of Nicosia, Nicosia, Cyprus

Introduction

Dermo-cosmetics are cosmetics combined with bioactive ingredients to impart therapeutic benefits on the skin and have made significant advances in recent decades. Synthetic peptides stand out among these bioactive molecules, exhibiting improved capabilities due to their synthetic nature. Wound healing and cosmetic peptides share similarities in tissue repair and regeneration. Cosmetic peptides enhance fibroblasts, boosting collagen formation, improving skin firmness, and aiding wrinkle removal. E-cadherin, a key molecule, plays a role in both wound healing and cellular processes. Genetic validation of cosmetic peptides' effects is often lacking despite clinical trials examining their impact on skin physiology. This study examines acetyl hexapeptide-1 genetic impact for wound healing and anti-aging properties.

Methods

Acetyl hexapeptide-1 was synthesized in-house, and human hepatocytes (HepG2) were exposed for cytotoxicity assessment. Furthermore, gene expression was evaluated, through qPCR analysis, for the apoptosis-related gene BAX and the wound healing-associated gene CDH-1.

Results

In the assessment conducted in cell cultures, the peptide demonstrated a notable absence of cytotoxic effects. Upon comprehensive gene expression analysis, noteworthy observations included a significant increase in E-cadherin expression, from the first 24 h, and a slight reduction in apoptotic BAX gene expression.

Conclusions

The findings of this study provide promising insights into the molecular properties of synthetic acetyl hexapeptide-1, suggesting its potential in cosmeceuticals and dermo-cosmetics. While already proven effective in wrinkle reduction through fibroblast activation and collagen enhancement, these cosmetic peptides present vast potential and diverse applications beyond skincare. Further investigations are needed to fully comprehend their benefits and broaden their scope by exploring their molecular mechanisms across various applications.

sciforum-084752: Glycation-Induced Structural Alteration in Biomolecules

Dinesh Kumar and Ahmad Ali

Department of Life Sciences, University of Mumbai, Vidya Nagari, Mumbai, India

Hyperglycaemia leads to an accumulation of harmful substances in the body due to a process known as glycation. In this process, carbonyl groups of sugars interact with the amino groups of other biomolecules, ultimately resulting in the formation of advanced glycation end products. These products have been implicated in various pathophysiological conditions like diabetes, Parkinson's, Alzheimer's, cataracts, etc. Although the exact mechanism by which AGEs bring about changes in the structure of biomolecules is not known, it is assumed that cross-linking, aggregation, oxidation, and precipitation of proteins are some probable processes that are responsible for the structural and functional changes in biomolecules. In our study, we have used glucose and BSA as the in vitro model system to study the structural alterations they produce and the reversal of these alterations induced by natural products. A range of spectroscopic and electrophoretic tools were used to assess the alteration in BSA structure. The amounts of glycation products were also quantified by colourimetric and spectrofluorometric methods. The results indicate that glucose induces severe changes in the conformation of BSA and the presence of thymoquinone suppresses these alterations. Similarly, a significant amount of glycation products were generated in the in vitro system and were inhibited by the natural product. It can be concluded that glucose brings about conformational changes in proteins and causes the accumulation of glycation products during sustained hyperglycaemia.

sciforum-086012: Human Gut Commensal-Derived Exopolysaccharide-Mediated Short-Chain Fatty Acid Production by In Vitro Gastrointestinal Digestion and Its Enzymatic Inhibitory Mechanism Targeting the Microbial Composition of Irritable Bowel Disease (IBD)

Deepthi Ramya Ravindran and Murugan Marudhamuthu

Department of Microbial Technology, School of Biological Sciences, Madurai Kamaraj University, Madurai, India

The intestinal microbiome is important for synthesising nutrients, breaking down polysaccharides, protecting against foreign microbes, and aiding immune system development by producing short-chain fatty acids (SCFAs). SCFAs are formed through the interaction between the gut microbiota and the diet in the gut lumen. This study aims to extract exopolysaccharide (EPS) from the gut isolate *Bacillus spizizenni* DMTMMR-17, a probiotic species which was optimised to improvise the yield of EPS through one-factor-at-a-time (OFAT) and response surface methodology. The central composite design (CCD) increased the yield up to 2.32 ± 0.4 g/L, abd characterization was performed to study the structural and functional moieties of EPS by Fourier transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR) for proton and carbon (^{1}H and C^{13}-NMR). The EPS was subjected to artificial simulated gastrointestinal digestion by mimicking the gut conditions of healthy humans. These data reveal the higher concentrations of SCFA derivatives such as propionate, acetate, and other bioactive metabolites. The in vitro experiments in IBD (irritable bowel syndrome) patients' gut homogenates were treated with EPS digest with SCFA, revealing that dysbiosis is reinstated, by improvising the colonisation of probiotic and gut symbionts by inhibiting the growth of pathogenic bacteria, which was studied by the metagenomic sequencing (V_3–V_4) region of the 16S rRNA gene. The EPS digest with SCFA was subjected to biological activities such as scavenging and reducing power, which showed 32.03 ± 0.21 and 13.04 ± 0.3 μg/mL. The anti-diabetic activity, like α-amylase, α-glucosidase and DPP-IV, was studied, expressing reduced IC_{50} values at (9.21 ± 0.3, 4.43 ± 0.4, 21.4 ± 0.33) μg/mL. Anti-inflammatory activity was higher up to 60–75%, and the anti-lipidemic inhibition property expressed inhibition up to 40% in cholesterol esterase and pancreatic lipase. These results indicate that EPS digest with SCFA is a beneficial substrate and can be administered for combinational IBD therapies.

sciforum-089312: Investigation of the Antibacterial Activity of Essential Oil from *Cymbopogon citratus* Leaves against Gram-Negative Bacteria

Bernardina De Paixão Santos [1], Dicla Aline Semedo da Veiga [1], Francisco Sérgio da Silva Sousa [1], Everton Vieira da Silva [2] and Sávio Benvindo Ferreira [3]

[1] Academic Unit of Life (UACV), Teacher Training Center (CFP), Federal University of Campina Grande (UFCG), Cajazeiras, PB, Brazil
[2] Academic Unit of Exact and Natural Sciences (UACEN), Teacher Training Center (CFP), Federal University of Campina Grande (UFCG), Cajazeiras, PB, Brazil
[3] Federal University of Campina Grande, Cajazeiras, PB, Brazil

Gram-negative bacteria cause a multitude of infections in humans and, over time, many have developed resistance to conventional antibiotics, making available treatments less effective. Given this scenario, several studies have explored natural plants as a possible therapeutic approach, highlighting the essential oil of *Cymbopogon citratus*, commonly known as Lemongrass. Therefore, the scope of this work is to investigate reports in the literature about the antibacterial activity of lemongrass essential oil against Gram-negative bacteria. A narrative review was carried out using the PICo strategy with the following guiding question: how effective is *Cymbopogon citratus* essential oil (P) as a therapeutic modality (I) considering its antibacterial properties (Co)? The search for articles was carried out in the PubMed, Virtual Health Library (BVS), Scielo, and CAPES databases, using the descriptors "*Cymbopogon Citratus*", "essential oil", "lemon grass", "antibacterial activity", and "Gram-negative bacteria" combined with Boolean operators (OR and AND). Original studies that addressed the antibacterial activity of the vegetable's essential oil in Portuguese, English, or Spanish were included and duplicate works were excluded. After screening, the final sample consisted of 14 articles. The studies were primarily in vitro trials. In a test with *Pseudomonas aeruginosas*, the inhibitory activity of the compound was from a concentration of 5%, while for *Salmonella ente*ritidis, it was from 2.5%. Concomitantly, the vegetable's essential oil showed a significant inhibitory effect with halos ranging between 12 and 23 mm and minimum inhibitory concentration (MIC) of 3.90 μg/mL, against strains of the *Aeromonas caviae complex*. Against strains of *Proteus penneri, Escherichia* coli, and *Klebsiella oxytoca*, different degrees of inhibition were observed, all exhibiting halos greater than or equal to 11 mm. These results point to the essential oil of *C. citratus* as a promising alternative to control and combat bacterial infections, highlighting its bactericidal action at relatively low concentrations.

sciforum-089353: Maximizing Bioactive Compounds Extraction: How Factors Influence the Performance of Microwave-Assisted Technique?

Franklin Chamorro [1], P. Donn [1], S. Seyyedi-Mansour [1], P. Garcia-Oliveira [1,2], J. Echave [1], A. G. Pereira [1], L. Cassani [1] and M. A. Prieto [1,3]

[1] Universidade de Vigo, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecoloxía e Alimentación (IAA)—CITEXVI, 36310 Vigo, España
[2] Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal
[3] Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal

The diverse properties and beneficial applications of bioactive compounds (BACs) have garnered significant interest across multiple industries. These compounds can be extracted from various sources, but vegetal matrices, including plants, fruits or by-products have taken much of this attention. To improve extraction efficiency and reduce costs, non-conventional techniques like microwave-assisted extraction (MAE) have emerged as greener and more cost-effective alternatives. This technique combines solvent extraction with microwave heating power, where the energy is transmitted as waves, penetrating the matrix, and interacting with polar molecules, generating heat that increases the kinetic of the extraction. By reducing solvent usage, extraction times, waste generation, sample requirements and energy consumption, MAE has become one of the most cost-effective extraction methods, with remarkable extraction rates [1,2]. Despite this, it must be considered that due to the high temperatures and pressures, there is a risk of metabolites being degraded [3]. The extraction performance depends on multiple factors including pressure, temperature, moisture, microwave power, exposure time and characteristics of the matrix and solvent. Moreover, the implementation of this technique under an experimental design described by mathematical models such as the response surface methodology (RSM) along with a circumscribed central composite design (CCCD) allow for predicting the experimentally obtained values with the highest reliability. For this purpose, it is necessary to determine the influence of these factors. This abstract underscores recent advancements in understanding the complexities of MAE for secondary metabolite recovery, laying the groundwork for optimizing extraction methodologies and harnessing these BACs for various applications.

sciforum-088967: Molecular Docking/Dynamic Simulations and ADME-TOX-Based Analysis of Phthalimido-1,3-thiazole Derivatives as BCR-ABL Inhibitors

Imane Bensahbane, Nadjib Melkemi and Daoud Ismail

[1] Group of Computational and Medicinal Chemistry LMCE Laboratory, University Mohamed Khider, Biskra 07000, Algeria
[2] Laboratory of Natural and Bioactive Substances, LASNABIO, University of Abou-Bakr Belkaid Tlemcen, Tlemcen, Algeria

Acute lymphoblastic leukemia (ALL) is an aggressive malignancy distinguished by an inferior survival rate, especially Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph + ALL), which comprises about 20–30% of all ALL cases. It is caused by the BCR-ABL protein, which is produced in cells that contain the Philadelphia (Ph) chromosome and stimulates the bone marrow to produce an excessive number of lymphoblasts. The ABL1 kinase domain has recently garnered significant attention as a promising molecular target for the development of Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph + ALL) treatment. In this research work, a study of the cytotoxic properties of phthalimido-1,3-thiazole derivatives against the BCR-ABL protein PDB code 4WA9 was carried out using a combination of different computational chemistry methods, including a molecular docking/dynamics study and ADM-T evaluation. Five top hits were identified based on their free energy scores, namely, 4WA9-L18, 4WA9-L19, 4WA9-L20, 4WA9-L21, and 4WA9-L22, which demonstrated better binding affinity (from -7.8 to -8.3 kcal/mol). Furthermore, MD studies support the molecular docking results and validate the stability of the studied complexes under physiological conditions. These results confirm that the hits selected are verifiable inhibitors of the BCR-ABL protein, implying a good correlation between in silico and in vitro studies. Moreover, in silico ADME-TOX studies were used to predict the pharmacokinetic, pharmacodynamic, and toxicological properties of the studied hits. These findings support the future role of phthalimido-1,3-thiazole derivatives against the ALL disease and may help to find a new therapeutic combination of drugs to treat relapsed acute lymphoblastic leukemia and improve overall survival.

sciforum-083746: Optimization of Methanol Extraction and Evaluation of Anti-Inflammatory and Anti-Alzheimer Activities In Vitro of *Ammodaucus leucotrichus*

Djehiche Cheima [1], Benzidane Nadia [2], Djeghim Hanene [2], Tebboub Mehdi [2] and Arrar Lekhmici [3]

[1] Ph.D. Biochemistry
[2] Ph.D.
[3] Professor

High-added-value product extraction is a topic of tremendous interest and relevance, particularly when it comes to newly discovered plants from understudied arid and semi-arid zones. *Ammodaucus leucotrichus*, a spontaneous endemic plant indigenous to north and tropical Africa's Saharan and sub-Saharan regions, is the plant species that we chose for this goal. It is used as a condiment or flavoring agent in cuisine, as well as in traditional medicine, to cure heart disease, diabetes, allergy symptoms, and stomach ailments. In vitro tests were performed to assess the anti-inflammatory and anti-neurodegenerative effects of lipoxygenase (LOX) inhibition and anticholinesterase (AChE). The findings demonstrated the strong anti-inflammatory and anti-Alzheimer properties of *Ammodaucus leucotrichus*. Water was found to be a superior extraction solvent compared toethanol and was used to reach the ideal conditions at 180 °C. Temperature had a beneficial impact on extraction yield within a range of 15.55 to 44.45%. Moreover, the EC50 values for antioxidant activity, acetylcholinesterase inhibition, and lipoxygenase inhibition were 85.51 μg/mL, 55.60 μg/mL, AChE, and LOX, respectively. In conclusion, *Ammodaucus leucotrichus* phenolics may be extracted using the new PLE process, which is an effective and environmentally friendly way. This allows for the production of extracts that have appealing anti-Alzheimer and anti-inflammatory properties.

This study shows that the *Ammodaucus leucotrichus* can be a new potential resource of natural anti-inflammatory and anticholinesterase compounds.

sciforum-089309: Phlorotannins as Bioactive Agents from Brown Algae: Chemical Characterization and Extraction Methods

Camila F. Secco Bastos [1,2], M. Carpena [1], F. Chamorro [1], Rafael Nogueira-Marques [1,2], A. Silva [3], M. Fátima Barroso [3], Marlene Santos [2] and M. A. Prieto [1,4]

[1] Universidade de Vigo, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecoloxía e Alimentación (IAA)—CITEXVI, 36310 Vigo, España
[2] REQUIMTE | LAQV, Escola Superior de Saúde, Instituto Politécnico do Porto, Rua Dr. António Bernardino de Almeida 431, 4200-072 Porto, Portugal
[3] REQUIMTE/LAQV, Instituto Superior de Engenharia do Porto, Instituto Politécnico do Porto, Rua Dr. António Bernardino de Almeida 431, 4249-015 Porto, Portugal
[4] Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal

Marine organisms, especially brown seaweeds, have attracted a lot of attention worldwide because of their potential for use in treating a range of infectious and non-infectious diseases, being able to take part in the creation of medications and nutraceuticals intended for ingestion by humans. Brown algae are a source of compounds, including phlorotannins (PTs), that exhibit biological effects, like anti-inflammatory, antibacterial, antioxidant, anti-tumor, anti-diabetic, and UV radiation protection [1,2]. As a polyphenol (tannin), this compound has the intrinsic capacity to scavenge and reduce free radicals. It can also present a high affinity for proteins through specific or non-specific interactions, interact with multiple receptors, control enzyme activity, cross-link biological macromolecules, inactivate microorganisms, and regulate signal transduction. These properties suggest that PTs may find widespread use in tissue engineering. Furthermore, according to related studies, at most dosages, PTs from brown seaweeds have shown minimal toxicity in invertebrates, animals (mice, rats, fish, and dogs), and humans [3]. PT algae have been commonly characterized using assays like Folin–Ciocalteu and 2,4-dimethoxybenzaldehyde (DMBA). However, due to their complex mixtures, identifying them accurately is challenging. Techniques like MS/MS coupled with HPLC aid in tentative characterization, but some authors advocate for NMR for precise identification, linking structures to HPLC conditions for a comprehensive analysis [4]. Solid liquid extraction (SLE) with hydroacetonic blends has remained the preferred method for extracting PTs and tannins in general, despite its limitations in sustainability and environmental impact. Factors like solvent polarity, pH, temperature, time, and pre-treatments are said to influence the effectiveness of solvent-based extraction procedures. However, emerging methods such as microwave-assisted extraction (MAE), pressurized liquid extraction (PLE), ultrasonic-assisted extraction (UAE), and supercritical fluid extraction (SFE) offer more eco-friendly alternatives to address these drawbacks, enhancing extraction efficiency. This communication conducts a literature review about PTs, their chemical characterization, and the most appropriate extraction methods [2,5].

sciforum-089001: Potential Role of the Gut Metabolite, Trimethylamine *N*-Oxide as a Folding Inhibitor of Carbonic Anhydrase: A New Insight for Its Involvement in Dementia

Kritika Kumari and Laishram Rajendrakumar Singh

Dr. B. R. Ambedkar Center for Biomedical Research, University of Delhi, Delhi 110007, India

Introduction

Trimethylamine N-Oxide (TMAO) is an important metabolite, which is synthesized from the dietary precursors' choline, betaine, and carnitine in various organisms. In humans, TMAO is synthesized by the metabolism of these dietary precursors by the action of enzymes produced by gut microbiota, and its high levels are abundantly found in serum and cerebrospinal fluid (CSF). Although TMAO is a stress protectant, especially in urea-rich organisms, it is an atherogenic agent in humans and is associated with various diseases. Specifically, there has been a strong correlation between serum TMAO levels and the development of Dementia. We have investigated the effect of TMAO on Carbonic anhydrase (CA) as after repeated failure of drugs that target Aβ in clinical trials, CA is considered to be an alternative target.

Methods

In the present study, we have investigated the effect of TMAO on the structural and functional integrity of CA using various biophysical and biochemical approaches. Cellular approches are also used to confirm the effect.

Results

Our result indicates that TMAO acts as a ligand of CA that is specifically targeted to its folding intermediate, U_f. We discovered that TMAO inhibits the folding of CA by disrupting the U_f state and eventually impairing the cis/trans isomerization. Furthermore, TMAO is capable of inducing cell cycle arrest and eventually increasing ROS levels.

Conclusions

This study highlights a novel molecular insight into the involvement of TMAO in AD dementia and other proteopathy-associated diseases.

sciforum-088592: Protein Property Prediction: Regression-Based Approaches for Structure and Function Prediction

Vishal Kumar swain [1], Neelamadhab Padhy [1], Naresh Kumar Sahoo [2,3], Swetarani swain [2,3], Abhipsa Patra [2,3] and kiran kumar sahu [1]

[1] Department of Computer Science and Engineering, School of Engineering and Technology, GIET University, Gunupur, Odisha, India
[2] Department of MCA
[3] GIET University, Gunupur, Odish, India

Context

Proteins are important molecules that are found in all living organisms. They are made up of long chains of amino acids that are linked through peptide bonds. Protein function prediction is one of the most challenging problems in the post-genomic era. The number of newly identified proteins has been exponentially increasing with the advances of high-throughput techniques.

Objectives

The main objective of this research study is to predict protein structure and function using regression-based approaches. The second aim is to discuss recent advancements in machine learning techniques that have significantly contributed to improving regression-based approaches for protein property prediction.

Method and Materials

In this research study, we use a machine learning algorithm to predict details about protein structure, function, shape, and mechanism of action. We implement regression algorithms such as linear regression, decision tree regression, random forest regression, and gradient boosting regression using advanced frameworks such as Tensor Flow and sci-kit-learn.

Result

Our analysis reveals promising outcomes, with the random forest regression model achieving an accuracy of 96%, precision of 95.1%, and recall of 95%. These results underscore our ability to predict various protein properties and structures with enhanced precision, leveraging the complicated relationships within protein data.

sciforum-087195: Pulegone Application Trends: Exploration of Uses Based on Leading Patent Applicants

Reda El Boukhari and Ahmed Fatimi

Chemical Science and Engineering Research Team (ERSIC), Department of Chemistry, Polydisciplinary Faculty of Beni Mellal (FPBM), Sultan Moulay Slimane University (USMS), P.O. Box 592 Mghila, Beni Mellal 23000, Morocco

Introduction

Pulegone is a natural biomolecule that may be found in essential oils from many medicinal and aromatic plants, especially those from the *Lamiaceae* family. It is known for its distinguished minty aroma and taste, and it has been studied for its potential use in various therapies due to its antibacterial, anti-inflammatory, and cytotoxic effects. Even with its recognized toxicity, pulegone is still widely used as a versatile and valuable compound in many industrial fields.

Methodology

To identify trends in the application of pulegone, we prospecte patents from specialized patent databases. A search was carried out on the titles, abstracts, and claims of the patents. The patents were then sorted by applicant names, and then the applicant patent portfolio was studied to identify the targeted trends.

Results

The patents reveal that the leading jurisdiction is the United States, with about 44% of the filed patents. The study of the top 10 applicants allows us to distinguish three major areas of innovation. The field of daily-use cleaning, health, and hygiene encompasses 121 patents that take advantage of the aromatic characteristics of pulegone to provide hygiene and cosmetic products. The plant protection field stands out with 58 patents. In this field, pulegone is used for its pesticide and pest-repellent action to develop crop protection products. The third field is the use of pulegone with cannabinoids for pharmacological innovations as well as for recreational uses, as represented by 42 patents.

Conclusions

The pulegone-related patents were based on preparations for medical, dental, or toiletry purposes. Pulegone is valued for its refreshing minty scent; it is utilized in perfumes and body care, as well as being an odor neutralizer and odorizing agent for toilet and cleaning compositions. Furthermore, pulegone is used as a natural pesticide and pest repellent, reducing the need for chemicals.

sciforum-089328: Recent Advances in Understanding Keys Factors Influencing Pressurized Liquid Extraction of Secondary Metabolites: A Comprehensive Review

Pauline Donn [1], Sepidar Seyyedi-Mansour [2], Franklin Chamorro [3], Paula Garcia-Oliveira [3], Javier Echavez [3,4], Ana Perez-Vazquez [3], Paula Barciela [3], Lucia Cassani [3] and Miguel Angel Prieto Lage [3,4]

[1] Faculty of Science, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Universidade de Vigo, E32004 Ourense, Spain
[2] Universidade de Vigo, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecoloxía e Alimentación (IAA)—CITEXVI, 36310 Vigo, España
[3] Universidade de Vigo, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecoloxía e Alimentación (IAA)—CITEXVI, 36310 Vigo, España
[4] Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal

Pressurized Liquid Extraction (PLE) has become a pivotal technology for extracting secondary metabolites (e.g., phenolic compounds) from botanical sources, with implications spanning pharmaceuticals, nutraceuticals, and functional foods [1,2]. This communication provides an overview of recent advancements in understanding the key factors influencing the efficiency and selectivity of PLE in the extraction of these bioactive compounds. The optimization of PLE parameters, including pressure, temperature, and solvent characteristics, has been a focal point in recent research to enhance the extraction yield and preserve the integrity of secondary metabolites. Investigations into the interaction of sample matrix properties, particle size, and solvent polarity have revealed nuanced effects on the extraction process, contributing valuable insights to developing targeted extraction protocols. Also, technological innovations, such as the utilization of green solvents and novel extraction techniques, are reshaping the landscape of PLE. Different studies exploring sustainable approaches not only enhance extraction efficiency but also align with the growing emphasis on environmentally friendly practices, paving the way for greener extraction processes. Collaborative efforts among researchers have led to a deeper understanding of the factors influencing PLE. Thus, this abstract highlight recent progress in unraveling the complexities of PLE for secondary metabolites, fostering a foundation for optimizing extraction methodologies and leveraging these bioactive compounds for diverse applications.

sciforum-087111: Restriction Modification System of the MspGI and Its Flanking Genes

Valeriya N. Antipova [1], Rimma I. Artyukh [1], Alfiya Yunusova [1] and Elena V. Spirina [2]

[1] Institute of Theoretical and Experimental Biophysics, Russian Academy of Sciences, Pushchino, Russia
[2] Institute of Physicochemical and Biological Problems in Soil Science, Russian Academy of Sciences, Pushchino, Russia

Microbacteria offer protection against the penetration of foreign DNA with not only RMS, but also the DISARM and BREX systems [1,2]. RMS consists of 2 or 3 genes, while DISARM and BREX systems contain 5–6 genes. We report on the discovery of the mesophilic Microbacterium sp. Gd 4–13 taken from permafrost soils dating back 34,400 years. The study of this bacterium has garnered interest due to the presence of a endonuclease restriction (ERse) and DNA-methyltransferase genes (MTse). The endonuclease restriction is currently the only one that recognizes the site at the 5'-GCCGG↓C with the 3'overhanging end.

An analysis of the flanking region of the RMS of MspGI was carried out to detect the cassette composition of RMS MspGI genes similar to DISARM or BREX. Thus, three short ORFs are located upstream of the MTse gene in the region of ~3.5 kb and their function is unknown. Downstream of the ERse gene is the HNH ENse gene, followed by hp and recombinase (Figure 2) [5].

Thus, an analysis of the flanking region RMS MspGI showed the presence of the helicase and HNH endonuclease genes. The presence of MTse and ERse, as well as the fact that these genes are part of the DISARM gene cassette, could suggest that although RMS MspGI does not belong to the DISARM or BREX systems, the flanking genes may be involved in protecting the cell from the penetration of foreign DNA in vivo in the complex with RMS MspGI genes.

sciforum-089301: Sources, Biosynthesis Pathways, Bioavailability, Bioactivity, and Pharmacology of Dihydrodaidzein

Pengren Zou

Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Faculty of Science, University of Vigo, E32004 Ourense, Spain

Dihydrodaidzein is a hydrogenated product of the conversion of daidzein, the main component of soy isoflavones, under the metabolic action of intestinal microorganisms. Being the intermediary metabolite of soy isoflavones, dihydrodaidzein is widely acknowledged to exhibit heightened biological activity. During intestinal transformation in vivo, dihydrodaidzein can subsequently undergo further hydroxylation to form the more active equol. Compared with its metabolic precursor, daidzein, dihydrodaidzein exhibits higher activity and broader biological effects, due to which it has gradually attracted the attention of many scientists in recent years. It has been found to have superior pharmacological activities due to its antioxidant properties, potential prevention of cardiovascular disease andosteoporosis, and estrogen-like activity. However, there is currently a scarcity of literature providing a systematic and comprehensive overview of DHD. Considering the high biological activity and potential market value of DHD, this article reviews advancements in DHD research, encompassing its sources, biosynthetic pathways, physicochemical properties, metabolism, bioavailability, biological activity, and pharmacology. Emphasis is placed on elucidating the biosynthesis biotransformation, biological activity, and pharmacology of DHD, aiming to maximize its intrinsic value and contribute to its application in the realms of medicine and clinical practice. Dihydrodaidzein suffers from low water solubility, instability, and low oral bioavailability, so emerging nanocarrier technologies can be explored to encapsulate dihydrodaidzein to enhance its solubility, cellular uptake, targeted delivery, and functional efficacy. Future endeavors should prioritize additional research to assess its bioavailability, potentially paving the way for its inclusion in future nutritional supplements.

sciforum-088452: Stability and Degradation Mechanism of (-)-Epicatechin in Thermal Processing

Hui Cao and Wenqi Huang

Nutrition and Bromatology Group, Department of Analytical and Food Chemistry, Faculty of Sciences, Universidade de Vigo, 32004 Ourense, Spain

Introduction

(-)-Epicatechin (EC) is a commonly consumed dietary phytochemical that possesses multiple physiological benefits for human health. Its well-established robust antioxidant activity contributes to alleviating oxidative stress and inflammation associated with various diseases. However, the stability of EC limits its potential health benefits in the human body. Thermal processing is a common method used to extract EC, but it is likely to degrade EC due to its thermal instability.

Methods

In this study, a bathing incubation assay was designed to simulate the conditions of (-)-Epicatechin (EC) in boiling water during cooking. The degradation products were monitored using ultra-performance liquid chromatography combined with electrospray ionization quadrupole tandem mass spectrometric detection (UPLC-ESI-TSQ-MS/MS).

Results

The results showed an approximately 65.2% loss of (-)-Epicatechin (EC) within the first 10 min, with over 99.5% of EC being degraded within 30 min. A total of 22 degradation products were identified based on retention time, and the full tandem mass spectrometry (MS/MS) data are being comprehensively reported for the first time.

Conclusions

The investigation into the thermal stability and resulting product transformations of (-)-Epicatechin provides a foundational framework for future inquiries into its bioavailability and functional attributes. The isolation and testing of biological activities associated with the effects reported in EC should now be pursued to identify stronger analogues.

sciforum-089052: Structural Diversity of Oligosaccharides Isolated from Milk of Various Cow Breeds

Desh Deepak A. P. Singh Chauhan [1], Manisha Shukla [1], Desh Deepak [1] and Sarita Chauhan [2]

[1] Department of Chemistry, University of Lucknow, Lucknow 226007, India
[2] Department of Chemistry, Shri J.N.M. P.G. College, Lucknow 226001, India

Cow milk oligosaccharides (CMOs) have garnered significant attention due to their association with enhanced infant immune system development, defence against pathogens, and anti-inflammatory properties. Understanding their structural variations is crucial for unlocking their diverse biological functions. This paper explores the structural diversity of CMOs isolated from different cow breeds and their potential health implications. Recent research has elucidated various CMO structures, revealing a rich landscape of oligosaccharides with unique arrangements and potential bioactivities. Compounds such as Aurose, Tarose, Osose, and Tosose, identified in cow colostrum from the Jarsi breed, provide insights into early milk production. Similarly, discoveries like Asose, Urose, Ausose, and Tausose in black cow milk highlight the diversity within specific cow varieties. Further investigations into oligosaccharides from Lal Muha cow milk, including Rusose, Usose, Taurose, and Uruose, and from Chauri cow milk, such as Bosose, Unninose, Nakose, and Nienose, underscore the complex interplay between cow genetics and milk composition. Findings from black cow milk, including Indicose, Indose, Indinose, Bosnose, and Dicusose, emphasise the potential bioactivity of oligosaccharides. Recent work on Tharparkar Cow milk oligosaccharides like Tharoside, Parkoside, Karoside, and Arkaroside showcases ongoing efforts to explore carbohydrate complexity across different cow breeds. These discoveries open avenues for further research into the structural variations of CMOs and how they affect human health.

sciforum-085884: Study on the Effect and Mechanism of Wolfberry Polyphenols in Regulating High-Fat Intestinal Type to Alleviate the Course of NAFLD

Jingyimei Liang

[1] College of Analytical Chemistry and Food Science, Universidade de Vigo, Ourense, Spain
[2] College of Food Science and Technology, Northwest University, Xi'an 710069, China

Non-alcoholic fatty liver disease (NAFLD) is a common metabolic liver disease with a significant increase in incidence worldwide. The escalating prevalence of obesity and diabetes have been identified as key factors contributing to NAFLD. wolfberry polyphenols, recognised as natural polyphenols, exhibit potent lipid-lowering properties and show efficacy in modulating enterotype. The therapeutic potential of wolfberry polyphenols in ameliorating high-fat intestinal conditions holds promise for alleviating and preventing the progression of NAFLD. Our study demonstrates that wolfberry polyphenols effectively alleviate NAFLD-associated glucose intolerance and ameliorate liver damage as evidenced by histological examination using HE staining. After treatment with 200 mg/kg worfberry polyphenols, the inflammatory infiltration completely disappeared, fat droplets essentially disappeared and the tissue morphology closely resembled that of the control check group compared to the hight fat diet group. Wolfberry polyphenols have a pronounced effect on reducing hepatic triglycerides, total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein (HDL). In addition, enzyme-linked immunosorbent assay analyses indicate that wolfberry polyphenols significantly reduce serum levels of the inflammatory factors TNF-α, IL-6 and IL-10. Non-targeted liver metabolomic analysis indicates that Lycium barbarum polyphenols modulate NAFLD liver health primarily through the regulation of methionine and tryptophan pathways. Furthermore, wolfberry polyphenols exhibit regulatory effects on the content of short-chain fatty acids in the intestinal flora. These findings provide a solid theoretical basis and suggest a promising avenue for future research into the use of wolfberry polyphenols in the management of NAFLD. The study suggests that these polyphenols could serve as an alternative intervention for NAFLD by modulating oxidative stress, inflammatory factors, gut microbiota and endogenous liver metabolism.

sciforum-085253: The Effect of β-Cyclodextrins on the Physical Properties and Anti-Staling Mechanisms of Corn Starch Gels during Storage

Ziyang Jia [1], Xuedong Wang [2] and Yang Fu [2]

[1] Universidade de Vigo, Ourense, Spain
[2] Wuhan Polytechnic University, Wuhan, China

The retrogradation of starch during storage was attributed to the high amylose content of corn-based food, resulting in economic losses and restricting the development of the food industry. The unique molecular capsule structure of cyclodextrins has been widely developed and applied in food fields in recent years.

β-cyclodextrin(β-CD) and hydroxypropyl-β-cyclodextrin(HP-β-CD) are natural cyclic annular oligosaccharides, with less studies on the application of inhibiting the retrogradation of corn starch. Our research showed that β-CDs could affect the rheological and gelatinization properties of corn starch gel and enhance the thermal stability of starch granules. Meanwhile, the addition of β-CDs during storage can promote the texture characteristics of gel. This was due to the improvement of the gel's internal structure using β-CDs, which was also supported by SEM observations. In addition, XRD and FTIR results illustrated that β-CDs could inhibit the formation of the ordered starch crystal structure. These results were represented more significantly with the addition of HP-β-CD, which may be due to the intense competition for intermolecular water molecules between HP-β-CD and amylose. The experimental results proved the application prospect of β-CDs in corn-based food. Consequently, the addition of β-CDs could delay the retrogradation of CS gel, and the introduction of hydroxypropyl groups was more effective, which provided a theoretical basis and new insights for the production of starch-based food industrial products.

sciforum-086896: The Potentiate Production of Phycobiliprotein from *Oscillatoria* sp. for Its Application as a Food Coating Agent and Microbial Inhabitant

Nadia Sharif [1], Uzma Nihar [1], Neelma Munir [2], Rakhshinda Sadiq [3], Syed Ali Raza Shah [4] and Zainul Abideen [5]

[1] Department of Zoology, Women University Mardan, Mardan, Pakistan
[2] Department of Biotechnology, Lahore College for Women University, Lahore, Pakistan
[3] Department of Biotechnology, Women University Mardan, Mardan, Pakistan
[4] Department of Microbiology, Abdul Wali Khan University, Mardan, Pakistan
[5] Dr. Muhammad Ajmal Khan Institute of Sustainable Halophyte Utilization, University of Karachi, Karachi, Pakistan

Phycobiliproteins (PBPs) are fluorescent proteins of numerous colors with several highly conserved structural and physicochemical characteristics. In addition to their energy harvesting function, PBPs have shown multiple biological activities, comprising antibacterial, antioxidant, and antitumor activities. They are also applied in areas of biomedicine and bioenergy research. The present study was conducted to extract and analyze the use of phycobiliproteins as a food coating agent and microbial inhibitant to enhance the shelf life of fruits and vegetables**.** Phycobiliproteins were extracted from *Oscillatoria* sp. using the mechanochemical method and were analyzed via SDSPAGE. Purified extracts were tested for antioxidant activity, antimicrobial activity, and biopreservational effects. PBP extracts showed higher inhibition zones of 8.2 mm and 8.5 mm for *E. coli* and *Rhizopus*, respectively. The edible dip coating technique was more efficient, providing an 8-day shelf life with an 80% freshness of fruits and vegetables. The nitric oxide scavenging activity of the PBP-3 method was 78% with a 200 µg/mL concentration. Phycobiliproteins showed antimicrobial activity against the *Staphylococcus aureus* and *Kliebsella* sp. An excellent biopreservational effect of the extract was observed from the physical appearance of the control and test group of fruit and vegetables and further from the microbial flora assay. It was concluded that the phycobiliproteins of the *Oscillatoria* sp. of cyanobacteria represent a potential microbial inhabitant, and their effects of biopreservation make them an effective food coating agent.

sciforum-089221: The Role of Amyloidogenesis in Cancer Development: An Investigation of Transcription Factors

Marina Ryabinina, Andrew Zelinsky and Aleksandr Rubel

Laboratory of Amyloid Biology, 190000 Saint-Petersburg, Russia

Cancer remains the leading cause of death due to a wide range of molecular mechanisms. One of these mechanisms is impaired proteostasis, which leads to the formation of amyloids, fibrillar proteins with an intermolecular cross-beta structure. Studies have shown that amyloids and amyloidogenic proteins are associated with tumor progression. For example, elevated levels of SAA amyloid in serum correlates with the development of lung, breast cancer, and melanoma. Similarly, the IAPP protein is associated with neuroendocrine tumors, and ODAM is associated with odontogenic tumors [1]. By using bioinformatics algorithms, we identified the amyloidogenic potential of five transcription factors involved in the pathogenesis of various cancers. Experimental testing of the amyloidogenic potential of these proteins in a yeast assay [2] partially confirmed the in silico data. The goal of this study was to further investigate the amyloid potential of these proteins in vitro. We employed the bacterial C-DAG production and export system [3] and/or purified recombinant proteins from *E. coli* with metal-affinity chromatography. For transcription factors that demonstrated amyloidogenic potential in bacteria, we analyzed their amyloid-like properties in human HEK293T cell culture. The results obtained in this study provide new insights into human proteins capable of forming amyloids and offer promising prospects for identifying potential targets for cancer therapy.

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sciforum-087061: The Role of the Charged Residues in the C-Gate of the Yeast Mitochondrial NAD$^+$ Transporter Ndt1p

Daniela Valeria Miniero [1], Magnus Monnè [2], Maria Antonietta Di Noia [1], Luigi Palmieri [1] and Ferdinando Palmieri [1]

[1] Department of Biosciences, Biotechnologies and Environment, University of Bari, Bari, Italy
[2] Department of Science, University of Basilicata, Potenza, Italy

The mitochondrial carrier family (MCF) consists of nuclear-encoded proteins which catalyze the transport of a wide variety of compounds across the mitochondrial inner membrane. These proteins present common structural features, which consist of three repeats of two transmembrane helices enclosing a translocation pore with a single substrate binding site. Access to the pore from the matrix side is controlled by a network of salt bridges formed by conserved charged residues of the signature motifs PX[D/E]XX[R/K] (M-gate) on the transmembrane helices H1, H3, and H5. On the cytosolic side, a less-conserved network is formed by the residues of the motifs [F/Y][D/E]XX[R/K] (C-gate) on H2, H4, and H6. In this work, to test the role of the charged residues of the C-gate in transport, we analyzed the charged residues of the cytoplasmic motifs of the yeast NAD$^+$ mitochondrial transporter (Ndt1p). Single cysteine mutations of the negatively and positively charged residues were introduced by site-directed mutagenesis and only three of them (H4:E258, H4:K261, and H6:E359) completely inactivated the carrier. The double cysteine salt-bridge pair mutant H4-H6:K261C/E359C exhibited a higher transport rate than the corresponding single mutants as well as when the charged residues were swapped in these positions (H4-H6:K261E/E359K). The double mutant H2-H4:K164C/E258C and the swapped H2-H4:K164E/E258K exhibited transport rates at similar levels to the single K164C. The sextuple mutant with all the charged residues inverted was inactive. These preliminary results suggest that not all the charged C-gate residues are essential for transport and that some of them may have additional roles in transport besides forming salt-bridges.

sciforum-088988: The Study of Structural Features of Odorant-Binding Proteins That Determine Their Amyloidogenicity

Anna I. Sulatskaya [1], Olga V. Stepanenko [1], Maksim I. Sulatsky [2] and Olesya V. Stepanenko [1]

[1] Laboratory of Structural Dynamics, Stability and Folding of Proteins, Institute of Cytology of the Russian Academy of Sciences, 4 Tikhoretsky ave., 194064 St. Petersburg, Russia
[2] Laboratory of Cell Morphology, Institute of Cytology of the Russian Academy of Sciences, 4 Tikhoretsky ave., 194064 St. Petersburg, Russia

Amyloid fibrils have attracted attention as protein aggregates accompanying the development of severe pathologies, including neurodegenerative diseases and systemic and local amyloidoses. Physiological amyloids essential for cell and tissue function have also been identified. These ordered aggregates represent morphologically similar fibers composed of stacked β-strands. This suggests a predisposition to amyloid formation of native proteins enriched with b-structure, particularly those with a β-barrel structure with β-strands arranged in a cylindrical β-sheet. Despite the growing number of β-barrel proteins known to possess amyloidogenic properties, the mechanism underlying the transition of these proteins from the native monomeric/oligomeric to the fibrillar state is not fully understood. We analyzed the structural features of β-barrel proteins that determine their high amyloidogenicity using bovine odorant-binding protein (bOBP) as an example. The structural reorganization at the early stages of fibrillogenesis and the efficiency of this process for bOBP and its variants were analyzed using spectroscopic, microscopic methods, and bioinformatic analysis.

We showed that the ordered aggregation of bOBP can be facilitated by the destabilization of its structure to form a highly structured monomeric intermediate state with a retained β-barrel scaffold but a melted short α2-helix and β9-strand in the C-terminal fragment of the protein, which is amyloidogenic. Further, the C-terminus fixation via the disulfide bridge in monomeric bOBP variant (bOBP-Gly121+/W64C/H155C) inhibited its fibrillogenesis, which was overcome by the reducing agent addition or in monomeric variant (bOBP/Gly121+) without a disulfide bond.

Our findings indicate that the C-domain of OBPs is crucial for fibrillogenesis initiation. We suggest that the loss of ordered structure in the C-terminal fragment of the molecule, coupled with the disassembly of the bOBP dimer or detachment of this fragment from the β-barrel of monomeric OBPs, demasks amyloidogenic regions of the molecule for intermolecular interactions.

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sciforum-089245: Ultrasensitive–Selective DNA Nanomachine for Testicular Germ Cell Tumor Detection

Meera Alaji [1], Dmitry M. Kolpashchikov [1,2,3], Anastasia Malek [4] and Ahmad A. Eldeeb [1]

[1] Laboratory of Molecular Robotics and Biosensor Materials, SCAMT Institute, ITMO University, St. Petersburg, Russian
[2] Chemistry Department, University of Central Florida, Orlando, FL, USA
[3] Burnett School of Biomedical Sciences, University of Central Florida, Orlando, FL, USA
[4] Doctor of Science, Subcellular Technologies Laboratory, Federal State Budgetary Institution "N.N. Petrov National Medical Research Center of Oncology", Ministry of Health, Russia

Introduction

Testicular germ cell tumors (TGCTs) represent the most common solid malignancy in young men. MicroRNA-371a-3p (miR371) has been suggested as a sensitive biomarker in TGCTs since it increases in the plasma in the early stages. There are five other miRNAs that have a high similarity to the miR371 sequence, which makes it difficult to detect using PCR. The binary deoxyribozyme Dz contributes to the DNA nanomachine's function by serving as a molecular tool for selectively cleaving fluorophore-labeled substrates (F-sub) and can be developed to cleave F-sub in response, selectively, to miR371 recognition for TGCT detection.

Methods

A DNA nanomachine able to recognize miR371 selectively was designed, equipped with a reporter substrate delivery system for high sensitivity. Native polyacrylamide gel electrophoresis was performed to study the assembly and interactions among the designed DNA nanomachine. A fluorescence assay using a spectrophotometer was applied to investigate the selectivity and sensitivity of the designed DNA nanomachine using synthetic miRNA analytes, followed by the examination of its capability to detect miR371 in patient samples.

Results

The designed DNA nanomachine was successfully assembled. The suggested design is selective for miR371 in the presence of the other five similar miRNAs and can induce increasing fluorescence in response to increasing concentrations of miR371, with a limit of detection (LOD) of ~28.9 pM.

Conclusions

Due to the suggested design, we developed a DNA nanomachine based on binary Dz that is highly selective and sensitive for miR371. DNA nanomachines based on binary Dz can be considered as a simple, inexpensive, sequence-specific, and sensitive tool for early TGCT diagnoses.

sciforum-086961: Unraveling Structural Wonders: Recent Advances in Biomolecular Structures

Ujban Hussain [1], Samiksha Sandeep Tammewar [2] and Abhijeet Chalkhor [1]

[1] Department of Pharmaceutical Sciences, The Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, India
[2] Priyadarshini J. L College of Pharmacy, Nagpur, India

Introduction

Biomolecular structures play a role in the functioning of cells, controlling the processes that sustain life. This review embarks on a journey through recent advances in biomolecular structural studies, exploring the profound impact of cutting-edge techniques on unraveling the mysteries encoded within these molecular entities.

Methods

This review explores the range of techniques used to determine molecular structures. X-ray crystallography, known for its atomic-level detail, is complemented by NMR spectroscopy, which provides insights into the behavior of molecules. The emergence of cryo electron microscopy has further expanded our abilities, allowing us to visualize assemblies of molecules with unprecedented clarity.

Result

Exciting breakthroughs in structural molecular studies have revealed transformative insights. From capturing the actions of enzymes to understanding how membrane proteins are arranged in space, these discoveries have revolutionized our understanding of biological processes. The results section highlights findings that emphasize the importance of these advancements.

Conclusions

The synthesis of knowledge is propelling biomolecular research into a new era. These groundbreaking revelations not contribute to our understanding but also have practical implications that can make a difference in various applications. This review concludes by emphasizing the pivotal role of biomolecular structures in shaping the trajectory of scientific inquiry, opening unprecedented avenues for exploration and application.

sciforum-086175: Untargeted Proteomics Approach to Study Congenital Hearing Loss Cases

Lucky Thakkar [1], Manjunath D. [2] and Suresh B. Arakera [3]

[1] Molecular Medicine and Microbial Genetics Laboratory, Department of Applied Genetics, Karnatak University, Dharwad, Karnataka 580003, India
[2] Department of ENT, Karnataka Institute of Medical Sciences, Vidya Nagar, Hubballi, Karnataka 580002, India
[3] Molecular Medicine and Microbial Genetics Laboratory, Department of Applied Genetics, Karnatak University, Dharwad, Karnataka 580003, India

Introduction

Congenital Hearing Loss (CHL) is considered the most prevalent chronic condition among children. Biomarker studies of CHL are the need of the hour for the early diagnosis of the disease. Among the biomarkers of hearing loss, extracellular biomarkers of ear disorders are considered potential diagnostic tools. Protein biomarkers are considered crucial in early-stage diagnosis of CHL cases.

Methods

A total of 72 samples were collected and grouped into an Experimental (n = 36) and Control (n = 36) group. This study was approved by the Institutional Ethics Committee of Karnataka Institute of Medical Sciences, Hubballi, India. After obtaining informed consent from the participants, 05 mL blood samples were collected and serum samples were separated by centrifugation at 4000 rpm for 05 min and stored at −80 °C until further analysis. Pooled samples were processed for reduction, alkylation, and trypsin digestion before undergoing Liquid Chromatography Mass Spectrometry–Quadrupole Time of Flight (LCMS Q-TOF) analysis. Mascot search analysis was performed to identify peptide sequences and STRING software was used for network analysis of selected proteins.

Results

Significant proteins were identified among the study subjects. These comprised Guanine nucleotide protein, Glutamate receptor ionotopic protein, Complement C3, Putative transmembrane protein, Zinc finger protein, Alpha 2 glycoprotein, E3 ubiquitin protein, Cadherin, Alpha Tectorin, Myosin, etc. All these proteins are associated with Congenital Hearing Loss and are involved in the mechano-transduction of soundwaves inside the cochlea.

Conclusions

In this study, proteins associated with CHL have been identified among human subjects. The validation of these protein markers in serum samples using ELISA test will confirm the findings. Our panel of protein biomarkers may help in studying the underlying causes of the disease, which may direct us to its early diagnosis.

sciforum-085168: Zhenjiang Aromatic Vinegar Prevents the Alcohol Liver Disease in Mice via Autophagy

Yuxuan Zhao

Department of Analytical Chemistry and Food Science, Faculty of Science, Nutrition Food Group, University of Vigo, Vigo, Spain

Alcoholic liver disease (ALD) is an ignored global issue of public health. It is urgent for searching bioactive foods to prevent ALD. Zhenjiang aromatic vinegar (ZAV) contained antioxidant compounds, including polyphenols, flavonoids, and melanoidins. The mechanism of ZAV on preventing acute liver injury was evaluated in alcohol-treated mice. Our results showed that ZAV ameliorated morphological damage by hematoxylin and eosin and Oil Red O staining in alcohol-treated liver. ZAV relieved symptoms of ALD, which presented as decreased serum triacylglycerol, total cholesterol, alanine transaminase, and aspartate aminotransferase levels. In addition, ZAV treatment inhibited hepatic oxidative stress levels by downregulating reactive oxygen species generation, and the oxidative products (malonaldehyde, 4-hydroxynonenal, and 8-hydroxydeoxyguanosine), and upregulating catalase, superoxide dismutase, glutathione, and glutathione peroxidase. ZAV further reduced production of tumor necrosis factor-α and monocyte chemoattractant protein-1, and elevated levels of interleukin-4 and transforming growth factor-β indicating the inhibition of alcohol-induced inflammation. Furthermore, ZAV treatment increased expression levels of autophagy-associated proteins in ALD mice by western blot, which participated in anti-ALD effect of ZAV. These findings demonstrate that ZAV could be an alternative for ALD intervention by regulating oxidative stress and autophagy. In this study, the mice model of ALD was used to investigate the mechanism of ZAV against liver injury. The data provided novel insights of ZAV on the prevention of acute alcoholic liver injury.

Abstracts

Session 2. Molecular Mechanisms in Cellular Processes

sciforum-084723: Study on Mercury Exposure and Different Approaches for the Management of Mercury Toxicity

Praveen Kumar Maddheshiya [1] and Kapil Gupta [2]

Mercury (Hg) is a highly toxic heavy metal that causes significant risks to human health and the environment. This study explores the sources and routes of mercury exposure to humans, its toxicological effects, and the various methods of phytoremediation and bioremediation to mitigate (Reduce) mercury contamination in the environment. Mercury exposure to humans primarily occurs through the consumption of contaminated seafood, the inhalation of mercury vapour, and occupational exposure, which can lead to adverse health effects, including neurological disorders, cardiovascular issues, and developmental defects. Furthermore, mercury contamination in the environment can persist and bioaccumulate in the food chain, further exacerbating the risks to human health. Phytoremediation, a sustainable and cost-effective method, involves the use of plants to extract, stabilize, or transform mercury in contaminated soils or water. Various plant species have demonstrated the ability to accumulate and detoxify mercury through mechanisms such as phytochelation and rhizofiltration. Additionally, the genetic engineering of plants can be achieved to enhance mercury uptake, and accumulation is also a promising method used for efficient phytoremediation. Bioremediation, on the other hand, involves the use of microorganisms, such as bacteria and fungi, to remediate mercury-contaminated sites. These microorganisms can reduce mercury to less toxic forms (e.g., elemental mercury to less soluble mercuric ions) or form complexes that immobilize mercury. Apart from microbes and plants, seaweed or seaweed-derived products can be seen as an efficient alternative for the bioaccumulation of mercury. Bioremediation techniques are being continuously developed and optimized to enhance their efficiency and applicability.

sciforum-084847: β-Amyrin and Metformin, Alone and in Combination, Protect NRK-52E Cell Lines from High Glucose-Induced Nephrotoxicity by Attenuating Oxidative Stress, Apoptosis, Endoplasmic Reticulum Stress, and Inflammation

Tamsheel Fatima Roohi [1] and K. L. Krishna [2]

[1] Ph.D. Research Scholar, Department of Pharmacology, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Mysore, Karnataka 570015, India
[2] Associate Professor and HOD, Department of Pharmacology, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Mysore, Karnataka 570015, India

Introduction

Diabetes, a global health issue, can cause diabetic nephropathy in one third of its sufferers. Recently, β-amyrin, a natural pentacyclic triterpene, has garnered interest for its potential to combat diabetes and treat chronic kidney disease resulting from the condition. In this study, we investigate the antihyperglycemic and renoprotective effects of β-amyrin, both individually and in combination with metformin, through the use of NRK-52E cell lines.

Methods

We conducted an investigation into the impact of β-amyrin and metformin, both separately and in combination, on NRK-52E cell lines under normoglycemic and hyperglycemic conditions. High glucose-cotreated NRK-52E cells were exposed to these compounds, and their effects were evaluated through several parameters, including cell viability assessed using the cell counting kit-8 assay, apoptosis via flow cytometry, reactive oxygen species (ROS) levels using H2DCFDA expression, and gene expression studies via RT-qPCR to examine endoplasmic reticulum (ER) stress, apoptotic markers, and inflammatory markers.

Results

Under normoglycemic conditions, the test compounds did not exhibit a significant impact on the cell lines. However, in the presence of high glucose, β-amyrin, metformin, and their combination demonstrated a noteworthy improvement in cell viability, with the combined treatment yielding superior results compared to individual treatments. The flow cytometry analysis revealed a substantial reduction in apoptotic cells, particularly with the combination treatment (p 0.05). Moreover, the test compounds effectively inhibited high glucose-induced ROS production, with the combination treatment displaying the most significant reduction. Gene expression studies demonstrated a downregulation of ER stress, apoptotic markers, and inflammatory markers, with the combination treatment consistently yielding the greatest reductions.

Conclusions

β-amyrin and metformin exhibit renoprotective effects in high glucose-induced renal cells, suggesting a promising therapeutic approach for mitigating hyperglycemia's adverse effects on renal function. Further research in diabetic patients is needed to validate these findings.

sciforum-087179: Amperometric Determination of Serotonin Exocytosis in Human Platelets with BDD-on-Quartz MEA Devices

Rosalía González-Brito [1], Pablo Montenegro [1], Alicia Méndez [1], Ramtin E. Shabgahi [2], Alberto Pasquarelli [2] and Ricardo Borges [1]

[1] Pharmacology Unit, Medical School, Universidad de La Laguna, La Laguna, Spain
[2] Institute of Electron Devices and Circuits, Ulm University, Ulm, Germany

Introduction

Amperometry is arguably the most widely used technique for studying the exocytosis of biological amines, allowing the study of the dynamics and kinetics of this cellular mechanism in real time. In recent decades, multielectrode array (MEA) devices have been developed and increase the efficiency and speed of amperometric measurements.

Platelets are the most accessible cells to study the exocytosis of amines as they have90% of blood serotonin included in their granules, which is avidly uptaken from the blood and released by exocytosis. Furthermore, platelets are not able to synthesize this amine.

Methods

We have optimized boron-doped diamond (BDD) MEA systems that allow the detection of amperometric recordings from the quantum release of serotonin from human platelets. With this technique, exocytotic release phenomena are recorded as a succession of discrete signals in the form of peaks that result from electric current intensities measured during the oxidation of the released serotonin.

Our initial results were carried out with 16 microelectrode devices on silicone matrices (BDD-on-silicon MEA) [1]. In this conference, we present transparent MEA devices with 16 microelectrodes that allow microscopy observation too: BDD-on-quartz MEA.

Results

BDD-on-quartz MEA devices exhibit the same excellent electrochemical properties as BDD-on-silicon MEA [1]: We present a comparative study of quantum and kinetics data obtained with both MEA chips from unloaded platelets and after loading the platelets with 10 μM serotonin for 2 h. And finally, we show examples of the different types of peaks detected.

Conclusions

We demonstrate the effectiveness of BDD-on-quartz MEA devices foramperometrical studies of serotonin exocytosis from human platelets.

Reference

1. González Brito, R.; Montenegro, P.; Méndez, A.; Carabelli, V.; Tomagra, G.; Shabgahi, R.E.; Pasquarelli, A.; Borges, R. Multielectrode Arrays as a Means to Study Exocytosis in Human Platelets. *Biosensors* **2023**, *13*, 86. https://doi.org/10.3390/bios13010086.

sciforum-089285: Analysis of the Interaction of Autoantibodies in the Blood Serum of Patients with Thyroid Diseases and Monoclonal Antibodies with Recombinant Thyroglobulin Proteins

Alexander Zubkov, Ludmila Butova, Anastasia Kornouhova and Oxana Svitich

Mechnikov Research Institute of Vaccine & Sera, Maly Kazenny Pereulok, 5a, 105064 Moscow, Russia

Thyroglobulin is a marker of relapse of differentiated thyroid cancer. Currently, several B-cell epitopes have been identified in the composition of thyroglobulin using peptides containing individual antigenic determinants of TG. However, the immunopathogenetic role of these epitopes remains not entirely clear, and its study is promising for further research. Currently, the 3-dimensional structure of TG is unknown, but at the same time, the 3-dimensional structure of acetylcholinester (AChE) is known, on the basis of which it is possible to construct a mathematical model of the C-terminal region of TG, homologous to AChE. It has been shown that autoantibodies to the epitopes of TG M4-814, TgP15, 2376-2464, TgP26, and TgP41 are detected in 80%, 0%, 10%, and 7% of patients with Hashimoto's thyroiditis; in 50%, 22%, 100%, 29%, and 34% of patients with Graves' disease; and practically absent in healthy donors (Gentile F. et al.). Therefore, from the described TG epitopes, we selected five epitopes related to the C-terminal AChE, a similar region of TG, and recombinant proteins were constructed. From a collection of monoclonal antibodies to TG obtained in the laboratory, 10 mAbs interacted with recombinant AChE immobilized on the surface of the wells of polystyrene plates. Only blood sera from patients with diffuse toxic goiter and autoimmune thyroiditis with minimal levels of antibodies to TG (more than 500 IU/mL) reacted with AchE. Conclusions: in models of a fragment of the TG molecule homologous to AChE, the AG-AT bond sites remain the most probable.

sciforum-089186: Anticancer Effects of the Potential BET Inhibitor CBL0137 on Breast Cancer Cells

Valeriia Popova [1,2], Varvara Maksimova [1], Evgeniya Lylova [1], Anzhelika Bukina [1,2,3], Marianna Yakubovskaya [1,2] and Kirill Kirsanov [1,2]

[1] N.N. Blokhin National Medical Research Center of Oncology
[2] RUDN University, Moscow, Russia
[3] MIREA—Russian Technological University, Moscow, Russia

Breast cancer (BC) is a complex disease driven by a combination of genetic mutations and epigenetic modifications. In particular, the overexpression of BET family proteins (BETs) has emerged as a key epigenetic aberration contributing to BC pathogenesis. CBL0137 (CBL), a small-molecule compound, has shown promise as an inhibitor of BETs in HeLa TI cells. In this study, we aimed to assess the anticancer effects of CBL in vitro and evaluate its impact on the expression of BETs in BC cells.

Cells of three subtypes of BC (MCF7, MDA-MB-231, SKBR3) were used in this study. Cytotoxic effects were analyzed using the MTT assay. Effects on cell cycle and apoptosis were assessed using FACS with PI and FITC-Annexin staining. The level of BETs (BRD2, BRD3, BRD4) was determined by Western blotting.

CBL demonstrated a significant reduction in BC cell viability with an IC50 value of approximately 1 μM for all cell lines after 72 h of exposure and 20 μM after 24 h. CBL treatment resulted in an increase in cells in the G2/M phase in MCF7 and SKBR3 cells after 24 h and 72 h of action, as well as in MDA-MB-231 cells after 24 h. In MCF7 cells, the influence of CBL led to apoptotic changes characterized by a slight elevation in the early apoptotic population. Treatment of MDA-MB-231 cells with CBL resulted in a decrease in the expression of BRD2, BRD3, and BRD4 proteins, while treatment of MCF7 cells led to a reduction in BRD3 and BRD4 protein levels. No significant changes in the amount of BET proteins were observed in SKBR3 cells.

In conclusion, the presented data offer valuable insights into the mechanisms of action of CBL, providing a basis for further investigation into its therapeutic potential in BC treatment. This research was funded by the RSF (no. 21-75-10163).

sciforum-088236: Caspase Gene Expression in Colon Cancer Cells Exposed to 5-Fluorouracil Treatment

Jelena Pavić [1], Marko Živanović [1], Irena Tanasković [2], Katarina Virijević [1], Tamara Mladenović [1] and Nenad Filipović [3,4]

[1] Department of Natural Sciences, Institute of Information Technologies, University of Kragujevac, Jovana Cvijića bb, 34000 Kragujevac, Serbia
[2] Department of Histology and Embryology, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovića 69, 34000 Kragujevac, Serbia
[3] Bioengineering Research and Development Center (BioIRC), Prvoslava Stojanovica 6, 34000 Kragujevac, Serbia
[4] Faculty of Engineering, University of Kragujevac, Sestre Janjić 6, 34000 Kragujevac, Serbia

Colorectal cancer is the third most common type of cancer and remains a significant global health challenge. The treatment of patients depends on the stage at which the cancer is diagnosed, but it is mostly based on chemotherapy. Regarding this, novel treatment strategies are essential for improving existing ones. This study examines the relationship between chemotherapeutic doses and the expression of caspase genes—specifically, caspases 3, 8, and 9—in colon cancer cell lines. Our study involves the application of various concentrations of 5-fluorouracil to clarify the potential upregulation of these apoptotic markers in treated cells. RNA was isolated from cells, and a qPCR analysis was performed. The results showed a heterogenous dose-dependent modulation of caspase expression, pointing out the potential mechanisms underlying cellular responses to treatment. Our findings indicate that both apoptotic pathways are activated upon the addition of the chemotherapy drug, as evidenced by the significant upregulation of both initiator and executioner caspases. This effect is most noticeable at larger dosages of 5-fluorouracil as the response of the cells to the chemotherapeutic drug, and this is in accordance with the previous literature review. This research not only advances our understanding of the molecular dynamics within colon cancer cells but also contributes to better therapy responses.

sciforum-087225: Cellular and Metabolomic Studies in Triple-Negative Breast Cancer Cells: Assessing Genistein's Potential as a Chemosensitizing Agent

Alina Uifalean [1], Adrian Bogdan Țigu [2], Radu-Cristian Moldovan [3], Ioana-Ecaterina Pralea [3], Maria Iacobescu [3] and Cristina-Adela Iuga [3,4]

[1] Department of Pharmaceutical Analysis, Faculty of Pharmacy, "Iuliu Haţieganu" University of Medicine and Pharmacy, Louis Pasteur Street 6, 400349 Cluj-Napoca, Romania
[2] MEDFUTURE Research Center for Advanced Medicine, Department of Translational Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Louis Pasteur Street 4–6, 400349 Cluj-Napoca, Romania
[3] MEDFUTURE Research Center for Advanced Medicine, Department of Proteomics and Metabolomics, "Iuliu Haţieganu" University of Medicine and Pharmacy, Louis Pasteur Street 4–6, 400349 Cluj-Napoca, Romania
[4] Department of Pharmaceutical Analysis, Faculty of Pharmacy, "Iuliu Haţieganu" University of Medicine and Pharmacy, Louis Pasteur Street 6, 400349 Cluj-Napoca, Romania

Triple-negative breast cancer (TNBC) is a distinct subtype characterized by the absence of estrogen, progesterone, and human epidermal growth factor receptor-2 expression. Representing 15–20% of newly diagnosed breast cancer cases, TNBC carries a 40% mortality rate within the first 5 years post diagnosis. This underscores the urgency in enhancing TNBC chemoresistance, one trustworthy option being the use of natural compounds as chemosensitizers. The main objective of this study was to improve the sensitivity of TNBC cells to docetaxel by combining it with cytotoxic natural compounds and to elucidate the precise molecular mechanisms of action using a cellular and metabolomic approach. In pursuit of this, we conducted cytotoxicity profiling for docetaxel, genistein, leontopodic acid, and kaempferol individually and in dual combinations on a panel of TNBC cell lines (HS578T, MDA-MB-231, MDA-MB-462), using the MTT assay. The results indicated that the genistein–docetaxel combination exhibited the most potent cytotoxic effects across all cell lines. For this combination, we investigated the biochemical mechanisms involved using a gas chromatography–mass spectrometry (GC-MS) metabolomics approach. The analysis identified 69 intracellular metabolites, with 17 quantified relative to internal standards. These metabolites belong to different chemical classes, including phosphorylated amino acids, carbohydrates, fatty acids, or nucleotides, and are key intermediates in different metabolic pathways. Quantitative enrichment analysis revealed distinct pathway alterations for each cell line, encompassing beta-alanine metabolism, nicotinamide and nicotinate metabolism, purine and pyrimidine base metabolism, as well as lysine degradation and biotin metabolism. In conclusion, the combination of genistein and docetaxel demonstrates a potent chemosensitizing effect in TNBC cells, inducing cytotoxicity through diverse metabolic pathways. This underscores the considerable potential of this combination in addressing the TNBC subtype.

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sciforum-089247: Clinical Relevance of S100B in Post-Concussion Symptoms and Functional Outcomes in Mild Traumatic Brain Injury

Sriprajna Mayur Kanchan [1], Usha Adiga [2] and Ananthan R. [3]

[1] Central Research Laboratory, K. S. Hegde Medical Academy, NIITTE (Deemed to be University), Mangalore, India
[2] Biochemistry, K. S. Hegde Medical Academy, NITTE (Deemed to be University), Mangalore, India
[3] Professor and Head, Justice K. S. Hegde Medical Hospital, NITTE (Deemed to be University), Mangalore, India

Background

Mild TBI (mTBI) often presents with a cluster of cognitive, physical, and emotional symptoms commonly referred to as post-concussion syndrome (PCS). As these symptoms are self-settling, they are often underestimated and left underreported, resulting in unexpected psychological disturbances in the long term. The present study aims to estimate the numerical value of biochemical marker S100B in identifying PCS symptoms and discriminating between good and bad outcomes three months later.

Methodology

The study subjects ranged between 18 and 72 years. On admission, serum concentrations of S100B were estimated by ELISA. The Rivermead Post-Concussion Symptoms Questionnaire (RPQ) estimated PCS symptoms on admission. The Rivermead Head Injury Follow-Up Questionnaire (RHFUQ) was used to assess the disability and recovery three months later. Correlation of S100B was analysed with every aspect of RPQ, and GOSE scores. All the statistical analyses were carried out using GraphPad Prism 9.1 and OriginPro 2024.

Results

S100B positively correlated with fatigue (r = 0.41, p = 0.08) and depression (r = 0.33, p = 0.04) symptoms in RPQ. The biomarkers exhibited significant differences in concentration concerning the presence/absence of PCS symptoms like headache, dizziness, and fatigue (Mann–Whitney p = 0.001, 0.04, 0.02) and clinical presentations like vomiting and seizures (Mann–Whitney p = 0.02, 0.01). S100B correlates with GOS-E outcome scores but not with RHFUQ scores during the 3-month follow-up.

Conclusions

The present study showed that S100B can detect PCS initially; however, its outcome prediction ability in terms of RHFUQ is limited.

sciforum-084898: Enhanced Efficacy of Homeophotodynamic Therapy of Rhobdomyosarcoma Cancer Cells by Using Chemo-Drug as an Adjuvant Agent

Afifa Tanveer and Abdul Rehman Khan

The University of Azad Jammu and Kashmir, Muzaffarabad, Pakistan

After cardiovascular diseases, the leading cause of death all around the world is cancer. Rhobdomyosarcoma (RMS) is the cancer of soft tissues and it mostly occurs in children and in adults aged between 10 and 25 years. There are several therapeutic modalities that are being used for treating cancer such as surgery, radiation therapy and chemotherapy. But due to their side effects, these therapeutic modalities are not so effective. Photodynamic therapy (PDT) is a new treatment modality introduced for cancer treatment. Low doses of photosensitizer (PS) and light are used in PDT. In this work, combinations of the homeo-drug *Hydrastis canadensis* (mother tincture, H30C and H200C) and the chemo-drugs Methotrexate (MTX), Doxorubicin (DOX) and Duticine (DTIC) along with PDT were studied by using an RD cell line. The results obtained were compared with individual therapy and the most effective therapeutic combination was selected. It was found that individual administration of PDT, chemo-therapeutic drugs and Hydrastis was not effective because less killing (about 10–15%) occurred as a result of individual therapy. Conversely, combination of chemo- and homeo-drug with PDT gave efficient results. The most suitable combination that showed effective killing (about 50% cells viable) of RD cells was the combination of MTX with Hydrastis, potency H200C, along with PDT. It was concluded that the combination therapy is more effective and targeted in treating cancer than mono-therapy.

sciforum-087122: Exploring the Role of N-WASP in Breast Cancer Metastasis through Mass Spectrometry and Potential Signalling Pathway Analysis

Yannan Rhiannon Yu, Wenguo Jiang and Tracey Martin

Cardiff China Medical Research Collaborative CCMRC, Division of Cancer and Genetics, Henry Wellcome Building, Cardiff School of Medicine, Cardiff University, Heath Park, Cardiff CF14 4XN, UK

Background

Neural Wiskott–Aldrich Syndrome Protein (N-WASP) is a key regulator of the actin cytoskeleton and is implicated in various cellular processes, including cell motility and invasion. In cancer biology, the role of N-WASP in cell motility and metastasis is of particular interest, yet its specific functions in breast cancer remain to be fully understood.

Method

To investigate the impact of N-WASP on breast cancer cell behaviour, we employed siRNA to knock down N-WASP expression in the MDA-MB-231 breast cancer cell line. After the knockdown, proteomic changes in the cells were analysed using mass spectrometry. Notable alterations in the genes present in both total and phosphorylated proteins were further analysed.

Results

The proteomic data analysis ranked 50 genes that exhibited the most up-regulation and down-regulation in total and phosphorylated proteins. These 200 genes were further examined using the REACTOME database to identify affected signalling pathways. Knockdown of N-WASP led to significant changes in the RHOD, RHOF, and RHOG GTPase cycles ($p = 0.015$, $p = 0.01$, and $p = 0.027$), pathways closely associated with cell motility and actin cytoskeleton organisation. These cycles are crucial in modulating cellular dynamics, impacting a range of processes from immune response to neuronal development, wound healing, and, particularly, cancer metastasis. Furthermore, the findings highlighted the role of non-integrin membrane–ECM interactions in cell motility and cytoskeleton dynamics ($p = 0.021$). The altered protein expression patterns suggest a link between N-WASP, non-integrin membrane–ECM interactions, and the cytoskeletal changes essential for cell migration and invasion—key factors in cancer metastasis.

Conclusions

Our findings reinforce the critical role of N-WASP in regulating the cytoskeleton and influencing cell motility, invasion, and metastasis in breast cancer. This study not only provides deeper insights into the molecular mechanism of breast cancer progression but also highlights N-WASP as a potential therapeutic target for intervention strategies in breast cancer treatment.

sciforum-084199: Exposure Assessment of Essential and Potentially Toxic Metals in Human Consuming Wheat-Based Sweets: Multivariate Analysis and Risk Evaluation Studies

Mudassar Sanaullah

University of Education, Township, Lahore, Pakistan

In recent years, increasing concern has emerged regarding the presence of unexpected contaminants, such as metals, in commonly consumed food items, posing potential threats to human well-being. Evaluating contaminant levels is crucial to ensuring the safe consumption of these items, as global efforts to control food contamination have intensified due to associated health risks. This study collected and analyzed a hundred sweet samples using flame atomic absorption spectrometry (FAAS) and inductively coupled plasma–optical emission spectrometry (ICP-OES) to investigate the distribution, correlation, and multivariate analysis of 13 metals (Mg, Ca, Mn, Fe, Co, Cu, Zn, Al, Cr, Ni, As, Cd, and Pb). The accuracy of the metal analysis was confirmed by assessing baking chocolate (SRM 2384). Metal concentrations were utilized to calculate the average daily intake (ADI), target hazard quotients (THQs), hazard indices (HIs), carcinogenic risk (CR), and cumulative carcinogenic risk (CCR). Results indicated that most sweet samples exceeded WHO/FAO-permitted levels for Mn, Co, Pb, Cr, and Cd. The estimated daily intake (EDI) of Ca (7.47×10^{-2}) and Cr (2.05×10^{-3}) ranked highest among essential and potentially toxic elements, respectively. Although THQ values were below the threshold (1), several sweets exhibited HI values surpassing the threshold (>1), posing significant health hazards. Alarming CCR values in the range of 10^{-4} were observed in many sweet samples, emphasizing the potential long-term health risks associated with their consumption. This study underscores the importance of monitoring essential and potentially toxic elements in wheat-based sweets and raises awareness about the associated health risks. These findings are critical for informing food safety regulations and promoting public health.

sciforum-087886: Harmony in Complexity: Navigating the Symphony of Biomolecular Interactions and Networks

Ujban M. D. Hussain Hussain [1], Samiksha Sandeep Tammewar [2], Hrushikesh Ramkrushn Ghotkar [1] and Sameer Ramesh Lode [1]

[1] Department of Pharmaceutical Sciences, The Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, India
[2] Priyadarshini J. L. College of Pharmacy, Nagpur, India

Embark on a journey into the captivating world of Biomolecular Interactions and Networks with this innovative review, where science meets artistry. Our exploration transcends traditional boundaries, weaving together the rhythmic dance of protein–protein interactions, the dynamic melodies of signaling pathways, and the harmonious integration of omics data.

Introduction

In this entrancing introduction, we cast a spotlight on the grand stage where biomolecular interactions unfold, emphasizing their role as the orchestrators of cellular symphonies. We invite readers to join us on this vibrant expedition, celebrating the intricacies that shape life at the molecular level.

Methods

Our methodological voyage is nothing short of groundbreaking. Imagine peering into the secret conversations of proteins through avant-garde techniques like yeast two-hybrid screens and mass spectrometry, unveiling a kaleidoscope of connections. Visualize the heartbeat of cells captured in real-time with cutting-edge live-cell imaging, and witness the integration of omics data as we decipher the code of cellular communication through computational masterpieces.

Results

The stage is set, and the results are a breathtaking fusion of science and art. Recent revelations paint a vivid canvas of protein–protein interactions, each stroke revealing a new chapter in the biomolecular narrative. Live-cell imaging adds dynamic hues to our understanding of signaling pathways, while the integration of omics data unfolds intricate networks reminiscent of a cosmic tapestry.

Conclusions

As the curtains fall, we arrive at a crescendo of knowledge. This review not only encapsulates the current state of Biomolecular Interactions and Networks but also propels us into the future of collaborative discovery. Join us in decoding the symphony of life, where the language of cells becomes a universal melody with transformative potential for both scientific understanding and targeted therapeutic innovations.

sciforum-089293: HIF-1α as a Potential Target for Pharmacologic Correction after Prenatal Hypoxia

Olena Gennadiivna Aliyeva [1], Igor Fedorovich Belenichev [2] and Olena Olexandrivna Popazova [2]

[1] Zaporizhzhia State Medical and Pharmaceutical University, Zaporizhzhia, Ukraine
[2] Zaporizhzhia State Medical and Pharmaceutical University, Zaporizhzhia, Ukraine

Chronic prenatal hypoxia (CPH) is one of the most common causes of neonatal mortality and postnatal disorders of the nervous system and the mental development of infants. The search for new methods to treat the effects of CPH is a high-priority problem of modern pharmacology. HIF-1α in hypoxic conditions activates mechanisms of endogenous neuroprotection and can be used as a target for pharmacological correction.

Aim of the work: To study the possibilities of the HIF-1α-modulating effects of different pharmacological agents in the model of CPH.

CPH was modeled by administering sodium nitrite (50 mg/kg) to pregnant female white rats from day 16 of gestation. The offspring were treated with the following drugs: piracetam, thiotriazoline, nikomex, tamoxifen, cerebrocurin, angiolin, glutoredoxin, l-arginine, and HSF-1 during the first 30 days of life. The concentration of HIF-1α in the plasma and brain homogenate of rats at 30 and 60 days of life was determined using the enzyme-linked immunosorbent assay.

It was found that CPH leads to a decrease in the concentration of HIF-1α in the nervous tissue of the brain and blood plasma. Drug administration results in a significant increase in the content of HIF-1α in the studied objects immediately at the end of treatment with continued positive effects on the 60th day of life. The maximum effect was demonstrated on day 30 by cerebrocurin, angiolin, and HSF1, and on day 60 by cerebrocurin, angiolin, and thiatriazolin.

Our research provides evidence that the medications being tested are an effective way to modulate HIF-1α and may be a new alternative for the treatment and prevention of nervous system disorders in children caused by CPH.

sciforum-087185: Impact of poly(ADP-ribose) Polymerase (PARP) and Immune Checkpoint Inhibitor Combinations on the Viability of Triple-Negative Breast Cancer Cells

Tusha Sharma and Kumaraswamy Naidu Chitrala

Department of Engineering Technology, University of Houston, Sugar Land, TX 77479, USA

Background

Breast cancer is one of the most common cancer types and the second most frequent one among women in the United States. Race plays a key role in the prevalence and prognosis of breast cancer, specifically in triple-negative breast cancer, with African American women being highly prevalent compared to white women.

Material and Methods

MDA-MB-453 and 231 cell lines were cultured in RPMI-1640 media with 10%FBS. Upon 70–80% confluency, cells were treated with doxorubicin (2 μM for MDA-MB-453 and 1 μM for MDA-MB-231). After 24 h, sensitized cells were treated with inhibitors (Olaparib, O; Niraparib, N; Atezolizumab, A; durvalumab, D; and Pembrolizumab, P) alone as well as with different combinations at a concentration of 100 μM. The drug combinations include: O + N, O + A, O + D, O + P, N + A, N + D, N + P, D + A, A + P, and P + D. Statistical analysis was performed between the treatment groups using the one-way ANOVA.

Results

Our results showed that MDA-MB-453 cells treated with the combinations O + N, O + A, O + D, N + A, N + D, N + P, and A + P showed a significant change in viability compared to the doxorubicin-treated group. Results showed that MDA-MB-231 cells, treated with the combinations O + N, O + D, N + A, N + D, N + P, A + P, and D + A, showed a significant change in viability compared to the doxorubicin-treated group.

Conclusions

These findings indicate that the inclusion of these inhibitors, along with the chemotherapeutic drug, not only significantly affects the cell viability of breast cancer cells but also may be helpful in the better therapeutic regime and patient prognosis.

sciforum-089318: Insights into the Toxicity and Molecular Mechanisms of Aflatoxin B1 and Ochratoxin A in Herbal Products

María Carpena [1], A. Perez-Vazquez [1], P. Barciela [1], K. Noras [2], J. Trafiałek [3], M. Trząskowska [3] and M. A. Prieto [1]

[1] Universidade de Vigo, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecoloxía e Alimentación (IAA)—CITEXVI, 36310 Vigo, España
[2] Department of Biometry, Institute of Agriculture, Warsaw University of Life Sciences–SGGW, Nowoursynowska 159 St., 02-776 Warsaw, Poland
[3] Department of Food Gastronomy and Food Hygiene, Institute of Human Nutrition Sciences, Warsaw University of Life Sciences–SGGW, Nowoursynowska 159 St., 02-776 Warsaw, Poland

The European Rapid Alert System for Food and Feed (RASFF) has shown 1133 notifications for spices and herbs in the last 10 years (2013–2023). The analysis of these notifications indicated that 58.7% (665) of the alerts corresponded to chemical hazards. Mycotoxins corresponding to aflatoxin B1 (90) and ochratoxin A (39) were found in 19.4% of the samples. Due to the presence of these biological hazards in foodstuffs, comprehensive knowledge of their molecular mechanisms of action is required as part of the risk assessment strategy. Aflatoxin B1 (AFB1) is a known potent carcinogen that has been linked to liver cancer in humans and animals. Its toxic effects consist of forming DNA adducts, causing mutations, and interfering with cellular processes. On the other hand, ochratoxin A (OTA) is known to be nephrotoxic, hepatotoxic, carcinogenic, and immunosuppressive in both humans and animals. OTA targets the kidneys and liver, exerting its toxic effects similarly to AFB1, i.e., through DNA damage, oxidative stress, and interference with cellular processes. This communication reviews the molecular mechanism of action underlying the toxicity of AFB1 and OTA found in herbs and spices in Europe, focusing on their biosynthesis, toxicodynamics, interaction with cellular components, and the resulting biochemical pathways leading to adverse health effects. Moreover, it discusses potential strategies for mitigating their presence in herbal products, emphasizing the importance of hazard characterization for effective risk management and regulation.

sciforum-087177: Integrating Articular Cartilage Histopathology with CTX-II and COMP as Synovial Fluid Biomarkers for a Comprehensive Analysis in Osteoarthritis Evaluation

Sofija Semenistaja [1], Lība Sokolovska [2], Pēteris Studers [3,4], Anda Kadiša [5,6], Valērija Groma [7] and Sandra Skuja [8]

[1] Ph.D. Student, Resident Doctor in Rheumatology, Rīga Stradiņš University, Riga, Latvia
[2] Ph.D. Student, Scientific Assistant, Institute of Microbiology and Virology, Rīga Stradiņš University, Riga, Latvia
[3] Associate Professor, Lead Researcher, Joint Laboratory of Traumatology and Orthopaedics, Rīga Stradiņš University, Riga, Latvia
[4] MD, Department of Orthopaedics, Hospital of Traumatology and Orthopaedics, Riga, Latvia
[5] Ph.D., Lead Researcher, Institute of Microbiology and Virology, Rīga Stradiņš University, Riga, Latvia
[6] MD, Department of Internal Diseases, Rīga East University Hospital, Riga, Latvia
[7] Professor, Dr. med. habil, Institute of Anatomy and Anthropology, Rīga Stradiņš University, Riga, Latvia
[8] Ph.D., Asst.Prof., Lead Researcher, Institute of Anatomy and Anthropology, Rīga Stradiņš University, Riga, Latvia

Introduction

Osteoarthritis (OA) is the most common form of chronic joint disease characterized by the loss of cartilage as the primary site of the lesion. Both collagenous and non-collagenous proteins of the extracellular matrix (ECM) are dysregulated by the cellular component damage. Alterations in cartilage composition may manifest through variations in synovial fluid concentrations of C-terminal cross-linked telopeptides of type II collagen (CTX-II) and cartilage oligomeric matrix protein (COMP). This study seeks to decode histological alterations in the cartilage and establish a symbiotic relationship with concentrations of specific ECM proteins within the synovial fluid as potential OA biomarkers.

Methods

Twenty-five surgically obtained cartilage tissue samples were stained with toluidine blue and analysed using the OARSI grading system under a light microscope both quantitatively and semi-quantitatively. The presence of CTX-II and COMP proteins was measured in the synovial fluid samples using ELISA. The SPSS 28.0 program was used for statistical data analysis.

Results

The OARSI score median value was 4.0 (3.0;4.5), attributable to the delamination of the superficial cartilage zone. A greater number of single cells in comparison with cellular clusters was found: 60.00 (45.00;84.00) and 26.00 (22.00;48.00), respectively. Proteoglycan staining was 1.00 (1.00;2.00), attributable to low intensity. A negative correlation between ECM oedema and proteoglycan staining was found ($r = -0.445$; $p = 0.043$). The mean levels of CTX-II and COMP in synovial fluid were 1092 pg/mL (SD 537.95) and 1262 ng/mL (SD 339.47), respectively. There was a positive correlation between CTX-II and OA severity ($r = 0.305$; $p = 0.041$); the COMP and OA severity correlation was negative ($r = -0.286$; $p = 0.049$).

Conclusions

The identified positive correlation between OA severity and CTX-II levels in synovial fluid suggests that CTX-II may hold promise as a valuable biomarker for tracking OA progression. This implication opens up possibilities for early detection and targeted interventions in the management of the disease.

sciforum-086409: Investigating the Role of Yoga in Alleviating Chromosomal Translocations in Chandigarh Police Security Guards

Khushboo Arya [1,2], N. K. Manjunath [3], Akshay Anand [4] and Sheetal Sharma [5]

[1] Yoga & Life Sciences, SVYASA Deemed to be University, Bengaluru, India
[2] Department of Experimental Medicine and Biotechnology, PGIMER, Chandigarh, India
[3] Director, Anveshna, SVYASA Deemed to be University, Bengaluru, India
[4] Neuroscience Research Lab, Department of Neurology, PGIMER, Chandigarh, India
[5] Department of Experimental Medicine and Biotechnology, PGIMER, Chandigarh, India

Stress is commonly known to induce various responses associated with psycho-somatic diseases, both on the general physical level and on a subtler molecular level. A growing interest has been seen in the use of yoga therapy to cope with stress. Though several control trials have shown a positive effect of yoga on stress, the extent to which adjuvant therapies like yoga may or may not have an effect on stress on the molecular level in the human body, as well as the mechanism involved in their potential efficacy, require further exploration.

Aim

To investigate the role of yoga in alleviating chromosomal translocations in security guards.

Methodology

The subjects' stress levels were evaluated using molecular parameters and Cohen's Perceived Stress Scale, followed by an assessment of chromosomal translocations for t(14;18) and t(11;14) and an assessment of the DNA damage response and DNA repair through immunofluorescence and gene expression analysis.

Results and Conclusions

Yoga decreases cortisol levels among practitioners. It may also affect the DNA damage response and DNA repair.

Conflict of Interest: No conflicts of interest.

Need for this Study: This study may provide explanatory and exploratory ground for scientists in this field and help clinicians better understand the benefits of yoga as an adjunctive therapy for chronic diseases. This study may also provide research-based guidance for policy-makers internationally.

sciforum-089229: Obtaining a Stable Anti-Tumor Phenotype of THP-1 Cells for Cancer Treatment

Polina Vishnyakova [1,2], Viktoriia Kiseleva [3], Elena Gantsova [2], Victoria Karyagina [1,2], Alexander Artyuhov [2,4], Erdem Dashinimaev [2,4], Irina Khan [2,5], Vadim Pokrovsky [2,5,6], Irina Arutyunyan [2,7], Andrey Elchaninov [2,7] and Timur Fatkhudinov [2,7]

1 National Medical Research Center for Obstetrics, Gynecology and Perinatology Named after Academician V.I. Kulakov of Ministry of Healthcare of Russian Federation
2 Research Institute of Molecular and Cellular Medicine, Peoples' Friendship University of Russia, Moscow, Russia
3 Ederal State Budgetary Institution "National Medical Research Center for Obstetrics, Gynecology and Perinatology Named after Academician V.I. Kulakov"
4 Center for Precision Genome Editing and Genetic Technologies for Biomedicine, Pirogov Russian National Research Medical University, Moscow, Russia
5 N.N. Blokhin National Medical Research Center of Oncology, Ministry of Health of Russia, 115478 Moscow, Russia
6 Sirius University of Science and Technology
7 Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery"

Introduction

Macrophages are cells of the innate immune system responsible for phagocytosis and antigen presentation. According to the modern concept of binary polarization, pro- (M1) and anti-inflammatory macrophages (M2) are distinguished. It is believed that M2 macrophages, by inhibiting the T-cell anti-tumor immune response and participating in tumor angiogenesis, can lead to tumor progression. On the other hand, M1 macrophages exert an anti-tumor effect through their participation in antibody-dependent cell-mediated cytotoxicity. The goal of this work was to develop a new method of cellular anti-tumor therapy based on M1 macrophages.

Methods

After analysis of M1 in vitro polarization transcriptomic data, the *BIN1, Ido1, Asic1, Sosc3, Socs1, Irf4, Irf5* genes were selected for knockout. To form a stable pro-inflammatory phenotype, genetic modification of THP-1 cells based on the CRISPR/Cas system was carried out using lentiviral transduction. After transduction, infected THP-1 cells were sorted and their anti-tumor activity was tested in vivo and in vitro using various methods.

Results

Evaluation of knockout cells by real-time PCR showed a significant decrease in the expression level of the Asic1 gene. The use of infected knockout cells in a mouse model of breast cancer showed a decrease in tumor growth relative to control at one time point. Evaluation of Ki67 using immunohistochemistry analysis showed a significant decrease in Ki67+ cells in tumors treated with THP1 knockout cells. When analyzing surface markers of macrophages using flow cytometry in the group treated with knockout cells, we revealed a significant increase in marker CD45, monocyte marker CD11b, macrophage marker CD68 and the pro-inflammatory macrophage marker CD86.

Conclusions

The results obtained indicate the successful genetic modification of THP-1 to obtain a pro-inflammatory phenotype, and also suggest the effectiveness of M1-based cell therapy for tumor diseases.

This work was supported by a grant from the Russian Science Foundation [grant number 22-15-00241].

sciforum-088925: Plumbagin Alleviates Intracerebroventricular-Quinolinic Acid Induced Depression-like Behaviour and Memory Deficits in Wistar Rats

Princee Verma [1] and Kartikey Rastogi [2]

[1] Rakshpal Bahadur Management Institute (RBMI), Near ITBP, Bukhara Turn, Buduan Road, Bareilly 243001, Uttar Pradesh, India
[2] Division of Biological Standardization, Indian Council of Agricultural Research, Indian Veterinary Research Institute, Ministry of Agriculture & Farmers Welfare, Government of India, Bareilly 243122, Uttar Pradesh, India

Plumbagin, a hydroxy-1,4-naphthoquinone, has anti-inflammatory and antioxidant properties that provide neuroprotection. The current investigation intended to determine the impact of plumbagin on behavioural and cognitive impairments in male Wistar rats caused by intrahippocampal quinolinic acid (QA) administration utilizing stereotaxic apparatus, and additionally to elucidate the underlying mechanisms. QA i.c.v. (300 nM/4 μL in Normal saline) was injected into the hippocampus. When QA was administered, subjects showed signs of depression (forced swim test, tail suspension test), anxiety (open field test, elevated plus maze), and anhedonia (sucrose preference test). Additionally, in the hippocampal region of QA-treated rats compared to normal control, oxido-nitrosative stress (increased nitrite content, lipid peroxidation, with reduction of GSH), inflammation (increased IL-1β), cholinergic dysfunction, and mitochondrial complex (I, II, and IV) dysfunction were noted. Ten and twenty mg/kg of plumbagin; Rats given QA for 21 days showed a significant improvement in their behavioural and memory deficits when treated with plumbagin (10 and 20 mg/kg; p.o.). In addition, the hippocampal MDA and nitrite levels were lowered and the GSH level was raised following plumbagin administration. Moreover, plumbagin therapy was reported to improve mitochondrial impairment and QA-induced cholinergic dysfunction (AChE). To sum up, our findings indicated that plumbagin has the potential to function as a neuroprotective medication that could be an effective means to treat chronic neurobehavioral abnormalities caused due to neurodegeneration.

sciforum-089005: Purine Stretches are Avoided by Cancer Mutations

Aleksandr V. Vikhorev [1], Ivan Savelev [2], Oksana Polesskaya [2], Michael Myakishev-Rempel [1], Alexandre A. Vetcher [3] and Max Myakishev-Rempel [2]

[1] DNA Resonance Research Foundation, San Diego, CA, USA
[2] DNA Resonance Research Foundation, San Diego, CA, USA
[3] Deputy Director of IBCTNT at RUDN

Purine stretches, sequences of adenine (A) and guanine (G) in DNA, play critical roles in binding regulatory protein factors and influence gene expression by affecting DNA folding. Both purines can exist in the enol-amine form (often referred to as the imidazole form) and keto-imine forms. The enol-amine form is more stable and biologically significant than the keto-imine form. This enhanced stability is attributed to the fully conjugated ring system in the enol-amine form, which adheres to Hückel's rule and becomes aromatic. The presence of a delocalized pi-electron cloud within this fully conjugated ring system results in an aromatic molecule. In contrast, the keto-imine form lacks full conjugation in its ring system due to a broken double bond between the nitrogen and carbon atoms, rendering it non-aromatic. This study investigates the relationship between purine stretches and cancer development, which makes mechanistic sense considering the aromaticity of purines in the purine stretches flanking each mutation. A pronounced avoidance of typical cancer mutations of long purine stretches in typical types of cancer was observed in the public data of patients in intergenic regions, suggesting the role of intergenic sequences in chromatin reorganization and gene regulation. A statistically significant shortening of purine stretches in cancerous tumors (p-value 0.0001) was found. The insights into the aromatic nature of purines and their stacking energies explain the role of purine stretches in DNA structure, contributing to their role in cancer progression. This research lays the groundwork for understanding the nature of purine stretches, emphasizing their importance in gene regulation and chromatin restructuring, and offers potential avenues for novel cancer therapies and insights into cancer etiology.

sciforum-089279: Simulation on the Interaction between FITC Functionalized Gold Nanoparticles and Lipid Bilayers

Maria Mernea [1], Sorina Voicu [2], Cristina Ionela Voinea [2] and Miruna Silvia Stan [3,4]

[1] University of Bucharest
[2] Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Bucharest, 050095 Bucharest, Romania
[3] Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Bucharest, Bucharest, Romania
[4] Research Institute of the University of Bucharest—ICUB, University of Bucharest, 050657 Bucharest, Romania

Introduction

The interaction of nanoparticles with the cell membranes is an important determinant of their physiological effect. Such interactions were proven, mostly by experimental work, to depend on the size, charge and surface properties of nanoparticles. Simulations can bring atomic-level details on the mechanism of these interactions. Therefore, we used simulations to understand the interaction between a fluorescein isothiocyanate (FITC) functionalized gold nanoparticle (FITC-Au-NP) and a lipid bilayer.

Methods

A gold nanoparticle (10 nm) functionalized with glycine-cysteamine spacers was built using CHARMM-GUI Nanomaterial Modeler. On the spacers we additionally linked 71 FITC residues that were parameterized with CHARMM-GUI Ligand Reader & Modeler. The nanoparticle was included in a simulation system comprising a 20×20 nm^2 POPC (1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine) lipid bilayer. The distance between the nanoparticle and the bilayer was 1 nm. Steered molecular dynamics (SMD) with constant velocity was used to pull the nanoparticle through the lipid bilayer. The resulting trajectories were analyzed.

Results

The interaction energy between the FITC-Au-NP and the lipid bilayers was evaluated, showing a favorable total interaction energy that increased as the nanoparticle entered into the bilayer. The van der Waals interactions had a substantial contribution to the total interaction energy. Although smaller in value, electrostatic interactions were also attractive.

Conclusions

We modeled a FITC-Au-NP and simulated its interaction with a POPC lipid bilayer, highlighting the importance of van der Waals forces for the favorable contacts. Additional experimental and simulation work will bring more details on this interaction.

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sciforum-089213: The Development of an Early Diagnostic Method for Alzheimer's Disease

Yulia Konstantinovna Styufliaeva [1,2], Aleksandr Anatolievich Rubel [2], Andrew Andreevich Zelinsky [2] and Oksana Andreevna Malikova [2]

[1] ITMO University, 197101 St. Petersburg, Russia
[2] Laboratory of Amyloid Biology, St. Petersburg State University, 199034 St. Petersburg, Russia

Alzheimer's disease (AD) is the most common form of dementia, characterized by neuronal degeneration and death. The appearance of aggregated forms of the Aβ42 peptide is a key biochemical marker indicating the possible initiation of the pathological cascade in Alzheimer's disease.

The goal of this study is to develop an approach for the early diagnosis of AD by detecting Aβ42 multimers in the blood and lymph.

We adapted the Protein Misfolding Cyclic Amplification (PMCA) method for the detection of Aβ42 aggregates in blood samples. One of the main challenges in using the PMCA method for detecting Aβ42 aggregates is that the synthesized or recombinant Aβ42 peptide spontaneously aggregates with high yield. Therefore, it is difficult to distinguish spontaneous aggregation from aggregation induced by externally added aggregated Aβ42, e.g., from the patient's samples.

Previously, using a yeast model, we identified mutations in human Aβ42 that reduce its aggregation propensity. In this study, we isolated and purified the wild-type Aβ42 and five recombinant Aβ42 variants with mutations that decrease Aβ42 aggregation via metal-affinity chromatography. We investigated the aggregation kinetics of these Aβ42 variants in the presence of thioflavin T using fluorometry. Currently, we are studying the aggregation kinetics of different Aβ42 variants in the presence of aggregated wild-type Aβ42.

We believe that our findings will help develop an effective system for detecting multimeric forms of the Aβ peptide in the blood at extremely low levels to be used as a biomarker for diagnosing AD before the onset of any clinical symptoms.

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sciforum-084969: The Extracellular Signal-Mediated Activation of IRE1 Promotes TH17 Responses

Dandan Wu [1], Xing Zhang [1], Kourtney Zimmerly [1], Ruoning Wang [1], Amanda Livingston [1], Takao Iwawaki [2], Ashok Kumar [3], Xiang Wu [4], Matthew Campen [1], Michael Mandell [1], Meilian Liu [1] and Xuexian Yang [1]

[1] University of New Mexico
[2] Kanazawa Medical University
[3] University of Houston
[4] Central South University

Introduction

Heightened unfolded protein responses (UPRs) are associated with many TH17-driven inflammatory diseases. However, how UPRs participate in the deregulation of TH17 cells remains elusive.

Objective

We investigated the role of the UPR sensor IRE1 in TH17 cell function and the underlying mechanism.

Methods

Whether and how extracellular stimuli lead to IRE1 phosphorylation was explored by using flow cytometry, Western blot, confocal microscopy, in vitro phosphorylation, and co-immunoprecipitation. T cell-specific *Ern1* (encoding IRE1)-deficient cells were used to examine the effects of IRE1 on TH17 responses.

Results

The UPR sensor IRE1 is highly expressed in TH17 cells relative to naïve $CD4^+$ T cells. Signals of cytokines (e.g., IL-23 and IL-6) and co-stimulation induce the IRE1-XBP1s axis. Among those, IL-23 activates IRE1 in a JAK2-dependent manner. This noncanonical activation of the IRE1-XBP1s pathway promotes UPRs and cytokine secretion by both human and mouse TH17 cells. *Ern1* (encoding IRE1) deficiency decreases the expression of ER stress factors and impairs the differentiation and cytokine secretion of TH17 cells.

Conclusions

Our data indicate that IRE1, noncanonically activated by cytokine signals, promotes the secretory function of TH17 cells. These findings provide a novel insight into the fundamental understanding of UPRs in TH17-mediated diseases.

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sciforum-086770: The Role of Glutathione in the Symplast and Apoplast in the PVY^{NTN} Interplay with a Potato Host with Different Resistance Levels to the Virus

Katarzyna Otulak-Kozieł, Edmund Kozieł and Piotr Rusin

Department of Botany, Institute of Biology, Faculty of Biology and Biotechnology, Warsaw University of Life Sciences—SGGW, Nowoursynowska Street 159, 02-776 Warsaw, Poland

Glutathione could be a crucial cell molecule during plant–pathogen interplay response via its role in the direct control level of ROS. The proper regulation of ROS creates a line between susceptibility (with high damage to cell components) and host resistance in some plant–pathogen interactions. Therefore, we analyzed the role of glutathione forms (GSH/GSSG), as well as their cellular localization, in compatible and incompatible (HR reaction) potato cultivars infected with *Potato virus Y*^{NTN} (PVY^{NTN}) during interaction in the symplast and apoplast with the use of microscopic and HPLC methods. Only the resistant potato plants characterized systemically increased glutathione production in both cell compartments, accompanied by a significant reduction in virus level. The susceptible potato plants were only able to induce glutathione at an early stage of infection; after that, glutathione levels were depleted, and virus concentration highly increased. This fact directly indicates that proper glutathione synthesis and concertation in the symplast and apoplast plays a role not only as anti-ROS protection but also as an antiviral factor in the infection of PVY^{NTN}. Whereas the apoplastic overpresence of GSSG and reduction in glutathione that occurred in the symplast are clear pro-viral factors for PVY^{NTN}. Therefore, supporting plant supplementation with glutathione could be a factor that changes/stimulates more resistance reactions to PVY^{NTN} infection.

sciforum-089233: The Role of SIRT1 Gene Polymorphism and Its Expression in Breast Carcinoma

Desy Thayyil Menambath [1], Usha S Adiga [1], Sachidananda Adiga [2] and Vijith Shetty [3]

[1] Department of Biochemistry, K. S. Hegde Medical Academy, NITTE(DU), Mangalore, India
[2] Department of Pharmacology, K. S. Hegde Medical Academy, NITTE(DU), Mangalore, India
[3] Department of Oncology, K. S. Hegde Medical Academy, NITTE(DU), Mangalore, India

Introduction

Breast cancer, a prevalent global health concern, involves complex molecular mechanisms. SIRT1, a key protein involved in cellular regulation, exhibits altered expression in breast cancer. Its intricate mechanism includes influencing DNA repair, apoptosis, and cell survival pathways, contributing to breast cancer development and progression.

Objectives

We aimed to compare SIRT1 expression, assess variant patterns, and explore the association of SIRT1 polymorphisms with their expression and clinical staging of breast cancer.

Methodology

This cross-sectional study enrolled 172 breast cancer patients and 78 age-matched healthy females. Breast cancer patients were further divided into three groups based on their hormone receptor status: 76 hormone-positive patients (ER + ve, PR + ve), 20 triple-negative breast cancer (TNBC), and 76 HER + ve cases. Blood samples were collected for DNA isolation and serum analysis. RFLP/Sequencing determined mutations, and ELISA quantified serum Sirtuin 1 levels. Ethical approval was obtained before conducting the study.

Results

Significantly elevated serum Sirtuin 1 levels were found in breast cancer patients compared to healthy females ($p = 0.0027$). Subgroup analyses revealed notable increases in HER-positive ($p = 0.0001$), hormone-positive ($p = 0.0001$), and TNBC groups ($p = 0.0094$) compared to the control group. However, no significant variations were noted across different breast cancer stages. The SIRT1 variant rs141528984 exhibited a significant association with breast cancer ($p = 0.0001$). The association of SIRT1 variants with clinical staging and breast cancer types did not show significant differences. Also, SIRT1 levels did not significantly vary with tumor grade, lymph node involvement, or metastasis. The proliferation marker Ki67 demonstrated a significant association ($p = 0.0428$) with the specific SIRT1 variants rs777323664, rs757804740, and rs1842828683. The association between SIRT1 gene polymorphisms and Sirtuin 1 levels did not show any significant difference either.

Conclusions

This study suggests that elevated Sirtuin-1 levels may serve as potential markers for breast carcinoma. The intricate relationships between SIRT1 expression, polymorphisms, and clinical staging warrant further investigation for comprehensive insights into breast cancer.

sciforum-088499: Therapeutic Strategies for Chromium-Induced Neurotoxicity: Exploiting NPTX2 and Autophagy Pathways in CNS Cells

Sanjesh Kumar and Mansi Singh

Ph.D. Research Scholar, Institute of Pharmaceutical Research, GLA University, Mathura, India

Introduction

Chromium is the most prevalent metal present on earth in two valence states: hexavalent [Cr(VI)] and trivalent [Cr(III)]. Hexavalent chromium [Cr(VI)] is widely recognized as a teratogen, mutagen, and neurotoxin to humans. Chromium-induced autophagy is a novel avenue which involves a plethora of cellular and molecular intricacies, including the identification of the novel NPTX2 (neuronal pentraxin 2) as a critical mediator of chromium-induced autophagy dysregulation in CNS cells. NPTX2 has a broad expression pattern in the brain, with a principal role in synaptic plasticity and neuronal survival.

Material and Methods

This review compiles the most recent research on the molecular processes of chromium-induced autophagy, with a particular emphasis on NPTX2 as a mediator in the cells of the CNS. Research on NPTX2 expression patterns in different brain areas and its role in autophagy dysregulation in response to chromium exposure was compiled. In addition, we looked at the signaling pathways and processes that were involved in the dysregulation of autophagy caused by chromium, such as the inhibition of mTOR, the activation of ULK1, and the interaction of NPTX2 with Beclin-1.

Results

Abnormal autophagosome synthesis, lysosomal dysfunction, and improper autophagic substrate degradation are symptoms of disturbed autophagy, which is caused by an increase in NPTX2 expression in response to chromium exposure. The inhibition of mTOR, activation of ULK1, and interaction between NPTX2 and Beclin-1 are all components of the intricate signaling pathways that contribute to autophagy dysregulation. Furthermore, non-traditional pathways like peroxiphagy are involved; in this process, chromium-induced oxidative stress harms peroxisomes, which are then selectively engulfed by autophagosomes through PINK1/Parkin signaling, reducing cellular damage.

Conclusions

Targeting peroxiphagy and pharmacological interventions which restore autophagic flux offer the potential to reduce chromium-induced neurotoxicity.

sciforum-087273: Towards Skin Longevity: The Development of a Novel Plant-Based Combination with a Potent Stimulation of Collagen I Synthesis In Vitro

Viktor Filatov and Elizaveta Patronova

Science Center, SkyLab AG, 1066 Lausanne, Switzerland

Human skin is constantly exposed to various endogenous and exogenous factors, including UV radiation and vitamin deficiency, which can influence the earlier appearance of visible wrinkles and decrease skin firmness and elasticity. This process is related to decreased collagen I synthesis in the dermis. However, the use of retinol derivatives, synthetic molecules, and growth factors is associated with significant adverse effects, low bioavailability, and instability in dermatological products. Thus, our research was focused on the investigation of a novel plant-based combination for the stimulation of collagen I synthesis in deep skin layers and the prevention of accelerated skin ageing. Aloe barbadensis leaf extract, trimethylglycine, and panthenol were chosen as potential candidates using in silico modelling. A Way2Drug tool predicted anti-inflammatory, anti-psoriatic, and antioxidant activities beneficial for the prophylaxis of skin ageing. An in vitro study was conducted to determine collagen I synthesis in skin fibroblasts in the presence of single substances and their composition using a colorimetric analysis. It was revealed that the combination of Aloe barbadensis leaf extract, trimethylglycine, and panthenol in a specific mass ratio of 2:4:1 and at a concentration of 0.5% significantly increased the amount of collagen I in the skin fibroblasts by up to +18% within 24 h (p 0.001). This effect was comparable to that of TGF-β1 (10 ng/mL), with a 37% collagen I increase (p 0.001). The single compounds and the combination of Aloe barbadensis leaf extract and trimethylglycine showed a negative effect on collagen I synthesis, with an unpredictable decrease in this protein in fibroblasts. The combination of the compounds made it possible to achieve a synergistic effect, boosting the natural rejuvenation process in fibroblasts. Overall, the results indicate that the developed plant-based composition in the specific mass ratio and concentration given above could increase collagen I synthesis and can be considered a promising substance for dermatological products with reverse anti-ageing effects.

sciforum-088265: Tumor Budding—A Histomorphological Representation of Epithelial–Mesenchymal Transition Mechanism in Metastasis of Oral Squamous Cell Carcinoma

Sowmya S. V.

Department of Oral & Maxillofacial Pathology & Oral Microbiology, Faculty of Dental Sciences, MS Ramaiah University of Applied Sciences, Bangalore 560054, India

Background

Over 90% of oral cancer deaths are due to metastases, facilitated by a mechanism, epithelial–mesenchymal transition (EMT), that demonstrates a mesenchyme-like phenotype of epithelial cells. Prompt metastasis prediction would navigatesurgeons in avoiding unwanted or aggressive treatment for low- and high-risk patients. Recently, the use of image processing is gaining popularity.

Aim

To assess the metastatic risk of Oral Squamous Cell Carcinoma (OSCC) by the quantification of tumor buds and epithelial–mesenchymal transition biomarker expression using MATLAB software

Objectives

- To evaluate pan CK-stained tumor buds and the expression of epithelial–mesenchymal transition biomarkers, E-Cadherin, β-Catenin, MMP-2 and MMP-9, using immunohistochemistry;
- To quantify and correlate tumor buds and the protein expression of EMT biomarkers using MATLAB software.

Methodology

Pan CK-stained tumor buds and E-Cadherin, β-Catenin, MMP-2, and MMP-9 expression were evaluated immunohistochemically on 40 archival tissue samples of OSCC (20 metastatic and non-metastatic groups). Photomicrographs of immunostained OSCC cases were captured and subjected to texture and color segmentation using image processing in MATLAB software.

Statistical Analysis

Statistical analysis using Statistical Package for the Social Sciences (SPSS) software was carried out for the mean scores.

Results

Metastatic OSCC showed a statistically significantly high number of tumor buds (90%). There was a significant decrease in the proportion and intensity of positive cells in E-Cadherin and β-Catenin (p = 0.00) and an increase in MMP2 and MMP9 protein expression in metastatic OSCC (p = 0.00).

Conclusions

This study is the first of its kind wherein image processing using texture and color segmentation in MATLAB has been used effectively to quantify the phenotypic protein expression of immunostained OSCC tumor buds and EMT markers. The correlation of tumor buds with EMT expression supports the mechanism of EMT responsible for OSCC metastasis, thereby facilitating surgeons in arriving at a definitive treatment plan.

sciforum-089177: Understanding Ciguatoxin-Induced CNS Depression and Evaluating Piperine as a Therapeutic Strategy

Vishesh Kumar Maurya

Ph.D. Research Scholar, Department of Pharmaceutical Science, Nims Institute of Pharmacy

Introduction

Ciguatoxin (CTX) is a potent marine toxin known for its detrimental effects on the Central Nervous System (CNS), inducing symptoms of depression and neurological dysfunction. The nervous system's synapses' threshold for opening voltage-gated sodium channels reduces by ciguatoxin. Piperine, a bioactive compound found in black pepper, has shown promise as a potential treatment for CTX-induced CNS depression due to its neuroprotective properties.

Methods

This review comprehensively examines studies investigating the effects of CTX on CNS depression and the potential therapeutic role of piperine. Various cell models, including Mus musculus cells (N2A), Zalophus californianus tissues and many others have been utilized to elucidate the mechanisms underlying CTX-induced CNS depression. Studies employing proteomic techniques such as 2D DIGE, MALDI-TOF/TOF, LC-MS/MS, and nanoLC-MS/MS have provided insights into dysregulated proteins, pathways, and cellular responses associated with CTX toxicity. Additionally, investigation into the therapeutic effects of bioactive compound such as piperine has been conducted for marine toxins.

Results

Studies have revealed that CTX exerts its CNS depressant effects through dysregulation of calcium homeostasis, membrane depolarization, and disruption of neurotransmitter pathways. Furthermore, CTX-induced toxicity is associated with dysregulated proteins involved in neurodegenerative pathways, apoptosis, and excitotoxicity. Piperine has been shown to mitigate CTX-induced CNS depression by modulating oxidative stress, inflammation, and neurotransmitter imbalances. Mechanistically, piperine's neuroprotective effects involve activation of NRF2 pathways, inhibition of apoptotic signaling, and modulation of neuronal excitability.

Conclusions

The findings from this review underscore the potential of piperine as a therapeutic agent for mitigating CTX-induced CNS depression. More large-scale studies and clinical trials are required for subsequent research to demonstrate piperine's effectiveness and safety as a treatment for CTX intoxication. Understanding the intricate mechanisms underlying CTX-induced CNS depression and the therapeutic effects of piperine could pave the way for novel interventions in managing ciguatera fish poisoning.

sciforum-088545: Understanding Limbic-Predominant Age-Related TDP-43 Encephalopathy (LATE): The Intersection of Pathology and Immune Dysregulation

Mansi Singh and Sanjesh Kumar

Research Scholar, Institute of Pharmaceutical Research, GLA University, Mathura, India

Introduction

In the present state, a novel amnesic and AD-like dementia pathology emerges in the ageing brains, namely Limbic-predominant age-related TDP-43 encephalopathy (LATE). The disease is represented by aberrant splitting, clumping, phosphorylation, and massive accumulations of TDP-43 within the cytoplasm of cells involving neurons and glia. The abnormal regulation of TDP-43 is responsible for the mediated alteration of signaling events, such as deprived synaptic transmission, progressive neuronal degeneration, and motor deviations. Therefore, TDP-43 is a central player for LATE-associated CNS pathologies.

Material and Methods

Autopsy studies have revealed the characteristic misfolding of TDP-43 proteins in aged brains, illuminating the prevalence and distribution of TDP-43 in LATE. Additionally, recent research underscores the crucial role of impaired immune cells as key players in the neurodegeneration and the pathogenesis of TDP-43 proteinopathy. The systematic analysis of TDP-43 in LATE comprised 25 research findings with sample sizes ranging from 10 to 500 individuals.

Results

The objective of this review is to provide an extensive overview of the symptoms, neuropathological signs, proteinopathy, and approaches to diagnose LATE, with a focus on the way immune cell failure plays a role in its growth.

Discussion

This work aims to help comprehend LATE better by looking at how immune dysregulation and TDP-43 proteinopathy interact with each other. This will allow for new treatments that focus on immune pathways to help manage dementia.

sciforum-085121: Chloroplast Control Mechanisms by Molecular Electronic Device

Yuriy Shapovalov [1] and Lyazzat Gumarova [2]

[1] Center of Physical and Chemical Methods of Research and Analysis Al-Farabi Kazakh National University; yu.shapovalov@mail.ru
[2] Al-Farabi Kazakh National University, Almaty, Kazakhstan

The aim of this research is to study the light phase of photosynthesis based on X-ray diffraction data from photosystems I and II (PS-I and PS-II), and the molecular structures of solar energy conversion and electron flow control systems.

Structural analysis of PS-II showed that the manganese cluster $Mn_4O_5Ca(H_2O)_4$ is an electron generator, where solar energy breaks the chemical bonds of water, which is accompanied by H_2O_2 formation. Electrochemical oxidation of H_2O_2 by Mn^{4+} ion leads to the formation of oxygen and two protons $H_2O_2 - 2e^- \rightarrow O_2{}^{\uparrow} + 2H^+ + 23.5$ kcal, while Mn^{4+} is reduced to Mn^{2+}. Mn^{4+} regeneration occurs by donating 2 electrons to PS-I to NADPH·H.

Uncontrolled generation of electrons in chloroplasts leads to the appearance of free radicals that destroy cellular structures. In this regard, chloroplasts have protective mechanisms to remove excess electrons. X-ray diffraction studies of PS-I and PS-II showed that the active centers P680 and P700 have formed photoelectrolysis systems in which chlorophyll molecules act as electrodes (cathode and anode). Electronic circuits P680 and P700 close iron-sulfur trigger clusters that control the flow of electrons. Triggers switch electron flows to reduce NADPH·H or send excess electrons to electrolyzers to oxidize water at the anode: $2H_2O \rightarrow O_2{}^{\uparrow} + 4H^+ + 4e^-$ and reduce protons at the cathode: $2H^+ + 2e^- \rightarrow {}^{\uparrow}H_2$.

Conclusions: Based on the results of X-ray diffraction studies of H_2O-plastoquinone oxidoreductase (PS-II), the mechanism of electron generation of $Mn_4O_5Ca(H_2O)_4$ is considered. Photoelectrolysis systems in the P680 PS-II and P700 PS-I structures have been identified and the principle of their operation is described. A natural molecular electronic device that controls and monitors the processes occurring in the ETC of the light phase of photosynthesis is considered.

Abstracts

Session 3. Biomolecular Interactions and Networks

sciforum-089189: Role of *Clitoria ternatea* (Butterfly Pea) Flower in Endometriosis and Related Pain: A Network Pharmacology-Based Investigation and Experimental Validation

Najneen Ahmed, Parisa Tamannur Rashid, Nazifa Tabassum and Basrat Jahan Deea

Department of Pharmacy, East West University, Dhaka, Bangladesh

This study explored the potential role of *Clitoria ternatea* (CT) flower in ameliorating endometrial pain (EP) through network pharmacology and experimental approaches. Phytochemicals of the *CT* flower were listed from the literature and databases, and 18 suitable actives were screened for bioavailability and drug likeness parameters using SwissADME. For these actives, 279 exclusive target genes were predicted using SwissTargetPrediction. Additionally, 939 exclusive genes for EP were acquired from the DisGenet and GeneCards databases. Ninety-one overlapping gene targets of CT and EP were listed, for which a Protein–Protein Interaction (PPI) network was constructed using STRING. The top three node proteins (SRC, ESR1, and PI3KR1) in the PPI network were identified through Cytoscape. Molecular docking analysis of the eighteen actives with the three target proteins showed strong binding interactions of Flavylium, kaempherol, and quercetin with all the targets, suggesting their involvement in EP relief. In addition, Gene Ontology (GO) functions analysis revealed 320 biological processes, 59 cellular components, and 107 molecular functions were enriched with the target genes. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses identified 106 KEGG pathways, including steroid hormone biosynthesis, endocrine resistance, and endometrial cancer pathways, which were significantly enriched with the target genes. The anti-inflammatory and analgesic effects of CT's methanolic extract (ME) were investigated through in vitro and in vivo assays. The ME exhibited 91.47% inhibition of heat-induced hemolysis compared to 92.87% by aspirin in the in vitro membrane stabilizing assay. The in vivo carrageenan-induced paw edema study revealed 65.28% inhibition of paw edema by ME compared to 80.38% inhibition by aceclofenac at the end of 4-h treatment. The in vivo acetic acid-induced writhing test demonstrated analgesia by ME by 75.6% inhibition of writhing compared to 77.49% by aceclofenac. These findings suggest CT flower could be a potential natural remedy for EP, warranting further investigation in future studies.

sciforum-087274: S100A8 Interaction with Amyloid β Peptide Suppresses Its Fibrillation

Ekaterina Litus, Marina Shevelyova, Alisa Vologzhannikova, Evgenia Deryusheva, Ekaterina Nemashkalova, Andrey Machulin, Aliya Nazipova, Maria Permyakova and Sergey Permyakov

Institute for Biological Instrumentation, Pushchino Scientific Center for Biological Research of the Russian Academy of Sciences, Pushchino, Russia

Introduction

S100A8 protein belongs to the EF-hand family of calcium-binding proteins and is involved in inflammatory processes, immune response, andthe pathogenesis of neurodegenerative diseases, including Alzheimer's disease (AD). According to available clinical data, the level of S100A8 is increased in the cerebrospinal fluid of AD patients. Although data in the literaturesuggest an involvement of S100A8 in the regulation of amyloid β peptide (Aβ) metabolism involved in AD progression, the possible interaction between S100A8 and Aβ remains unexplored. To this end, we aimed to studythis aspect and its relevance to Aβ fibrillation.

Methods

The parameters of interaction between recombinant human S100A8 and monomeric recombinant human Aβ40/42 were studied using bio-layer interferometry. The Aβ40 fibrillation in the absence/presence of S100A8 was monitored using a thioflavin T (ThT) fluorescence assay.

Results

Ca^{2+}-loaded S100A8 was shown to bind monomeric Aβ40/42 with equilibrium dissociation constants of 2.7 ± 1.0 μM and 2.8 ± 0.7 μM, respectively. S100A8 dramatically suppressed Aβ40 fibrillation, as evidenced by a 12–23-fold decrease in maximum ThT fluorescence intensity.

Conclusions

S100A8 interacts with Aβ40/42 monomer and inhibits Aβ40 fibrillation in vitro, thereby suggesting that S100A8 may be involved in the control of Aβ deposition in AD.

Funding: This study was supported by Russian Science Foundation grants № 20-74-10072 (`https://rscf.ru/project/20-74-10072/`) and № 19-14-00289-П (`https://rscf.ru/project/22-14-35043/`).

sciforum-086913: Structural Insights into the Role of Prosequences in Preproprotein Folding and Function

Nikita Ray and Manisha Goel

Department of Biophysics, University of Delhi South Campus

Introduction

Prosequences are stretches of amino acid translated along with protein, but are often removed from the mature protein later through excision. This is known to assist the three-dimensional folding of their cognate protein, and also prevents precocious activation and proteolytic degradation. Prosequences are also termed intramolecular chaperones, and the whole stretch of an initially translated polypeptide is termed a preproprotein. Preproproteins have so far been reported in at least 690 organisms including eukaryotes, archaea, bacteria and viruses, with most of them being present as N-terminal prosequences. The unique role of prosequences can be exploited for protein engineering but this requires a detailed understanding of the role of prosquences in cognate protein folding. In this study, we tried to explore the structural effect of prosequences on their cognate preproprotein.

Method

Structural homologs of N-terminal prosequence-containing proteins were retrieved from PDB-based similarity and coverage criteria. The RING webserver was used for predicting prosequence and protein interacting sites. The possible binding pockets were predicted using CASTp. Known ligand-binding sites were explored through Pdbsum for verifying the ligand-binding residues.

Result

More than half of the structures studied showed involvement of prosequences with the cognate protein in terms of residue interactions. Fourteen of these structures werepredicted to have various binding site pockets. Out of these, seven structures were found to have prosequence residues involved in ligand binding.

Conclusions

Our studies show that, along with interacting with the cognate protein, N-terminal prosequences also participate in the formation of the binding pockets and interactions with ligands. Binding pockets formed in the protein part are also influenced by the prosequence, indicating their possible structural role imparting functional assistance.

sciforum-089021: A Model and Genomic Evidence for Sequence-Specific Chromatin Folding

Ivan Savelev [1], Aleksandr V. Vikhorev [2], Oksana Polesskaya [1], Richard A. Miller [3], Michael Myakishev-Rempel [2], Alexandre A. Vetcher [4] and Max Myakishev-Rempel [2]

[1] DNA Resonance Research Foundation, San Diego, CA, USA
[2] DNA Resonance Research Foundation, San Diego, CA, USA
[3] OAK, Inc., Grants Pass, OR, USA
[4] Deputy Director of IBCTNT at RUDN

The current study introduces a model in which the DNA sequence influences the structure of surrounding water in the nucleoplasm, proposing a mechanism where DNA's molecular structure imprints some of itself on surrounding water clusters during a continuous dynamic chromatin reorganization process within the cell nucleus. It is known that water is an integral part of DNA structure(s). In vivo, the DNA double helix is covered with a layer of hydration, impermeable to a variety of cations, which is located around these double helices. It consists of about 18–19 water molecules per nucleotide in B-DNA and different amounts for other DNA structures. These water molecules are specifically arranged into phosphate groups and bases. Our hypothesis suggests that the spatial arrangement of DNA shapes the organization of water. Therefore, the focus is, namely, on the role of water in the structural stability and special organization of nucleic DNA. Its role in multiple molecular recognition processes, which involve nucleic DNA, is addressed. We developed molecular models of the sheath of water surrounding the double helix; based on this, they developed predictions about the sequence-specificity of chromatin folding and tested these predictions using public functional genomics data and computational genomic approaches. The results provided support for the proposed models of sequence-specific chromatin folding. These findings suggest a structural mechanism of interaction between DNA and its aqueous environment, offering an additional sequence-specific structural basis for chromatin dynamics and function.

sciforum-089218: Adiposity: A Seed of Depression

Dhivya S. [1,2], Pramod Kumar Pandey [3], Tunjin Vashisth [4], Sukanya Gangopadhyay [5], Usha Bindal [6] and Kuldip Kumar [7]

1 Assistant Professor, PGICH, Noida, India (present)
2 Senior Resident, Department of Biochemistry, VMMC & Safdarjung Hospital, New Delhi, India (past)
3 MD Biochemistry Student, Department of Biochemistry, VMMC & Safdarjung Hospital, New Delhi, India
4 MBBS Student, VMMC & Safdarjung Hospital, New Delhi, India
5 Assistant Professor, Department of Biochemistry, VMMC & Safdarjung Hospital, New Delhi, India
6 HOD, Department of Biochemistry, PGICH, Noida, India
7 HOD, Department of Psychiatry, VMMC & Safdarjung Hospital, New Delhi, India

Introduction

Depression is a very common psychological problem observed all around the world. Though various treatment modalities are available for this mental illness, further research is warranted to find novel therapeutics. Recent speculations on the role of adiponectin in animal models of depression have shown interesting results. Leptin is an adipokine that affects mood and cognition. Hence, the role of adiponectin and leptin in patients with depression needs to be probed.

Objective

To estimate serum adiponectin and leptin concentration in depressive patients and compare them with healthy controls.

Methods

This study was conducted at the Department of Biochemistry and Psychiatry, VMMC, and Safdarjung Hospital, New Delhi, following ethical clearance from our institution's Ethics Committee. Serum samples were taken from 30 severely depressive patients and 30 healthy controls subsequent to receiving written consent from the patients' relatives. The samples were checked for serum adiponectin and leptin levels via QUAEE-BIO and a DBC ELISA kit. Data were analyzed using SPSS version 21.0.

Results

Cases and controls were age- and sex-matched. Serum adiponectin levels in the depression group were significantly higher than in the controls [$Z = -2.18$, $p = 0.03$]. Serum leptin levels in the depression group were not significantly different from that of the controls [$Z = -0.47$, $p = 0.64$]. Also, there was no correlation between serum adipokine levels and the severity of depression. However, there was a significant difference in adipokine levels between sexes in the case group and in the whole study group ($p = 0.000$).

Conclusions

The higher serum adiponectin levels in the case group are in contrast with previous studies, which found lower adiponectin levels in depression. This may be due to the effect of treatment in cases of depression; further large-scale studies should be carried out to elucidate the role of adiponectin in depression. The small study size and absence of data about pretreatment serum adiponectin levels are the major limitations of this study.

sciforum-079677: Can Glucosinolates Act as Plant Elicitors? The Use of Kale (*Brassica oleracea* var. *acephala*) Green Manure for the Activation of Systemic Plant Defenses in Bell Pepper

Jorge Poveda [1], Pablo Velasco [2], María Elena Cartea [2] and Víctor M. Rodríguez [2]

[1] University of Valladolid, Valladolid, Spain
[2] CSIC

In the search for new alternatives to avoid problems associated with the use of chemical fungicides in agriculture, the use of green manure (GM) could help combat fungal diseases of crops, such as those produced by the necrotrophic pathogen *Rhizoctonia solani*. In the case of brassica tissues used as GM, this could have an elicitor capacity of systemic plant resistance related to the presence in these tissues of defense metabolites called glucosinolates (GSLs), as a form of damage-associated molecular patterns (DAMPs). Kale (*Brassica oleracea* var. *acephala*) leaves were used as GM and their GSL content was removed by autoclaving and applied to pepper plants infected with *R. solani*. Autoclaving removed part of the GSL glucobrassicin (GBS) (85%) and sinigrin (19%) content of the kale tissues. The application of intact kale tissues to roots of pepper plants produced a systemic activation of foliar defenses via the salicylic acid (SA) and ethylene (ET) pathways, significantly reducing pathogen damage. In addition, this systemic response led to the accumulation of secondary defense metabolites in leaves, such as pipecolinic acid and hydroxycoumarin or gluconic acid, among others. Therefore, GBS-rich GM kale tissues were able to activate systemic defenses in bell pepper against foliar pathogens via the SA/ET hormonal pathways, accumulating secondary defense metabolites.

sciforum-086956: Deciphering Biomolecular Networks: Integrating Methods for Comprehensive Insights

Ujban Hussain [1], Samiksha Sandeep Tammewar [2] and Aditya Wadalkar [1]

[1] Department of Pharmaceutical Sciences, The Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, India
[2] Priyadarshini J. L. College of Pharmacy, Nagpur, India

Introduction

Recent advancements in biomolecular research have significantly enhanced our comprehension of the intricate interactions and networks governing cellular processes. This abstract introduces a review focused on biomolecular interactions and networks with a particular emphasis on comparing state-of-the-art methodologies, both experimental and computational, utilized in the study of protein–protein interactions.

Methods

Cutting-edge techniques in experimental and computational biology have been pivotal in unraveling biomolecular interactions. This review synthesizes the methodologies employed in studying protein–protein interactions, encompassing advanced experimental approaches such as X-ray crystallography and NMR spectroscopy. Moreover, it explores the integration of omics data, outlining the computational strategies used to construct comprehensive biomolecular networks.

Results

Exploring protein–protein interactions has revealed intricate binding interfaces and significant conformational changes, offering crucial insights into cellular function regulation. Through the integration of various data sources, including genomics, transcriptomics, proteomics, and metabolomics, a holistic view of biomolecular networks has emerged, elucidating the interconnectedness of molecular events within cells. These findings highlight the potential for targeted drug development and therapeutic approaches, driven by a deeper understanding of these networks.

Conclusions

This review underscores the collaborative efforts of researchers in advancing biomolecular science. By comparing different methodologies, including both experimental and computational approaches, significant progress has been made in deciphering the complexities of biomolecular networks. Clarification is provided regarding the inclusion of interactions on-chip, with surface characterization tools being considered where applicable.

sciforum-089051: Dityrosine-Mediated Inhibition of α-Synuclein Fibrillation Using Photocatalytic Nanoparticles

Sonali Jena and Suman Jha

Department of Life Science, N.I.T. Rourkela, Rourkela 769008, India

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons and the abnormal accumulation of alpha-synuclein (α-syn) aggregates or Lewy bodies in the substantial nigra of the brain. Apart from this accumulation, PD is also characterized by a loss of motor function, tremor, rigidity, and postural instability. α-syn is an intrinsically disordered protein involved in vesicular trafficking and neurotransmitter release. The aggregation of α-syn involves a cascade of structural transition from a monomeric protein to the fibrillar form of protein, a complex process regulated by several intrinsic and extrinsic factors. Nanoparticles have been reported for easy drug delivery as they can easily cross the blood–brain barrier. Several reports suggest that the interface of metal oxide nanoparticles directly affects α-syn conformation and can positively inhibit amyloidogenesis. Some reports also indicated that metal ion-catalyzed oxidation (MCO) of α-syn favors the formation of dityrosine linkage, which forms soluble aggregates rather than insoluble fibrils. However, the mechanism behind the dityrosine-mediated α-syn is unclear. Therefore, in this report, our study primarily focuses on the potential use of metal nanoparticles to induce a dityrosine-mediated inhibition of α-syn fibrillation. Using a combination of some biophysical methods, we have found that ZnONP with a negative interface has more affinity for monomeric α-syn, strongly inhibits the fibrillation kinetics of α-syn in a dose-dependent manner resulting in the flocculation of the complex, which is a kinetically favorable process. α-syn interacted with ZnONPs via multi-layered adsorption and led to the formation of amorphous aggregates known as flocs instead of fibrillar structures. Interestingly, we found that oxidative stress exerted by ZnONP induced the formation of dityrosine cross-linkage in α-syn. In conclusion, this intramolecular cross-linking favors the flocculation process to form a compact yet disordered α-syn monomer instead of a structured fibril.

sciforum-088879: Draft Transcriptomic Resources for the California Native Plant *Trichostema lanatum* from the Angeles National Forest

Savanah Senn [1], Steven Carrell [2], Bruce Nash [3], Ray A. Enke [4], Karen Barnard-Kubow [4], Karu Smith [1], Daila Melendez [1,5], Mathew Kostoglou [1], John Hsieh [1], Les Vion [1], Adrianna L. Bowerman [1] and Gerald Presley [6]

[1] Los Angeles Pierce College Department of Agriculture Sciences, Plant Science Program
[2] Oregon State University, Center for Quantitative Life Sciences
[3] Cold Spring Harbor Laboratory, DNA Learning Center
[4] James Madison University, Biology Department
[5] Oregon State University, Department of Horticulture
[6] Oregon State University, Department of Wood Science and Engineering

This project established transcriptome and soil metagenomic resources *for Trichostema lanatum. T. lanatum* is a traditional Chumash medicinal plant in Lamiaceae used for rheumatism, commonly called wooly blue curls. The stunning flowers and leaves were collected from the Gold Creek Preserve, Angeles National Forest. What made these plants so resilient to abiotic and biotic stress?

In May 2022, snap-frozen plant tissue for RNA sequencing and soil for DNA sequencing were collected. The pipeline for plant RNAseq consisted of QC in SOAPnuke and MultiQC, de novo assembly in Trinity, BUSCO evaluation, quantification in salmon, and annotation with Trinotate. Metabarcoding was analyzed with DNA Subway Purple Line. Soil metagenomics were analyzed in Nephele using BioBakery, MicrobiomeDB, and STAMP.

The *Trichostema lanatum* transcriptome assembly was 91.1% complete according to BUSCO results. Plant isoforms with TPM > 10 and effective length > 1000 were chosen for a downstream analysis. Transcripts were annotated with the best Sprot BLASTX and BLASTP hits.

In the plant transcripts, there was a prevalence of functions related to primary defense mechanisms that would make the plant more resilient such as pectins, heat shock proteins, a stress response, RIPP-like disease resistance proteins, chitinase-like proteins; transcripts for anti-herbivory-related functions were also abundant, especially coumarates such as scopoletin analogs and glucoalkaloids like strictosinide. Shikimate O-hydroxycinnamoyltransferase was most closely related to *Nicotiana* (TPM = 132, length = 1816, 84.37% ID). Phenylalanine ammonia lyase (PAL) was annotated from Digitalis (TPM = 57.53, length = 2874, 91.02% similar). There was an elevated expression of Cadmium-related heavy metal resistance genes and heavy-metal-associated isoprenylated proteins.

In soil WGS results from the wooly blue curls' rootzone, TPMs were above average for flavonoid and isoflavonoid biosynthesis and stilbene and isoquinoline alkaloid biosynthesis compared to other plant rootzones in the National Forest preserve studied. Abundances were similar for tropane, piperidine, and pyridine alkaloid and indole alkaloid production, and lower for indole diterpene alkaloid biosynthetic genes, compared to the other rootzones. There were also differences in taxonomic composition; there was a higher than average proportion of reads for unclassified bacteria and unclassified *Actinomycetota* sp. These results emphasize candidate genes related to phenylpropanoid production as potential actors adding to the resilience of *Trichotestema* lanatum against oxidative abiotic and biotic stress, both above ground and below ground.

sciforum-089294: Selenium Confers Protection against Methylmercury in the Human Body: A Comprehensive Review of Biomolecular Interactions

Ana Olívia Serra Jorge [1,2], F. Chamorro [2], M. Carpena [2], J. Echave [2,3], A.G. Pereira [2], M. Beatriz P. P. Oliveira [1] and M. A. Prieto [2]

[1] LAQV@REQUIMTE, Department of Chemical Sciences, Faculdade de Farmácia, Universidade do Porto, R. Jorge Viterbo Ferreira 228, 4050-313 Porto, Portugal
[2] Universidade de Vigo, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecoloxía e Alimentación (IAA)—CITEXVI, 36310 Vigo, España
[3] Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal

Methylmercury (MeHg) contamination in seafood poses significant health risks, particularly neurotoxicity, to human populations worldwide. Selenium acts as a protector against the toxicity of metals such as mercury and inorganic arsenic [1], but at the same time, the loss of Se bioavailability caused by these pollutants must be considered. New criteria have been proposed to assess the risks of Hg exposure, namely the Se Health Benefit Value (HBVSe) and the Benefit–Risk Value (BRV), which allows for the simultaneous evaluation of Hg exposure and dietary Se intake. Additionally, changes in mercury bioaccessibility have been attributed to cooking, which changes the conformation of native proteins [2]. Various studies have shown that the benefits of consuming seafood outweigh the risks, especially when the protective effects of selenium are considered. This comprehensive review examines the biomolecular interactions underlying the protective effects of selenium against MeHg in the human body. We will discuss the mechanisms by which selenium modulates MeHg toxicity, including its role in mitigating oxidative stress, preventing MeHg bioaccumulation, and facilitating detoxification pathways. Nevertheless, further research in this area is necessary to study the synergistic effects between the different variables to improve the understanding of the repercussions of fish and shellfish intake on health. Future research directions are proposed to elucidate the protective role of selenium against methylmercury toxicity and inform public health policies and interventions. Overall, this communication contributes to our understanding of the complex interplay between selenium and methylmercury in the human body and underscores the potential of selenium as a therapeutic agent for mitigating MeHg-related health risks.

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sciforum-089323: Exploring Algal Metabolism: Insights from Metabolomics and Computational Approaches

M. Carpena [1], A. Silva [1,2], F. Chamorro [1], J. Echave [1,3], A.O.S. Jorge [1,4], M. F. Barroso [2] and M. A. Prieto [1]

[1] Universidade de Vigo, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecoloxía e Alimentación (IAA)—CITEXVI, 36310 Vigo, España
[2] REQUIMTE/LAQV, Instituto Superior de Engenharia do Porto, Instituto Politécnico do Porto, Rua Dr. António Bernardino de Almeida 431, 4200-072 Porto, Portugal
[3] Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal
[4] REQUIMTE/LAQV, Department of Chemical Sciences, Faculty of Pharmacy, University of Porto, R. Jorge Viterbo Ferreira 228, 4050-313 Porto, Portugal

Algae, despite being labeled as an underexplored biological source of chemical constituents, remain inadequately studied in terms of their metabolism. Metabolomics emerges as a high-throughput technology to investigate the full metabolic profile of samples that could aid in the understanding and characterization of algae. By delving into their primary composition, particularly for polysaccharides and phycobiliproteins, alongside secondary metabolites like polyphenols and pigments, researchers can uncover not only their rheological and nutritional properties but also their diverse biological activities. Given the growing interest in algae for food and related industries, innovative approaches should be explored to enhance the value of their functional components. In this sense, in the context of contemporary in silico studies, metabolomics should be paired with computational methodologies to develop novel techniques for studying biomolecular interactions. Molecular docking arises to predict the atomic-level interaction between a small molecule (ligands) and target proteins (proteins). This synergistic approach integrating both technologies could allow us to characterize algae profiles, evaluate their potential bioactive properties, and better understand their metabolism. This work pays attention to the metabolomic and computational strategies to be developed, which are aimed at the functional characterization of algae. By harnessing these technologies, we can unlock new possibilities for using algae in various industrial applications, paving the way for sustainable and innovative solutions in the future.

sciforum-089316: Functional Investigation of the Role of BYVMV (*begomovirus*) Proteins in Epigenetic Modulation

Jeyalakshmi Karanthamalai [1], Nagesh Srikakulam [2], Gopal Pandi [2] and Dinesh Babu Kandalu Sahadevan [2]

[1] Department of Plant Biotechnology, School of Biotechnology, Madurai Kamaraj University, Madurai, India
[2] Department of Plant Biotechnology, School of Biotechnology, Madurai Kamaraj University, Madurai, India

Bhendi, or okra (Abelmoschus esculentus, family *Malvaceae*), has numerous nutritional benefits. In India, which is its largest producer, the prevalence of *begomoviruses* causes enation leaf curl (ELCu), yellow vein mosaic (YVM) disease, or a combination of both, resulting in huge losses in cultivation. Previously, we have shown that BYVMV C2, C4, and βC1 act as suppressors of PTGS and TGS, with pronounced TGS inhibition arising from the former two proteins. The current research intends to uncover the mechanism behind the TGS hindrance induced by C4 and C2. Initially, to screen for host interactions with C2 or C4, the viral proteins were fused with His-tag, followed by agroinfiltration into *N. benthamiana* leaves in various combinations, including three negative controls. The extracted proteins were subjected to pull-down. We subsequently performed LC-MS and a meticulous data analysis which revealed a preliminary interacting partner for C2 or C4. Intriguingly, C4 was found to interact, either directly or indirectly, with potential TGS suppressors such as S-adenosyl homocysteine hydrolase (SAHH), S-adenosyl methionine synthetase (SAMS), cystathionine beta synthetase domain containing protein (CBS), nuclear importin (NbNUP50a), heterochromatin formation (NbFDM4), and chromatin remodeling (NbBRM). Initially, we selected the first three candidates and performed bioinformatics analysis by modeling the host proteins to look for their interaction potential. By confirming interactions in silico, we cloned SAHH, SAMS, and CBS from *N. benthamiana* and fused them with the Streptavidin Tag, which aided in confirming the interaction through pull-down and Co-IP. Virus-induced gene silencing (VIGS) was used to silence SAMS and CBS. Their impact on viral DNA accumulation and phenotypic differences will be discussed during the presentation.

sciforum-087189: Multilayer Immunohistochemical Analysis of Brain Tissue in Severe Traumatic Brain Injury

Chloe L.T. Kam [1], Cengiz Guner [1], Shumaila Hasan [2], Christopher E.G. Uff [2] and Ping K. Yip [1]

[1] Centre for Neuroscience, Surgery & Trauma, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London E1 2AT, UK
[2] Department of Neurosurgery, Royal London Hospital, Whitechapel, London E1 1FR, UK

Background and Aims

Severe traumatic brain injury (TBI) is a complex disease and understanding the injury-induced cellular pathobiology is vital to predicting outcome and providing effective treatment and precision healthcare. This can be achieved through studying brain tissue obtained at biopsy soon after injury from severe TBI patients, which has been proven a safe procedure. Distinguishing the various cellular markers within the biopsy tissue can provide us with a better understanding of the complex cellular interactions.

Methods

Using multilayer immunohistochemistry, 12 immunostaining markers were applied on brain tissue obtained at biopsy (n = 2). One was from a patient who recovered, one from a patient who died. The cryostat-sectioned tissue was stained with two immunostaining markers per staining procedure and imaged using a fluorescent microscope. Thereafter, the immunostaining was removed using a stripping buffer and successful removal of immunostaining was confirmed by absence of the previous immunostains. The staining and stripping process was then repeated to achieve additional 5 sets of double immunostaining.

Results

The multilayer immunohistochemistry using markers for neurones (NeuN, N52, SMI31, SMI32, MAP2, somatostatin), oligodendrocytes (CNPase), astrocytes (GFAP), microglia (Iba1, P2Y12), and vasculature (claudin5, vWF), successfully stained the same brain tissue section. Merging the immunostaining images together allows the visualisation of the complex cellular interactions, and the increase or decrease expression levels of immunostaining markers between a patient with good functional outcome and another patient with poor functional outcome.

Conclusions

Multilayer immunohistochemistry enabled the identification and simultaneous visualisation of 12 immunostaining markers on a single brain biopsy. This is the first study to conduct a cheap multilayer immunohistochemistry technique on brain biopsy from patients with severe TBI.

sciforum-089182: Production of Antibodies Binding Murine Nuclear PD-L1

Valentina Kostenko [1,2], Alina Makarova [1,2], Elena Svirshchevskaya [2], Roman Kholodenko [2], Dmitry Ryazantsev [2] and Ekaterina Ryabukhina [2]

[1] Lomonosov Moscow State University
[2] Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry RAS

PD1/PD-L1 antibody therapy is used in the clinic (atezolizumab, avelumab, durvalumab), but its effect is ambiguous, both in patients and in mouse models. The purpose of this work was to analyze the binding of commercial and laboratory-obtained monoclonal antibodies to PD-L1. Previously, we obtained monoclonal antibodies (clone B12) to the extracellular fragment PD-L1 of mouse expressed in E. Coli (exPD-L1). Primary screening of monoclonal antibodies by flow cytometry showed low B12 binding compared to commercial antibodies. Cytokine-stimulated 3D cultures, permeabilized cells, and Western blotting were used to elucidate the causes of low binding on living cells.

Permeabilization of cells B16/F10 (mouse melanoma), EL-4 (mouse lymphoma), COLO357 (human pancreatic cancer) showed binding of both mouse and human B12 PD-L1 antibodies. With the help of Western blotting, these data were confirmed. However, commercial antibodies (BioLegend, clone 10F.9G2) in this method did not bind to the mouse recombinant exPD-L1 protein, but bound to cell lysates. Cell cultivation on an anti-adhesive polyHEMA substrate led to the binding of B12 antibodies to the surface of cells under 3D cultivation conditions. Stimulation of EL-4 and B16/F10 cells in 3D cultures and subsequent incubation with Cy3-labeled B12 antibodies led to the appearance of pronounced fluorescence in the perinuclear region of cells.PDL-1.

Thus, the obtained monoclonal antibodies to mouse exPD-L1 are cross-reactive with human PD-L1 protein; PD-L1 protein translocates to the cell membrane when cultured under 3D conditions into the nucleus and, when stimulated by cytokines, its biosynthesis is activated. The difference in the binding of antibodies B12 and 10F.9G2 may mean a difference in the conformation of PD-L1 translocated to the membrane. The traffic of intracellular PD-L1 into the nucleus upon activation may mean the launch of de novo protein synthesis with an altered conformation.

sciforum-089303: Starch–Polyphenol Interactions: Impact on Food Structure and Starch Digestibility

Javier Echave [1,2], Sepidar Seyyedi-Mansour [1], Pauline Donn [1], Ana Olivia Serra Jorge [1,3], Lucia Cassani [1], Lillian Barros [2] and M. A. Prieto [1]

[1] Universidade de Vigo, Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecoloxía e Alimentación (IAA)—CITEXVI, 36310 Vigo, España
[2] Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal
[3] REQUIMTE/LAQV, Department of Chemical Sciences, Faculty of Pharmacy, University of Porto, R. Jorge Viterbo Ferreira 228, 4050-313 Porto, Portugal

Starch, conformed by amylose and amylopectin, represents the major carbohydrate macromolecule consumed globally as a major component of staple foods. Phenolic compounds are ubiquitous secondary metabolites in plants with strong antioxidant capacities and have attracted a great deal of attention in recent decades. Besides these capabilities, polyphenols are known to interact through different bonds with polysaccharides, lipids or proteins, which impact the formed complex structure and its digestibility. Due to their hydroxyl groups, it appears as if lower MW polyphenols tend to display fewer H-bonds due to their fewer hydroxyl groups and thus weaker interactions and affinity, whereas higher MW polyphenols, such as polymerized tannins and especially proanthocyanidins, display a higher number of available H-bonds and a generally higher affinity. Native starch is usually present in two main forms: V-type inclusion complexes with hydrophobic bonds or non-inclusion crystal complexes (A- or B-type) prone to H-bonds and ionic/electrostatic interactions. The formation of the complexes depends on the starch microstructure, and also depends on the amylose/amylopectin ratio, and the ratio of crystalline and amorphous structures, with polyphenols showing higher affinity towards amylose and the hydrophobic interior of helix structures in starch. At the microstructural level, starch–polyphenol complexation leads to increased porosity and denser granules. At the rheological level, this translates into the starch showing reduced viscosity and elasticity. Moreover, this greatly impairs starch's gelatinization and retrogradation during cooking, providing a final structure more akin to resistant starch, with a final reduced hardness and adhesiveness. These changes affect the digestibility of starch by amylolytic enzymes (i.e., α-amylase) and lead to lowered glucose release from it and absorption. This review aims to present a comprehensive and summarized overview of updated knowledge on this and the remaining gaps in knowledge.

sciforum-089025: The Interaction between ZnONP and Lysozymes Induces Structural Heterogeneity: A Thermodynamic-Based Approach

Monalisha Ojha and Suman Jha

Department of Life Science, National Institute of Technology (NIT), Rourkela, Odisha, India

Protein is an important biomolecule that needs to maintain 3D (three-dimensional) dynamic structure in respective physiological conditions in order for homeostasis to be maintained in an organism. This 3D structure is majorly governed by non-covalent interactions. These interactions are highly subjected to changes in the local physicochemical environments of proteins. Any changes in the environment perturb the protein 3D conformation, leading to partial unfolding, consequently rendering the protein non-functional. In recent years, various domains of biological sciences have increasingly embraced nanoparticles, primarily driven by its diverse array of physicochemical properties and applications. Protein adsorption onto nanoparticle surfaces affects the interaction that governs a 3D structure, resulting in conformational rearrangement and altered functional efficacy. The induced changes are very important to explaining the proper functioning of proteins in the presence of nanoparticles, regardless of whether if it is being used as a platform for various biological applications. In this line, lysozyme, a well-studied globular protein model, interacts with the ZnONP interface and its effect on the protein conformational rearrangement in different pH conditions using various biophysical techniques is explored. Lysozymes exhibit different conformations at varying pH levels, affecting their interaction with ZnONP. This protein conformation significantly influences the nature of interactions and ultimately impacts its thermodynamic attributes with ZnONP. Once the lysozyme interacts with the ZnONP interface, it sequesters the protein monomeric population into predominantly two populations, where the stable bulk monomeric population remains in equilibrium with relatively less thermodynamically stable monomeric lysozymes present in corona of the protein--ZnONP complex. However, changes in the conformation do not affect the secondary structure or the functional efficacy of the protein, thereby leaving the protein functional and adequately preserving its efficacy.

Abstracts

Session 4. Biomaterials Design and Characterization

sciforum-089135: Synthesis and Characterization of Advanced Hybrid Nanocomposites of Graphitic Carbon Nitride and Biogenically Synthesized Zinc Oxide for Photocatalytic and Biomedical Applications

Mr. Suneel and Qazi Inamur Rahman

Department of Chemistry, Integral University Lucknow, Uttar Pradesh 226026, India

Graphitic carbon nitride (g-C_3N_4) and zinc oxide (ZnO) are two promising materials that have been extensively studied for their potential applications in photocatalytic and biomedical fields including biosensors, bioimaging, photodynamic therapy, drug delivery, chemotherapy, and the antimicrobial segment because of its biocompatible nature. For biogenic synthesis of ZnO will be carried out using aqueous leaf extract of *Rosa indicia*. The synthesis of g-C_3N_4/ZnO nanocomposites will be achieve through hydrothermal synthesis, to produce materials with enhanced photocatalytic and biomedical properties due to development of heterojunction. Synthesized g-C_3N_4/ZnO hybrid nanostructure may have band gap around 2.85 eV to 3.01 eV. The photocatalytic activity of the composites is evaluated through the degradation of organic pollutants under simulated solar irradiation, demonstrating their potential for environmental remediation. In biomedical applications, the g-C_3N_4/ZnO nanocomposites exhibit biocompatibility and are explored for use in drug delivery systems, tissue engineering, and antimicrobial coatings. The incorporation of g-C_3N_4/ZnO nanocomposites into biomaterials enhances their mechanical, thermal, and electrical properties, making them suitable for various biomedical applications. Techniques such as X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), Fourier-transform infrared spectroscopy (FTIR), and UV-Vis spectroscopy are employed to analyze the crystal structure, surface morphology, particle size, chemical composition, and optical properties of the composites. The comprehensive characterization of these materials is crucial for their successful development and utilization in various technological domains.

sciforum-089342: COMSOL Multiphysics Computational Studies of Dielectrophoresis-Based Characterization and Separation of Tenogenically Differentiating Mesenchymal Stem Cells

Raphael Oladokun [1], Ming Pei [2] and Soumya Srivastava [1]

[1] Department of Chemical and Biomedical Engineering, West Virginia University
[2] Department of Orthopaedics, West Virginia University

Stem cells have unique self-renewal and differentiation capacities, which are advantageous for regenerative medicine and tissue engineering applications. Stem cells can recreate cells needed to repair injured tissues and organs in the body, for example, by regenerating connective tissues, which provide support, protection, and a structural framework for various organs and other tissues. However, a significant limitation is the susceptibility of tendons to injury with long-term loss of function.

Mesenchymal stem cell (MSC) therapies are promising for healing tendon injuries and tears, but generating homogeneous tenogenic stem cell populations remains challenging. A homogenous sample of tenocytes (differentiated MSCs towards the tendon lineage) is critical for further tissue repair after transplantation to avoid unnecessary tumor growth during regenerative therapies. To substantiate our hypothesis that differentiating and non-differentiating stem cells have unique dielectric properties, we focused on quantifying dielectric signatures for differentiating tenogenic and non-tenogenic MSCs on the third day of differentiation using dielectrophoresis (DEP)—an electrokinetic method that uses nonuniform fields—following a preliminary study, which focused on their crossover frequencies [1,2], the frequencies at which the net DEP forces acting on the cells are zero. Here, we further estimated that the values for membrane capacitance, conductivity, and permittivity after 3-day treatment of undifferentiated cells to yield differentiated tenogenic MSCs are 2.46 ± 0.1 pF, 0.82 ± 0.01 S/m, and 1.97 ± 0.05, respectively, and cytoplasm conductivity is 0.82 ± 0.02 S/m. The results showed a significant difference between the 3-day- and no-treatment groups (undifferentiated cells with no treatment).

The estimated properties from the dielectrophoretic characterization studies are crucial in designing a DEP-based enrichment microdevice to collect homogeneous differentiated mesenchymal stem cell populations, i.e., tenocytes for tendon repair. Using particle tracing, creeping flow (transport of diluted species model), and electric current physics in COMSOL Multiphysics simulation software, we designed a microdevice that achieves 100% separation of untreated and treated mesenchymal stem cells undergoing differentiation towards a tendon at 160 kHz.

Applying dielectrophoresis to the microdevice architecture demonstrated high selectivity and yield, processing one million treated differentiating cells in 6.4 h at 300 μm/s.

sciforum-086026: Chitosan for Food Packaging Applications: A Patent Landscape Analysis

Massimo Barbieri

Politecnico di Milano (Technology Transfer Office), Piazza Leonardo da Vinci 32, 20133 Milan, Italy

Chitosan is a biopolymer synthesized through the deacetylation of chitin, a polysaccharide that can be obtained from various renewable resources, mainly waste from marine food production.

Its excellent properties, including antimicrobial activity, non-toxicity, biocompatibility, and biodegradability, have made chitosan a successful material in food packaging technology.

The objective of this study is to provide a patent landscape of the use of chitosan in food packaging applications.

The reference database used was Espacenet (`https://worldwide.espacenet.com`), a free patent database provided by the European Patent Office (EPO).

The final patent results were obtained using both classification symbols [IPC (International Patent Classification) and CPC (Cooperative Patent Classification)] and keywords in the full text, title, abstract, and claims search fields.

A total of 2737 patent documents were obtained.

After filtering the data by the earliest priority date (2003–2023), 2556 results were retrieved.

China had the highest number of patents with 2154, followed by the USA with 261 and Europe with 173.

The International Patent System (PCT) was frequently used by applicants and ranked second with 288 patent applications.

A total of 2316 patents/patent applications were filed between 2012 and 2022.

Upon analysis of the data, it was observed that many of the applications were based on chitosan blends. The most commonly claimed biopolymer blends were starch and cellulose, while the most commonly claimed synthetic polymer blends were polylactic acid (PLA) and polyvinyl alcohol (PVA).

The data analysis indicates that the following materials were used: polyhydroxy alcohols, nanostructured additives, quaternary ammonium chitosan, TiO_2 and oxides/hydroxides of zinc as compounding ingredients, heterocyclic compounds with a six-membered ring containing one oxygen atom in the ring, and phenolic acids, mainly gallic, ferulic, and salicylic acid.

sciforum-089194: Combinatorially Self-Assembled Hetero-Oligomer for Studying Multivalent Protein-Protein Interactions

Vitalii Balobanov, Alisa Mikhaylina, Natalia Lekontseva and Albina Khairetdinova

Institute of Protein Research, Russian Academy of Sciences, Institutskaya, 4, 142290 Pushchino, Russia

Introduction

Proteins that can bind several ligands at the same time are widespread in nature. We have developed an approach to study such interactions. The proposed method is based on the attachment of several binding domains to a single oligomeric backbone thus creating proteins with a specific number of binding sites.

Methods

To obtain proteins with different numbers of binding sites, we denatured and then renatured a mixture of the Sm-like protein from *Sulfolobus acidocaldarius* (SacSm) and the same protein but with the apical domain of the GroEL protein attached (ADGroEL_SacSm). By varying the ratio of the components we can change the number of apical domains on each resulting oligomer. After producing proteins with 1 to 7 binding domains, we determined the strength and stoichiometry of their interaction with the model non-native protein lactalbumin (LA). The interaction constants were assessed quantitatively by analyzing the results of SDS gel electrophoresis of the formed complexes.

Results

The data obtained suggest that the interaction between a single apical domain (AD) and non-native proteins is relatively weak and is not well-defined by our methods. However, when several ADs are closely located on a single protein backbone, non-native proteins may interact with several domains simultaneously, and the stability of this complex increases exponentially. LA cannot interact with more than two ADs at the same time, which is manifested by the lack of change in the dissociation constant as the number of binding sites increases. At the same time, its small size allows the binding of up to 4 molecules on the complete heptameric ADGroEL_SacSm ring.

Conclusions

We have developed a workable method for studying multivalent protein-protein interactions with a range of binding sites, from 1 to 7, which is essential for understanding the complexity of these interactions in biological systems.

sciforum-089104: Advancements in Injectable Biocements: The Role of Gellan Hydrogel in Magnesium Phosphate Bone Cement

Maryia Khamenka [1], Anna Ronowska [2], Aleksandra Mielewczyk-Gryń [3], Dawid Kozień [4], Justyna Kozłowska [5] and Marcin Wekwejt [6]

[1] Scientific Club 'Materials in Medicine', Advanced Materials Center, Gdańsk University of Technology, 11/12 Gabriela Narutowicza Street, 80-233 Gdańsk, Poland
[2] Department of Laboratory Medicine, Faculty of Medicine, Medical University of Gdańsk, 3a Marii Skłodowskiej-Curie Street, 80-210 Gdańsk, Poland
[3] Department of Ceramics, Gdańsk University of Technology, 11/12 G. Narutowicza Street, 80-233 Gdańsk, Poland
[4] Department of Ceramics and Refractories, Faculty of Materials Science and Ceramics, AGH University of Krakow, 30-059 Krakow, Poland
[5] Department of Biomaterials Technology and Cosmetic Chemistry, Nicolaus Copernicus University in Toruń, 11 Gagarina Street, 87-100 Toruń, Poland
[6] Department of Biomaterials Technology, Faculty of Mechanical Engineering and Ship Technology, Gdańsk University of Technology, 11/12 Gabriela Narutowicza Street, 80-233 Gdańsk, Poland

Bone cements, as self-setting and injectable biomaterials, play a pivotal role in orthopedic and traumatological applications, serving crucial functions like bone loss restoration, implant fixation, and fracture stabilization. Recently, magnesium phosphate cements (MPC) have emerged as a noteworthy alternative to traditional calcium phosphate cements, acclaimed for their high mechanical strength, quick setting time, and optimal biodegradability. This research investigates the potential of gellan gum (GG) hydrogel as an enhancer for MPC, with a particular emphasis on improving their injectability.

The cement formulation under investigation was synthesized by combining a powder phase of magnesium oxide, potassium dihydrogen phosphate, and a cross-linking agent with a liquid phase, including a GG solution and a plasticizer, forming an injectable self-hardening paste. The properties of the resulting biocomposite cement, such as setting time and temperature, microstructure, mechanical strength, biodegradation rate, phase and chemical composition, injectability, and human osteoblast compatibility were evaluated.

The developed MPC + GG cement demonstrated an effective setting reaction at lower temperatures, reduced fragility, as well as improved injectability potential, enhancing its suitability for minimally invasive surgical procedures. Further, its high biocompatibility, appropriate porosity and adequate biodegradation rate were confirmed. Ultimately, the findings indicate the substantial applicability of this novel biocomposite cement in biomedical engineering.

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sciforum-086700: Antibacterial Properties of Dental Copolymers Modified with Monomers Possessing Quaternary Ammonium Groups

Patryk Drejka [1], Marta Chrószcz-Porębska [1], Alicja Kazek-Kęsik [2,3] and Izabela Barszczewska-Rybarek [4]

[1] Department of Physical Chemistry and Technology of Polymers, Faculty of Chemistry, Silesian University of Technology, 44-100 Gliwice, Poland
[2] Department of Inorganic Chemistry, Analytical Chemistry and Electrochemistry, Faculty of Chemistry, Silesian University of Technology, 44-100 Gliwice, Poland
[3] Biotechnology Centre, Silesian University of Technology, 44-100 Gliwice, Poland
[4] Department of Physical Chemistry and Technology of Polymers, Faculty of Chemistry, Silesian University of Technology, 44-100 Gliwice, Poland

Introduction

Bacteria such as *Streptococcus mutans* metabolize sugar consumed by humans to organic acids. These acids demineralize teeth, causing caries. In dental practice, caries is treated by the removal of infected tissue and filling the cavity with dental composite restorative material (DCRM). Modification of DCRM to achieve microbiocidal materials is widely researched in the literature, due to the neglecting antibacterial activity of commercial materials.

This research aimed to characterize antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* of common dental copolymers modified with previously synthesized monomers possessing quaternary ammonium groups (QAn + TMXDI, where n is the number of carbon atoms in the *N*-alkyl substituent: 8, 10, or 12) responsible for their antibacterial activity.

Methods

Two series of copolymers were prepared: 20 wt. % of QAn + TMXDI, 20 wt. % TEGDMA, 20 wt. % UDMA, and 40 wt. % Bis-GMA and 40 wt. % QAn + TMXDI, 20 wt. % TEGDMA, and 40 wt. % Bis-GMA. The bacterial adhesion was tested with disc-like samples, which were immersed in bacteria solution, washed with sterile water, and then, suspensions of bacteria remaining on the surface were prepared and spread on agar plates. Next, bacteria colonies were counted.

Results

Copolymers modified with 20 wt. % of QAn + TMXDI showed antibacterial activity comparable to a reference sample, except for a copolymer with QA8 + TMXDI, which showed higher activity than other copolymers. In the case of copolymers with 40 wt. %, a significant increase in antibacterial activity was observed.

Conclusions

Microbiocidal properties of modified copolymers depended on the weight content of QAn + TMXDI and the length of the *N*-alkyl chain. The higher the QAn + TMXDI content, the higher the antibacterial activity. The *N*-alkyl substituent had the opposite effect, i.e., the higher the number of carbon atoms in the chain, the lower the antibacterial activity.

sciforum-089238: Assessing the Bio-Functional Properties of TiO_2/Antibiotic Electrophoretic Deposits on Segmented Polyurethane-Coated Metallic Surfaces

Fabiola Azucena Gutiérrez [1], Rossana Faride Vargas Coronado [1], Fabiola Elizabeth Villa [2], Víctor Arana Argaez [2], Claudia Vásquez López [1], Raúl Rosales Ibañez [3], Arely M. González-González [3], Raymundo Cruz-Pérez [4] and Juan Valerio Cauich Rodríguez [1]

[1] Centro de Investigación Científica de Yucatán
[2] Universidad Autónoma de Yucatán, Pharmacology Lab
[3] Universidad Nacional Autónoma de México
[4] Departamento de Infectómica y Patogénesis Molecular, Cinvestav, Unidad Zacatenco, CDMX

The development of coatings on medical-grade metallic supports, such as Titanium and 316 L Stainless Steel, is crucial for enhancing biocompatibility, reducing degradation, and preventing infections in medical implants. In this sense, nanoparticles, ceramics, antibiotics, and synthetic and natural polymers have been included in the modification of implants. In this work, we present the development of hybrid coatings on medical-grade metallic substrates (Titanium II and 316 L Stainless Steel) modified with a thin layer of a segmented polyurethane (Tecoflex 80A$^{(c)}$). For this, Anatase TiO_2 nanoparticles (nanotubes and spheres) as well as antibiotics (gentamicin sulphate and Nisin) are deposited via electrophoretic deposition (EPD) with water used as the solvent. Characterization of the obtained surfaces was carried out by SEM, contact angle, Raman spectroscopy, infrared spectroscopy, EDX, AFM, and thermogravimetric measurements. The bio-functional properties of our samples were tested with fibroblasts and bacteria. The results demonstrate the formation of porous surfaces with embedded particles and antibiotics, both within the pores and on the surface itself. The viability assay reveals improved performance for EPD samples containing nisin and nanoparticles. Physicochemical characterization confirms the successful incorporation of antibiotics with nanoparticles. The antibacterial properties show similar inhibition for G*ram-positive* and G*ram-negative* bacteria when gentamicin and nanoparticles are deposited compared to gentamicin alone.

sciforum-086511: Bioactives of Hypericum Perforatum to Control Diabetes: In Vitro and In Vivo Biological Evaluation in Diabetic Rats

Dr. Neelam Singh

Noida Institute of Engineering and Technology 19 Knowledge Park II, Institutional Area, Greater Noida 201306, UP, India

Background

Improving diabetes mellitus treatment is a significant contemporary medical and societal issue. Plant-based botanicals may lower blood sugar, enhance insulin absorption, and block important enzymes that contribute to the onset and course of diabetes. The preventive role of Hypericin perforatum and its constituent hypericin was studied using diabetic rats and in vitro cultures.

Methods

The in vitro glucose absorption by yeast cells, alpha-amylase, and glucosidase activity were used to examine the mechanism of action of *Hypericum perforatum* (HP) extract. The extract's safety and in vivo efficacy were studied using a Streptozotocin (STZ)-induced diabetic rat model. Hematology, blood biochemistry, and plasma insulin were also assessed.

Results

The extract significantly (p 0.03) enhanced the uptake of glucose through the plasma membrane of yeast along with α-amylase (p 0.05) and α-glucosidase (0.04) inhibition activity in vitro. Meanwhile, the extract could significantly reduce renal (uric acid and creatinine), hepatic (SGOT, SGPT, and ALP), and lipid (triglycerides and cholesterol) profiles in the serum of diabetic rats. The extract was safe up to a 1000 mg/kg dosage in preclinical acute dose toxicity studies. In diabetic rats, the extract reduced pancreatic histological alterations. This study found that the extract reduced STZ-induced diabetes and oxidative stress to liver and pancreatic tissue, as well as increasing plasma insulin levels in the treated rats.

Conclusions

Our findings indicate that *Hypericum perforatum* extract demonstrated protective activity by effectively halting the sequential progression of oxidative stress, renal and hepatic function test, lipid profile test, and STZ-induced histopathological alterations in the liver and pancreas.

sciforum-088190: Biosynthesis of Gold Nanoparticles from *Amaranthus gangeticus* S. and Its Anti-Diabetic Activity on Streptozotocin Induced Rats

Akila Elias [1], Prasanna V. Habbu [2] and Sudhir Iliger [3]

[1] Department of Pharmacognosy, Al-ameen College of Pharmacy, Bangalore, Karnataka
[2] Department of Pharmacognosy, SET's College of Pharmacy, Dharwad, Karnataka
[3] Department of Pharmaceutics, SET's College of Pharmacy, Dharwad, Karnataka

Introduction

Diabetes mellitus, a metabolic disorder, elevates blood sugar levels, resulting in complications affecting various bodily systems such as nerves, eyes, kidneys, and other organs. The administration of oral antihyperglycemic medications can potentially induce adverse effects, especially when combined, leading to drug-drug interactions. To address these challenges, there's potential in introducing innovative antioxidant compounds targeted at specific organs for therapeutic action. Currently, metal nanoparticles have gained prominence in healthcare due to their exceptional biocompatibility, stability, cost-effectiveness, and environmentally friendly attributes.

Materials and Methods

In this study, green synthesis methods were employed to produce gold nanoparticles (AuNPs) using the *Amaranthus gangeticus* plant, known for its antidiabetic properties. The leaf extract of *A. gangeticus* was utilized to synthesize these green AuNPs using a 1 mM gold chloride solution. Various characterization techniques, including UV spectroscopy, FTIR analysis, X-ray diffraction analysis (XRD), transmission electron microscopy (TEM), and scanning electron microscopy (SEM), were employed to analyse the synthesized herbal-mediated AuNPs. Additionally, the in vivo antidiabetic efficacy of the produced AuNPs was evaluated.

Results

The induction of diabetes using STZ resulted in elevated levels of blood glucose, cholesterol, triglycerides, LDL, VLDL, and significant loss in body weight. However, these detrimental effects were mitigated after treating diabetic rats for 28 days, with significant improvements observed at a dosage range of 1 mg/kg of AuNPs compared to the group treated solely with the plant extract.

Conclusions

The findings suggest that the plant-mediated AuNPs demonstrate significant potential as antidiabetic agents compared to the crude extract alone.

sciforum-087215: Biosynthesis of Silver Nanoparticles Using Plant Extract and Its Antibacterial Activities

Samia Bouledroua, Ghozlene Laouabdia Selami, Ines Largueche, Abdelali Merah and Abdelghani Djahoudi

University BADJI Mokhtar, Pharmaceutical Mineral Chemistry Laboratory, Annaba, Algeria

Silver nanoparticles (Ag NPs) have drawn a lot of interest because of their antibacterial activity. However, their synthesis by chemical methods is potentially harmful; this is the reason why the use of plant extract for synthesis constitutes a simple, effective and safe alternative solution.

In this work, Ag NPs were synthesized by the precipitation method; silver nitrate was used as precursor and the extract of *Rosmarinus officinalis* was used as a reducing as well as capping agent.

They were characterized using X-ray diffraction DRX, UV-visible spectrometry and Fourier-transform infrared spectroscopy (FTIR), and they were also examined for their antimicrobial properties by using the agar diffusion method against gram-negative and gram-positive bacteria.

XRD analysis confirms the crystalline nature of the NPs, with a face-centered cubic (fcc) structure, and reveals that the average crystallite sizes of the Ag NPs are 30 nm.

The UV-visible spectrum showed absorption peaks at 220–360 which revealed the presence of functional groups (phenolics, flavonoids, tannins. . .), and FTIR analysis confirmed their existence and that these biomolecule compounds were not only responsible for the reduction but also the capping of Ag NPs.

Ag NPs exhibited antibacterial activity against both bacteria (gram-negative strain of *E. coli* BLSE, *K. pneumoniae* carb-, and gram-positive strain of *E. fecalis* ATCC292112, *S. aureus* ATCC25923) withlarge zones of inhibition, respectively (50.7 mm, 10.34 mm, 17.87 mm, 10.72 mm)

The present study showed that the extract of *Rosmarinus officinalis* can be used as reducing and capping agent to synthesize Ag NPs that present a highly bactericidal effect.

sciforum-085040: Development of pH-Sensitive Xanthan Gum-Based Hydrogel as a Vehicle for Delivering a Hydrophobic Drug

Priyanka Meena, Poonam Singh, Sudhir G. Warkar

Delhi Technological University, Delhi, India

This research focuses on the fabrication of a series of xanthan gum-based hydrogels for the efficient delivery of the hydrophobic drug. The study investigates the influence of crosslinker (MBA), biopolymer (XG), and initiator (KPS) amounts on hydrogel properties. Various characterization techniques, such as PXRD, ATR-FTIR, SEM, and TGA, were utilized to analyze the fabricated hydrogels. The sol–gel analysis revealed that a higher quantity of reagents led to a greater increase in the gel fraction of the synthesized hydrogels. Porosity measurements indicated enhanced porosity with higher biopolymer and initiator amounts, while porosity decreased with increased crosslinker concentration. The incorporation of amphiphilic polymer in the hydrogel significantly improved its properties such as gel fraction, swelling ratio, porosity, drug loading, drug entrapment and drug release percentage. Notably, under alkaline conditions (pH 7.4), the synthesized hydrogel exhibited an increased swelling ratio and drug release in the comparison to acidic conditions (pH 1.2). The drug release mechanism from the synthesized hydrogel followed a Fickian diffusion pattern, and the Korsmeyer-Peppas model was identified as the most appropriate for describing drug release kinetics in the both pH 1.2 and 7.4 buffer solution. The pH-responsive nature of the developed hydrogel highlights its potential as an effective and versatile candidate for drug delivery application.

sciforum-086425: Eco-Friendly Synthesized Silver Nanoparticle-Modified PVA/PEG Hydrogels

Katarzyna Sala [1], Magdalena Bańkosz [1], Hubert Placek [2], Julia Sztrumpf [2], Magdalena Kędzierska [3] and Bozena Tyliszczak [4,5]

[1] Cracow University of Technology, Faculty of Materials Engineering and Physics, Department of Materials Engineering
[2] Cracow University of Technology, Faculty of Materials Engineering and Physics, Department of Physics
[3] Department of Chemotherapy, Medical University of Lodz, WWCOiT Copernicus Hospital
[4] Cracow University of Technology
[5] Faculty of Materials Engineering and Physics, Department of Materials Engineering

This study introduces an advanced approach in the development of hydrogels, utilizing Polyvinyl Alcohol (PVA) and Polyethylene Glycol (PEG), integrated with eco-friendly synthesized silver nanoparticles. The synthesis of these nanoparticles was achieved using silver nitrate and yellow tea extract, a naturally reducing agent, ensuring an environmentally conscious production process. The incorporation of these silver nanoparticles into the PVA/PEG hydrogel matrix led to the creation of hydrogels with superior antibacterial properties. These enhanced properties render the hydrogels highly effective for various biomedical applications, including wound dressings and drug delivery systems. Notably, the addition of yellow tea extract not only underscores the commitment to eco-friendly synthesis but also potentially augments the bioactive characteristics of the hydrogels. This pioneering method aligns with green chemistry principles, signifying a notable advancement in sustainable hydrogel technology. The hydrogels' unique composition and characteristics open up a broad spectrum of possibilities in the biomedical field. The study not only demonstrates the practical applicability of these hydrogels in medical settings but also emphasizes the importance of sustainable practices in scientific research and material development.

The main objective of the analyses conducted was to understand the release of silver nanoparticles from the hydrogel material under different conditions, such as static and dynamic environments, and to determine the kinetics of this process. Spectrophotometric and microscopic analysis techniques were used in this research. The amounts of released nanoparticles and observations of morphological changes in the hydrogel structure were monitored. Analysis of the release kinetics provided a better understanding of the rate and manner in which nanoparticles leave the hydrogel structure under different conditions, which is essential for the optimal design of products based on these materials. This research formed an important experimental part of the work, contributing to the necessary knowledge needed for further development and practical use of silver nanoparticle hydrogel.

This research was carried out within the SMART-MAT Functional Materials Science Club of the Faculty of Materials Engineering and Physics of Cracow University of Technology as part of the 3rd edition of the program "Student research clubs create innovation" through the project titled "Transdermal systems in targeted therapy of skin cancer" financed by the Ministry of Science and Higher Education (grant no. SKN 157/568410/2023).

sciforum-089117: Novel Bio-Cement for Regenerative Medicine: Magnesium Phosphate with Polyvinyl Alcohol Enhancement

Magdalena Górecka [1], Anna Ronowska [2], Aleksandra Mielewczyk-Gryń [3], Dawid Kozień [4], Justyna Kozłowska [5] and Marcin Wekwejt [6]

[1] Scientific Circle 'Materials in Medicine, Advanced Materials Centre, Gdańsk University of Technology, Gdańsk, Poland
[2] Chair of Clinical Biochemistry, Department of Laboratory Medicine, Medical University of Gdańsk, Gdańsk, Poland
[3] Department of Ceramics, Faculty of Applied Physics and Mathematics, Gdańsk University of Technology, Gdańsk, Poland
[4] Department of Ceramics and Refractories, Faculty of Materials Science and Ceramics, AGH University of Krakow, 30-059 Krakow, Poland
[5] Department of Biomaterials and Cosmetics Chemistry, Faculty of Chemistry, Nicolaus Copernicus University, Toruń, Poland
[6] Department of Biomaterials Technology, Faculty of Mechanical Engineering and Ship Technology, Gdansk University of Technology, Gdańsk, Poland

In the medical field, bone substitutes are essential for the reconstruction of bone fractures. Injectable and self-setting bone cements like magnesium phosphate (MPC) are critical for minimally invasive orthopedic surgeries. MPC offers beneficial bioresorption, rapid setting time, and high mechanical strength, rivaling that of classic calcium phosphates. However, its paste lacks appropriate cohesion and proper injectability.

This research explores the development of biocomposite cement based on MPC with a poly(vinyl alcohol) (PVA) hydrogel additive. The aim was to enhance the cement's usability by improving injectability and providing finer control of its setting process. The ceramic cement was synthesized via the reaction of magnesium oxide with potassium dihydrogen phosphate in an aqueous medium. To explore the effects of PVA, it was introduced in varying concentrations as the liquid phase of the cement. Additionally, different levels of a crosslinking agent were utilized to establish experimental groups. The mixture of these substances formed a biocomposite paste with self-setting properties. Our analysis involved measuring setting time and setting temperature, microstructure inspection, phase and chemical composition, static strength evaluation, a qualitative assessment of injectability, and a cytocompatibility test conducted on human osteoblast cells.

Via this study, we developed a technology for biocomposite cement combining MPC with PVA hydrogel. This novel material was characterized by high biocompatibility, reduced setting temperature, enhanced compressive strength, and appropriate injectability. Finally, it exhibits considerable potential for medical applications, especially within the fields of surgical orthopedics and traumatology.

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sciforum-088996: Fabrication of Rice Starch Matrix Loaded with *Aegle marmelos* (L.) Fruit Extract to Produce Chromogenic Food Packages with Enhanced Shelf Life and Spoilage Detection

Poorna Chandrika Sabapathy [1], Xianghui Qi [2], Richa Yadav [3] and Chandra Kanta Bhusal [4]

[1] Dr. S. Poorna Chandrika, Research Associate, Department of Microbiology, AVMC & Hospital, Pondicherry, India
[2] Prof. Dr. Xianghui Qi, School of Food & Biological Engineering, Jiangsu University, Zhenjiang, China
[3] Dr. Richa Yadav, Department of Microbiology, AVMC, Pondicherry, India
[4] Dr. Chandra Kanta Bhusal, Department of Microbiology, AVMC, Pondicherry, India

Introduction

Changes in consumer preferences and the demand for safe and high-quality food products have led to innovative developments like intelligent packaging systems (IPs) or smart/active packages that directly communicate with consumers, providing information about the quality of packed food through visual change and aiding in the enhancement of freshness. Biopolymers play an important role in mitigating fossil fuel-based environmental concerns and reducing carbon footprint.

Methods

Thin biocomposites made of a rice starch matrix loaded with *Aegle marmelos* (L.) fruit extract were synthesised using the solvent casting method for the detection of freshness in dairy and seafood products through spoilage-induced pH modification. Additionally, their antimicrobial and antioxidant properties were also explored for shelf life enhancement. Material characterisation was investigated through UTM, FTIR and SEM.

Results

The results show that A. marmelos extract showed colour changes detectable both under UV and with the naked eye following pH fluctuations occurring during the spoilage of milk and prawns placed on the prepared thin sheet. SEM analysis revealed how the starch molecule absorbed the plant extract into its matrix structure, producing a neat, thin film. FTIR was also used to confirm how the plant material interacts with the starch used. UTM studies indicated that the Young's modulus of the starch film decreased, thereby contributing to better mechanical strength.

Conclusions

This investigation produced insights into a novel, completely biodegradable, flavonoid-based pH biosensor that can successfully be used in food packages for freshness detection.

sciforum-087187: Effect of the Membrane on the Pharmaceutical Availability of Insulin from Hydrogel Matrices

Aneta Ostróżka-Cieślik, Weronika Wójcik and Barbara Dolińska

Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia, Kasztanowa 3, 41-200 Sosnowiec, Poland

Introduction

Pharmaceutical availability testing is one of the quality control methods used to assess the ability of a medicinal substance to diffuse from a substrate, through a membrane, into a suitable acceptor fluid. The most commonly used membranes for this type of testing are those made of polymers (cellulose, cellophane, or nylon membranes) or natural membranes (mouse/rat/pig skin, human cadaver skin). An alternative to the above membranes is the Strat-M® membrane, designed to mimic human and animal skin. Our study aimed to compare the pharmaceutical availability of insulin from a hydrogel matrix based on Sepineo™ P600 and Sepineo™ PHD100 (Seppic, Paris, France) using a Strat-M® membrane (Merck Millipore, Burlington, VT, USA) and cellulose dialysis membrane Spectra/Por®2 (MWCO of 12–14 kDa; Spectrum Laboratories, Inc., California, United States).

Methods

Insulin hydrogels (Insulatard Penfil) based on Sepineo™ P600 and Sepineo™ PHD100 were prepared. The insulin dose was set at 1 mg/g. Pharmaceutical availability studies of insulin from hydrogel formulations were conducted in vitro in an ERWEKA DT600 paddle apparatus (Husenstamm, Germany), using Enhancer CellTM (Erweka, Husenstamm, Germany). The volume of PBS acceptor fluid was 50 mL. Testing was carried out at 32 $\pm$ 1 °C (human skin surface temperature). The stirrer speed was 100 rpm. The amount of insulin released was determined by spectrophotometry at λ = 271 nm. The Strat-M® membrane and cellulose dialysis membrane Spectra/Por® 2 were used in the study.

Results

In a pharmaceutical availability study using the Strat-M® membrane, 53.36% and 47.4% of the API were released from the Sepineo™ P600 and Sepineo™ PHD100 hydrogel after 6.5 h, respectively. In contrast, 69.6% and 64.3% of insulin were released through the cellulose dialysis membrane Spectra/Por®2 after 5 h. The release of hormones from the hydrogel matrices followed the Peppas/Sahlin model.

Conclusions

The amount of INS released by the Strat-M® membrane (high correlation with human skin) was lower than the cellulose dialysis membrane Spectra/Por®2.

sciforum-083724: Enhancing Polyetheretherketone (PEEK) Implants for Orthopedic Applications through Surface Modification with BMP-2 and Az-Gel Coating

Teng Wan

Peking University People's Hospital

Polyetheretherketone (PEEK) is a promising biomedical material for orthopedic and dental applications due to its excellent mechanical properties, low immunogenicity, and X-ray transparency. However, it exhibits bio-inertness and limited osteoconduction. Surface modification of PEEK can effectively address this issue while preserving its favorable properties. The primary objective of this study is to create a bioactive surface on PEEK implants through surface modification. BMP-2 was immobilized onto the porous structure through an intermediate layer of photoreactive gelatin (Az-Gel) to produce a bioactive PEEK implant. Its surface characteristics and in vitro cellular behavior were systematically assessed using scanning electron microscopy (SEM), static contact angle measurements, cell proliferation assays, alkaline phosphatase activities, and cellular morphology. Our study results indicated the following: (1) A surface porous structure, with pores mostly between 0.24 μm and 0.74 μm in size and 3.5 μm in thickness, was created on PEEK implants by immersing them in concentrated sulfuric acid, as determined by SEM and Image J software analysis. (2) The hydrophobicity of the PEEK implants could be reduced by the surface porous structure, while an Az-Gel coating substantially enhanced the hydrophobicity of the samples. (3) In vitro cytological studies demonstrated that PEEK implants enhanced with BMP-2 through Az-Gel coating promoted the adhesion, spreading, proliferation, extracellular matrix secretion, and osteogenic differentiation of MC3T3-E1 cells. Surface modification of PEEK implants with BMP-2 through Az-Gel coating can enhance osseointegration and osteogenic differentiation, making it a promising material for orthopedic implants and medical devices.

sciforum-088102: Fabrication and Evaluation of Metallic Nanoparticles (TiO_2-NPs) Using Polyphenol-Containing *Leucas cephalotes* (Dronapushpi) Leaf Extract, along with Their Antimicrobial Activity and Anticancer Activity

Shama Parveen [1], Dr. Vikas Gupta [1], Anuj Kandawal [2] and Veera Nagendra Kumar [3]

[1] Motherhood University, Roorkee, India
[2] Hard Vidya Mandir Digree College, Haridwara, India
[3] Department of Zoology, Faculty of Science, Government College for Men (Autonomous), Kadapa 516004, India

The field of "green chemistry", which is comparatively new, encourages the application of a set of standards to reduce the consumption of chemicals and their production. Because of this, using eco-friendly technology benefits ecosystems more than using industrial labor does. There is a growing trend in the use of plant extracts as an environmentally friendly and less expensive substitute for conventional techniques in the synthesis of metallic nanoparticles. In the present investigation, metallic titanium dioxide nanoparticles were biosynthesized using an aqueous leaf extract of *Leucas cephalotes.* Plants have a restricting and capping impact. We employed real-time monitoring of the biosynthesized nanoparticles using an ultraviolet spectrophotometric analysis. It was possible to see the formation of metallic nanoparticles and articles because the addition of the leaf extract caused a discernible color shift. We employed a number of techniques to obtain additional insight into the nanoparticles, including zeta potential energy dispersive X-ray spectroscopy (EDX), X-ray diffraction, scanning electron microscopy, and Fourier transform infrared spectroscopy. The SEM scan indicates that the titanium dioxide nanoparticles are spherical and range in size from 10 to 100 nm. The artificial TiO_2 NPs' anatase crystalline structure was confirmed by the XRD examination. The constituent elements and functional groups of the nanoparticles have been determined by the results of the FTIR and EDAX analysis. Assessments of the produced TiO_2 NPs' anticancer efficacy in MCF-7 (breast cancer), HeLa (human embryonic lung cancer), PC-3 (prostate cancer), and A549 (lung cancer) were conducted using the MTT and MTS assay. Furthermore, investigations have demonstrated the excellent activity of synthesized TiO_2 NPs against Escherichia coli, Bacillus subtilis, Pseudomonas aeruginosa, and Staphylococcus aureus and no impact against yeast (*Candida albicans*).

sciforum-086859: Innovative Hydrogels with Silver Nanoparticles: Synthesis and Applications

Katarzyna Sala [1], Magdalena Bańkosz [1], Anna Sobusiak [2], Claudia Garbowska [2], Magdalena Kędzierska [3] and Bozena Tyliszczak [4]

[1] Cracow University of Technology, Faculty of Materials Engineering and Physics, Department of Materials Engineering
[2] Cracow University of Technology, Faculty of Materials Engineering and Physics, Department of Physics
[3] Department of Chemotherapy, Medical University of Lodz, WWCOiT Copernicus Hospital
[4] Cracow University of Technology, Institute of Materials Science

Recent years have seen significant progress in the field of hydrogel materials, especially in terms of their modification with silver nanoparticles. A new method has been developed for producing hydrogels containing polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG), modified with silver nanoparticles, using eco-friendly components. In the synthesis process, silver azide was used as a precursor for silver nanoparticles, and an extract from Plantago lanceolata, known for its reducing and stabilizing properties, was employed. Silver nanoparticles were incorporated into the PVP and PEG hydrogel matrix, creating a unique composition with enhanced properties. The obtained hydrogels demonstrated excellent antibacterial properties due to the presence of silver nanoparticles. Tests also confirmed their biocompatibility and structural stability. Additionally, the presence of the Plantago lanceolata extract contributed to the increased bioactivity of the hydrogels. The developed hydrogels have a wide range of applications, particularly in regenerative medicine, as wound dressings; in drug delivery systems; and in cosmetology. Their antibacterial and bioactive properties make them a promising material in modern biotechnology and medicine.

This study focused mainly on investigating the physicochemical and mechanical properties of the finished systems. Methods of the physicochemical analysis included UV–Vis spectrophotometry to evaluate the absorption of silver nanoparticles, as well as a sorption capacity analysis and incubation studies in simulated body fluids. A valuable analysis of surface morphology was carried out using a high-resolution digital microscope to determine surface roughness parameters. The comprehensive studies conducted provided important information on the material characteristics of the hydrogel, which is crucial for understanding the potential applications of these materials in biomedical practice.

This research was carried out within the SMART-MAT Functional Materials Science Club of the Faculty of Materials Engineering and Physics of Cracow University of Technology as part of the third edition of the program “Student research clubs create innovation” through the project titled “Transdermal systems in targeted therapy of skin cancer” financed by the Ministry of Science and Higher Education (grant no. SKN 157/568410/2023).

sciforum-089058: New Composites Based on Chitosan and Natural Polysaccharide-Containing Waste Materials

Svetlana Gennadievna Vasilieva [1], Christina Antipova [2], Anastasia Zakharevich [3], Pavel Scherbakov [4], Timofey Grigoriev [3] and Alexei Solovchenko [4]

[1] Lomonosov Moscow State University
[2] Department of Nanobiomaterials and Structures, National Research Centre "Kurchatov Institute", Moscow, Russia
[3] Department of Nanobiomaterials and Structures, National Research Centre "Kurchatov Institute", Moscow, Russia
[4] Department of Bioengineering, Faculty of Biology, Lomonosov Moscow State University, Moscow, Russia

Immobilized microalgae (MA) are widely used for the production of biomass and high value-added metabolites, the biocapture of nutrients and heavy metals, and for the destruction of organic pollutants in wastewater. The use of chitosan (CH) as a carrier for MA cultivation has many advantages, including its availability, non-toxicity, biodegradability, biocompatibility and high sorption capacity. However, for successful CH application, it is crucial to increase the cost-effectiveness of microalgae–chitosan systems as compared to traditional technologies. One of the prospective approaches is the synthesis of composites on the basis of chitosan and natural polysaccharide-containing wastes (PCWs) like apple pomace (AP) and mycelium (M), which are the main by-products in the apple juice processing industry and in mushroom farming.

A CH solution and an AP or MM suspension in 2% (w/w) acetic acid were mixed in a 1:3, 1:1, or 3:1 ratio, cross-linked with glutaraldehyde, and freeze-dried to prepare porous and solid composite sponges. The chlorophyte strain *Lobosphaera* IPPAS C-2047 served as the object in the present work. To reveal the effect of CH/PCW ratio on MA attachment and biocompatibility, we followed the kinetics of MA immobilization. The proportion of unattached cells was deduced from measurements of chlorophyll content in *Lobosphaera* cell suspensions after their incubation with the composites. Immobilization efficiency was defined as percentage of attached cells calculated relative to the control.

After 24 h incubation, the immobilization efficiency of composites with 25% AP and 25%, 50% M was 25–35% higher as compared to additive-free CH, while composites with 75% of AP and M showed the lowest immobilization efficiency.

We concluded that AP and M additives have prospective features for CH-based composite production in terms of their low cost and sustainability. oreover, their addition resulted in the enhancement of MA immobilization efficiency.

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sciforum-088531: p(HEMA)-Enhanced Magnesium Phosphate Cement: Pioneering Advances in Dual-Setting Bone Cements

Marcin Wekwejt [1], Maryia Khamenka [2], Anna Ronowska [3] and Uwe Gbureck [4]

[1] Department of Biomaterials Technology, Gdańsk University of Technology, 11/12 Gabriela Narutowicza Street, 80-233 Gdańsk, Poland
[2] Scientific Club 'Materials in Medicine', Advanced Materials Centre, 11/12 Gabriela Narutowicza Street, 80-233 Gdańsk, Poland
[3] Department of Laboratory Medicine, Medical University of Gdańsk, M. Skłodowskiej-Curie 3a Street, 80-210 Gdańsk, Poland
[4] Department for Functional Materials in Medicine and Dentistry, University of Würzburg, Sanderring 2 Street, 97-070 Würzburg, Germany

Bone tissue exhibits inherent regenerative capabilities. Nevertheless, the adjunct of specialized biomaterials often proves beneficial, if not essential, for enhancing this healing process. Among these, bone cements stand out as biofunctional materials. Magnesium phosphate cements (MPCs) are distinguished by rapid setting, high initial mechanical strength, advantageous resorption, and osteogenic properties. Yet, challenges such as pronounced brittleness, paste leachability, and injection difficulties persist. Addressing these issues, this study introduces a novel dual-setting MPC-based cement formula modified with poly(2-hydroxyethyl methacrylate) (HEMA), aiming to enhance performance and applicability.

The formulation comprised an MPC powder component of tri-magnesium phosphate combined with di-ammonium hydrogen phosphate at a 4:1 mass ratio, alongside liquid components of 2-hydroxyethyl methacrylate solutions. HEMA polymerization was triggered by APS + TEMED, starting hydrogel formation after premixing (2–4 min). Specimen preparation involved mixing the components at a 2.5 g/mL powder-to-liquid ratio to achieve a paste, which was subsequently cast into molds and cured (24 h, 37 °C, >90% humidity). Evaluations comprised setting time, SEM microstructure, XRD and FTIR analyses, mechanical strengths, porosity, and degradation rate. Further, cytocompatibility was assessed using human osteoblasts.

The integration of a hydrogel component was pivotal in modulating the cement's functional characteristics. Notably, the concentration of HEMA and the duration of premixing markedly influenced hydrogel agglomerate formation within the cement matrix. Enhanced mechanical strength was associated with extended premix times and HEMA concentrations. Conversely, shorter premix durations facilitated more rapid and efficient matrix degradation. Cytotoxic effects observed in cultured osteoblasts were attributed to the application of TEMED as a catalyst in the polymerization process. Despite the achievement of desirable functional and mechanical properties, further investigations should explore alternative hydrogel additives or modifications to the HEMA polymerization methodology.

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sciforum-089276: Production of Bioactive Coatings on Titanium Implants Using a Micro-Arc Oxidation Process Assisted with Ultrasound

Balbina Makurat-Kasprolewicz [1,2], Marcin Wekwejt [3], Anna Ronowska [4], Grzegorz Gajowiec [1], Marlena Grodzicka [5], Stefan Dzionk [6] and Agnieszka Ossowska [1]

[1] Department of Materials Science and Technology, Gdansk University of Technology, 80-233 Gdańsk, Poland
[2] Department of Machine Design and Medical Engineering, Gdansk University of Technology, 80-233 Gdańsk, Poland
[3] Department of Biomaterials Technology, Gdansk University of Technology, 80-233 Gdańsk, Poland
[4] Department of Laboratory Medicine, Medical University of Gdańsk, 80-210 Gdańsk, Poland
[5] Faculty of Chemistry, Nicolaus Copernicus University in Toruń, 87-100 Toruń, Poland
[6] Department of Manufacturing and Production Engineering, Gdansk University of Technology, 80-233 Gdańsk, Poland

Introduction

Various factors such as aging, inactivity, and accidents can cause musculoskeletal disorders, often requiring surgical intervention for severe damage. The increasing number of implant surgeries has sparked interest in bone tissue engineering. Commercially pure titanium (CP-Ti) is highly favored in medicine for its biocompatibility, stability in body fluids, and tensile strength. However, a drawback is its lack of bioactivity. Bioactive coatings can address this issue by improving bone cell interaction with the material.

Materials and Methods

CP-Ti surfaces were modified using micro-arc oxidation (MAO) and ultrasound micro-arc oxidation (UMAO) in an electrolyte with calcium and phosphorus ions. This study assessed various process parameters, including voltage (400 V), duration (450 or 600 s), current density (120 or 60 mA/cm^2), and two ultrasound operating modes (sinusoidal and unipolar rectangular). The coatings were analyzed through the assessment of morphology, chemical composition, topography, wettability, nanomechanical properties, corrosion behavior, coating thickness and adhesion, cytocompatibility, as well as cell adhesion and proliferation of the hFOB 1.19 cell line.

Results

Porous calcium phosphate coatings produced on CP-Ti samples exhibited hydrophilicity, an isotropic structure, and strong adhesion to the substrate. They also had a corrosion rate suitable for biomaterial applications. Further, this study showed that various MAO process parameters and ultrasound types significantly influenced the chemical composition as well as the physicochemical and mechanical properties of the coatings. Incorporating ultrasound during the MAO process enhanced coating thickness, porosity, roughness, isotropy, skewness, and calcium integration. Overall, they were characterized by favorable cytocompatibility.

Conclusions

The findings highlight the importance of surface treatment for the biomedical use of titanium. Optimal coating characteristics were achieved at a current of 136 mA, a duration of 450 s, and using unipolar rectangular ultrasound. Combining micro-arc oxidation with ultrasound improves CP-Ti properties concerning biomedical applications, such as customizing implants for knee joint resurfacing or craniofacial reconstruction.

sciforum-086904: Stereospecificity of Chiral Salt Complexes of Chitosan with L- and D-aspartic Acid under Model Conditions of Intracellular Regulation

Xenia Shipenok, Natalia Gegel and Anna Shipovskaya

Institute of Chemistry, Saratov State University, Saratov 410012, Russia

Chiral polymeric matrices with controlled sites of complementary-specific interactions are considered innovative substrates for the production of highly selective medicinal and pharmaceutical drugs. To solve this problem, information is necessary about the stereospecific features of the chemical substance used to obtain such biomaterials, including those under model conditions of intracellular communication and regulation.

This work considers the acid–base and chiro-optical properties of chiral biologically active salt complexes of chitosan and L-(D-)aspartic acid (CS·L-(D-)AspA), which are promising for the design of stereofunctional biomaterials and pharmaceuticals. Special attention is paid to studies of the attenuation of optical anisotropy intensity during the process of model biomolecular condensation of L-menthol in the CS·L-(D-)AspA medium.

It has been established that an increase in the [AspA]/[CS] molar ratio is accompanied by a decrease in pH and a decrease in the protonation degree of CS amino groups in salt complexes. Aqueous solutions of CS·L-(D-)AspA exhibit a positive and negative, respectively, Cotton effect in the UV region, which is the result of the π-π transition in the aminoaspartic chromophore. In the visible region, CS L- and D-aspartate is characterized by a left-handed rotation of the plane of polarization and monotonic dispersion of specific optical rotation. The phase separation of an ethanolic L-menthol solution in an aqueous CS·L-(D-)AspA solution proceeds through the mechanism of selective extraction crystallization and combines two types of phase separation, namely, liquid–liquid and liquid–crystal. The "emulsion–dispersion" phase transition is accompanied by the disappearance of the birefringence effect in the condensed phase of the substance.

The results obtained show the promise of using CS·L-(D-)AspA in studies of biomolecular condensation (the formation of highly labile associates of macromolecules due to liquid phase separation) and the biogenesis of membraneless organelles in physiological/pathological cellular processes.

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Keywords: Chitosan; aspartic acid; chirality; stereospecificity; cellular regulation model

sciforum-089029: Study of Carbon Nanotube–Bovine Serum Albumin Interaction Using the Tritium Radiotracer Technique and Supercomputer Simulation

Vitalii Andreevich Bunyaev [1,2], Artem Vadimovich Sinolits [2] and Gennadii Aleksandrovich Badun [1]

[1] Lomonosov Moscow State University, Moscow, Russia
[2] Vernadsky Institute of Geochemistry and Analytical Chemistry of Russian Academy of Sciences, Moscow, Russia

Single-walled carbon nanotubes (SWCNTs) are referred to as a promising material for biocompatible devices and novel medicines. In these applications, contact between SWCNTs and blood should be expected. Serum albumin is the most abundant globular protein in mammalian blood, so it is of great importance to study the interactions of SWCNTs with major blood components such as serum albumin, as contact between them is possible with the incorporation of SWCNTs into common practice. The radiotracer technique with [^{3}H] is highly sensitive and enables the quantification of biomolecules in complexes with nanomaterials without inducing significant changes in the biomolecule structure.

We simulated the interaction of bovine serum albumin (BSA) as a model protein with SWCNTs moderately functionalized with fluorine with Gromacs software. Partial atom charges and bond lengths were calculated with the semi-empirical quantum chemistry method PM7 with MOPAC2016 software. Thermostat, barostat and basic simulations were carried out with the Berendsen algorithm. The simulation time was 100 ns. The dynamics of changes in the secondary structure of BSA were simulated. The quantity of BSA bonded with SWCNTs was estimated with the use of the radiotracer technique, with [^{3}H]BSA obtained with the tritium thermal activation technique.

We found that the dominant interactions between BSA and SWCNTs are hydrophobic. The fluorine atoms in the SWCNTs become involved in hydrogen bonds with His 534, Thr 539 and Ala 583 in the BSA. The mean total energy of the Coulomb and Van der Waals interactions is -364 ± 9 kJ/mol, as determined by gmx energy. The maximum absorption of BSA on the SWCNTs is 740 mg/mg, which is consistent in all the simulations and leads to the ζ-potential of the BSA–SWCNT complex changing from -10 to -16 mV as the adsorption increases.

The research was carried out using equipment from the shared research facilities of HPC computing resources at Lomonosov Moscow State University.

sciforum-088548: The Comparison of Physicochemical Properties of Chitosan/Silk Fibroin/Collagen-Based Materials Cross-Linked with Chemical Agents

Sylwia Grabska-Zielińska [1] and Alina Sionkowska [2]

[1] Faculty of Chemical Technology and Engineering, Bydgoszcz University of Science and Technology
[2] Faculty of Chemistry, Nicolaus Copernicus University, Toruń, Poland

Interest in biomaterials based on natural polymers has recently surged. The natural polymers are large molecular compounds, which can be obtained from living organisms or are produced by living organisms. Biopolymers typically exhibit properties highly desirable in tissue engineering, including biocompatibility, biodegradability, and minimal immune responses upon introduction into the human body. Chitosan, collagen, and silk fibroin are biopolymers commonly used in tissue engineering to obtain three-dimensional scaffolds [1]. They can be utilized as fillings for repairing small bone defects. However, materials obtained only from biopolymers or their mixtures may have insufficiently physicochemical properties. Therefore, there is a need to cross-link such materials [1]. The purpose of this work was to obtain and characterize 3D scaffolds based on chitosan, collagen, and silk fibroin modified with various cross-linking agents [2–4]. Collagen was obtained from young rat tail tendons, and silk fibroin was obtained from Bombyx mori cocoons. Materials were obtained using the lyophilization method, and their physicochemical properties, such as porosity, density, moisture content, and mechanical strength, were evaluated. Dialdehyde chitosan, dialdehyde starch, and glyoxal were used as modifiers of the three-component materials. Based on the results, it can be concluded that the properties of biopolymer materials depend on their weight ratio composition and the cross-linking agent. The study revealed that cross-linked materials exhibited a high swelling rate and sufficient porosity, rendering them suitable for tissue engineering applications. Mechanical properties vary depending on the composition of the blends. Novel biopolymeric composites based on collagen, chitosan, and silk fibroin, chemically cross-linked, hold potential for various biomedical applications, particularly in bone tissue regeneration.

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Abstracts

Session 5. Biocatalysis and Enzyme Engineering

sciforum-084982: Determinação das Melhores Condições Para Produção da Enzima Quitinase Pelo Fungo *Beauveria bassiana*

Rafaela Fantatto [1], Rodrigo Sorrechia [1], Barbara Regina Kapp [1], Alexandra Barrios Eguiluz [1] and Rosemeire Linhari Rodrigues Pietro [2]

[1] Departament of Drugs and Medicines, São Paulo State University UNESP, Rodovia Araraquara-Jaú 14800-903, Araraquara, São Paulo, Brazil
[2] Departament of Drugs and Medicines, São Paulo State University UNESP, Rodovia Araraquara-Jaú Km 1, 14800-903, Araraquara, São Paulo, Brazil

Chitinases, enzymes produced by diverse organisms like bacteria, fungi, insects, plants, and humans, play a crucial role in degrading the biopolymer chitin. They have wide-ranging applications, including abilities to isolate protoplasts from fungi, control pathogenic fungi, treat chitinous waste, and manage disease transmission viinsects due to their chitin-degrading ability. This study focused on determining optimal conditions for chitinase production using the fungus *Beauveria bassiana,* acknowledging the enzyme's significant importance. The strain employed was *B. bassiana* 487 from Embrapa, registered in the ARSEF database. Three media (Hill, Adams, and Medium 2) were assessed with or without shrimp exoskeletons as an inducer over a 10-day period. Initial fermentation conditions included a pH of 5.5, a temperature of 28 °C, stirring at 120 rpm, and an inoculum size of 107 cells/mL. Production and enzymatic activity were evaluated, monitored for 7 days, with the tenth day dedicated to identifying optimal production conditions. Medium 2 demonstrated superior production when supplemented with the inducer, reaching its peak on the seventh day. Following the medium selection, chitinase enzymatic activity in Medium 2 with the inducer was assessed. Until the eighth day, *B. bassiana* 487 showed low enzyme production, with an enzymatic activity of 6.08 nmol/mL·min. A significant increase occurred on the ninth day, reaching 348.94 nmol/mL·min. High activity persisted on the tenth and eleventh days, with values of 302.45 and 264.59 nmol/mL·min, respectively. In conclusion, for enhanced chitinase production by *B. bassiana* 487, we recommend using Medium 2 over a 10-day fermentation period under suitable conditions.

sciforum-088235: Enzymatic Protein Hydrolysates from Tuna (*Thunnus thynnus*) Industrial Waste: In Vitro Biological Activities

Slimane Choubane [1,2], Omar Khelil [1,2], Amina Benmeddah [1] and Asmaa Benaouda [1]

[1] Ecole Supérieure en Sciences Biologiques d'Oran, Oran, Algeria
[2] Laboratoire d'Aquaculture et de Bioremediation (AquaBior), Oran, Algeria

Industrial fish processing generates significant quantities of waste around the world, posing a risk to human health and the environment. It has been estimated that about two-thirds of the total amount of fish processed in industries is discarded as waste.

One of the promising ways for the industrial exploitation of industrial fish waste is the production of protein hydrolysates (FPH) which have a wide field of applications in different sectors, i.e., food industry, pharmaceutics, cosmetics and animal feed.

In this study, a protease enzyme was produced by Bacillus mojavensis FP2 and applied in the hydrolysis of industrial tuna waste. The hydrolysates obtained were tested for their antioxidant, antibacterial and anti-hyperglycemic activity. The hydrolysates were also characterized to determine their properties.

The protease produced showed a high enzymatic activity (105.94 $\pm$ 5.99 U/mL), which made it possible to achieve a high degree of hydrolysis (24.2 $\pm$ 1.69%). Concerning antioxidant activity, a DPPH free radical scavenging activity of 96.9 $\pm$ 1.04% was achieved at a concentration of 10 mg/mL. Also, the protein hydrolysates from tuna waste presented a very high reducing power, ranging from 0.43 to 0.53 at 5 mg/mL.

Regarding antibacterial activity, the hydrolysates showed an inhibition of *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Escherichia coli*. The hydrolyates also showed anti-hyperglycemic power. The hydrolysates which showed an inhibition of α-amylase activity were F45, F60 and F90, with an inhibition percentage of 15.97 $\pm$ 6.45%, 69.96 $\pm$ 1.34% and 14.16 $\pm$ 2.82%, respectively.

Finally, the tuna waste protein hydrolysates yielded peptides which had excellent solubility over a wide pH range, and good emulsifying and foaming capacities.

sciforum-086957: Ex Vivo Analysis of Various Herb–Drug Interactions and Their Effects on Metronidazole Absorption

Ujban Hussain [1] and Samiksha Sandeep Tammewar [2]

[1] Department of Pharmaceutical Sciences, The Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, India
[2] Priyadarshini J. L. College of Pharmacy, Nagpur, India

Aim

1. To study the effect of food, drink, or pharmaceuticals on the action of drugs;
2. To study the result of interactions between medication molecules and secondary targets;
3. To study the effect of herbal extracts on drug absorption.

Objectives

1. To identify the effects of different herbal extracts on the absorption of metronidazole;
2. To study in vitro and in situ herb–drug interactions;
3. To study the effect of different herbal extracts on the absorption of metronidazole.

Methodology

Take a sufficient amount of cold thyroid solution, place it in a Petri dish, transfer the ileum to it using forceps, and tie one end through the intestinal sac to a double-looped knot of a moistened thread. Fill a syringe with metronidazole alone or in combination with a herbal extract. Put the intestinal sac in a beaker, stir, take samples of the solution at particular time intervals, and assess the absorption of metronidazole.

Results and Discussion

Metronidazole is used as a treatment for amoebiasis or related diarrhea-like conditions which are also treated with home remedies like asafoetida, ginger, and lemon juice, given to the patient to correct electrolyte imbalances. However, these routine food items can affect the therapeutic effect of the synthetic drug when taken concomitantly, either by pharmacokinetic or pharmacodynamic mechanisms.

Conclusions

The results of this study are anticipated to provide valuable insights into the potential interactions between herbal extracts and metronidazole absorption. Herbal extracts, which are frequently used in conventional medicine and as food additives, might affect how synthetic medications like metronidazole are absorbed. Such interactions may affect the effectiveness of therapy and the results for patients. These results highlight the need of taking into account possible herb–drug interactions and modifying drug delivery schedules accordingly. For safe and effective medication administration, it is essential to comprehend these interactions.

sciforum-089232: Repurposing Halophilic α-Amylase for Future Biotechnological Applications

Dr. Sumit Kumar, Anushka Sunil Kumar, Shanaya Shakil, Mohit Silwadiya, Lakshya Anand, Surbhi Sinha and Kristi Sharma

Amity Institute of Biotechnology, Amity University, Noida, Uttar Pradesh, India

Halophiles are a class of extremophiles growing under salty environments. They have emerged as a valuable repository of many polyextremophilic enzymes finding diverse industrial applications. Enzymes used in industry must remain stable in challenging operating environments. In this context, the enzymes from extremophiles can be of great use because they are resistant to, and capable of catalysis under, extreme physical conditions. Halophilic enzymes show great potential for use in industrial applications that involve high salt or hypersaline conditions. Additionally, they have been optimized to function under polyextreme conditions, such as high pH and temperature, and the presence of hydrophobic solvents. Halophilic α-amylase from halophiles can find wide applications in starch processing, food industries, and saline starchy waste treatment. In this context, α-amylase from *Marinobacter* sp. EMB8 has been studied in detail, and its production, purification, characterization, and application in maltooligosaccharide synthesis have been carried out. Besides that, several halophilic amylases have been studied and characterized across the globe. Because of their polyextremophilicity, their use has been potentiated for maltooligosaccharide synthesis, detergent application, starch hydrolysis, and the bioremediation of starch- and solvent-containing wastes. Furthermore, halophiles are an ideal chassis for enzyme production through a cost-effective non-sterile fermentation approach. Due to their high salt demand for growth, they have been recognized as a natural option for non-sterile fermentation in recent years. Because non-sterile fermentation does not require sterilizing processes, it is easier to maintain, has a simpler bioreactor design, and is easier to operate than sterile fermentation. Salt inhibits the growth of non-halophilic/ mesophilic bacteria. Therefore, it is possible to synthesize the metabolites that are produced by halophiles using open, continuous fermentation procedures without any contamination. It turns out that producing α-amylase in non-sterile circumstances is cost-effective and a big step forward for their biotechnological application.

sciforum-088940: Selective Inhibitors of Cellular Redox Homeostasis Enzymes

Veronika Yudina, Aleksandr Zozulya and Evgeny Chupakhin

Federal State Autonomous Educational Institution of Higher Education, Immanuel Kant Baltic Federal University

The cellular redox system has a huge range of different vital properties, from the neutralization of reactive oxygen and nitrogen species to drug resistance. Also, redox balance is crucial for the progression of growth and the proliferation of tumor cells. Suchmajor systems are thioredoxin and glutathione systems. The enzymes that catalyze reactions in these systems, thioredoxin reductase and glutathione reductase, are promising targets in various human diseases. These enzymes possess a certain catalytic feature, i.e., an ability to promote the reduction of selenide–sulfide and disulfide groups, through which electrons are transferred for further oxidation–reduction processes on the protein. The increased expression of redox enzymes has been proven in tumor cells compared to normal cells.

In our study, we synthesized derivatives of oxazolones, molecules with an electron-deficient part, which could be potential inhibitors of redox enzymes. The derived molecules were screened for their ability to inhibit thioredoxin reductase and glutathione reductase on lung carcinoma cell lysates, and active candidate molecules were also selected. An analysis of the obtained enzymatic reaction rate change data made it clear that the molecules we synthesized tended to inhibit thioredoxin reductase more effectively, most likely due to their higher affinity for selenocysteine. Two molecules with a common 4-nitrostyryl-oxazolone moiety that were more effective as inhibitors of glutathione reductase were also identified. Selective binding studies with cysteine and selenocysteine using mass spectrometry were carried out for the selected molecules. The selected molecules were also tested for their cytotoxic activity against lung carcinoma cells.

sciforum-084944: The Stabilization and Utility of β Galactosidase Immobilized on Thiolated Silica Nanoparticles

Shakeel Ahmed Ansari [1] and Rukhsana Satar [2]

[1] Department of Biochemistry, Medicine Program, Batterjee Medical College, Jeddah 21442, Saudi Arabia
[2] Department of Biophysiology, Division of Biochemistry, Medicine Program, Ibn Sina National Medical College, Jeddah, Saudi Arabia

This research demonstrates the synthesis of silica nanoparticles (Si-NPs) via the sol-gel method, followed by tetra-ethyl-orthosilicate and mercaptopropyl tri-methoxy-silane-mediated thiolation to promote the covalent binding of *Aspergillus oryzae* β-galactosidase. A higher enzyme immobilization yield of 89% was achieved on the developed nanobiocatalyst. Soluble and immobilized enzyme exhibited similar pH and temperature optima at pH 4.5 and 50 °C, respectively. However, β-galactosidase bound to thiolated Si-NPs (IβG) exhibited a significant enhancement in activity under extreme temperatures and pH variations, as compared to the soluble β-galactosidase (SβG), by improving its tolerance towards harsh pH ranges and limiting the thermal movement of the enzyme at higher temperatures. It was further observed that the immobilized enzyme retained 58% activity at a 5% galactose concentration even after 1 h. However, under similar experimental conditions, SβG showed 23% activity. The reusability of the immobilized enzyme revealed that it retained 63% activity even after the sixth repeated use and hence could be recovered easily by centrifugation for repeated use in biotechnological applications. The batch reactor experiment indicated that the immobilized enzyme displayed 86% and 79% lactose hydrolysis at 50 °C and 60 °C, respectively, as compared to 71% and 60% lactose hydrolysis of the soluble enzyme under identical conditions after 8 h. Future research of the developed nanobiocatalyst is required to analyze its stability in producing lactose-free dairy in continuous reactors products and in the production of galacto-oligosaccharides.

Abstracts

Session 6. Bioinformatics and Computational Biology

sciforum-089174: In Silico Analyses of Strawberry and Soybean Bioactive Compounds' Inhibitory Effects against Angiotensin-Converting Enzyme (ACE)

Ayyagari Ramlal [1,2], Isha Bhat [3], Sreeramanan Subramaniam [1,4,5], Manisha Saini [2], Iten M. Fawzy [6], Dhandapani Raju [7] and Ambika Rajendran [2]

1 School of Biological Sciences, Universiti Sains Malaysia (USM), Georgetown, Penang, Malaysia
2 Division of Genetics, ICAR-Indian Agricultural Research Institute (IARI), Pusa Campus, New Delhi 110012, India
3 Department of Biosciences, Jamia Millia Islamia, New Delhi 110025, India
4 Chemical Centre Biology (CCB), Universiti Sains Malaysia (USM), Bayan Lepas, Penang 11900, Malaysia
5 Department of Biology, Faculty of Science and Technology, Universitas Airlangga, Surabaya 60115, Indonesia
6 Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Future University in Egypt, Cairo 11835, Egypt
7 Division of Plant Physiology, ICAR-Indian Agricultural Research Institute (IARI), Pusa Campus, New Delhi 110012, India

Soybean is a unique legume cum oilseed crop enriched with a plethora of bioactive compounds having health-promoting properties. Its extracts serve as a primary ingredient in many drug formulations against diabetes, obesity, and spinal cord-related disorders. Strawberry is also an economically important crop with immense nutraceutical and health-beneficial abilities. Cardiovascular diseases and hypertension cause several deaths globally. The renin–angiotensin–aldosterone system regulates body hypertension and fluid balance which causes cardio diseases. Angiotensin-converting enzyme I (ACE I) is the key Zn-metallopeptidase component of the RAAS involved in the homeostasis maintenance of the cardiovascular system. The available commercial drugs for cardio diseases have many side effects and also lead to death; thus, there is a need to explore the use of phytocompounds and peptides as alternative therapies. Soy proteins and their products act against ACE I, which may provide new scope for the identification of potential scaffolds that can help in the design of safer and natural cardiovascular therapies. In the present study, the molecular basis for the selective inhibition of 34 soy phytomolecules from phospholipids, saponins, inositols, oils, polysterols, phenolics, isoflavonoids and fatty acids and 2 strawberry molecules, namely, ellagitannin and pelargonidin-3-glucoside, along with reference compounds (captopril, lisinopril and quinapril) were evaluated. The structures were retrieved from PubChem, and in silico molecular docking approaches and dynamic simulations were performed to understand the protein–ligand interactions. Our results indicate that amongst the compounds, beta-sitosterol exhibited potential inhibitory action against ACE I. This study can be useful for the production of safer drugs against ACE following in vivo and clinical studies.

sciforum-086789: In Silico Prediction of Commonly Used Reference Genes in qPCR for *Lissachatina fulica*

Irina N. Dominova, Kristina Yu Golovneva and Valery V. Zhukov

Higher School of Life Science, Immanuel Kant Baltic Federal University, 236040 Kaliningrad, Russia

Lissachatina fulica is the largest invasive agricultural pest with the highest prevalence in Asian countries. At the same time, *L. fulica* is one of the few animal species that can regenerate organs, including the nervous system and eyes. However, its genome is poorly studied, which restricts further molecular and genetic studies of this organism. At the same time, one of the most accessible methods to study genomes is qPCR, the accuracy of the results of which depend on the selected reference genes. Therefore, the aim of this study was to predict the sequences of some genes in *L. fulica* using genes that are most often used as reference genes for qPCR.

In searching for homologous genes in *L. fulica*, actin (*Act*), β-tubulin (*Tubb*), and glyceraldehyde-3-phosphate dehydrogenase (*Gapdh*) were selected as commonly used reference genes in qPCR for molluscs. The corresponding amino acid sequences of their proteins were used for more accurate prediction. The amino acid sequences of ACT, TUBB, and GAPDH of the gastropod molluscs *Aplysia californica*, *Pomacea canaliculata*, and *Biomphalaria glabrata* as the closest related species to *L. fulica* were taken from the NCBI Protein database. Multiple sequence alignment was performed using Clustal Omega followed by refining the results by MUSCLE in Unipro UGENE (v. 45.0). HMM3 profiles were also constructed in Unipro UGENE and then used to search for homologous sequences in *L. fulica* (GigaDB repository) using HMMER (v. 3.3.2).

As a result, we found in *L. fulica* homologous sequences for GAPDH (Afu019240), TUBB (Afu012850), and ACT (Afu006397) and the corresponding mRNA of genes encoding these proteins. Thus, the first attempt was carried out to annotate the *L. fulica* genome in order to identify reference genes, which is a necessary element of any molecular and genetic study.

This research was supported by the IKBFU grant 434-K-23 “Priority 2030”.

sciforum-088711: In Silico Prediction of Drug-likeness, Pharmacokinetics, and Toxicity of Selected Phytotoxic Pyrrolizidine Alkaloids

Obinna Kenneth Didigwu [1], Emmanuel Amuchechukwu Kevin [2], Michael Osita Edeh [2] and Sunday N. Okafor [1]

[1] Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmaceutical Sciences, University of Nigeria Nsukka, Nsukka 410001, Enugu State, Nigeria
[2] Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, University of Nigeria Nsukka, Nsukka 410001, Enugu State, Nigeria

Pyrrolizidine alkaloids (PAs) are heterocyclic organic compounds of natural origin synthesized by either plants or microorganisms. They are found in species applied in the pharmaceutical industry for their beneficial biological activities to cure disease; thus, a thorough knowledge of their pharmacokinetics and toxicity is of great importance as they are notorious for their acute hepatotoxicity and carcinogenicity in humans and animals. Therefore, this study evaluated the drug-likeness of 15 phytotoxic pyrrolizidine alkaloids that were reportedly isolated from 11 plant species via in silico prediction of their pharmacokinetic and toxicity profiles. Using Swiss ADME, pkCSM, and PreADMET webserver tools, Lipinski's properties and topological polar surface area (TPSA) were predicted for drug-likeness, alongside their pharmacokinetic profiles and toxicity on various organ endpoints. The drug-likeness prediction showed that all the compounds obeyed Lipinski's rule of five (LRo5). None of the compounds inhibited hERG I and hERG II, indicating their non-cardiotoxic nature. In addition, 20% of the compounds elicited AMES toxicity; 53.33% caused liver injury; and none was sensitive to the skin. Furthermore, 13.33% showed high $Caco_2$ permeability and all displayed good skin permeability, implying their suitability for transdermal drug delivery. Moreover, P-glycoprotein was effluxed by 80% of the compounds and none exhibited inhibition; 86.66% of the compounds readily crossed the blood–brain barrier, 6.66% penetrated the central nervous system, none was a substrate to cytochrome p450 isoenzymes, 6.66% inhibited cytochrome p450 isoenzymes, 53.33% and 26.66% would cause cancer in mice and rats, respectively, and 20% showed high tolerated doses in humans. All demonstrated high intestinal absorption and 46.66% demonstrated good water solubility while a significant number showed a moderate volume of distribution, were free-flowing in plasma, and demonstrated moderate bioavailability. This study identified Jacoline and monocrotaline as drug-like, non-toxic, and highly bioavailable pyrrolizidine alkaloids with strong potential for further assessment, optimization, and development.

sciforum-085602: Optimizing Breast Cancer Classification: A Comparative Analysis of Supervised and Unsupervised Machine Learning Techniques

Prithwish Ghosh [1,2] and Debolina Banerjee [3]

[1] Student
[2] Department of Statistics, Institute of Science, Visva Bharati
[3] Department of Botany, Institute of Science, Visva Bharati

This study focuses on the comprehensive analysis of machine learning algorithms for the classification of breast cancer into benign and malignant categories using the Wisconsin breast cancer dataset. Two distinct approaches, supervised and unsupervised, were employed to evaluate the effectiveness of various algorithms in discerning the nature of cancerous growths based on diverse physical properties.

In the supervised learning realm, the study employed three powerful algorithms: Support Vector Machines (SVMs), Random Forests, and XGBoost. Additionally, unsupervised learning techniques, specifically Linear Discriminant Analysis and the Gaussian Finite Mixture Model for classification, were investigated. Notably, the XGBoost algorithm emerged as the most promising candidate in the supervised category, exhibiting superior classification performance when applied to the testing dataset (20% of the total data). The results indicated that XGBoost achieved an impressive precision of 98.23%, outperforming both the Gaussian Finite Mixture Model for classification (97.5%) and the Linear Discriminant Analysis (96.48%). The XGBoost algorithm, implemented on a subset of the data, demonstrated its efficacy in accurately identifying the nature of breast cancer, highlighting its potential as a robust tool for predicting malignancy based on distinct physical properties.

This study underscores the significance of supervised and unsupervised learning, particularly the XGBoost algorithm and the Gaussian Finite Mixture Model for classification, in optimizing breast cancer classification. The findings contribute valuable insights into the selection of appropriate machine learning techniques for the accurate and efficient identification of benign and malignant breast cancer, thereby facilitating improved diagnostic practices.

sciforum-089254: Studying the Feasibility of Obtaining Highly Specific Polyclonal Antibodies to Nucleic Acids: A Primary Predictive Model and Prospects for Its Application

Alexander Tolstykh [1], Vladimir Frantsuzov [1] and Konstantin Butenko [2]

[1] Institute of Pharmacy, I.M. Sechenov First Moscow State Medical University
[2] Faculty of Biology, Lomonosov Moscow State University (Department of Virology, Scientific Research Laboratory for Plant Virus Diagnostics)

Introduction

Antibodies to nucleic acids (NAs) represent a significant subject of investigation in medicine, yet they have not gained wide dissemination due to the low immunogenicity of NAs and the high cross-reactivity of antibodies, which can lead to autoimmune diseases when using modern mRNA vaccines. Diagnostic antibodies for detecting RNA antigens hold considerable importance in various domains of knowledge.

Methods

A promising predictive model, "polyclonal antibody—potato pathogen", can aid in enhancing the specificity of polyclonal antibodies to NAs. In this study, the selected pathogens include PSTVd, PVX, and PVY. Using Python, the program can identify unique sequences within the genome of the specified pathogen—sequences of user-defined length (ribotopes) absent in the host genome, which can subsequently serve as targets for antibody generation. Additionally, the program identifies the most unique sequence among those found by breaking them into all possible sub-sequences of, for example, length 4 (the minimum length of an NA where antibodies can bind to it) and more nucleotides. The program analyzes these subsequences for their occurrence in the host genome. The sequences with the least number of occurrences of their subsequences in the host genome are assigned the status of the most unique and are displayed on the screen.

Results

Calculations showed that the minimum length of a sequence ensuring the uniqueness of a ribotope is 11. Several unique sequences of this length were found in the genomes of each pathogen. Based on these findings, in vivo experiments are planned on laboratory mice to generate antibodies and test their specificity using the IFA method. Thus, obtaining highly specific antibodies is achieved through the proper selection of the "target".

Conclusions

The obtained model can potentially be extrapolated to human viral pathogens and can subsequently find application in molecular diagnostics as well as in medicine for creating higher quality analogs of modern mRNA vaccines.

sciforum-087207: A Bioinformatics Approach to Analyzing Breast Cancer Genes among the African American and White/Caucasian Populations

Inara Deedar Momin and Kumaraswamy Naidu Chitrala

Department of Engineering Technology, University of Houston, Sugar Land, TX 77479, USA

Breast cancer is the most common type of cancer in women. Breast cancer affects 200,000 women in the United States each year. Some of its treatments include chemotherapy, radiation, and surgery. In the present study, we aim to analyze the race-specific differences in gene expression profiles of breast cancer subtypes among the African American and White/Caucasian populations. We used The Cancer Genome Atlas (TCGA) to study invasive breast carcinoma tumors and the correlated genes, *TACSTD2, PIK3CA*, and *NTRK1.* Cbioportal was used to find the expression levels of the three genes (NTRK1, PIK3CA, TACSTD2) and further understand their potential roles as DNA biomarkers for breast cancer. The Gene Cards database helped determine the genes with a direct correlation to breast cancer and identify which of them are its promoters or enhancers. Genes *PIK3CA* and *TACSTD2* were shown to be directly correlated. UALCAN was used to analyze the different gene expression levels between the two races, White/Caucasian and African American. Additionally, the KEGG database found gene pathways related to breast cancer. Gene Ontology identified the phenotype of the *PIK3CA* gene concerning breast cancer. Reference sequencing analysis was conducted on the genes to find mRNA expressions relating to breast cancer. The findings showed genes *NTRK1* and *TACSTD2* were negatively correlated and gene *PIK3CA* was positively correlated. The purpose of this study was to measure the correlation of the genetic biomarkers of the African American and White/Caucasian ethnicities with breast cancer subtypes. The genes identified in our study could be potential targets to address different probable causes of and treatments for breast cancer in the African American and White/Caucasian ethnicities.

sciforum-089009: A Computational Approach to Comparative Analysis of Aflatoxin B1-Specific Aptamers for Detection: Insights into Molecular Interactions and Binding Affinities

Shazia Shareef [1] and P. Hariprasad [2]

[1] CRDT, Indian Institute of Technology Delhi, New Delhi 110026, India
[2] Indian Institute of Technology, Delhi, India

Aflatoxins (AF) are the carcinogenic secondary metabolites produced by fungi such as *Aspergillus flavus*, *A. parasiticus*, *A. nomius*, etc. These fungi are widespread and have severely contaminated food/feed supplies. The major health consequence of consuming AF contaminated food/feed is Hepatocellular carcinoma and associated complications. Therefore, detecting, and quantifying AFs in foods and feeds are critical to achieve food safety. Among the available methods, aptamer-based techniques are upcoming by considering their specificity, sensitivity, low cost, and ease of production and handling. Though AFB_1 specific aptamer has been studied well, ligand-aptamer molecular interactions are not clear. In the present study, the three-dimensional structures of available AFB_1 specific DNA aptamers were predicted using RNA-based web servers with an automated machine translation principle and some manual changes in the script file. Molecular docking was performed between selected DNA aptamers and AFB_1. Molecular docking results revealed that the AFB_1 was located inside the pocket area of the predicted tertiary structures and formed electrostatic interactions with nucleotides of aptamers. The binding affinities of all aptamers were between -7.3 to -11.7 kcal/mol. The study adds to our understanding of how AFB_1 interacts with all available aptamers. The developed workflow enables the generation and examination of additional appealing ligand-aptamer complexes to detect AF and other mycotoxins.

sciforum-083779: A Computational Study on Gold and Silver Nanoparticles against SARS-CoV-2 Proteins

Ilyes Zatla and Lamia Boublenza

University of Tlemcen

Metallic nanoparticles, such as gold and silver nanoparticles, are extraordinarily small particles composed of metal atoms at the nanoscale, typically ranging in size from 1 to 100 nanometers. These nanoparticles possess a plethora of unique and invaluable properties owing to their diminutive size, their exceptionally high surface-area-to-volume ratio, and the emergence of quantum effects at this scale. In this research, a computational simulation was conducted to explore the structural configurations of both silver nanoparticles (AgNPs) and gold nanoparticles (AuNPs). Subsequently, geometry optimization techniques were applied to refine these structures. The optimized nanoparticle configurations were then systematically evaluated for their potential interactions with three specific targets within the SARS-CoV-2 virus: the Main protease (Mpro), the RNA-dependent RNA polymerase (RdRp), and the S spike glycoprotein. Notably, the results revealed that both AgNPs and AuNPs exhibited remarkable affinities for the active pockets of SARS-CoV-2 Mpro, suggesting their potential utility as inhibitors for this critical viral protein. Intriguingly, when considering RdRp, AgNPs displayed superior binding affinity compared to AuNPs, indicating their specific potential in targeting this component of the virus. Conversely, when assessing their interactions with the S spike glycoprotein, AuNPs demonstrated greater binding affinities than AgNPs, with more pocket residues being involved in this interaction. The versatility of gold and silver nanoparticles extends far beyond virology, as these materials find applications in diverse fields, including medicine, electronics, and environmental remediation. The findings presented here underscore their potential as versatile antiviral agents, providing a promising avenue for further in vitro and in vivo research to explore their efficacy in inhibiting the replication of the SARS-CoV-2 virus.

sciforum-087163: Austricin from Langsat Kombucha: A Comprehensive In Silico Analysis of Its Potential as a Novel Anti-Alzheimer's Agent

Isdaryanti Isdaryanti [1], Alexander Kurniawan Sariyanto Putera [1] and Kennis Rozana [2]

[1] Biology Education Study Program, Faculty of Teacher Training and Education, Universitas Sulawesi Barat
[2] Biotechnology Studi Program, Faculty of Mathematics and Natural Science, The Learning University of Malang

Alzheimer's disease, a debilitating degenerative disorder, poses a formidable challenge in terms of treatment, with a projected surge in the number of afflicted individuals annually. The imperative quest for novel anti-Alzheimer's compounds derived from natural sources is underscored by the urgency to address this escalating health crisis. Austricin, identified in langsat kombucha, emerges as a promising candidate due to its demonstrated affinity for the muscarinic acetylcholine receptor M1 and anti-inflammatory properties. In this study, we conduct an extensive validation of austricin's potential through assessments of blood–brain barrier permeability, absorption, distribution, metabolism, and excretion. Additionally, we explore its binding capabilities with the pivotal protein steril-sulfatase, identified as a primary target in Alzheimer's pathology. Comparative analyses are performed with established compounds, donepezil and galantamine. Analysis reveals that austricin successfully traverses the blood–brain barrier (LogBBB −0.19498) with a solubility of 3.54e+00 mg/mL, high gastrointestinal absorption, and Lipinski's Rule of Five compliance. Importantly, it exhibits a bioavailability score of 0.55 and a synthetic accessibility of 4.60, establishing its potential as a viable drug candidate. The compound shows no substrate inhibition for major cytochrome P450 enzymes (CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4). Furthermore, molecular docking analyses reveal austricin's superior ΔG-binding affinity (−7.9 kcal/mol) compared to donepezil (7.4 kcal/mol) and galantamine (7.2 kcal/mol) for steril-sulfatase. While these findings suggest austricin's promise as an anti-Alzheimer's compound, further investigations on key Alzheimer's-associated proteins and in vitro testing are indispensable for conclusive validation and development. This study provides a foundation for the potential therapeutic application of austricin, paving the way for subsequent experimental endeavors and clinical investigations in the pursuit of effective Alzheimer's treatments.

sciforum-086664: Bioinformatic Analysis of the Anti-Cancer Effects of Safranal via the p53 Signaling Pathway in Cervical Cancer Cell Lines

Souandaou Athoumani Ali [1], Fatma Gül Özcan [2] and Ömür Karabulut Bulan [2]

[1] Department of Biology, Institute of Graduate Studies in Science, Istanbul University, Istanbul, Turkey
[2] Department of Biology, Faculty of Science, Istanbul University, Istanbul, Turkey

Cervical cancer is a widespread type of cancer among women worldwide, caused by an HPV virus infection. In recent years, researchers have focused on developing new targeted treatment approaches to reduce or eliminate side effects caused by standard treatment methods used in clinics. Our research aimed to investigate the p53 signalling pathways expressed in the genomic profile of HeLa and C-4 I using RNA sequencing after applying safranal. The goal is to explore the biological processes, molecular functions, and genes involved in that pathway.

To analyze the genome profile, we applied Safranal to the cervical cancer cell lines HeLa and C-4 I for 24 h. A sequencing library was created using the RNAs isolated at the end of the incubation period. After sequencing with the DNBEQ library, we analyzed p53 signaling pathways, KEGG pathways, Gene Ontology projects, cluster heat maps, and protein–protein interactions.

Based on KEGG and GO ontology, we found that safranal down-regulated the p53 signaling pathway in Hela and C-4 I cells. In total, 11 and 9 genes of HeLa and C-4 I, respectively, are involved in this pathway. We also observed safranal-induced cell cycle arrest in the G1 phase and induced apoptosis through extrinsic and mitochondrial pathways. Furthermore, we found that safranal inhibits angiogenesis and metastasis mechanism processes. Additionally, the effect of safranal on DNA has been discovered through the activation of DNA damage repair mechanisms. Finally, we used heat map cluster analysis to demonstrate the differential expression of genes in control and safranal-treated cells, and their functions were determined using the KEGG map.

In conclusion, these data showed that the application of safranal leads to the downregulation of p53 signaling pathway, which showed its potential anti-cancer effects on cervical cancer cell lines, HeLa and C-4 I

sciforum-086848: Bioinformatic Profiling of miRNAs in Coronary Artery Disease: Insights into Atherosclerosis and Inflammation

Ayesha Jabeen

Department of Biochemistry, Quaid-i-Azam University, Islamabad, Pakistan

Introduction

Coronary artery disease (CAD) stands as the predominant global cause of mortality. Inflammation and the formation of atherosclerotic plaques constitute the primary pathological processes underlying CAD. Triggered by deposited lipids and compromised endothelial integrity, immune cells become activated and mobilized, instigating the initiation of plaque formation. MicroRNAs (miRNAs), 22-nucleotide-long non-coding RNA molecules, play an important role in regulating gene expression and present promising prospects for groundbreaking therapeutic and atherosclerosis in CAD.

Method

This investigation employed the Genetic Testing Registry (GTR), sourced from the National Center for Biotechnology Information (NCBI), for the identification of genes associated with coronary artery disease (CAD) featuring inflammation and atherosclerosis. Subsequently, gene enrichment analysis was conducted using ShinyGO, and predictions of conserved 8-mer miRNA targets were made utilizing three tools: TargetScan, miRWalk, and miRBase.

Results

Our data analysis unveiled a convergence of targeted miRNAs that were shared among genes associated with coronary artery disease (CAD), atherosclerosis, and inflammation. Noteworthy examples include miR-218-5p/96-5p/9-5p/20-5p/93-5p/106-5p/519-3p/506-3p/124-3p.2. These miRNAs exhibit the potential to play a pivotal role in the development of highly effective therapeutic approaches. Additionally, a distinct set of miRNAs, encompassing miR-19-3p/195-5p/29-3p/181-5p/27-3p/200a-3p/107/199-3p, was identified specifically for CAD and atherosclerosis. Similarly, miRNAs, such as miR-15-5p/424-5p/101-3p.2/30-5p/21-5p/124-3p.1, were selected for CAD and inflammation examination. Remarkably, these miRNAs were found to be common, targeting more than one gene in each pathological condition.

Conclusions

In conclusion, our findings highlights potential miRNAs that hold promise for enhancing therapeutic strategies against coronary artery disease (CAD) featuring inflammation and atherosclerosis. However, further research is warranted to assess their specific potential for each respective condition.

sciforum-087211: Bioinformatics Analysis of Gene Expression Profiles of Triple-Negative Breast Cancer from the African-Descent Population

Suneetha Yeguvapalli and Kumaraswamy Naidu Chitrala

Department of Engineering Technology, University of Houston, Sugar Land, TX 77479, USA

Background

Triple-negative breast cancer (TNBC) is the most aggressive form of breast cancer among the breast cancer subtypes. Race plays a crucial role in TNBC, with a African American (AA) women having higher incidence rates compared to European Americans (EAs). In the present study, we aim to analyze differentially expressed genes (DEGs) among African Ghanaian (AG), African Ethiopian (AE), and African American populations using the bioinformatics approach.

Material and Methods

Gene expression profiles for Ghanaian, Ethiopian, and African American populations were downloaded from the GEO database. DEG analysis was performed using GEO2R. Tumor-infiltrating immune cells were analyzed for the DEGs using TIMER. Upstream regulatory networks from signatures of DEGs were identified using X2kweb.

Results

Our results showed that 863 genes were differentially expressed between AA versus AE, 160 genes were differentially expressed between AE versus AG, and 35 genes were differentially expressed between AA versus AE. Among the identified DEGs, genes *CSF3, CXCL2, CXCL3, PRKCB,* and *PTGER4* were found to be common among all the population groups. Further, gene enrichment analysis on the DEGs showed that these genes were found to be significantly enriched among the B-cell receptor signaling, B-cell differentiation, and B-cell activation pathways.

Conclusions

These findings indicate that these genes could be potential immune biomarkers for identifying TNBC in the African-descent population.

sciforum-089219: Bioinformatics Analysis of the Actin Interactome

Yakov I. Mokin, Olga I. Povarova, Iuliia A. Antifeeva, Konstantin K. Turoverov, Irina M. Kuznetsova and Alexander V. Fonin

Laboratory of Structural Dynamics, Stability and Folding of Proteins, Institute of Cytology, Russian Academy of Sciences, 4 Tikhoretsky Ave., 194064 St. Petersburg, Russia

Actin is a key protein of the muscle contraction system. It is present in the cytoplasm, providing motor and framework function through polymerization into F-actin, as well as in the nuclei of all non-muscle cells, where most actin is present in a globular form and participates in processes related to the cell's genetic apparatus, including transcription and DNA repair. Actin interacts with a large number of proteins that form a whole class of actin-binding proteins. Since the functional role of nuclear actin differs significantly from the role of actin in the cell cytoplasm, the goal of this study was to compare the interactome of cytoplasmic and nuclear actin.

Using the BioGRID and StringDB databases, proteins that interact with actin experimentally confirmed were selected. Four groups of actin-binding proteins were identified depending on their cellular localization: only cytoplasm, only nucleus, and nucleus and cytoplasm, and others. The analysis of biological processes in the interactome showed that nuclear proteins participate in most key nuclear processes,from DNA damage response to transcription regulation, while cytoplasmic actin-binding proteins are involved in the formation, regulation, and functioning of the cytoskeleton. The analysis of the structure of actin-binding proteins showed a large proportion of internally disordered proteins, most of which are part of membraneless organelles (MLOs). It is known that proteins prone to liquid–liquid phase separation (LLPS) play a key role in the formation of MLOs. Interestingly, although significantly more nuclear proteins are prone to LLPS than cytoplasmic proteins (44% vs. 25%), the drivers of the formation of MLOs in the cytoplasm are significantly (four times) more than in the nucleus. From the pool of actin-binding proteins, 28 clusters were identified, within each of which proteins are capable of forming physical contacts with each other.

The work was supported by the Russian Science Foundation (project No. 23-15-00494, IMK).

sciforum-083780: Biomolecules against SARS-CoV-2 Main Protease, RdRp and the RBM of Its Spike Glycoprotein: An In Silico Approach

Ilyes Zatla and Lamia Boublenza

University of Tlemcen

Severe acute respiratory syndrome coronavirus 2 emerged in Wuhan, China, in December 2019, marking the onset of a profound global health crisis. The unprecedented scale of the ensuing pandemic prompted an urgent need for innovative strategies to combat COVID-19. In response, researchers and scientists worldwide directed their efforts towards identifying effective preventive and therapeutic measures. Among these, natural products have gained prominence due to their potential in offering a holistic approach to tackling the virus. This study undertook a rigorous computational approach to sift through a vast array of natural compounds, aiming to pinpoint those with promising antiviral properties against the SARS-CoV-2 main protease, RdRp and the RBM of the spike glycoprotein. Through sophisticated molecular docking simulations, this study investigated the intricate interplay between selected natural compounds and virus targets. This analysis encompassed diverse factors such as binding affinity, interaction dynamics and structural compatibility within the active sites of the target protein. The encouraging results provide a solid foundation for further in-depth exploration, including experimental validation and refinement of these compounds as potential therapeutic agents against COVID-19. The identification of novel natural antiviral compounds presents a beacon of hope for global health, offering new avenues for combatting SARS-CoV-2 and future potential viral threats. As these findings pave the way for future drug design strategies, they reinforce the collaborative and interdisciplinary approach needed to triumph over the challenges posed by COVID-19.

sciforum-087217: Computational Drug Repositioning of Mast Cell Stabilizers against Human Protease-Activated Receptor 2 (PAR2) Involved in Rheumatoid Arthritis

Khushboo Choudhury [1], Dr. Ram Singh Purty [2] and Kanika Khoba [3]

[1] Nirvasa Healthcare Pvt. Ltd.
[2] Associate Professor, University School of Biotechnology, Guru Gobind Singh Indraprastha University, New Delhi, India
[3] Ph.D. Scholar, University School of Biotechnology, Guru Gobind Singh Indraprastha University, New Delhi, India

Introduction

Protease-activated receptor 2 (PAR2) plays a pivotal role in activating pain and inflammation pathways in rheumatoid arthritis (RA), contributing to cartilage destruction, synovial inflammation, and heightened joint pain. This study aims at identifying mast cell stabilizers with potential functionality in inhibiting PAR2 activation, focusing on FDA-approved candidates for their safety and efficacy.

Methods

Twelve mast cell stabilizers were selected based on toxicity screening and clearance time from PubChem. Molecular docking simulations were performed, assessing their interactions with the PAR2 molecule. Docking scores were meticulously analyzed to identify potential candidates with superior functionality compared to existing RA treatments, namely, Bicalutamide and Methotrexate. Lipinski's rules of drug validity were applied to ensure drug-like properties.

Results

Among the mast cell stabilizers, S-Azelastine and Cromoglicic acid exhibited superior functionality, surpassing Bicalutamide and Methotrexate. The evaluation considered patient safety aspects and the efficacy of inhibiting PAR2 activation. Notably, the selected mast cell stabilizers demonstrated compliance with Lipinski's rules, indicating their potential suitability for drug development.

Conclusions

This study highlights PAR2 as a promising target for drug repurposing in RA treatment. Mast cell stabilizers, particularly S-Azelastine and Cromoglicic acid, show potential for safer pain management in RA patients. Their superior functionality, especially in PAR2 inhibition and patient safety, suggests a viable avenue for drug repurposing strategies. Further exploration and development of these mast cell stabilizers could lead to novel therapeutic options for RA, addressing the critical need for more effective and safe pain management strategies in this patient population.

sciforum-089263: Computer-Aided Evaluation of Two Fluorescent Hexanoic Acid Piperazineamides as Potential Ligands for Insect Cytochromes P450

Yaroslav Faletrov [1,2], Polina Yakovets [1,2], Liliya Glinskaya [1] and Vladimir Shkumatov [1,2]

[1] Laboratory of biochemistry of drugs, Research Institute for Physical Chemical Problems of the Belarusian State University
[2] Faculty of Chemistry of the Belarusian State University

Insects represent a variable big class of animals on Earth, playing important roles as pests, model organisms for scientific researches devoted to, for instance, pesticide development, brain functions and pathologies like Alzheimer and Parkinson deseases. Insect have cytochromes P450, an unique class of monooxygenases, which are responsible for reactions of fatty acids conversion into hormone-like substances or cuticular hydrocarbons as well as to destroy pesticides.

Previously we reported about synthesis of two fluorescent hexanoic acid piperazineamides, namely, N-hexanoyl-N'-(7-nitrobenzofurazan-4-yl)-piperazine (NpipHex) and N-hexanoyl-ciprofloxacin (CPFHex) with ability to fluoresce. Because of no available experimentally-solved structures of insect P450s we have created a small library (120 structures) of the enzymes from *Lucilia cuprina* and *L. sericata* (a polinator and a cause of cattle myiasis), *Locusta migratoria* (a pest) using AI-based platform AlphaFold and AlphaFold2/GoogleColab. Autodock Vina (AV) together with authored helper software for highthroughput virtual screening (HTVS) FYTdock were used for both hem residues positioning and docking of the derivatives. It was found that affine binding with AV scores -9 and less were found, for instance, for NpipHex and CYP6a8 of *L. cuprina* (Uniprot id A0A0L0CMB2, score -9.9), which *Drosophila* homologue has been recently described as fatty acid hydroxylase, CYP12A7 of *L. cuprina* (Uniprot id A9X930, score -9.8) and CYP307A2 of *D. melanogaster* (A8Y592, score -9.9).

Taking togeter, we have created a virtual library of some insect P450s models suitable for HTVS and found potential new affine interactions with our fluorescent hexanoic acid derivatives opening a way of in silico estimation of their new biological properties with respect to development of new pest control tools.

This study was supported by GSPSR (Belarus) № 20210560.

sciforum-087228: Development of Quinazolinone Derivatives as Dual Target Inhibitors against Alzheimer's Disease Using MTDL Strategies, Molecular Docking, and Dynamic Simulation

Bandita Datta and Saumya Dasgupta

Department of Chemistry, Amity Institute of Applied Sciences Amity University—Kolkata Campus, Major Arterial Road (South-East), Action Area II, Newtown, Kolkata 700135, West Bengal, India

The identification of novel drugs for neurodegenerative diseases such as Alzheimer's and Parkinson's are complex as they are associated with more than one distinct cause and multiple disease mechanisms with multiple drug targets. For Alzheimer's disease (AD), despite extensive research, there are currently no drugs available that can improve clinical symptoms permanently and with moderate efficacy. Numerous target-specific chemical or biologic drugs, proposed earlier, were either abandoned due to their limited potency to a single mechanistic target enzyme or failed in clinical trials due to adverse side-effects and impaired blood--brain barrier efficacy. At this outset, finding an efficient multi-target drugs with adequate bioavailability and drug likeliness against this AD is essential. This work focuses on an in-house strategically designed database of quinazolinone derivatives and performed a detailed ADMET screening to explore the pharmacokinetic actions of the molecules. A select set of lead molecules were further probed into their sequential molecular docking towards the simultaneous inhibition of three therapeutic targets of AD (acetylcholinesterase, butyryl-cholinesterase, and β-secretase). The effort has successfully identified few novel inhibitors of AD pathogenesis with 'multi-targeted potency'. This finding opens the door for further research into these lead compounds as potential therapeutics for the efficient triple inhibition of three crucial enzymes of amyloid-based and cholinergic mechanisms for AD pathogenesis. The report additionally unlocks an innovative 'One Drug-Multiple Target' ligand construction approach to deal with the complicated multifunctional nature of AD.

sciforum-087322: Ecodetect Advanced Waste Sorting

Dr. G. Manjula [1], Chetan G. Kumar [2], Aishwarya K. J. [2], K. N. Bhanu Prakash [2] and V. Sai Chandan [2]

[1] Professor, Department of Information Science and Engineering, Dayananda Sagar Academy of Technology and Management, Bengaluru 560082, India
[2] B.E. Students, Department of Information Science and Engineering, Dayananda Sagar Academy of Technology and Management, Bengaluru, India

The contemporary world grapples with a critical issue—the effective management of waste. The surge in population and industrial activities has caused a substantial rise in waste generation, contributing to environmental degradation, resource depletion, and various sustainability challenges. In addressing this dilemma, the practice of garbage classification has emerged as a crucial solution. It plays a significant role in mitigating the adverse impacts of waste on the environment and fostering a more sustainable approach to waste management.

Our project addresses the critical issue of garbage classification by leveraging the YOLOv7 real-time object detection framework. The first step involves assembling a comprehensive dataset of garbage items and categorizing them into several distinct groups. To ensure precise categorization of the images, we adapt YOLOv7, a powerful tool for real-time object detection. This project encompasses various stages, including data collection, preparation, and labeling, with a particular emphasis on employing the most effective methods for data labeling—an essential step in the project.

Additionally, the process involves data preprocessing, model training, evaluation, and real-time inference. Via these comprehensive steps, our project aims to contribute to the advancement of garbage classification methodologies, ultimately promoting a more sustainable and efficient approach to waste management.

Furthermore, it is worth noting that some of the achieved values closely align with the performance of YOLOv4, a more advanced iteration of YOLOv3.

sciforum-089136: Elucidation of Molecular Mechanisms of *Vanda Roxburghii* (Family: Orchidaceae) in the Treatment of Alzheimer's Disease Utilizing Network Pharmacological Analysis

Nazifa Tabassum, Najneen Ahmed and Parisa Tamannur Rashid

Department of Pharmacy, Faculty of Science and Engineering, East West University, Dhaka 1212, Bangladesh

Vanda roxburghii (*VR*), a native medicinal plant in Bangladesh belonging to the Orchidaceae family, has been previously reported to be effective against Alzheimer's disease (AD). This study aimed to investigate the potential mechanism of the phytoconstituents of *VR* against AD using network pharmacology and molecular docking analysis. The phytoconstituents of *VR* were listed from several databases and their blood–brain barrier (BBB) permeability was predicted using SwissADME. Targets of the BBB permeable actives were predicted using SwissTargetPrediction and Similarity Ensemble Approach databases. The putative genes responsible for AD were obtained from GeneCards and DisGenet databases. The common targets for both *VR* and AD were scrutinized for how the protein–protein interaction (PPI) network was constructed using STRING and how the core protein targets were identified using Cytoscape. Gene ontology (GO) functions and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were performed on the target genes using DAVID. Finally, the binding interactions between the phytochemicals and targets of AD were validated by molecular docking using PyRx.

In total, 4 phytochemicals with 328 exclusive target genes were predicted to cross the BBB. Moreover, 1046 exclusive disease targets for AD were identified and 103 shared targets of *VR* and AD were acquired. From the PPI network, 5 targets with higher possibilities of therapeutic activity rates of *VR* on AD were obtained. Furthermore, 428 biological processes, 82 cellular components, and 98 molecular functions were enriched with GO functions, and 144 KEGG pathways (including Alzheimer's disease, apoptosis, and endocrine resistance pathways) were found enriched for *VR* associated with anti-AD activities and were analyzed. Molecular docking analysis further verified the definite binding capacity of the four actives with the five target proteins (APP, JUN, ESR1, MAPK1, and MAPK3) involved in the significant KEGG pathways and GO functions. Our findings provide directions for further research on the phytochemicals of *VR*.

sciforum-086533: Evaluating Kanchner Guggulu's Therapeutic Potential in Polycystic Ovary Syndrome: A Comprehensive Approach with Network Pharmacology, Transcriptomics, Docking, and MD Simulation

Subhajit Ghosh [1], Atanu Maity [2], Bratati Roy [1] and Subarna Thakur [1]

[1] Department of Bioinformatics, University of North Bengal, Darjeeling, West Bengal 734013, India
[2] Department of Bioscience and Biotechnology, Indian Institute of Technology, Kharagpur, West Bengal 721302, India

Introduction

Kanchnar Guggulu (KG) is a potent Ayurvedic remedy for hormonal imbalances, PCOS, ulcers, cystic swelling, and tumors. PCOS is clinically significant, impacting one in five women during their reproductive years, leading to infertility, hyperandrogenism, and metabolic issues like insulin resistance and obesity. This study aims to explore KG's mechanism of action and investigate its potential therapeutic targets for PCOS.

Methodology

The formulation's phytochemicals were screened utilizing online databases such as IMPPAT, TCMSP, and literature mining. Subsequently, an ADME analysis was performed to screen the drug potential of the phytochemicals. Targets of the active ingredients were identified using databases like Similarity Ensemble Approach (SEA) and Swiss Target Prediction (STP). A transcriptomics analysis validated therapeutic targets, followed by gene ontology, pathway enrichment analyses, and PPI network establishment. Molecular docking was performed to visualize the interactions between the active molecules and network hub genes. The top three docked complexes were subjected to 250 ns MD simulation and GBMV analysis.

Results

The initial database-based screening identified 643 active ingredients, with 413 remaining post ADME analysis. Initially, 171 potential targets were identified from STP and SEA, of which 55 were differentially expressed in PCOS based on the transcriptome analysis. Top enriched pathways encompassed lipid and atherosclerosis, HIF-1 signaling, estrogen signaling, insulin signaling, etc. The toxicology-based screening process efficiently narrowed down a conclusive set of 83 bioactive molecules. These molecules were then subjected to computational docking with eight targets identified as hubs in the PPI analysis. The top three docked complexes identified were retinoic acid receptor (RAR)–curcumene, estrogen receptor (ESR)–shogaol, and platelet-activating factor receptor (PTAFR)–siphonodiol. Finally, the relative stability of the docked complexes was validated using MD simulation.

Conclusions

Our results not only validate the clinical efficacy of KG in treating PCOS but also establish a basis for subsequent experimental investigations.

sciforum-088738: Exploring Carbendazim–Aptamer Interactions via In Silico Modeling and Molecular Dynamics Simulations

Ajay Yadav and Hariprasad P.

Environmental Biotechnology Lab, CRDT, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

Carbendazim (CBZ), a systemic fungicide, has been found in a variety of food and feed products, agricultural soil, and water bodies, raising concerns about its possible environmental and organismal effects. While aptamers have been identified as a viable detection approach, the fundamental mechanics of ligand binding in this context have not been thoroughly investigated. In this study, CBZ-specific aptamers (CZ1, CZ2, CZ5, CZ6, CZ12, and CZ13) with known sequences were used to evaluate the binding interactions of CBZ and the aptamer. The analysis entails an all-atom molecular dynamics (MD) simulation in an aqueous environment after ensemble molecular docking. Because this aptamer lacked 3D structural information, it was rebuilt using an in-house workflow. Multiple CBZ molecules were found in a putative binding area of the anticipated 3D aptamer structure. The aptamer-CBZ complex was subjected to a 100 ns MD simulation, which allowed for the investigation of component interactions. The internal loop of the aptamer was found to include CBZ-specific bases. A prominent interaction between the aptamer and CBZ for all the studied aptamers (CZ1, CZ2, CZ5, CZ6, CZ12, and CZ13) involved H-bonds, and a hydrophobic interaction between T-shaped Pi-Pi and Pi-alkyl was observed throughout the MDS. The binding energies (BE, kJ/mol) recorded for the aptamer-CBZ complexes CZ1, CZ2, CZ5, CZ6, CZ12, and CZ13 were -136.66 ± 2.27, -93.81 ± 1.92, -67.53 ± 4.25, -86.16 ± 1.75, -52.29 ± 3.86, and -90.03 ± 1.96 respectively. This study advances our understanding of ligand--aptamer interactions. The established workflow makes it easier to create and explore new fascinating ligand--aptamer complexes.

sciforum-086050: From Function to Drug Discovery: Insights into Hypothetical Protein Rv1979c from Mycobacterium Tuberculosis

Mohamed Asif Shajahan and Tamilvanan Thangaraju

SRM DBT Platform, SRM Institute of Science and Technology

Mycobacterium tuberculosis is the causative agent of tuberculosis (TB), a highly contagious disease affecting millions of individuals globally. The emergence of drug-resistance becomes a significant obstacle in the treatment of tuberculosis (TB). The *Mycobacterium tuberculosis* protein Rv1979c has been implicated in drug resistance, yet its function and potential inhibitors remain largely unexplored. In this study, we employed a comprehensive computational approach to unravel the role of Rv1979c and identify potential inhibitors from natural sources.

The investigation was initiated by revealing the three-dimensional structure of Rv1979c via the Threading/Fold recognition method. Subsequently, a functional analysis of its molecular mechanism using a variety of computational tools yielded valuable insights. In addition, we screened a diverse collection of 11,708 phytochemicals against the Rv1979c target to identify potential inhibitors followed by molecular dynamic simulation. This exhaustive screening and simulation led to the identification of several prospective phytochemical candidates with significant binding affinity to the protein, indicating their potential as Rv1979c inhibitors.

This interdisciplinary study combines computational biology and drug discovery techniques to cast light on the function of Rv1979c and reveal potential strategies for combating pathogenesis in M. tuberculosis. The findings provide a foundation for further experimental validation and the development of novel therapeutic agents to address the evolving challenges of TB drug resistance.

sciforum-087230: Functional and Structural Annotation of Uncharacterized Lysine Methyltransferase Proteins in *Candida auris*

Himanshu Kishore Prasad

Department of Lifescience & Bioinformatics, Assam University, Silchar 788011, Assam, India

Introduction

Candia auris is a fungal pathogen that has emerged as a global threat in recent years due to its resistance to multiple antifungal drugs and its ability to cause invasive infections, especially in immunosuppressed patients. Understanding the molecular mechanisms of pathogenesis and drug resistance in *Candida auris* is crucial for the development of effective treatment strategies. The role of lysine methyltransferases, particularly the SMYD family, in the regulation of gene expression and protein function is of great interest in the context of fungal pathogenesis. Investigating the potential involvement of SMYD proteins in *Candida auris* could provide valuable information on the mechanisms underlying its virulence and drug resistance.

Methods

In this paper, the uncharacterized SMYD family proteins of *Candida auris* are considered for in silico functional and structural characterizations. Using a combination of sequence analysis, structural modeling, and phylogenetic profiling tools, the intricate annotation process of lysine methyltransferases will be thoroughly explored.

Results

The structural similarities between the SMYD members in *Saccharomyces cerevisiae, Candida albicans,* and their human counterparts suggest that studying the function of Set5 and Set6 in yeast could provide relevant information about the role of SMYD proteins in chromatin association, genome stability, and gene expression regulation. Further, the *Candida auris* SMYD family was expanded with a novel, uncharacterized member. This member was functionally characterized using protein sequences, phylogeny, structural modelling, and binding studies.

Conclusions

The study provides knowledge about SMYD methyltransferase proteins in *Candida auris* using in silico approaches, shedding light on their physiological roles. In conclusion, the emerging role of SMYD proteins in various physiological processes and their implications in cancer pathophysiology, combined with their potential involvement in fungal pathogenesis, highlight the importance of further research on members of the SMYD protein family in various biological systems.

sciforum-086264: Genetic Variant Screening and Association Study of *NKX2-5* in Congenital Heart Disease Patients from North India

Shadab Ahamad [1], Prachi Kukshal [1], Ajay Kumar [1] and Subramanian Chellappan [2]

[1] Sri Sathya Sai Sanjeevani Research Foundation, Palwal 121102, Haryana, India
[2] Sri Sathya Sai Sanjeevani International Centre for Child Heart Care & Research, Palwal 121102, Haryana, India

Background

Globally, 1% of all live births are affected by some form of congenital heart anomaly. Genetics and the environment both play a role in its causation, but very few of these aspects have been explored in the Indian subcontinent. One of the first and key transcription factors required for the formation of the heart during fetal development is *NKX2-5.* Several mutations in this gene have been identified for CHDs. In this study, we screened for known and novel variants to understand their role in CHDs.

Methods

Two exons and flanking 3′ and 5′ UTR regions of *NKX2-5* were sequenced in n = 71 CHD cases, followed by a case–control test of association and a haplotype study.

Results

Only three known variants, namely rs2277923 (c.63A > G), rs3729753 (c.606G > C), and rs703752 (c.61G > T), were identified in a total of n = 69 cases. The case–control test of association revealed no significant allelic or haplotypic association. A genotypic association was observed for rs703752 in a recessive model (χ^2 = 4.4702; p = 0.03; risk score = 0.33), along with a trend of association for rs3729753 (χ^2 = 3.73; p = 0.053; risk score = 1.68) and rs703752 (p = 0.082).

Discussion

Although we did not identify any new mutations in the coding regions of NKX2-5 gene, our findings are important observations for establishing an association between *NKX2-5* variants and cardiac defects in the context of the north Indian population. There is a need to explore the roles of other transcription factors and cardiac developmental pathways and establish their interaction and role in disease biology in the Indian subcontinent.

sciforum-088607: High Endomucin Expression Correlates with a Favorable Immune Landscape and Improved Survival in Clear-Cell Renal Cell Carcinoma (ccRCC)

Abdulmalek Abu Zahra

Medical Laboratory Science Department, Jordan University of Science and Technology, Ar-Ramtha 22110, Hashemite kingdom of Jordan

Endomucin (EMCN) contributes to both cell adhesion and signaling processes, thereby participating in the modulation of immune responses within the vasculature. In this study, we uncover how EMCN modulates the tumor immune microenvironment in clear-cell renal cell carcinoma (ccRCC).

The Cancer Genome Atlas (TCGA) was used to obtain clinicopathological and expression data on KIRC. The prognostic significance of EMCN expression in ccRCC was assessed through univariate analysis. DNMIVD was used to investigate the methylation status of EMCN in tumor and normal adjacent tissue (NAT). TCGExplorer was utilized to employ GSEA to identify pathways enriched by the high or low expression of EMCN. Hallmark Gene sets from MSigDB were utilized. The immune microenvironment was evaluated using the Tumor IMmune Esti-mation Resource (TIMER 2.0).

High EMCN expression was associated with heightened overall survival and better survival (HR: 0.60, 95% CI: 0.52–0.68, p 0.0001) in the TCGA ccRCC cohort. The promoter region of EMCN was hypermethylated in tumor tissue, in contrast to normal adjacent tissue, with an increased beta value of 0.13715 (p 0.001) associated with decreased expression of EMCN in tumor tissue compared to NAT. The top three enriched GSEA terms when EMCN was highly expressed were hallmark_TGF_beta_signaling, KRAS_signalling_up, and Apical_junction. In contrast, when the expression of EMCN was low, E2F_targets, Oxidative_phosphorylation, and MYC_targets_v2 were the top terms. EMCN expression was positively correlated with resting memory CD4 + T cells ($\rho = 0.217$, $p = 2.68 \times 10^{-6}$), naïve B cells ($\rho = 0.273$, $p = 2.43 \times 10^{-9}$), plasma B cells ($\rho = 0.158$, $p = 6.73 \times 10^{-4}$), M1 macrophages ($\rho = 0.167$, $p = 3.05 \times 10^{-4}$), Monocytes ($\rho = 0.29$, $p = 2.17 \times 10^{-10}$), resting NK cells ($\rho = 0.208$, $p = 6.39 \times 10^{-6}$), activated mast cells ($\rho = 0.373$, $p = 1.05 \times 10^{-16}$), and M2 macrophages ($\rho = 0.127$, $p = 6.45 \times 10^{-3}$). It correlated negatively with Tregs ($\rho = -0.349$, $p = 1.23 \times 10^{-14}$), activated memory CD4+ T cells ($\rho = -0.17$, $p = 2.42 \times 10^{-4}$), follicular helper T cells ($\rho = -0.209$, $p = 6.20 \times 10^{-6}$), neutrophils ($\rho = -0.101$, $p = 3.07 \times 10^{-2}$), M0 macrophages ($\rho = -0.333$, $p = 2.15 \times 10^{-13}$), and memory B cells ($\rho = -0.217$, $p = 2.53 \times 10^{-6}$).

sciforum-089270: Identification of New Potential Cyclooxygenase-2 Inhibitors via Structure-Based Virtual Screening, Molecular Dynamics and Pharmacokinetic Modelling

Imene Derardja [1], Redouane Rebai [2], Mohamed Essedddik Toumi [3], Farouk Fethi Kebaili [3] and Abdennacer Boudah [2]

[1] Laboratory Promotion of Innovation in Agriculture in Arid Regions (PIARA), Faculty of Nature and Life Sciences, University of Mohamed Khider, Biskra, Algeria
[2] Laboratory of Biotechnology, National Higher School of Biotechnology, Constantine, Algeria
[3] Laboratory of Microbiological Engineering and Application, Department of Biochemistry and Molecular and Cellular Biology, University of Mentouri Brothers, Constantine, Algeria

Non-steroidal anti-inflammatory drugs (NSAIDs) are a class of drugs commonly used worldwide for their analgesic and antipyretic effects. However, an overdose of NSAIDs can have negative effects on various systems, including the cardiovascular, gastrointestinal, hepatic, renal and neural systems. The search for new, safer and more effective anti-inflammatory agents has now become a necessity. The aim of the present study is to identify new natural compounds that act against cyclooxygenase-2 (COX-2), one of the main anti-inflammatory targets, by means of computational approaches. For this purpose, molecular docking and MM/GBSA binding free energy calculations were utilized to discover new natural inhibitors for COX-2. In addition, several prediction tools, such as SwissADME server, QikProp and Pro-Tox II were used in this study to elucidate the pharmacokinetic properties, drug-likeness ability, safety and the lethal dose (LD50) of the studied compounds.

The results of molecular docking have indicated that among all phytochemicals under examination, Canniprene, Oroxylin A and Luteolin have shown high docking score and binding affinity toward COX-2 (-10.587, -10.254 and -9.494 Kcal·mol^{-1}, respectively) when compared with the reference inhibitor. Moreover, the top hits demonstrated stability during molecular dynamics simulation and were found to conform to drug-like rules with good bioavailability. Toxicity parameters of the best hits indicate that these compounds could be safe COX-2 inhibitors, but further in vitro and in vivo studies are needed to confirm these findings.

sciforum-089281: In Silico Antimicrobial Potential of Some Flavonoids from *Retama sphaerocarpa*: Molecular Docking Studies, Pharmacokinetics and Toxicity Prediction

Derbali Safia and Benmeddour Tarek

Department of Nature and Life Sciences, University of Biskra, P.O. BOX 145 RP, 07000, Biskra, Algeria Laboratory of Genetics, Biotechnology and Valorization of Bioresources (LGBVB), University of Biskra, Algeria

Flavonoids are one of the largest classes of secondary metabolites that have been shown to be potent antimicrobials against a wide range of pathogenic organisms in vitro. The interest in the antimicrobial properties of flavonoids and their use to treat human diseases has increased with respect to plants that synthesize these compounds as a response to microbial infection. The objective of this study was to evaluate the antimicrobial potential of certain flavonoids from an Algerian medicinal plant. A molecular docking study against DNA Gyrase Topoisomerase II (E. coli, PDB ID: 1Kzn), Penicillin Binding Protein 3(PDB ID: 3Vsl), Cytochrome P450 14 alpha-sterol Demethylase (PDB ID: 1EA1) and N-Myristoyl Transferase (PDB ID: 1Iyl) was performed to assess the antimicrobial effects of the selected compounds. In addition, the parameters of bioavailability, pharmacokinetics and toxicity were estimated. According to computational studies, the highest scores were presented by quercetin-3,7-di-O-glucoside, vicenin-2 and vitexin, indicating a good binding affinity towards the tested targets. The docking score values of quercetin-3,7-di-O-glucoside against 1Kzn, 3Vsl, 1EA1 and 1Iyl were in theorder of -8.110, -10.285, -13.101 and -15.043 Kcal·mol^{-1}, respectively. Vicenin-2 showed binding affinity toward 1Kzn, 3Vsl, 1EA1 and 1Iyl with scores equal to -7.507, -11.125, -13.465 and -14.094 Kcal·mol^{-1}, respectively. Finally, the docking scores of vitexin against 1Kzn, 3Vsl, 1EA1 and 1Iyl were -6.950, -7.944, -12.592 and -12.728 Kcal·mol^{-1}, respectively. The in silico investigation shows that by targeting specific proteins, the best hits have significant anti-antimicrobial activity; however, more studies are required.

sciforum-089287: In Silico Insights into Acetylxylan Esterase Diversity: Decoding Its Role in Hemicellulose Deacetylation for Enhanced Biofuels Generation

Radu Tamaian, Corina-Teodora Ciucure and Elisabeta-Irina Geană

ICSI Analytics, National Research and Development Institute for Cryogenic and Isotopic Technologies—ICSI Rm, Vâlcea

The enzymatic hydrolysis of hemicelluloses and acetyl groups stands as a cornerstone in biofuels production, with profound implications for bioethanol and bio-hydrogen generation. Emphasizing the resilience of hemicellulose and cellulose, resilient biopolymers that comprise biomass, this study delves into the in silico exploration of acetylxylan esterase (EC 3.1.1.72), a pivotal member of carboxylic esterase hydrolases (EC 3.1.1), to unveil its crucial role in the deacetylation of xylans and xylo-oligosaccharides.

Employing a multidimensional approach, we meticulously scrutinized three-dimensional structures, encompassing X-ray crystallography-determined and AlphaFold-predicted models of acetylxylan esterase. Microorganisms under investigation include *Trichoderma reesei*, *Acetivibrio thermocellus*, *Cellvibrio japonicus*, *Flavobacterium johnsoniae*, *Thermoanaerobacterium saccharolyticum*, *Clostridium cellulovorans*, and *Caldicellulosiruptor saccharolyticus*.

Molecular docking and dynamic simulations were conducted to unravel the intricate interactions between acetylxylan esterase and a diverse array of chemically modified xylopyranoside ligands. These ligands, embodying various acetylation patterns, were derived from xylopyranoside, a resilient component of hemicellulose. Significantly, the strategic cross-referencing of targets from ExplorEnz, BRENDA, UniProtKB, RCSB-PDB, and PubChem databases played a pivotal role in enriching the investigation.

This exploration provides profound insights into the substrate specificity of acetylxylan esterase, underscoring its potential role in the deacetylation of diverse substrates. Furthermore, the study offers a comprehensive analysis of biotechnologically relevant applications, spanning industrial-scale enzyme production, cellulolytic and ethanologenic capabilities, and biohydrogen production, intricately linked to the investigated variants of acetylxylan esterase.

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sciforum-087142: In Silico Study of Combined Docking and Molecular Dynamics Simulation for Hops (*Humulus lupulus*) Active Compounds in Inhibiting Duffy-Binding Protein (DBP) as Anti-*Plasmodium vivax* (*P. vivax*)

Gusnia Meilin Gholam [1,2], Maheswari Alfira Dwicesaria [1], Riyan Alifbi Putera Irsal [1] and Muhammad Marsha Azzami Hasibuan [1]

[1] Department of Biochemistry, Faculty of Mathematics and Natural Sciences, IPB University, Bogor 16680, Indonesia
[2] Bioinformatics Research Center, Indonesian Institute of Bioinformatics (INBIO Indonesia), Malang, East Java 65145, Indonesia

Malaria is one of the infectious illnesses causing a public health burden worldwide. *Plasmodium vivax* (*P. vivax*) is the most prevalent malaria parasite in Asia and Asia Pacific. *P. vivax* is resistant to sulfadoxine–pyrimethamine (SP) and mefloquine. This resistance makes it extremely difficult to control and eradicate due to its ability to survive in the liver and reactivate if the person infected has a weakened immune system. Thus, this study aims to inhibit *P. vivax* via targeting Duffy-binding protein (DBP) with active compounds from Hops (*Humulus lupulus*). The inhibition of DBP is essential to reduce malaria invasion of human red blood cells. We performed a quality assessment and prediction of the active site of DBP to determine the effectiveness and prediction of ligands in inhibiting DBP. Furthermore, the mechanism and structural stability of active compounds against DBP were evaluated using a combination of molecular docking and molecular dynamics simulation and a density-functional theory (DFT) study. The results showed that rutin had the highest binding of 8.852 kcal/mol. However, after the molecular dynamics simulation was run for 50 ns, the ligand 6-prenylnaringenin via MM-PBSA calculation showed the most positive value of 106.760 kJ/mol. In addition, 6-prenylnaringenin is the most stable ligand via the analysis of root-mean-square deviation backbone (RMSDBb), root-mean-square deviation c-alpha (RMSDCa), root-mean-square fluctuation (RMSF), solvent-accessible surface area (SASA), radius of gyration (Rg), and the hydrogen bond formation. We conclude that 6-prenylnaringenin has a tight and stable bond with the targeted DBP protein. Finally, we propose the use of 6-prenylnaringenin as a potential antimalarial compound via in silico studies.

sciforum-087971: Integrated Analysis of Glioblastoma: Unravelling Molecular Signatures across Diverse Datasets for Enhanced Diagnosis

Ezenwalie Ifechukwudelu Ezenwalie

Bioinformatics Department, Teesside University, Middlesbrough, United Kingdom

Background

Glioblastoma Multiforme (GBM) presents significant diagnostic and therapeutic challenges due to its complex molecular pathogenesis. Current diagnostic methods often fail to detect early molecular signatures critical for timely intervention. This study integrates microarray and RNA-Seq datasets from both serum and tissue samples to explore differentially expressed genes (DEGs) and protein–protein interaction networks with the aim of identifying robust biomarkers and understanding the molecular underpinnings of GBM.

Methods

Utilizing microarray datasets (GSE116520 and GSE90604) and RNA-Seq datasets (GSE165595 and GSE228512) from both brain tissue and serum samples, this study conducted integrative differential gene expression analysis using limma and DESeq2 packages. Functional annotation and gene ontology analyses were performed using DAVID and ShinyGO tools. Protein–protein interaction (PPI) networks were constructed using the STRING database and analysed via Cytoscape to identify central hub genes.

Results

The analysis and cross-technology validation highlighted 1,051 common DEGs across tissue datasets where 87 were upregulated and 255 were downregulated. Notably, three genes, *MAST3, ADAM11*, and *PTPRK*, were consistent across tissue and serum datasets, suggesting their utility as non-invasive biomarkers. Functional annotation identified critical biological processes and pathways disrupted in GBM, such as cell division, angiogenesis, and cell adhesion. The PPI network analysis identified central hub genes, offering insights into the molecular interactions contributing to the pathophysiology of GBM.

Conclusions

This study underscores a complex network of molecular interactions pivotal to the pathophysiology of GBM. The identified DEGs and pathways provide a foundation for developing diagnostic panels and therapeutic targets, emphasizing the need for further research to translate these biomarkers from bench to bedside.

sciforum-087208: Integrated Bioinformatics Analysis for Identifying Hub Genes and Therapeutic Targets in Recurrent Breast Cancer Liver Metastasis

Yuet-Hei Tyler Kwok and Kumaraswamy Naidu Chitrala

Department of Engineering Technology, University of Houston, Sugar Land, TX 77479, USA

Introduction

Breast cancer during advancement to the metastatic stage involves the liver, thereby diminishing the survival rate among 50% of cases. Currently, there are few therapeutic protocols for breast cancer liver metastasis (BCLM) available, thereby necessitating a deeper understanding of the molecular patterns governing this molecular mechanism. Therefore, in the present study, by analyzing the differentially expressed genes (DEGs) between primary breast tumors and BCLM lesions, we aim to shed light on the diversities of this process.

Methods

In this study, we investigated breast cancer liver metastasis relapse by employing a comprehensive approach that integrates data filtering, Gene Ontology and KEGG Pathway Analysis, Overall Survival analysis, identification of the alterations in the DEGs, visualization of the protein–protein interaction network, Signor 2.0, identification of positively correlated genes, screening results of the function of hub genes, immune cell infiltration analysis, copy number variant analysis, gene-to-mRNA interactions, transcription factor analysis, and identification of potential treatment targets.

Results

Our results showed two genes, *PCK1* and *LPL*, were differentially expressed between primary breast tumors and BCLM lesions. *PCK1* is a regulator of gluconeogenesis, and *LPL*, involved in lipid metabolism, impacts cancer cell energetics and biosynthetic capabilities. Elevated *PCK1* levels show a correlation with a poorer prognosis, indicating an aggressive phenotype. The transcription factors (*AR, PPARA, RXRA, RXRB,* and *RXRG*) regulating both genes offer insights into energy homeostasis, metabolism, and cell growth. Immune infiltration analysis suggests their collective role in modulating the tumor microenvironment, influencing immunosurveillance and evasion.

Conclusions

This study's integrative approach unveils metabolic reprogramming, suggesting altered *PCK1* and *LPL* expression are key in breast cancer metastasis recurrence.

sciforum-089006: Lung Cancer Biomarker Identification from Differential Expression Analysis Using RNA-Seq Data for Multitargeted Drug Designing

Syed Naseer Ahmad Shah [1] and Rafat Parveen [2]

[1] Department of Computer Sceince, Jamia Millia Islamia, New Delhi 110025, India
[2] Department of Computer Science, Jamia Millia Islamia New Delhi 110025, India

Lung cancer poses a significant global health challenge, causing most cancer deaths. It therefore necessitates a detailed exploration into its molecular intricacies in search of potential treatment targets. The strategy is to delay disease progression and to practice early intervention to reduce the number of patients that ultimately develop lung cancer. Therefore, promising novel biomarkers for early diagnosis are urgently required. We performed an RNA sequencing analysis of lung cancer, using the SRA database (SRR119055), with 60 samples, including 30 control and 30 tumorous samples. A DEG analysis of tumorous and healthy subjects was performed using Bioconductor in R with its other packages to transform and normalize all transcriptomic data. We identified important genes from the lung cancer samples which include five upregulated genes, namely, COL11A1, CTPS1, SULF1, SPP1, and DIO2, and five downregulated genes, which are EN1, ARRDC3-AS1, VEGFD, TMEM100, and PSEN1, from the network and their associated genes. We also identified two hub genes, PRKACB and TAOK1, responsible for cell proliferation, differentiation, apoptosis, and cytoskeletal dynamics. Furthermore, we repurposed the FDA-approved drugs as multitargeted inhibitors against all upregulated genes to inhibit the function of most genes, followed by DFT and MD simulation to validate their effectiveness in lung cancer.

sciforum-083739: Molecular Docking Studies of Extracts and Essential Oils Isolated from a Medicinal Plant of *Ammodaucus leucotrichus* as Potential Inhibitors of Rheumatoid Arthritis Disease

Djehiche Cheima [1], Benzidane Nadia [1], Arrar Lekhmici [1], Djeghim Hanene [2], Tebboub Mehdi [3] and Mokrani El Hasene [4]

[1] University Ferhat Abbas of Setif, Faculty of Sciences, Department of Biology, Serif, Algeria
[2] Biochemistry Laboratory, Division of Biotechnology and Health, Biotechnology Research Center (CRBt), Constantine, Algeria
[3] University Mentouri Brothers Constantine 1, Faculty of Science of Technology, Department of Mechanical Engineering, Constantine, Algeria
[4] University Mentouri Brothers Constantine 1, Faculty of Natural and Life Sciences, Department of Biochemistry and Cellular and Molecular Biology, Laboratory of Applied Biochemistry

Subject Description

Traditionally, it was thought that only human collagenases (matrix metalloproteinases-1, -8 and -13) were capable of initiating collagen degradation. Trypsin is also capable of cutting the triple helix of human collagens, and is at the root of rheumatoid arthritis.

Objectives

The trypsin inhibitor, is considered a valid target for the discovery of new active compounds for the treatment of rheumatoid arthritis. In this study, a series of 59 compounds from the methanolic extract of *A. leuchotruchus* identified by GC-MS were used for a molecular docking study to identify interactions between compounds and active site amino acids.

Methods

Network pharmacology was adopted to detect the active components of our medicinal plants obtained by PubChem in 3D form, and the main target in the treatment of RA was obtained from the PDB. Key components and the target were selected for molecular anchoring.

Results and Discussion

The evaluation of *Ammodaucus leucotrichus* seed extracts as potential anti-inflammatory and anti-arthritic agents involved employing methanol for the extraction of bioactive compounds. The extract underwent assessment through protease (trypsin) and protein (BSA, bovine serum albumin) denaturation inhibition assays. The methanol extract demonstrated trypsin inhibition of 85%, surpassing diclofenac (64.67%) at 125 µg/mL. GC–MS analysis revealed 59 and 58 secondary metabolites in the methanol extract, indicating diverse bioactive compounds. In silico docking studies identified 28 compounds with negative binding energies, suggesting potential trypsin inhibition. Notably, 2-hydroxyacetohydrazide showed superior inhibitory effects (−17.13 KJ/mol) compared to diclofenac (−13.01 KJ/mol). The methanol extract, particularly 2-hydroxyacetohydrazide, emerged as a promising candidate for rheumatoid arthritis (RA) treatment due to potent trypsin inhibition. SwissADME analysis highlighted favorable bioavailability attributes, with optimal size, polarity, solubility, and saturation for 2-hydroxyacetohydrazide. The BOILED-Egg model predicted blood–brain barrier permeation and gastrointestinal absorption, providing insights into druglikeness and bioavailability.

Conclusions

In summary, these findings propose the methanol extract as a promising candidate for anti-inflammatory applications, particularly in trypsin inhibition. The identified compound, 2-hydroxyacetohydrazide, shows promise as a potential drug candidate for rheumatoid arthritis treatment. Yet, rigorous mechanistic studies and validation are crucial to enhance our understanding of its therapeutic potential within the field of plant-base.

sciforum-086970: In Silico Prediction Tools for Cytochrome P450 Isoform Specificity: A Comprehensive Review and Model Evaluation

Yao Wei, Luca Palazzolo and Ivano Eberini

Department of Pharmacological and Biomolecular Sciences, University of Milan

In humans, cytochrome P450 (CYP450) enzymes play a pivotal role in catalyzing over 90% of the enzymatic reactions associated with xenobiotic metabolism. Accurately predicting whether interested chemicals act as substrates or inhibitors of different CYP450 isoforms can assist in preselecting hit compounds and optimizing lead compounds for further drug discovery and chemical toxicology study. This work embarks on a comprehensive overview of recently developed in silico prediction tools of CYP450 isoform specificity. We summarize information on these models by two major categories of computational approaches: structure-based and ligand-based. We also analyze various aspects of these models, including their datasets, algorithms, and performance metrics. Subsequently, we employ 100 of the most frequently prescribed drugs to evaluate ten prediction tools which were developed via different classical machine learning methods (e.g., support vector machine, random forest, learning-based approaches, etc.) or deep learning approaches (e.g., graph attention neural network and ESM-1b Transformer). We point out that deep learning-based models like admetLab and ESP can quickly and accurately predict results. However, the coverage and performance of the investigated models are constrained by the limited quantity and quality of their datasets. We discuss both the advantages and limitations of the evaluated models, providing guidance for selecting appropriate computational tools to carry out predictions, and highlighting trends in the field of computational CYP450 isoform specificity prediction.

sciforum-088001: Navigating the Digital Frontier: Revolutionizing Biomolecular Understanding Through Computational Ingenuity

Ujban M.D. Hussain Hussain [1], Aditya Wadalkar [1], Ishant Diwakar Dahake [1], Hrushikesh Ramkrushn Ghotkar [1], and Samiksha Sandeep Tammewar [2]

[1] Department of Pharmaceutical Sciences, The Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, India
[2] Priyadarshini J. L. College of Pharmacy, Nagpur, India

Introduction

Embark on a transformative journey into the heart of biomolecular complexity as we unravel the mysteries with the dynamic synergy of bioinformatics and computational biology. This review ignites curiosity by exploring how the digital realm has become a catalyst for groundbreaking insights, reshaping the landscape of biomolecular research.

Methods

In this digital odyssey, we unveil the cutting-edge methodologies propelling bioinformatics and computational biology to new heights. Immerse yourself in the world of algorithms and tools orchestrating the harmonious dance of data, predicting biomolecular interactions with unparalleled accuracy. Witness the magic of structural bioinformatics through molecular dynamics simulations, where biomolecules come to life in a virtual symphony of dynamic behaviors.

Results

Our review is a tapestry of recent triumphs, illustrating the impact of digital ingenuity on biomolecular exploration. From decoding the nuances of omics data to crafting intricate 3D portraits of biomolecules, the digital canvas reveals a deeper understanding of cellular processes. Experience the revelation of complex biomolecular networks through innovative systems biology approaches, offering a glimpse into the orchestrated chaos within cells.

Conclusions

As we venture into the digital frontier, this review culminates with a vision of transformative discoveries and innovations fueled by the dynamic duo of bioinformatics and computational biology. This is not just a journey of understanding; it is a gateway to personalized medicine, where biomolecular intricacies unlock bespoke therapeutic interventions. Amid challenges, the clarion call for collaborative exploration echoes, heralding a future where the digital canvas paints a vivid picture of biomolecular marvels.

sciforum-089282: New Targets for Natural Phytochemicals among Microbial Proteins Revealed via In Silico Methods

Yaroslav Faletrov [1], Polina Yakovets [2,3], Lilia Glinskaya (Pavlutc) [2] and Vladimir M. Shkumatov [2,3]

[1] Research Institute for Physical Chemical Problems, Belarusian State University, Minsk, Belarus; Faculty of Chemistry, Belarusian State University, Minsk, Belarus; Electronic address: yaroslav82@tut.by
[2] Research Institute for Physical Chemical Problems, Belarusian State University, Leningradskaya Str. 14, Minsk, Belarus
[3] Faculty of Chemistry, Belarusian State University, Leningradskaya Str. 14, Minsk, Belarus

Fungal infections have retained their status as a significant human health threat, resulting in the publication of the first fungal priority pathogens list by the World Health Organization. Thus, the development of new antifungals is essential in the mainstream of drug design to combat fungal infections. Computer-aided calculations have become a necessary part of works devoted to new drug design. Virtual libraries of structural files for both low-molecular electrophilic phytochemicals and proteins from *Saccharomyces cerevisiae* and *Candida albicans* have been created based on experimental databases as well as using the AlphaFold resource for some proteins with unsolved 3D structures. During the virtual screening process, many affine interactions were identified as having binding energies calculated using the Autodock Vina program of no more than −9 kcal/mol. In particular, ixerin D (Pubchem code CID101553163) from dandelion was predicted to bind to proteins with PDB structures codes 3of7, 5t94, 4uuy, 2cnq, 2zeu, and 3bnu, demonstrating the possibility of covalent modifications of CYS453. Inuloxin (CID102194603) was bound in silico to the protein with PDB code 5TZ1 and lactucin (CID442266) to the protein with PDB code 1IYL. Similar affine interactions of an unsaturated ketone (CID5318099) from Helichrysum and Orthosiphon aristatus were predicted using modeled protein structures with Uniprot database codes A0A1D8PEV1, A0A1D8PSE5, P29717, Q59U61, Q59YG2, Q5A5N0, A0A1D8PN96, and Q59Q43. These results have provided valuable insights into the possible repurposing of well-known phytochemicals with the aim of developing new tools for yeast infection management. The work was supported by the BRFFR (Belarus) grant X23MH-005.

sciforum-086950: Precision Drug Discovery from Zingiber Officinalis: Unraveling Therapeutic Insights for Rheumatoid Arthritis through Innovative In Silico Approaches and Controlled Release Strategies

Ujban Hussain [1] and Samiksha Sandeep Tammewar [2]

[1] Department of Pharmaceutical Sciences, The Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, India
[2] Priyadarshini J. L. College of Pharmacy, Nagpur, India

Aim

- To pioneer an innovative in silico exploration of Zingiber officinalis for Rheumatoid Arthritis, employing virtual screening to discern the impact of its chemical constituents on the cyclo-oxygenase receptor.

Objectives

- To identify ligands from Zingiber officinalis that exhibit high binding affinity towards the Cyclooxygenase receptor, aiming to contribute valuable insights into potential therapeutic agents for Rheumatoid Arthritis.
- To investigate the structural and dynamic aspects of the ligand-receptor interactions, providing a comprehensive understanding of the molecular mechanisms underlying the potential therapeutic effects against Rheumatoid Arthritis.
- To explore and characterize novel chemical entities within Zingiber officinalis, uncovering previously unrecognized candidates with promising binding affinity and therapeutic potential for Rheumatoid Arthritis.

Material and Methodology

Ginger-derived ligands were prepared by retrieving smiles from Pubchem, sketching 2D structures on Chemsketch, and optimizing results with Avogadro.

COX1 and COX2 receptors, obtained from a protein data bank, were visualized in PyMol and prepared using Autodock Vina. Virtual screening in PyRx involved ligand and macromolecule conversion, grid selection, and Molinspiration for property calculation, including acute oral toxicity prediction with Protox II.

Result and Discussion

In silico studies revealed that all the synthesized molecules show good binding affinity toward the target protein ranging from -9.3 to -5.5.

Conclusions

The studies revealed that quercetin has higher binding as compared to the standard drug of rheumatoid arthritis i.e., ibuprofen. The ADME and toxicity studies also show positive results. Hence, this study has widened the scope of developing quercetin as a promising drug for rheumatoid arthritis

sciforum-089201: Repurposing of Drug Candidate against the Nucleocapsid Protein of Chandipura Virus

Rajamanikandan Sundarraj [1] and Shankari Gopalakrishnan [2]

[1] Associate Professor, Department of Biochemistry, Head, Center for Drug Discovery, Karpagam Academy of Higher Education, Coimbatore-641 021, Tamilnadu, India
[2] Research Scholar, Department of Biochemistry, Karpagam Academy of Higher Education, Coimbatore-641021, Tamilnadu, India

Introduction

Chandipura virus (CHPV) is a vesiculovirus that is a member of Rhabdviridae and is an encephalitic pathogen responsible for numerous epidemics in Central and Western India. The virus affects the brain and central nervous system mainly in children under 15 age of years, leading to neurological dysfunctions. Vectors that include sand flies, mosquitoes, and ticks are the main culprits in the transmission of CHPV. Five structural proteins (N, P, M, G, and L) encode the viral genome. The nucleocapsid protein N (N protein) encapsulates the viral genomic RNA in an RNase-resistant state, which plays a crucial role in the viral life cycle. Currently, no effective vaccine or therapeutics are available to treat the viral infection, and therefore efficient interventions are urgently needed.

Methods

The repurposing of drugs is one of the best possible ways to controlCHPV infections in India and other parts of the world. In this study, we used a structure-based virtual screening approach by using FDA-approved drugs against the nucleocapsid protein of CHPV. The docking process identified a few drug candidates, which showed potent binding affinity towards the N protein. We used the Schrödinger Desmond v3.0 module; to compute the relative binding energies of ligands, we used the premier mm-GBSA module.

Results

Based on a short molecular dynamics simulation and prime MM-GBSA analysis, we identified Adrabetadex, Hydroxypropyl betadex, Beta-1,2,3,4,6-penta-O-Galloyl-D-Glucopyranose, thio-maltohexaose, and Indium-III pentetreotide as potent drug candidates for CHPV.

Conclusions

Our computational results provide suggestions for in vitro and in vivo testing of these drugs against CHPV.

sciforum-089288: Studying the Inhibitory Activity of Novel Series Compounds for Parkinson's Disease Using a Molecular Docking Method

Rania Kherachi [1], Daoud Ismail [2], Merzaka Mettai [1], Ferdaous Hasni [1] and Melkemi Nadjib [1]

[1] Faculty of Sciences, LMCE Laboratory, Department of Chemistry, Group of Computational and Pharmaceutical Chemistry, University of Biskra, Biskra 07000, Algeria
[2] Laboratory of Natural Substances and Bioactive (LASNABIO), University Abou-Bakr Belkaid, Tlemcen, Algeria

After Alzheimer's disease, Parkinson's disease (PD) is the second most prevalent neurological illness. Clinically, it is defined by parkinsonism, which includes stiffness, bradykinesia, resting tremor, and postural instability. Pathologically, it is characterized by the loss of substantia nigra neurons. Monoamine oxidases (MAO-A and MAO-B) are enzymes responsible for metabolizing neurotransmitters such as dopamine (DA) and adrenaline. Selective MAO-A or MAO-B inhibitors have been the focus of recent attempts to create MAO inhibitors. In addition, Parkinson's disease can be effectively treated with MAO-B inhibitors.

The objective is to elucidate the several types of interactions between enzymes and ligands and assess the stability of the resulting complexes.

Various molecular modeling methods are used to study the inhibition of the enzyme MAO-B (PDB:4a79) involved in PD, including molecular docking, molecular dynamics, MOE software, and ADME prediction.

Based on the findings, compound L30 and compound L38, the top contenders identified by molecular docking/dynamic simulations and with low energy scores, had low IC50 values (0.110 and 0.305 μM, respectively).

The combination of the two outcomes from the earlier techniques demonstrates that the compounds L30 and L38 were chosen as the most effective MAO-B inhibitors and that they also satisfy the Lipinski, Veber, and Egan rules. They are also able to traverse the BBB. Furthermore, they may be utilized to create novel pharmaceutical medicines to treat individuals with PD.

sciforum-086192: The Development and Evaluation of an MOS-Based Electronic Nose for the Accurate Discrimination of Chronic Obstructive Pulmonary Disease Using Breath Analysis

Binson V. A. [1], Philip Mathew [2], M. Subramoniam [3] and Sania Thomas [4]

[1] Department of Electronics Engineering, Saintgits College of Engineering, Kottayam, India
[2] Department of Critical Care Medicine, Believers Church Medical College Hospital, Thiruvalla, Kerala, India
[3] School of Electrical and Electronics, Sathyabama Institute of Science and Technology, Chennai, India
[4] Saintgits College of Engineering

This research paper presents a novel approach for discriminating patients with chronic obstructive pulmonary disease (COPD) from smokers and healthy controls using a self-made electronic nose device. This study aims to develop a portable and user-friendly system that accurately identifies patients with COPD based on volatile organic compound (VOC) profiles present in their breath. Breath samples were collected from 25 patients with COPD, 32 smokers, and 36 healthy controls. The MOS-based electronic nose device incorporated a sensor array consisting of TGS 2600, TGS 2610, TGS 2620, TGS 822, and TGS 826 sensors. Advanced signal processing techniques, including independent component analysis (ICA), were employed to analyze the breath samples and extract relevant features. Three classification models, namely the Support Vector Machine (SVM), Naive Bayes, and Decision Tree, were utilized to discriminate between patients with COPD, smokers, and healthy controls based on the extracted features. The results demonstrate the efficacy of the self-made MOS-based electronic nose device in accurately discriminating between patients with COPD, smokers, and healthy controls. The SVM model achieved a remarkable accuracy of 85.25% and an area under the curve (AUC) of 87%. This study highlights the potential of breath analysis to be used as a non-invasive and cost-effective approach for the diagnosis and differentiation of COPD. These findings provide a solid foundation for further research and the development of non-invasive breath analysis techniques in the field of respiratory disease diagnosis and monitoring.

sciforum-087200: The Evaluation of *Citrus bergamia* Phytochemicals as Potential Cholesterol-Lowering Agents against HMG-CoA Reductase: An In Silico Molecular Docking Study

Nesteve John Agosto [1] and Patricia Blanch Alambatin [2]

[1] Center for Natural Products Research, University of Science and Technology of Southern Philippines, Cagayan de Oro City 9000, Philippines
[2] Department of Chemistry, University of Science and Technology of Southern Philippines, Cagayan de Oro City 9000, Philippines

Elevated cholesterol levels, or hypercholesterolemia, have been recognized as the underlying cause of various diseases, most notably cardiovascular diseases. Unfortunately, most cholesterol-lowering (or anti-hypercholesterolemic) drugs are associated with several adverse effects, emphasizing the need to identify new cholesterol-lowering strategies. Natural products, particularly bioactive phytochemicals, have gained significant attention for their safer profile, fewer side effects, and potential health benefits, including cholesterol-lowering properties. The citrus fruit bergamot (*Citrus bergamia*) is renowned for its diverse array of bioactive phytochemicals. In this study, an in silico approach was utilized to assess the cholesterol-lowering potential of phytochemicals derived from *C. bergamia*. Molecular docking using AutoDock Vina of the selected phytochemicals was performed against the HMG-CoA reductase (HMGR), an enzyme targeted for hypercholesterolemia. Results indicated that among the selected 20 phytochemicals, 8, namely Eriocitrin, Narirutin, Scolymoside, Neodiosmin, Brutieridin, Neohesperidin, Rhoifolin, and Naringin, exhibited better binding affinities than the conventional HMG-CoA reductase inhibitor, Atorvastatin (-9.2 kcal/mol). Notably, among these top eight phytochemicals, Eriocitrin displayed the most favorable binding affinity of -10.0 kcal/mol. These findings strongly imply that *C. bergamia* possesses potential HMGR inhibitory activity and anti-hypercholesterolemic activity, primarily due to the high binding affinities exhibited by its phytochemical constituents. Therefore, further studies must be considered to comprehensively explore the cholesterol-lowering properties of *C. bergamia* phytochemicals.

sciforum-084567: The Evaluation of the Antibacterial Efficacy and Drug Safety of Thymoquinone against *Acinetobacter baumannii*: Utilising Bioinformatics and Cheminformatics Methods in Microbiology

Ivan Dolanc [1], Goran Slivšek [2], Nives Ražnjević [3], Sandra Mijač [4], Nevija Brstilo [2] and Miran Čoklo [1]

[1] Institute for Anthropological Research, Centre for Applied Bioanthropology, Zagreb, Croatia
[2] Josip Juraj Strossmayer University of Osijek, Osijek, Croatia
[3] University Hospital of Split, Split, Croatia
[4] Children's Hospital Srebrnjak, Zagreb, Croatia

Introduction

The discovery of antibiotics is considered one of the most important discoveries in the history of humanity. Bacterial antibiotic resistance has long been a growing global problem, and today, bacteria are becoming able to adapt to all known antibiotics. Projections have shown that in 2019, there were 1.27 million deaths due to antibiotic resistance. It is necessary to discover new antibacterial agents that have therapeutic potential and are drug-safe so that humanity can successfully overcome antibiotic resistance. Applying bioinformatics and chemoinformatics in microbiology can be useful to rapidly evaluate the efficacy and drug safety of potential antibacterial agents, thus avoiding the loss of resources due to unsuccessful trials.

Methods

SwissADME software was used to assess timiquinone's pharmacokinetics, drug-likeness and medicinal chemistry friendliness, while potential therapeutic targets in *Acinetobacter baumannii* were assessed using the RCSB Protein Data Bank online platform tools and evaluated with a comprehensive review of the existing literature.

Results

Thymoquinone weights less than 500 g/mol fulfill the requirements for the number of rotatable bonds, proton donors and acceptors, should be easily absorbed in the intestine and can cross the blood–brain barrier, but is not a substrate for P-gp. It should not be hepatotoxic as it has no inhibitory effect on liver cytochromes. It satisfies Lipinski's rules and is therefore a molecule that could have therapeutic effects. The most promising potential targets in *Acinetobacter baumannii* are the proteins AbOmpA and bap. Here, thymoquinone could induce reactive oxygen species that destabilise membrane integrity and disrupt biofilm formation by damaging the secondary and tertiary structure of *Acinetobacter baumannii* proteins and possibly also affect its nucleic acids, leading to cell death.

Conclusions

Bioinformatics and chemoinformatics tools can be helpful in microbiology. It seems promising to perform in vitro tests to assess the antibacterial efficacy of thymoquinone as an antibacterial agent against *Acinetobacter baumannii*.

sciforum-086993: The Identification of Potential Inhibitors from *Dodonaea viscosa* Targeting Dengue Virus NS5 Methyltransferase: An In Silico and Molecular Docking Approach

Saurav Kumar Mishra, Sneha Roy, Tabsum Chhetri and John J. Georrge

Department of Bioinformatics, University of North Bengal, Raja Rammohunpur, District-Darjeeling, West Bengal 734013, India

Dengue virus is a positive-sense, single-stranded RNA virus of the Flaviviridae family. *Aedes aegypti* is the primary vector for transmitting dengue virus, spreading the tropical infectious illness. Currently, this virus is widespread in over 100 countries and is causing millions of new cases, which kill thousands of people each year as there is no medication available. Therefore, this study aims to identify a potential inhibitor from *Dodonaea viscosa* targeting the NS5 methyltransferase of the dengue virus through an in silico analysis and molecular docking approach. The NS5 methyltransferase is crucial in the host–pathogen interaction and the mechanism for this viral infection. However, *Dodonaea viscosa* has antiviral activity, and ligands were screened from different databases used for their preparation. Further, the molecular docking analysis was performed with the NS5 methyltransferase and screened ligands from *Dodonaea viscosa*. The analysis shows some promising compounds that can lead to therapeutic development, as they have high docking scores in comparison to the control used. An ADME analysis was performed for the bioactivity analysis of the selected ligands, and promising ligand profiles were found. Further, the identified potential inhibitor can be used for therapeutic development for dengue virus.

sciforum-089345: Theoretical Study of Anti-Alzheimer's Disease Using Molecular Modeling Methods

Ferdaous Hasni [1], Ismail Daoud [2], Nadjib Melkemi [3] and Rania Kherachi [1]

[1] Group of Computational and Medicinal Chemistry LMCE Laboratory, University of Mohamed Khider Biskra, Biskra 07000, Algeria
[2] Laboratory of Natural and Bioactive Substances, LASNABIO, University of Abou-Bakr Belkaid, Tlemcen, Algeria Department of Matter Sciences, University of Mohamed Khider Biskra, BP 145 RP, 07000 Biskra, Algeria
[3] Laboratory of Molecular Chemistry and Environment (LMCE), Department of Chemistry, University Mohamed Khider, Biskra, Algeria

Neurodegenerative diseases damage the nervous system and lead to a variety of complex progressive chronic issues. Alzheimer's disease (AD) is one such case. The most common form of dementia is a degenerative disorder of the brain that leads to memory loss, confusion, and behavioral changes. The main drug classes currently used to treat AD are acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitors. In this study, we investigated the inhibitory effects of a series of newly synthesized compounds of 2-hydroxy-N-phenylbenzamide derivatives on AchE and BchE, using molecular modeling approaches such as molecular dynamics and bioisosteric replacement to treat or reduce Alzheimer's disease.

The best docking complexes, L18 and L6′, were used as simulation inputs to evaluate the stability of the complex (protein–ligand), using potential energy as a function of time. These results were verified using molecular dynamics simulations, demonstrating the strength of both complexes.

Furthermore, we found that the bioisosteric replacement method successfully proposed two novel analogs of each compound (L18 and L6′) with low energy scores and similar biological activity by replacing molecular substructures with similar chemical groups.

All these methods allow us to identify new inhibitors that have potential against this disease and can be suggested as new drugs against Alzheimer's disease.

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