NINTH INDO-US WORKSHOP ON MATHEMATICAL CHEMISTRY

with Application to Drug Discovery, Computational Toxicology, Cheminformatics and Bioinformatics

JAN 06-10, 2025

BOOK OF ABSTRACTS

Workshop Series Founder Chairman: Dr Subhash C. Basak, USA
Ninth Workshop Organizer: Dr Ramanathan Natarajan, India

Host Institute

SARANATHAN COLLEGE OF ENGINEERING, TIRUCHIRAPPALLI, TAMIL NADU, INDIA

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INVITED LECTURES

Neuroprotective AMPA receptor modulators: from computer-aided drug design to synthesis and preclinical studies

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The glutamate receptors are of crucial importance in CNS functioning. Among the substances acting on the glutamatergic system, the most promising are allosteric modulators of AMPA and KA receptors.[1] The positive allosteric modulators (PAMs) of AMPA receptors as compared to direct agonists are more safe and able to perform the fine tuning of the glutamatergic system since they do not cause any effects in the absence of the natural ligand in the synapse. PAMs of AMPA receptor reveal such neurophysiological effects as significant increase of nerve growth factors expression as well as induction of long-term potentiation of synaptic excitation, considered as a substrate for learning and memory. This makes them privileged compounds for the development of nootropic and neuroprotective agents. The negative modulators of AMPA receptors can be employed as antiepileptic drugs.

The *de novo* design of AMPA receptor modulators using previously refined receptor models was supplemented in our work with molecular dynamics simulation of the modulator-agonist-receptor complexes for various possible receptor binding sites. The Molecular Field Topology Analysis (MFTA) QSAR technique was quite beneficial in the modeling of ligand potency within the series of closely related compounds. The 3D QSAR and pharmacophore models of the AMPA receptor PAMs as well as predicted ADMET parameters served as useful additional filters. That allowed us to find a series of new positive and negative highly potent allosteric modulators based on several new scaffolds. They include novel tricyclic derivatives of bispidine, substituted bis(pyrimidines) and bis-amides with various linkers/spacers. Convenient synthetic approaches were elaborated and scaled-up for the designed compounds. Electrophysiological patch clamp *in vitro* experiments have demonstrated the pronounced influence of the studied compounds in sub-nanomolar concentrations on the kainate-induced currents recorded for Purkinje neurons from rat cerebellum. The *in vivo* studies based on behavioral models have shown cognition-enhancing properties for the designed positive modulators. The combinations of these properties with low toxicity allowed several compounds to successfully pass preclinical studies.

This study was supported by the Russian Science Foundation, grant No. 22-15-00041.

Keywords: AMPA receptor; positive allosteric modulators; molecular dynamics; QSAR; neuroprotective agents.

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Adventures in the evolving landscape of mathematical descriptors of molecules and biomolecules: A tortuous journey of fifty years

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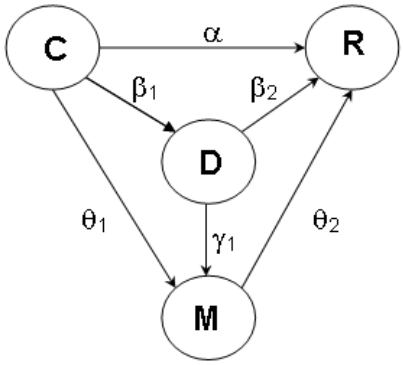
Although graph theory was developed by Euler in 1736 and researchers like Cullen, Cayley and Sylvester in the eighteenth century realized that conventional chemical structures are graphs, the current growth spurt in the use of graph theoretic descriptors began in the middle of the twentieth century. Subhash C. Basak observed that the recent upsurge of research in mathematical chemistry and its applications was catalyzed by three main factors: (a) Development of novel concepts in the characterization of molecular structure, (b) Easy accessibility to software and high-speed computers capable of calculating relevant molecular properties from molecular structure fast, and (c) Availability of sufficiently large databases of experimental properties as well as statistical and machine learning methods for the development and validation of robust predictive models for basic research and their practical applications in decision support systems in current regulatory and industrial protocols for chemical evaluation. Graph theoretic descriptors of molecules and biomolecules have been used in the characterization of closely related structures like isospecral graphs, quantification of similarity/ dissimilarity of chemical and biological structures, quantitative structure-activity relationship (QSAR) studies and development of biodescriptors to quantify aspects of DNA/ RNA sequences as well as experimental proteomics patterns. Such wide applications of graph theoretic descriptors in wide areas of chemistry, drug discovery, predictive toxicology and chemobioinforamtics follows from the basic philosophy of the structure-property similarity principle (SPSP) as shown in the figure below:



An empirical property is a function α:C → R that maps the set C of molecules or biomolecules into the real line R. A non-empirical structure-activity relationship (SAR) may be looked upon as a composition of a description function β1:C → D mapping each molecular/ biomolecular structure of C into a space of non-empirical structural descriptors (D) and a prediction function β2:D → R which maps the descriptors into the real line. When [α(C) - β2 β1(C)] is within the range of experimental errors, we say that we have a good non-empirical predictive model. On the other hand, the property-activity relationship (PAR) is the composition of θ1:C → M which

maps the set C into the molecular property space M and θ2:M → R mapping those molecular properties into the real line R. PAR seeks to predict one property (usually a complex property) of a molecule/ biomolecule in terms of another (usually simpler) property. This presentation will give an overview of my personal journey into the emerging landscape of descriptors of molecules and biomolecules from 1975 till date,

Keywords: Graph theory; Molecular descriptor; Chemodescriptor; Biodescriptor; Structure-property similarity principle (SPSP); Isospectral graphs; Molecular similarity; Property-activity relationship (PAR); Structure-activity relationship (SAR).

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Pharmacophore recognition of bioactive molecules may aid in more efficient AI -driven database searches for discovery of potent compounds

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Pharmacophore is a combination of steric and electronic features of a molecule responsible for optimal interaction with a biological target to trigger or inhibit its biological response. Pharmacophore developed for mosquito repellents will be discussed here. Mosquitoes are the most notorious vectors for transmission of lethal diseases, such as malaria, dengue fever virus, yellow fever, chikungunya virus, West Nile virus, lymphatic filariasis, Zika virus, and Japanese encephalitis. Suitable vaccines and drugs are still not available for countering the infections. Thus, mosquito repellents became the most effective preventive measures. However, most mosquito repellents have certain toxicity issues, such as greasiness, strong odors, irritation to the skin and mucous membranes. In addition, majority of them are not also resistant to abrasion or rub-off. Therefore, efforts for finding a compound that circumvents the issues continue to be the goal for repellent research community despite many challenges.

In pursuit of the goal, we developed a three-dimensional a pharmacophore model for potent repellent activity from eleven known diverse insect repellent compounds. The protection time for experimental repellent activity of the compounds was taken from an earlier study. The pharmacophore was found to have three hydrophobic sites (two aliphatic and one aromatic) and a hydrogen-bond acceptor site in three-dimensional space. The pharmacophore showed an excellent correlation between the experimental and predicted protection time of the compounds in the training set. By mapping the model on the most potent analogue, a 3-dimensional shape-based template was created for search of our in-house database of three hundred compounds. This allowed discovery of four new insect repellents. The validity of the pharmacophore was tested by excellent mappings on a variety of other known insect repellents including a compound recently isolated from samples of greasy gaur hair. Thus, the repellent pharmacophore model is clearly predictive and therefore, suitable for search of more effective nontoxic repellents from large compound databases. Searches or virtual screening for compounds from large databases serve as complimentary to high throughput screens (HTS) by facilitating selection of a smaller number of compounds. Blum, L.C. et al. in 2009 reported that there are about a billion (drug-like) compounds in the chemical space from which about thirty million are available for targeting ~105 human proteins. Therefore, search for a lead compound against a disease specific target is highly challenging for high throughput screens (HTS). Machine learning (AI) methods with intelligent augmentation (IA) may better accomplish the task. Predictive pharmacophore models developed from experimental activities can provide an intelligent augmentation (IA) to the machine learning and thereby significantly enabling a short listing of compounds for experimental evaluations.

Keywords: Pharmacophore; mosquitoes; repellents; virtual screening; database searches; machine learning and intelligent augmentation (IA).

Bioinformatics, computer modeling and mosquitos: Insect sodium channels functioning from a theoretical perspective

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Many concepts of mathematical chemistry are useful in bioinformatics and computer modelling of proteins. In this talk we will present new examples of useful synergy stemming from interactions between these disciplines. Everybody knows how serious threat to humans pose vector borne diseases (VBD). One of the most dangerous animals is a little female mosquito. Despite many scientific efforts we still have no effective repellents nor insecticides – resistance develops quickly. One of molecular targets are insects' voltage dependent ion channels. We have created a realistic model of such channel and performed extensive MD simulations of transport pathways of several ligands inside fenestrations present in this system. We have identified transport pathways of DCJW, metaflumizone, and a non-ester pyrethroid etofenprox and calculated, using metadynamics free energy profiles. We showed that those mutations which warrant resistivity to pyrethroids (i.e.F1852Y) are linked with mechanical hampering of insecticides access to the central cavity [1]. Data may help to develop better chemicals to control VBD.

Keywords: Bioinformatics; computer modelling; sodium channel; VBD; transport pathways.

Support from NCN grants no. 2021/41/N/NZ3/02165 (BN),2021/43/D/ST4/00920 (JR) and NCU IDUB #MEMO-BIT(WN) has been obtained.

Simulating optical properties of organic and biomaterials

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Photochemical reactions have been the focus of research interest for decades. However, photochemistry has only recently evolved from a relative niche topic to a major research field.

From the theoretical side this transition has been driven alike by a plethora new concepts and painstaking advances in photodynamics methods. Unraveling the mechanism of a photochemical reaction requires monitoring the electronic and structural transformations that the molecular system undergoes after light absorption. Through a series of examples of productive collaborations with experimental partners, we will illustrate how photochemical concepts are manifested in the experiments [1-3] and how the mechanisms of fundamental photochemical reactions, for instance the isomerization of cyclohexadiene, are often more complex than expected [4].

Also, I'll present our efforts to develop computational tools for simulating photoinduced processes and calculating spectroscopic signals, which are more accessible to non-experts. Useful information will be presented that can help interested researchers to perform their simulations and explore photochemical processes at their own pace.

Keywords: Optical properties; photochemistry; mixed quantum-classical dynamics; surface hopping.

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Topological indices: Physicochemical significance in QSARS

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Quantitative Structure Activity Relationship (QSAR) studies play a key role in drug discovery research. The QSARs describe the correlations between biological activity as dependent parameter and physicochemical and structural descriptors, including topological indices (TIs) as independent parameters. There are several commonly used topological indices viz Balaban(J), the Platt(F), the Hosoya(z), Zagreb(M), Wiener(W), Molecular connectivity (chi), Randic´(χ), Kappa(K), and Information content(IC) etc. The TIs of molecules have been extensively used in describing their physicochemical properties like study of Entropy, boiling point, enthalpy, molecular weight, Gibb's energy Motor octane number, Standard enthalpy of vaporization and Acentric factor. The QSAR models developed by correlating the biological activity with TIs are useful in predicting activity, and in virtual screening. They may also provide meaningful insights into the mode of action of the bioactive molecules if the physicochemical significance of TIs is interpreted. The efforts in this direction were initiated in 90s and are being continued where the physicochemical parameters like hydrophobic (LogP/π) electronic (σ) and steric (MR) are correlated with different TIs and even some computational parameters CAA, CMA CSEV of ChemDraw and Au, Nc, Vs, TIC3, ATS2p of Dragon software's. It has been observed that mostly these parameters correlate better with steric parameter MR than the hydrophobic parameter (LogP) or other parameters. The QSAR models using TIs have been developed for different disease like Alzheimer's, viral COVID-19 and tuberculosis in recent years. The QSAR model describing antitubercular activity in substituted quinoline in terms of MR, PC and CMA was not only a good predictive model but also provided insight into the ATP synthase target for antitubercular activity.

Keywords: QSAR- Quantitative Structure Activity Relationship; TI- Topological Indices; MR- molar refractivity.

Higher-dimensional structures for a better understanding of the chemical space and its evolution

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Modelling the evolution of the chemical space, spanned by all chemicals and reactions reported in the literature, requires the development of mathematical and computational frameworks that encode the dynamics of the entire network linking chemicals through chemical reactions. In this presentation, I will explore some of the current computational ontologies for chemistry, their importance and shortcomings, and the need for a stable ontological framework for the future of chemistry and its computational scope. Additionally, I will provide a mathematical framework that relates the various ontologies of chemistry and their interconnections.

In the second part of the talk, I will examine the available models for chemical space, focusing particularly on those based on hypergraphs, in contrast to the traditional graph-based approaches. I will discuss the advantages of the hypergraph framework, along with its associated challenges. Some results will be presented on the use of hypergraphs, covering the evolution of the chemical space from 1800 to the present day. I will also address the significance of random hypergraphs and their chemical relevance, as well as recent advances in exploring the mathematics behind these random structures. Lastly, I will highlight the role of generative models for hypergraphs, along with their chemical significance and implications.

Keywords: Chemical space; hypergraphs; higher-order structures; chemical ontologies.

A novel pyruvate kinase activator - From a HTS impurity to a ead series

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Pyruvate kinase (PK) is an essential component of cellular metabolism, converting ADP and phosphoenolpyruvate (PEP) to pyruvate in the final step of glycolysis. Of the four unique isoforms of pyruvate kinase, (PKR) is expressed exclusively in red blood cells and is a tetrameric enzyme that depends on fructose-1,6-bisphosphate (FBP) for activation. PKR deficiency leads to hemolysis of red blood cells resulting in anemia. Activation of PKR in both sickle cell disease and beta-thalassemia patients could lead to improved red blood cell fitness and survival. The discovery of a novel series of substituted urea PKR activators, via the serendipitous identification and diligent characterization of a minor impurity in a High Throughput Screening (HTS) hit will be discussed. Details on the mining of the HTS data and computational chemistry applications leading to the design of the lead molecule will also be presented.

Keywords: Pyruvate Kinase Activator; HTS impurity; data mining; molecular design.

Assessment of JNK3 enzyme inhibition of piceatannol - *in silico* & *in-vitro* studies

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Stress induced apoptosis is major concern as it leads to neuronal cell death following cerebral ischemia. JNK3, a neuronal kinase activated by stress, plays a role in stress-induced apoptosis. Natural products continue to serve as antioxidants that have important implications on apoptosis pathway.

In this context, this study aims to investigate the neuroprotective effects of piceatannol (PCT) in SHSY-5Y neuroblastoma cells after hypoxic injury and its interaction with JNK3.

The crystal coordinates, interaction energies, and amino acid interactions to determine PCT's selectivity for JNK3 was done. Density functional theory was implemented to compute the electrostatic potential, while molecular dynamics assessed the stability and structural consistency of the JNK3-PCT complex. The reference compound taken for this study is SP600125 (SP6), a JNK3 inhibitor. In addition to this MTT assay and cell-free JNK 1, 2, and 3 kinase assays to evaluate the cytotoxicity and isoform selectivity of PCT respectively.

In silico studies against JNK1, JNK2 and JNK3 revealed a stronger binding affinity between PCT and JNK3 compared to JNK1 and JNK2. The molecular dynamic studies demonstrated the stability of JNK3-PCT complex. The in vitro kinase assay showed that PCT-treated cells exhibited a decrease in Cyt-c and caspase-3 expression and an increase in Bcl-2 level, compared to hypoxic control ($p < .001$). PCT also demonstrated superior efficacy over the reference compound SP6 in inhibiting JNK3 phosphorylation ($p < .001$).

Keywords: Piceatannol (PCT)J; NK3; *in silico*; molecular dynamics; neuronal kinase.

Modelling adsorption of small structures onto fullerene graphs

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A **matching** *M* of a graph *G* is a collection of edges of *G* such that each vertex of *G* is incident with at most one edge from M. Matchings serve as mathematical models of many interesting phenomena; among the best known are various types of dimer coverings. Packings are generalizations of matchings that facilitate the study of coverings of a given substrate by disjoint copies of the same smaller structure: A **packing** of *H* into *G* is a subgraph of *G* whose every connected component is isomorphic to *H*. Hence, matchings are the simplest non-trivial coverings, in which each component is a single edge.

This talk presents some recent results on packings of various small structures into classical and generalized fullerene graphs.

Keywords: Fullerene graphs; packing; isomorphism.

Unravelling the complex immunorepertoire of an immune library

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Antibodies are highly sought after biomolecules due to its unique ability to identify and capture targets with high specificity. The antibody repertoire generated is in response to the exposure to an infection. The understanding of antibody gene diversification processes underpinning the complex gene sequence make-up provides in-depth information to further dissect the gene diversification and preference during infections. In this study, in-depth analysis of the antibody repertoire against Lymphatic filariasis was carried out. Using high-throughput sequencing of antibody repertoires (Ig-Seq/Rep-Seq), immunome analysis of LF-IgG (LG) and LF-IgM (LM) repertoires includes V(D)J gene segment usage, diversity, length, and amino acid compositions of CDR3, SHM and clonality were studied. Unique V-gene patterns were visible in both repertoires. Higher SHM level were observed in LG sequences and presence of oligoclonal sequences indicates the extent of clonal expansion. Monoclonal antibodies against closely-related parasitic infections were present within the LG repertoire suggest that immune repertoires are not as exclusive and biased against the target infection as initially thought. The characterization of the immune repertoire can provide critical insight into the antibody response patterns in disease state, antibody generation process during infections and future antibody designs.

Keywords: Immunorepertoire; CDR3; SHM; lymphatic filariasis.

Entrapment of flow of substrate to diversion pathway for combating persistent tuberculosis: Bioinformatics Approach

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The post genomic era provided the leap into the quantitative biology and introduced biologists into the "omes" & "ics" world. For biologists it is utmost important to know the biology of disease and the mechanism of action of medicines. But no longer are these contained in the domain of physiology & medicinal chemistry. The importance of reorganizing our thinking process is mostly reflected in the merger & acquisition of Biotechnology, Bioinformatics and Chemoinformatics companies by/with large pharmaceutical companies recently.
The development in the field of molecular modeling and simulation has played the leading role in drug design technology in the pharmaceutical industry. Starting from Genomics, alignment of genes of interest amongst the species, three-dimensional structure prediction from the knowledge of sequence of amino acids, prediction of active sites, searching for lead compounds using databases and structure-based design, prediction of binding efficiency prior to the experiment and lead optimization using physico-chemical properties of the compounds [JCIM 2006,46,17-23] are a few to cite.

One such case study using *in silico* attempt towards the designing from known anti-tuberculosis chemicals a set of novel inhibitors and finding the drug target (s) using pathway simulation and analysis [BMC Journal 2006, 3, 3-27& JBSD 2009, 26,663-895] will be discussed in brief.

Recent news has warned the medical community that war against pathogenic bacteria is not yet over, repeated breaking of different drug resistance in different range of pathogen has been observed in the patient especially in developing & underdeveloped countries. Many researchers, probably the next to cancer, are experimentally using many prongs attack on the understanding the mechanism and developing new strategies of inhibitors for combating this phenomena, resurging XDR, MDR, PDR. Extensive discussion to define these classes, cause & treatments is available in literature [Acc. Chem. Res. 2021, 54, 2361−2376].

Research work engaging with clinicians, epidemiologists, biologists, microbiologists etc. in this field is emerging to highlight the complexity of the problem. However, many chemicals have been developed to combat the MDR/XDR TB yet have not been fully successful for a long time. Tuberculii, bacteria have shown to have multiple spontaneous mutations at a predictable rate and independent of different drug administration. Such phenomena are prevalent to many bacterial & more common to viral disease which leads researchers to develop multiple target drug designing.
Present discussion will open the future of understanding of disease, inter relationship within biochemical pathway & effect of protein-protein interaction identified as target for combating persistence stage in bacteria.

Keywords: Latent TB; biochemical pathway; structure modelling & dynamics.

Building better computational toxicology solutions with AI and ML

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Machine learning (ML) and artificial intelligence (AI) techniques, integral to a wide range of data-driven disciplines, unsurprisingly, also useful for enhancing computational toxicology workflows. This presentation will explore both basic and advanced ML/AI strategies used to assess toxicological properties of chemical compounds. Emphasis will be placed on methodologies that extend beyond mere prediction, providing meaningful explanations and rationales that facilitate a collaborative interface between computational models and human experts, ultimately supporting more informed decision-making processes. Additional topics include the application of quantitative structure–activity relationship (QSAR) models, expert rule-based systems, deep learning–derived molecular fingerprints, as well as best practices for model validation and the application of domain applicability principles.

Keywords: Machine learning (ML); artificial intelligence (AI); toxicology; QSAR; applicability domain.

Assessment of Blood-Brain Barrier entry of a structurally diverse set of chemicals using computed descriptors

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In this paper, we used five different statistical methods, viz., Principal Component Logistic Regression, Logistic LASSO, Random Forest, Support Vector Machines and Neural Networks, to estimate blood-brain barrier (BBB) entry of a structurally diverse set of 7775 molecules using 1189 computed molecular descriptors. For training and optimal model selection, the data was split into training and validation subsets in the 90%-10% ratio. Out of the five methods, the SVM with polynomial basis and random forest model emerged as the top two classifiers. Based on the results derived from a large and data set of chemicals, it can be concluded that the top two modelling methods can be used for the computer-assisted estimation of BBB entry of chemicals in general.

Keywords: BBB (blood-brain barrier) entry; Logistic LASSO; Random Forest; Support Vector Machines; Neural Network.

Growing counter-propagation artificial neural networks

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Teuvo Kohonen developed the original self-organizing maps (SOM) neural network algorithm in the 1980s. Even in those early years, Kohonen proposed SOMs with dynamically changing topology. The idea at the time, according to Kohonen, was to use standard rectangular SOM and if the distance between two neighbouring neurons is too large, the corresponding connection between them is *turned off*. This could be considered as *top-down* approach in changing of the network topology. Another interesting variant of SOMs with changing topology, this time using *bottom-up* approach, was developed in the 2000s. This algorithm, which is almost unknown for chemists, is called growing self-organizing maps (GSOM). In cases like this the network grows faster (adds new neurons and connections between them) in a direction of larger probability distribution of the data.

Here a supervised version of GSOM algorithm called *growing counter-propagation artificial neural network* (GCPANN) is presented. This algorithm, as its analogue with fix topology, is used for modelling purposed. Due to the variable size, GCPANN converges faster toward models with good performances. An additional advantage of the algorithm, because of its dynamically changing topology and network size, is that it usually solves the same modelling problem with smaller number of neurons.

Keywords: Neural networks; self-organizing maps; Kohonen networks; growing self-organizing maps; counter-propagation artificial neural networks; growing counter-propagation artificial neural networks.

Assessment of mutagenicity using computed molecular descriptors and support vector machines

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The assessment of toxicity of chemical is important for the protection of human and environmental health as well as for new drug discovery. Because of the cost of laboratory testing of chemicals and unavailability of necessary toxicity data needed for the hazard assessment of a large number of candidate chemicals, both in United Stated of America and European Union in recent years there is increased interest in the use of *in silico* models in the prediction of toxicity of commercially important chemicals. As part of this trend, development of quantitative structure-activity relationship (QSAR) models for prediction of mutagenicity is of interest for regulatory purposes and for understanding the structural features of chemicals, which determine mutagenicity.

This work describes the use of support vector machines (SVMs) coupled with genetic algorithms (GAs) for automated search for important parameters needed for good classification models for a set of 508 structurally diverse chemical mutagens each molecule represented by 275 computed descriptors that included topostructural, topochemical, geometrical (3-D), and quantum chemical (QC) indices. The results emphasize development of best performing models as well as descriptor selection. Five-fold cross-validation applying Kennard-Stone algorithm along with Euclidean distance as well as Mahalanobis distance was used for evaluation of the performances of the models during the optimization. In addition to this, our own method for automatic adjustment of the relative importance of the selected descriptors was applied to get additional information during the interpretation of the final models. The best models produced by genetic algorithms were able to correctly classify between 85 and 90% of the chemicals, which were used for external validation of the models.

Keywords: quantitative structure-activity relationships; molecular descriptors; support vector machines; variable selection; genetic algorithm; cross-validation; machine learning.

Emotions Extraction of Autism children through Art using Deep Learning Techniques

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Autism spectrum disorder (ASD) comprises neuro-degenerative disorders associated with social, communication, and behavioral difficulties. It is necessary for early detection to mitigate the adverse effects of this disorder by starting special education in a school and rehabilitation center to enhance children's daily lives. Most children with Autism Spectrum find difficult to socially and verbally communicate. Some children tend to be completely non-verbal whereas others face challenges while trying to hold a conversation and are unable to read the body language and faces of others successfully. One common way to allow people with autism spectrum disorder (ASD) to communicate, is through art therapy. This effectuates people to use their visually-minded brains to communicate through artistic media. It allows them to record images and scenes, as well as other visualize the data, express ideas, and process information in an accurate manner. Additionally, children with ASD are often unable to express their emotions properly. It leads to have a solution which can address the aforementioned challenges This research mainly deals with the implementation of Deep Learning techniques to analyze and extract the emotions of autism children through their art using Deep Learning techniques. Feature extraction for the effective recognition of emotions is obtained. It also targets on identifying the emotions through the artwork of children diagnosed with autism spectrum disorder (ASD) by implementing the predictions of their emotions. This leads to the result of contributions to the state-of-the-art results in this research field. DL algorithms help to analyze the ASD children's key emotions and the perceptions enabling them to analyze their emotional state thereby helping the doctors, therapists, parents and care takers such that they are in safe hands of the society.

Key words: ASD, Prediction; non-verbal; languages; art; detection and classification; deep learning techniques.

VEGFR2 chemical space: Stimulator and inhibitory peptides

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The kinase pathway plays a crucial role in blood vessel function. Particular attention is paid to VEGFR type 2 angiogenesis and vascular morphogenesis as the tyrosine kinase pathway is preferentially activated. In silico studies were performed on several peptides that affect VEGFR2 in both stimulating and inhibitory ways. This investigation aims to examine the molecular properties of VEGFR2, a molecule primarily involved in the processes of vasculogenesis and angiogenesis. These relationships were defined by the interactions between Vascular Endothelial Growth Factor receptor 2 (VEGFR2) and the structural features of the systems. The chemical space of the inhibitory peptides and stimulators was described using topological and energetic properties. Furthermore, chimeric models of stimulating and inhibitory proteins (for VEGFR2) were computed using the protein system structures. The interaction between the chimeric proteins and VEGFR was computed. The chemical space was further characterized using complex manifolds and high-dimensional data visualization. The results show that a slightly similar chemical area is shared by VEGFR2 and stimulating and inhibitory proteins. On the other hand, the stimulator peptides and the inhibitors have distinct chemical spaces.

Keywords: Peripheral artery disease; molecular modelling; docking, angiogenesis; vascular morphogenesis; chimeric protein.

Rhombelane based vaccines

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Coronaviruses have a changing surface protein expression, making it impossible to design an efficient vaccine. To have protection against coronavirus, one has to be immunized periodically. Efforts to create a polyvalent vaccine are increasing. Bio nanosystems represent a tempting strategy for designing polyvalent vaccines. In this paper, some nanoparticles- rhombelanes are studied computationally to be used as a core for polyvalent vaccines. Rhombhelanes were analyzed with an antibody database characterizing their interacting feasibility as agents designed to neutralize COVID-19 particles. Results show that nanoparticles and vaccines based on such carriers are feasible candidates. A polyvalent vaccine against viruses that present unstable surfaces must be further developed.

Keywords: COVID 19; polyvalent vaccine; rhombelanes; antigens.

Mediated vasculogenesis and morphogenesis

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The Prostaglandin E1 (PGE1) is a molecule that widens blood vessels and is used for several medical purposes, such as treating erectile dysfunction and critical limb ischemia. Nevertheless, its involvement in vasculogenesis and morphogenesis is a more specific subject in the field of developmental biology and therapeutic research. Vasculogenesis is the embryonic phenomenon in which endothelial progenitor cells generate new blood vessels. This phenomenon is distinct and divergent from angiogenesis, which entails the creation of novel blood vessels extending from pre-existing ones. Morphogenesis is the biological phenomenon responsible for the development of an organism or its components into a specific shape. Embryonic development and tissue re-generation are essential components. Current research is investigating the broader consequences of prostaglandins, such as PGE1, in the fields of developmental biology and regenerative medicine. Gaining knowledge about the impact of PGE1 on morphogenesis could provide valuable insights into congenital vascular abnormalities and innovative approaches for tissue repair and regeneration, especially in limb ischemia. A histologic and morphogenesis study was carried out on Artemia Salina PGE1 as the top molecule with vasoactive properties. The study uses wet experiments together with computational methods. Results show that PGE1 can initiate the shape of the vessel formation. Overall, PGE1 plays a significant role in mediating vasculogenesis and morphogenesis through its vasodilatory, anti-inflammatory, and pro-proliferative effects on endothelial cells. The ability to enhance blood circulation and support the appropriate functioning of endothelial cells makes it a valuable tool in both developmental biology research and therapeutic interventions aimed at tissue regeneration and vascular repair.

Keywords: vasculogenesis; morphogenesis; angiogenesis; VEGFR2; PGE1.

On the nature of chemical bond: Quantum molecular polyhedra and collective bond description

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The nature of the quantum mechanical LCAO-MO Mulliken's description of the chemical bond is analyzed in light of constructing basis function enfolded spaces. As a result, the concept of the chemical bond transforms into a collective functional structure, where one considers the whole set of molecular atoms as bearing the chemical bond.

Keywords: LCAO-MO; Enfolded Spaces; Basis Sets; Collective Chemical Bonds; First Order Density Function.

Clustering/classification of chemicals, proteomic data and emerging global viruses considering different kinds of representations

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In the contribution we present the classification scheme for three sets of chemicals described with different descriptors. The first clustering exercises were performed on sets of 1654/1522 compounds published by the ToxCast EPA project. The in vitro measurements were performed in the framework of CoMPARA project studying their agonist/antagonist activity to androgen receptor [1]. The second example shows the chemometrical analysis of proteomic data. The proteomics were recorded from three kinds of cells treated with two kinds of nanoparticles under different regimes (doses and time of exposure). In the following, we present the classification of RNA virus sequences of Zika virus [2], SARS, MERS and SARS-COV2 (COVID-19) virus [3]. The sequences were represented by 48, or 64 alignment free descriptors. In all examples the different chemometrical methods for clustering and data analysis were applied, viz., Euclidean distance (ED), Mahalanobis distance (MD), principal component analysis (PCA), and self-organizing map (SOM) or Kohonen network.

Keywords: clustering; emerging viruses (COVID-19); proteomics data from cells treated with different nano-particles; in vitro activity to estrogen/androgen receptors.

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Information-entropy descriptors for chemical reactions

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Previously, we deduced the general formula for information entropy of molecular ensemble (h_{ME}), which behaves super additively relative to the information entropies of the constituting molecules (h_i) and contains additional term called the cooperative entropy H_Ω:

$$h_{\mathrm{ME}} = H_\Omega + \sum_{i=1}^{m} \omega_i h_i$$

where ω_i are fractions of the molecules in the ensemble. Cooperative entropy H_Ω is an emergent quantity reflecting the mixing of the molecules.

In the present talk, we discuss the application of this formula to the analysis of simple (one-stage) and complex (multi-stage) chemical reactions. In the case of the simple reactions, our approach allows calculating the change in information entropy at the chemical reaction and its components associated with molecular-structure and molecular-size changes. We demonstrate that both total information entropy change and its contributions are characteristic for the selected classes of chemical reactions.

For complex reactions consisting of K stages, we derived the relation between the stage information entropies ($\Delta h_{\mathrm{R},k}$) and the total value (Δh_{R}) that corresponds to the scheme:

$$\Delta h_{\mathrm{R}} = \sum_{k=1}^{K} \omega_k \Delta h_{\mathrm{R},k}$$

where ω_k are the fraction of the atoms participating in the k-th reaction in the number of atoms appearing in the summative chemical equation of the reaction scheme. The application of this relation to the sets of successive, parallel, catalytic, and conjugated chemical reaction are discussed. The insights into digital classification of different reaction schemes based on the information entropy are considered.

This research was funded by the Russian Science Foundation, project “Information entropy of chemical reactions: A novel methodology for digital organic chemistry”, grant number 22-13-20095.

Keywords: Information entropy of molecular ensemble; cooperative entropy; information entropy of chemical reactions.

Topological isomers of DNA dodecahedral links

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The comprehensive understanding of DNA nanostructures is a major challenge given their enormous potential applications in various fields. The DNA polyhedral links are considered as optimal templates for controlling the chemical synthesis of DNA nanostructures. To provide a comprehensive understanding, this paper addresses the periodicity and topological isomers of DNA dodecahedral links. We have successfully constructed a series of DNA dodecahedral links with consistent strands number and genus using two distinct strategies. Our results demonstrate the presence of periodic variations in both strand number and genus of these structures. As a result, we calculated the HOMFLY-polynomials of these structures to effectively distinguish between them and defined these structures as topological isomers. Our research not only provides valuable insights into the comprehensive understanding of DNA nanostructures, but also offers scientists with clues for the screening and synthesis of unexplored DNA nanostructures.

Keywords: DNA dodecahedral links; strands number; genus; topological isomers; HOMFLY polynomial.

Perturbation response scanning analysis for drug-target networks

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The Perturbation Response Scanning (PRS) method, based on linear response theory, provides a means to evaluate how network dynamics respond to external forces. Initially developed in conjunction with elastic network models, PRS was designed to simulate protein dynamics and identify intraprotein communication interactions. Signal propagation, however, is not confined to proteins; it can dynamically traverse cellular environments. From a biophysical perspective, PRS offers unique advantages in studying the higher-order organization and synergy within cellular networks. Therefore, we extended the PRS method to drug-target network analysis, assessing the impact of drug-induced perturbations on target dynamics by considering network dynamics. By integrating artificial intelligence and biological network algorithms, we applied this method to drug repurposing studies for cancer and neurodegenerative diseases.

Keywords: Network dynamics; target module; drug repurposing.

All-metal aromaticity and conceptual DFT

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Several metal clusters exhibit aromatic behaviour. Conceptual density functional theory has been found to be useful in analyzing the behaviour of all- metal aromatic compounds like Al_4^{2-} and all-metal antiaromatic compounds like Al_4^{4-} and their complexes in terms of different global and local reactivity descriptors as well as the nucleus independent chemical shift. Aromaticity and antiaromaticity in cyclic alkali clusters like Na_6 and K_6, polyacene analogues of inorganic ring compounds, multivalent superatoms, trigonal cyclic π- bonded dianions like Be_3^{2-} and Mg_3^{2-} as well as their different sandwich and multi- decker complexes are analyzed in terms of those reactivity descriptors and the associated electronic structure principles. The hydrogen storage ability of these clusters has been explored.

Keywords: DFT; aromaticity; polyacene; superatoms.

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The application of the QSPR methodology can help improve the prediction of protein folding rates

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Understanding the protein folding process is considered one of the most important topics in chemistry and biology. Understanding the underlying factors that are mainly responsible for the folding rate of proteins has been intensively researched over the last 25 years [1]. Many studies have been published in which models have been developed to predict the rate of folding using different data sets. However, it remains unclear which are the most important descriptors/attributes of protein structure for the folding rate of proteins. We found shortcomings in the quality of validation methods used in the model optimisation phase, which are very primitive. We investigated the possibilities for improving model validation methodology in the area of protein folding rate modelling. We utilised basic insights already used in the classical quantitative structure-property relationship (QSPR) methodology, such as cross-validation and external validation of models. We compared three types of models from the literature developed for sets of 80-100 proteins and developed our own models based on the logarithm of protein sequence length. It turned out that the primary structural descriptors that determine the folding rate of proteins are (1) the length of the protein sequence, (2) the secondary structure content of the protein and the average physical/chemical properties of a protein sequence, and (3) the average contact order distance between amino acids in the 3D structure. The last descriptor is related to the concept of graph theory, for which the term connectivity is defined, i.e. the connection through non-covalent interactions between atoms in amino acid residues that are in close contact in the 3D structure of the protein. However, a more rigorous validation of the models by cross-validation, and in particular a validation of the accuracy of the prediction of protein folding rates on external proteins not used in the model development phase, shows that in real predictions the most stable model is based on the logarithm of the number of amino acid residues in proteins (sequence length). This is an important result that confirms that the protein folding process and folding rates are primarily determined by the size of the protein.

Keywords: Protein folding rates; QSPR modelling; cross-validation; external validation; sequence length; contact order distance.

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Molecular descriptors or machine-generated features? Their impact in predictive modelling and QSAR

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Chemical properties can be studied using physical models, simulation, or non-physical predictive models as (Quantitative) Structure Activity Relationships - (Q)SAR. Non-physical models are heavily data driven and use statistical or machine learning (ML) methods. Machine-interpretable representations of data have been a research issue for a long time, with molecular descriptors and fingerprints being the most common molecule representations. While molecular descriptors account for global properties of the molecules, fingerprints codify the presence/absence of functional subgroups.

Classical QSARs consider a dataset of molecules and activity, compute a large number of chemical descriptors, apply some method to reduce them to a few, and build a model to predict the activity. During the years the model building algorithms changed, and ML methods prevailed, pushed by their success in modeling difficult tasks as images understanding. Moreover, ML methods are non-parametric and do not make any assumption about the function connecting molecular descriptors and molecular property. ML is able to mine large quantities of data even in case no theories are available. Among the ML methods neural networks (NN) are appealing for their ability to learn complex and non-linear functions; the functions are more and more complex when they grow deep, as in the deep neural networks (DNNs).

Different input formats can be given to DNNs, because they can learn directly the relevant features from data, without the need of computing features a priori. First, the input is taken to discover a good representation, then the representation is used to provide the output. DNNs contain simple non-linear processing units, each transforming the representation at one level into a representation at a higher level. DNNs avoid the bias introduced by the selected descriptors; instead, using the full molecule, either represented as a graph or as a string, allows using the whole information and generating important substructures, to be eventually scrutinized for possible roles as structural alerts. Since DNN models generate no rules and no equations, understanding them can be done looking at the internal states of the net; differently from the models expressed as equations, those internal representations are more complex.

The presentation will analyze the pros and cons of DNN models for chemistry, and discuss future prospective about the way models could be created, understood, and distributed.

Keywords: molecular descriptors; predictive modeling; deep neural networks; features extraction.

Use of alignment-free sequence descriptors (AFSDs) in the computer assisted unified vaccine design.

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Now a days viral epidemics are occurring in a frequent manner and creating deadly issues for human health worldwide. Designing a suitable vaccine to protect the population against invading pathogen is the most pivotal approach to combat the problem. Protocols of traditional vaccine design are time-consuming and expensive. The latest advancements of technologies in computer science, bioinformatics, immunology, and genetics have generated new possibilities for development of vaccines within a very short time and at a low cost.

In the process of computer assisted vaccine design, researchers are interested to identify the specific target regions, instead of the whole genome sequence of a virus, from where the maximum efficacy of a vaccine candidate would be possible. In this approach, alignment-free sequence descriptors (AFSDs) play a critical role to identify the targeted regions.

In this presentation, we would like to emphasize the detailed in silico vaccine design protocol to identify specific regions (vaccine candidates) of any new strains of a virus by employing mathematical algorithm and considering the chemical basis of the selected sequence elements. Furthermore, as viruses mutate very frequently, it would be better if one unified vaccine candidate effective against all possible strains (both existing and coming in future) of a virus could be identified. This presentation also includes the detailed process of identification of unified regions to suggest potential vaccine candidates for further practical validation by synthesis of the proposed candidate molecule and wet laboratory testing.

Keywords: AFSD; computer assisted vaccine design; unified vaccine candidate.

Decoding proteomic mysteries: advanced graphical user interfaces for FASTA harmonization and *in-silico* mutation engineering

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Proteomic research relies heavily on the accuracy and efficiency of bioinformatics tools for analyzing and modifying protein sequences. In this work I have introduced two cutting-edge graphical user interfaces (GUIs) designed for FASTA file harmonization and *in-silico* mutation engineering, bridging the gap between user accessibility and computational precision. The developed tools simplify the management of protein sequence data, enabling users to harmonize sequences, validate inputs, and perform up to quadruple mutations across multiple chains in a user-friendly environment. Advanced features include customizable amino acid matrices, interactive error handling, and automated output generation with unique identifiers for seamless data integration.

These GUIs empowers researchers to explore conformational changes and functional impacts of mutations with enhanced accuracy. Extensive tests with single, dual, and multi-chain sequences demonstrate the tool's robustness in handling complex proteomic scenarios, including combinatorial sequence generation and error detection. By combining a streamlined workflow with versatile functionality, this innovation represents a significant leap forward in computational biology, offering a valuable resource for both academic research and applied proteomics.

Keywords: Proteomics; bioinformatics; mutation engineering; FASTA Harmoniser; graphical user interface.

Mathematical chemodescriptors for the characterization of molecular chirality

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Beginning in the middle of the twentieth century there has been an upsurge of interest in the formulation and use of novel mathematical chemodescriptors of molecules and biomolecules. Hierarchical quantitative structure-activity relationship (QSAR) studies using graph theoretical, three dimensional (3-D) and quantum chemical indices found that in many cases the graph invariants gave good quality predictive models which were not much improved after the addition of 3-D and quantum chemical descriptors to the set of independent variables. More recently, we developed the concept of relative chirality index (RCI) to differentiate enantiomers and diastereomers. The first test of any useful index is to check whether it can discriminate closely related structures, which are the enantiomers and diastereomers in case of chiral molecules. For QSAR of molecules with chiral centers only one chirality index that can discriminate among the chiral forms may not be sufficient. The neighborhood where the chiral atom(s) are embedded in the molecule will affect the interaction of chiral ligands with bioreceptors. The type and extent of such interactions cannot be predicted a priori. We need a collection of mutually different chirality indices for the QSAR of chiral molecules of different chemical classes or different bioactivities of the same set of molecules. With this end in view, we designed a series of RCI descriptors based on the weighted graph models of the neighborhoods of chiral centers in the molecules.

This presentation will discuss the results of research in the applications of the novel family of RCI in the quantitative chiral structure-activity relationship (QCSAR) studies of different classes of chemicals.

Keywords: Chirality indices; QSAR; molecular descriptors; numerical characterization.

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Recent trends in the study of Molecular descriptors using Graph theoretic approach

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This paper addresses the prominent study of topological indices through the polynomial representation of graphs, a well-established field with extensive literature. We present a comprehensive survey of graph polynomials and the robust techniques for computing vertex-degree-based indices, along with their significant applications to a variety of chemical structures.

The *M-polynomial* of a graph $G(V(G), E(G))$ is defined as $M(G; u, v) = \sum_{i \leq j} m_{ij} u^i v^j$, where m_{ij} denotes the number of edges $xy \in E(G)$ such that $\{d_x, d_y\} = \{i, j\}$, and d_x, d_y denotes the degree of the vertices x and y in the graph $G(V(G), E(G))$. In this talk, we demonstrate how to compute various degree-based indices, such as the Forgotten Index, Reduced Second Zagreb Index, Sigma Index, Hyper-Zagreb Index, and Albertson Index, using the *M-polynomial*. Additionally, we present an effective method for quickly calculating degree-based topological indices using the M-polynomial for two carbon nanotube structures: $HC_5C_7[p, q]$ and $VC_5C_7[p, q]$. Furthermore, we will discuss the application of the graph operation known as edge corona in the study of chemical structures.

This talk is based on the joint work with Dr. Abhay Rajpoot and Ms. Smrati Pandey.

Keywords: Edge Corona; Graph polynomials; NM Polynomial; degree-based indices; M Polynomial;

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ORAL PRESENTATIONS

Essential oils from a tropical medicinal plant, *Ruta chalepensis* as a potential raw material in the manufacture of vector control formulations

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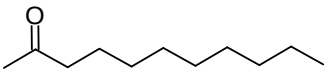
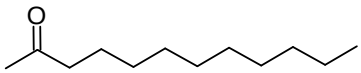
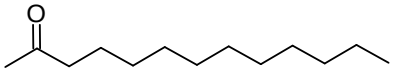
There are several plants that produce methyl ketones such as undecanone (**1**), tridecanone (**2**), dodecanone (**3**) and all these *n*-aliphatic methyl ketones.



undecan-2-one
(1)



dodecan-2-one
(**2**)



tridecan-2-one
(**3**)

These methyl ketones have strong smell and can repel several insects and some reptiles. There are several studies on using *n*-aliphatic methyl ketones as insect repellents. A commercial product by trade name BIO-UD-8 Spray is marketed by Homs, LLC, Pittsboro, NC, USA. The major active content in the spray is 2-undecanone. There are no repellent products available in India with aliphatic methyl ketones as active ingredient. As the essential oil from Ruta plant is a natural botanical extract in this toxicity for human beings will be definitely very low. Hence, it was decided to explore the essential oils from the various parts of the plant *Ruta chalepensis* as a potential alternative to insect repellent that contain synthetic chemicals such as DEET, Picaridin etc.

The plant *Ruta chalepensis* grows in Ooty and in Nilgiris hills of Wester Ghat region Tamil Nadu. Local people and the tribals conventionally use the plant for repelling insects and small reptiles. They tie a small amount of the aerial parts of the plants in toddlers' hands to repel insects and reptiles such as snakes. The plant has a very characteristic strong smell which indicative of high ketone content.

The fruit of *Ruta* is the terminal part and is in the form of a textured capsule which is divided into pointed lobes. The composition of the essential oil extracted was analysed by GC-MS. The GC-MS analysis clearly shows that the methyl ketones are the major contents and constitute to 65.9% of the essential oil and of the methyl ketones 2-undecanone alone constitutes 50.7% [2-nonanone (11.8%), 2-undecanone (50.7%), 2-decanone (1.4%) and 2-tridecanone (2.0%)]. The results are very encouraging to pursue further studies on exploring the extraction of essential oils from various parts of the *Ruta* plant and optimize the distillation conditions for maximum yield.

Keywords: 2-undecanone; *Ruta chalepensis*; essential oil; distillation; methyl ketones.

Bioactive compounds from *Ocimum tenuiflorum* as vector agent against *Aedes albopictus*

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This study investigates the larvicidal potential of *Ocimum tenuiflorum* extracts against *Aedes albopictus*, a key vector for dengue and chikungunya viruses. The objective was to assess the plant's larvicidal activity as a natural alternative to synthetic insecticides, aiming for environmentally safe mosquito control strategies. Immature mosquitoes were collected from the Thiruvarur district, India, and reared to obtain the F1 generation. The third- and fourth-instar larvae were exposed to ethanolic extracts of *Ocimum tenuiflorum* at concentrations of 100, 250, 500, and 1000 ppm using a larvicidal bioassay, which followed World Health Organization (WHO) guidelines, with larval mortality recorded at 24, 48, and 72 hours. Lethal concentration (LC50 and LC99) values were determined using log-probit analysis.

The findings demonstrated a dose- and time-dependent larvicidal efficacy, with LC_{50} values decreasing from 335.7 ppm at 24 hours to 247.5 ppm at 72 hours, indicating sustained potency. Gas chromatography-mass spectrometry (GC-MS) analysis identified several bioactive compounds, including eugenol, methyl eugenol, caryophyllene oxide, phytol, and squalene, suggesting their synergistic contribution to larvicidal activity. Microscopic examination revealed morphological changes in larvae, such as blackened abdomens and extended cephalothoracic regions, likely caused by cellular necrosis or interference with spiracle functionality.

This research highlights the potential of *Ocimum tenuiflorum* as a natural larvicide, contributing to sustainable and eco-friendly vector control strategies. Further studies are recommended to isolate and optimize the active compounds for broader application. This work supports the growing shift towards plant-based solutions in integrated pest management.

Keywords: *Ocimum tenuiflorum*; *Aedes albopictus*; larvicidal bioassay; gas chromatography-mass spectrometry; natural vector control.

Exploring the phytoconstituents and therapeutic potential of *Plumeria rubra* flower extract for SGLT-2 receptor targeting: GC–MS and an *in silico* approach

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Plumeria rubra plants within the *Apocynaceae* family of plants are currently known to be found in India. It holds ethnobotanical importance and is frequently employed in traditional medicines. This research aimed to assess the antidiabetic properties of *Plumeria rubra* flowers by targeting SGLT-2 receptors and determining several phytoconstituents present via GC–MS. The main objective of this research to identify the various phytoconstituents and their potential in targeting the SGLT-2 receptors. We employed GC-MS for the identification of phytoconstituents in the extract. Additionally, in our investigation, we harnessed computational modeling using the Schrödinger Maestro 11.2 edition to leverage interactions among bioactive components. In the methanolic extract of *Plumeria rubra* flowers, various preliminary phytochemical studies revealed the presence of glycocides, terpenoids, flavonoids, and steroids and various types of phytoconstituents, notably Mome Inositol, plumericin, 2-furanmethanol, benzeneacetaldehyde, and 4-ethenylphenol, were detected through GC–MS. Molecular docking studies of 32 phytoconstituents revealed that plumericin, 2-furanmethanol, benzeneacetaldehyde, and 4-ethenylphenol had better docking scores with 7VSI. In this work, a wide array of phytoconstituents were detected in the methanolic extract of *Plumeria rubra* flowers. Four identified compounds will be created as novel antidiabetic drugs for targeting SGLT-2 receptors after proper in vivo and other clinical studies

Keywords; *Plumeria rubra;* GC-MS*;* molecular docking; phytochemical.

In silico evaluation of the isolates of *Calotropis procera* and *Nigella sativa* as anti-cancer potentials

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Cancer is a deadliest disease in which abnormal cells tend to divide uncontrollably and destroy body tissue. They primarily appear in one area, further spreads throughout the body through lymph nodes. Various factors are involved in the progression of disease such as usage of tobacco, genetic causes, unhealthy diet. In the case of breast cancer, gets predominant occurrence in females over 2.3 million, where 6 lakh attained death which is being recorded globally by 2020. There are many plants which chemical constituents are more potential against the breast cancer targets such as ER and HER. *Calotropis procera* is a plant which comes under the family apocynaceae. It is also called as Neela erukku in Tamil which is easily available in tropical and subtropical regions of Asia and have been reported to have cytotoxic, antioxidant, analgesic properties. *Nigella sativa* is a plant which come under the family Ranunculaceae. It is also known as karunjeeragam in Tamil. The pharmacological studies reveal that the plant has anticancer activity. Various phytochemicals namely isovitexin, isoorientin are isolated from *Calotropis procera* and nigellimine *N*-oxide, apigenin, quercetin, epicatechin from *Nigella sativa* for their rich cytotoxic, antioxidant and analgesic properties.

This study aims to unfold the anti-cancer effect of phytochemicals on hormonal targets associated with breast cancer using computational studies.

The phytochemicals were collected after thorough literature review and downloaded from PubChem database. The 3D structure of hormonal targets such as ER alpha and HER 2 were retrieved from protein databank. *In silico* docking studies had been performed using glide, Schrodinger in order to determine the ligand - protein affinity, various interactions within their binding domain and to furnish the docking score. The molecular docking studies were further validated simulation studies using Desmond, Schrodinger.

Upon performing *in silico* docking studies, the number of hydrogen bond and amino acids involved in hydrogen bonding were noted. Binding affinity between ligand and target protein was identified with good interaction and among the phytochemicals' top docking score was shown by isoorientin (-10.227) against HER 2 by hydrogen bonding interaction with ASN 170, SER40, ASN 135 amino acid linkages and apigenin (-10.374) against ER alpha by establishing hydrogen bonding with LEU 346, GLY 420 amino acid residues. Simulation studies revealed the stability of the complex of phytoconstituents such as nigellimine *N*-oxide, isovitexin, isoorientin, apigenin, quercetin, epicatechin with breast cancer target. The important interactions related to anti-cancer activity showed by the phytoconstituents were validated by simulation studies.

This study enables the exploration of anti-breast cancer activity of plant-based products that leads the cancer research to obtain potent anticancer moieties.

Keywords: Isoorientin; apigenin; *in silico* docking studies; simulation studies; anti-cancer activity.

Molecular docking studies of phytomolecules against multi targets associated with antioxidants, anti-inflammatory and anticancer pathways

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Phyto principles remain to possess significant therapeutic applications invariably in treating broad category of diseases through their antioxidant properties. Anti-cancer properties of many natural products are associated with the combined anti-inflammatory and antioxidant properties (AAA). During hypoxia/tumorigenic environment, excessive ROS production leads to activation of oncogenes such as PI3K, MAPK, HIFs, NF-κB. Similarly, during inflammatory conditions high levels of ROS would activate NF-*κ*B pathway, inflammasomes and produces cytokines.

In silico docking studies were carried out on different scaffolds to explore the AAA properties of less studied phyto principles. Hence the present study focused to screen known antioxidants against endogenous targets related to antioxidant enzymes, pro-inflammatory proteins and cancer promoting pathways.

Thirty standard Phyto principles that are known for their AAA property and thirty test phyto principles that are needed to be explored for their AAA properties was chosen for this study. Six targets interrelated with AAA property such as SOD, CAT, PI3, NFkb, MAPK and HO-1 were selected to understand the multiple action of the selected phyto principles on AAA associated pathways. The proposed hypothesis is validated with the known and less explored phytochemicals on AAA response. The molecular docking studies were carried out using Glide, Schrodinger especially using XP mode.

Among different scaffolds selected for the study flavones, flavonoids, and isoflavones are likely to show multiple interactions with AAA targets. The phyto principles form psychotria plant showed highest activity on multiple targets comparable with that of standard molecules. This initial screening delineated the multiple target mediated actions of phytochemicals and the link between antioxidant, anti-inflammatory, and anti-cancer (AAA) responses. Thus, the multiple actions of these Phyto principles can be used as prophylactic agents against AAA related disorders through their immune modulatory activities.

Keywords: Phyto principles; oxidative stress; antioxidant; anti-inflammatory; anti-cancer; In silico studies.

Structural insights into 4-bromomandelic acid as a potent M2 muscarinic receptor antagonist: A molecular docking approach

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The muscarinic acetylcholine receptor (mAChR) subtype M2 plays a crucial role in modulating cardiac, pulmonary, and central nervous system functions. Homatropine, a well-known anticholinergic agent, acts as an antagonist of mAChRs, thereby inducing pupil dilation, alleviating uveal tract inflammation, and suppressing cough reflexes. In this study, molecular docking was conducted to explore the binding interactions of 4-bromomandelic acid, a novel homatropine derivative, with the human M2 muscarinic acetylcholine receptor (PDB: 3UON). The structural modification of homatropine aimed to enhance receptor binding affinity and specificity. The ligand was prepared using molecular modeling approaches, including energy minimization and topology generation. Molecular docking simulations were performed to predict binding conformations and interaction profiles within the orthosteric binding site of the M2 receptor. Key binding interactions, such as hydrogen bonds, hydrophobic contacts, and halogen interactions, were analyzed to understand the contributions of each functional group to receptor affinity. The docking results revealed that 4-bromomandelic acid exhibited stronger binding affinity relative to the parent homatropine molecule. The presence of the bromine atom facilitated halogen bonding and enhanced hydrophobic interactions, which contributed to the improved binding affinity. Analysis of key amino acid residues within the orthosteric site provided insight into the structure-activity relationship (SAR) of this derivative. These findings highlight the potential of 4-bromomandelic acid as a promising M2 receptor antagonist with enhanced binding characteristics. This study provides valuable insights into the SAR of homatropine analogs, offering a rational basis for the development of more potent and selective anticholinergic agents. Future studies will focus on in silico ADMET profiling and molecular dynamics simulations to further evaluate the pharmacokinetic and dynamic properties of this promising derivative.

Keywords: mAChR; 4-bromomandelic acid; homatropine; docking; ADMET profiling.

Optimizing large-scale molecular docking: A novel software prototype for efficient drug discovery

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Drug discovery is a complex and resource-intensive process, where identifying the right lead compound is crucial to the project's success. Molecular docking has become a key tool in this process. Through computer-aided drug design (CADD), significant reductions in time and cost can be achieved by efficiently guiding experimental research toward more promising compounds. Techniques like molecular docking and virtual screening (VS) complement traditional experimental methods, providing valuable insights early in the discovery process.

Molecular docking involves predicting the optimal position, orientation, and conformation of a small molecule (drug candidate) when it binds to a target protein. This approach aids in identifying potential drug candidates and streamlines lead optimization. By docking compounds from large databases, virtual screening enables the rapid identification of promising hits from vast compound libraries.

However, large-scale molecular docking has several challenges. Docking hundreds of thousands or even millions of compounds against a target protein demands substantial computational resources and time. For example, calculating the binding affinity of a large database like Enamine's xREAL space, containing around 666 million compounds, could take days or even weeks. This process becomes a significant bottleneck due to its computational intensity.

Another challenge arises when training machine learning (ML) models on publicly available data to predict docking results. A limitation of this approach is that the receptor used for training might have a different binding surface area compared to the receptor being docked, leading to discrepancies in predictions.

To address these challenges, we developed a software prototype that enhances both the speed and accuracy of the docking process. Instead of docking every compound in the database, our approach first docks a random sample of 5,000 to 10,000 compounds. This sample data is then used to train a machine learning model on the fly. We use a random forest regressor model, which is trained during the docking process. The model predicts docking scores based on key properties such as molecular weight, logP, receptor binding area, and the number of rotatable bonds—data collected during the docking procedure.

Additionally, the data generated during docking can help identify structure-activity relationships (SAR), providing insights into how compound modifications can influence binding affinity. While the predicted docking scores may not be highly accurate, they serve as an initial filter to eliminate compounds with little potential, thereby reducing the number of candidates for further investigation.

Beyond docking predictions, our software prototype also forecasts other key properties like synthetic accessibility, drug-likeness, and adherence to Lipinski's Rule of Five and the Rule of Three. By integrating these capabilities, our software aims to accelerate the early phase of drug discovery, improving efficiency and helping researchers focus on the most promising drug candidates more quickly.

Keywords: Large-scale docking; computational efficiency; binding score prediction; enamine xREAL space; random forest regressor.

Inter- and intra-molecular interactions and dielectric dispersion studies of amino acid solubilized in anionic surfactant solution

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The effectiveness of surfactant-amino acid molecular level interactions in chemical, biological and industrial applications make them highly important to study. Soft condensed matter physics has been active in studying the impact of micellar stability on technological process. The strong impact of the co-solvent on self-aggregation leads to Critical Micelle Concentration (CMC) and strong binding affinity with small and medium biomolecules. Amino acid-surfactant interactions are high epicenters. Dielectric Relaxation Spectroscopy (DRS) is a strong and versatile tool to monitor the dynamic process of such a micellar system. Complex permittivity spectra of the surfactant SDS with the amino acid LM were studied in the frequency range 10 MHz to 50 GHz, Changes in dielectric parameters (dielectric constant, dielectric loss) of the medium and the relaxation time of micellar solution (SDS) with water in the presence and absence of LM will be discussed. Time Domain Reflectometry (TDR) was used to obtain the dielectric data of the samples in reflection mode. A sampling oscilloscope and plug-in-model were used in TDR technique. The results show that the dielectric constant and relaxation time decrease up to equal volume fraction and then increase gradually. The dielectric constant and relaxation time were also found to increase with increase in temperature (288 K to 303 K). The same trend reflected in dielectric strength and activation energy. The relaxation time of the samples obtained is in the order of 11 to 13 ps which is greater than that of Debye rotational relaxation of monomer species. Our findings show that in amino acid-surfactant mixtures, the amine groups are highly solvated at the surface of SDS micelles, due to the interaction at the surfactant-water-amino acid interface.

Keywords: Sodium dodecyl sulfate (SDS); L-methionine (LM); Dielectric RelaxationmSpectroscopy (DRS); Time Domain Reflectometry (TDR).

Dielectric Relaxation Spectral and molecular interaction analysis of aqueous pyrazine in ethanol using Time domain reflectometry (TDR)

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The dielectric behavior of aqueous pyrazine + ethanol mixtures was studied by using time domain reflectometry (TDR) at various temperature (303 K-288 K) in steps of 5 K. The study was carried out in various concentrations and in the frequency range 10 MHz to 30 GHz. Dielectric Relaxation Spectroscopy (DRS) gives the type of molecular interactions of solute-solvent and co-solvent interaction specifically. The complex permittivity spectra of the mixture were recorded using TDR. The dielectric parameters such as relaxation time, dielectric permittivity at low and optical frequency, and static dielectric constant calculated from the spectra indicate the relaxation properties of the complex solutions. The π electron cloud of aromatic ring creates a through bond interaction, and the swapping of hydrogen by wait and switch type in nitrogen of pyrazine with ethanol create variations in the dielectric parameters. This variation validates the intra- and inter-molecular interactions.

Keywords: Dielectric parameter; TDR; complex permittivity; relaxation time; molecular interaction.

Computational insights into photoactive systems: exploring photoswitching, TADF, and photosensitization

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This presentation showcases a series of computational investigations into photoactive systems, emphasizing their unique functionalities and potential applications.

We begin with an exploration of potential **photoswitches**, analyzing their structural and electronic responses under varying conditions to uncover insights into their photochromic behavior. These studies highlight how specific environmental factors influence switching efficiency and stability, offering guidelines for their practical implementation.

The focus then shifts to **thermally activated delayed fluorescence (TADF)** capabilities, where we investigate singlet-triplet energy gaps, spin-orbit coupling, and Reverse Intersystem Crossing (rISC) rates. Through detailed excited-state analyses, we examine how molecular architectures and donor-acceptor interactions contribute to the realization of efficient TADF properties.

Lastly, we delve into **photosensitization processes** critical for singlet oxygen generation in photodynamic therapy (PDT). Computational studies unravel the mechanisms of intersystem crossing and triplet-state dynamics, providing valuable insights into designing efficient and non toxic photosensitizers.

These studies, carried out through computational approaches, demonstrate the critical role of theoretical methods in understanding and advancing photoactive systems for diverse applications.

Keywords: photoactive systems; photoswitches; TADF; photodynamic therapy.

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Prosopis juliflora leaf extract assisted synthesized tin oxide nanoparticles for applications high-performance supercapacitor electrode

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The advancement of supercapacitor technology is impeded by a dearth of advanced electrode materials that can augment energy storage capabilities. In this-work, we adapte a novel, sustainable methodology for synthesizing tin oxide nanoparticles (SnO_2-PJ NPs) utilizing *Prosopis juliflora* aqueous leaf extract as a stabilizing and reducing agent for the first time. These nanoparticles were evaluated in comparison to those synthesized via traditional chemical methods (SnO_2-pure NPs). The samples were analyzed using an array of techniques including ultraviolet spectroscopy (UV), Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDX), photoluminescence (PL), powder X-ray diffraction (XRD)and X-ray photoelectron spectroscopy (XPS). The results indicated that the SnO_2-PJ NPs exhibited superior performance as supercapacitor electrodes in both three-electrode and two-electrode system configurations. They displayed a high specific capacitance (189 F/g at 1 A/g) and energy density (31 Wh/kg at 0.35 kW/kg) in an acidic electrolyte of1 MH_2SO_4. Additionally, the SnO_2-PJ NPs demonstrated exceptional cycling stability, maintaining 100% of their specific capacitance after 10,000 cycles. In conclusion, the SnO_2-PJ NPs exhibit tremendous potential as a next-generation energy storage material, owing to their high-powerdensity, high-energy density, and outstanding capacity.

Keywords: Green synthesis; *Prosopis juliflora* leaf extract; SnO_2 nanoparticles; supercapacitor electrode.

Green synthesis of zinc oxide nanorods using *Ficus benghalensis* aerial root extract and enhanced antibacterial activity

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In the present work zinc oxide nanorods and *Ficus benghalensis* – zinc oxide nanorods were developed by hydrothermal method. The physiochemical characteristics of the nanorods were investigated. X-ray diffraction spectrum confirms the formation of well crystalline nanorods along (101) orientation. The particle size of nanorods was noticed to be lesser than the chemically synthesized Zinc Oxide nanorods. The PL spectrum shows a broad red emission peak and a sharp blue emission peak. The width of the energy gap of nanorods is lesser than the chemically synthesized ones. The functional groups of the Nanorods were determined by Fourier Transformation Infrared analysis. Scanning Electron Microscope - Energy Dispersive X-ray analysis micrograph reveals the morphology of the nanorods and elements present. The antibacterial efficiency of the Nanorods was evaluated by the Agar well diffusion method against some multi-drug safe oral microbes.

Keywords: ZnO nanorods; bacteria; *Ficus benghalensis* root; microstructural parameters; photoluminescence; antibacterial.

One-pot bioinspired synthesis of PbO/CuO/FeO trimetallic oxide nanocomposite using *Vitis vinifera* fruit juice for highly sensitive electrochemical detection of 4-nitrotoluene

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The determination of explosive nitroaromatic chemicals has prompted concerns about human safety around the world. In this work, we demonstrate an electrochemical sensor based on trimetallic oxide nanocomposites modified screen-printed carbon electrode (SPCE) for the detection of nitroaromatic compounds. Trimetallic oxide nanocomposites are multiphase materials containing ternary metal oxides. Because of their high specific surface area, superior electron transport capabilities, and favourable catalytic behaviour, they are frequently employed as antibacterial materials, catalysts, and sensors. In order to combat the problems associated with high manufacturing costs, low selectivity, and low sensitivity of conventional sensors, this paper reports on the construction of an electrochemical sensor for 4-nitrotoluene (4-NT) using a trimetallic oxide nano-sensor. The nano-sensor is composed of transition metal oxides copper and iron combined with post-transition lead metal oxide. In this study, we prepared a PbO/CuO/FeO TMO NCs/SPCE (PbO/CuO/FeO TMO NCs/SPCE) sample with different individual metal oxides synthesized by a green reduction method using *Vitis vinifera* fruit juice. SEM was used to observe and validate structural and morphological variations brought on by various metal compositions. The four bio-synthesized materials comprise dispersed multiphase matrices containing varying shapes of nanoparticles with different morphologies. The elemental and phase arrangements of the synthesized samples were investigated employing UV, FT-IR, XRD, and EDAX approaches. The findings of the electrochemical measurements indicate that the SPCE modified with PbO/CuO/FeO TMO NCs/SPCE has enhanced sensing capabilities over CuO, FeO, and PbO NPs for 4-NT; the limit of detection is 4.512 nM and sensitivity is -0.531μA nM^{-1} for the developed sensor. Notably, recovery values (99.2–101.7%) in water samples showed that evaluating interfering species from different contaminants had no effect on the sensing of 4-NT. All of these findings show that the newly developed sensor performs well in terms of reproducibility, selectivity, and sensitivity for the detection of 4-NT.

Keywords: Green synthesis; *Vitis vinifera* fruit juice; Trimetallic oxide nanocomposites; electrochemical sensor; 4-nitrotoluene.

Characterization of sequence similarity using BLAST versus novel alignment-free information theoretic sequence descriptors: A case study with Infectious Salmon Anemia Virus (ISAV) sequences

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Nucleic acid sequences determine the biological properties of organisms in a complex manner. Structure (sequence) -property similarity principle (SPSP) is applied to compare sequences in order to characterize their bioactivities. One alignment-based sequence comparison approach is the BLAST analysis. Because of the complexity of the situation methods other than BLAST can be applied to analyze sequence-property similarity of biologically important nucleic acids. Therefore, in this work we carried out a comparative study of sequence similarity with a set of Infectious Salmon Anemia Virus (ISAV) sequences using BLAST versus novel alignment-free method derived based on Euclidean distance derived from our novel information theoretic sequence descriptors.

Keywords: Sequence comparison; BLAST analysis; Structure (sequence) -property similarity principle (SPSP); Infectious Salmon Anemia Virus (ISAV); novel information theoretic sequence descriptors; Euclidean distance.

Predicting mutagenicity of a diverse set of chemicals using mathematical molecular descriptors and different statistical methods

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Assessment of potential mutagenicity of chemicals is important for environmental protection and new drug discovery. Because the cost of laboratory testing of chemicals is prohibitively costly, both in the United Stated of America and European Union there is an increased interest in the use of *in silico* models for the prediction of mutagenicity of commercially important chemicals. Development of quantitative structure-activity relationship (QSAR) models from purely computed descriptors is a cost-effective way of deriving mutagenicity data for decision support systems. In this presentation we have used a suite of statistical/ machine learning methods to develop QSAR models for the assessment of mutagenicity of a structurally diverse set of 508 chemicals from their computed structural descriptors. Our results show that we can achieve a high classification accuracy greater than 70% by using an appropriate machine learning method. The use of only numerical structural molecular descriptors as independent variables was sufficient for this classification purpose. The addition of atom pairs (APs), a type of substructures, to the set of predictors does not improve the prediction accuracy significantly.

Keywords: Quantitative structure-activity relationshi0p (QSAR); molecular descriptors; Atom pairs (APs); Penalized logistic regression with MCP penalty; Generalized partial least square; Random Forest; mutagenicity.

Machine learning-integrated template-guided docking: a novel approach for identifying potent HIV-1 NNRTIs

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The present study highlights the enhanced performance of template-guided docking compared to simple docking in achieving improved binding efficacy within the non-nucleoside inhibitor binding pocket (NNIBP) of NNRTI-class HEPT derivatives. This method establishes an efficient docking protocol that ensures superior binding orientations and binding energies for HEPT analogues. The analysis revealed that lipophilic interactions play a pivotal role in determining the antiviral potency of the inhibitors. Although electrostatic interactions have a lesser impact, they are compensated by aromatic π-π stacking with nearby polar residues. Water molecules in the active site appear to have minimal influence, likely due to their greater distance and the absence of favorable hydrogen bonding. Notably, the 3-N of the pyrimidine ring significantly contributes to hydrogen bonding by forming an H-bond with LYS101. The data-mining capabilities of the proposed model surpass those of the simple docking protocol, effectively identifying novel and potent hits from large datasets. Additionally, the model demonstrates promise in overcoming drug resistance by leveraging structural interactions and conformational flexibility, facilitating multiple binding modes. This approach offers a robust strategy for improving antiviral efficacy and mitigating susceptibility to drug-resistant mutants.

Keywords: AIDS; HEPT; template-guided docking; MLR; ANN; antiviral activity.

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A DFT study of lead-free halide perovskites $GaMX_3$ (X= Sr, Ba; X= F, Cl) for solar cell applications

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Halide perovskites are an important class of materials with unique physicochemical properties. Lead-free halide perovskite materials have gained a lot of popularity in recent decade among researchers due to its applications in photovoltaic devices. In this work, lead-free halide perovskites such as $GaMX_3$, M = Ba, Sr and X = F, Cl are examined using Density Functional theory (DFT) technique. Optimization of $GaMX_3$ is performed using functionals LSDA/DEF2TZVP within DFT framework. HOMO-LUMO energy gap of $GaBaF_3$, $GaSrF_3$, $GaBaCl_3$ and $GaSrCl_3$ are found as 2.608, 2.879, 3.509 and 3.4002 eV. Computed data shows their probable uses in photovoltaic devices. CDFT based global descriptors are also calculated.

Keywords: Density Functional Theory; lead-free perovskite materials; $GaSrF_3$; $GaBaCl_3$; HOMO-LUMO gap.

Design and evaluation of quercetin-5-fluorouracil conjugates and other similar conjugates as anti-cancer agents

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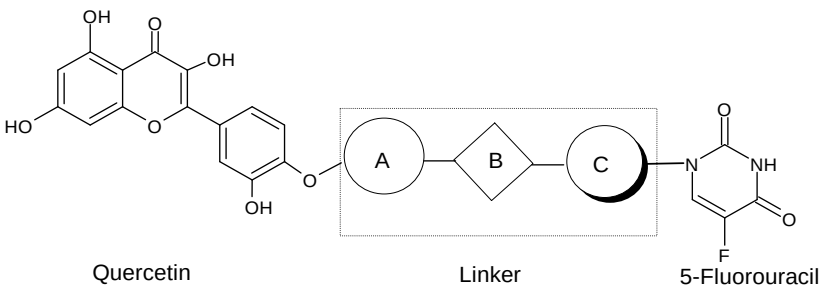
The main objective is to identify new molecules to treat cancer in general and colorectal cancer (CRC) in particular. Natural molecule namely, quercetin which has anticancer property was the choice and the conjugates of quercetin and 5-fluorouracil were explored. The conjugates of quercetin are like prodrugs/dual drugs, owing to their susceptibility to undergo metabolism in human body and lead to quercetin and 5-fluorouracil, both of them eliciting anticancer property individually. The molecules designed herein are a new class of compounds that have not been reported and used earlier. The new molecules are expected to be more potent because of their anticancer properties with synergistic effect through the combination of quercetin and 5-fluorouracil, a well-known chemotherapeutic agent

Nine proteins were identified as the target for treating CRC. The nine proteins and their PDB ids are:

1. Matrix Metalloproteinase-2 (**1HOV**)
2. Poly [ADP-ribose] polymerase-1(**1UK0**)
3. Cyclin dependent kinase CDK-2 (**2A4L**),
4. Chk1 (**2R0U**),
5. Nitric oxide synthase (**3E7G**),
6. Cytochrome P450 CYP17A1(**3RUK**),
7. Cyclin A (**6GUE**),
8. TRAF2 & NCK interacting protein kinase (**2X7F**)
9. Apoptosis regulator Bcl-2 (**4LXD**).



Each of the eight quercetin conjugates of the general structure shown above were docked on to the nine target proteins using AutoDock/Vina and the docking scores were recorded. They were compared with the docking scores of standard reference compounds. Several of the new molecules, quercetin-5-fluorouracil conjugates were found to have higher docking score than the reference molecules indicating better potency as a drug candidate. Further investigation and synthesis are in progress. The *in-silico* docking study with various colorectal cancer targets resulted in the identification of compounds having the best fit. These shortlisted compounds form the basis for further optimization and evaluation for potency and safety.

Keywords: Conjugates; quercetin; 5-fluorouracil; colon rectal cancer; molecular docking.

A novel bio-indicator of soil fertility

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Medicinal plants are a pride to our nature. It is estimated that there are more than 45,000 species of medicinal plants present in our country. Of these only 60% of plants are officially used by practitioners and 40% of plants are used traditionally. One such traditionally used ethanomedicinal plant is *Pergulariadaemia* which is used to treat several ailments. It is a latex plant, pungent smelling and perennial twinning herb belonging to the family Asclepiadaceae. Seeds of this plant have velvety hairs and are dispersed through wind with cottony appearance. This is one of nature's gifts that the plant spread widely across the planet, thus acting as floating fairies. Hence, these plants are found mostly along the roadsides forming hedges of tropical and subtropical regions. It is commonly known as "Veliparuthi" in Tamil and "Hariknot" in English. In Tamil, the term "Veli" denotes "a guardian" or "a protector". It is interesting to note that the Siddha medicine had named only two medicinal plants which act as a shield for humans. One is Veliparuthi (*Pergulariadaemia*) and the other is kodiveli (*Plumbago zeylanica*), as they both have multiple valuable properties. *Pergulariadaemia* is mainly used to cure emmengogue and asthma. It also has anti-diabetic, anti-inflammatory, antipyretic, anti-bacterial, anti-fungal, anti-oxidant, anti-helmintic, depurative, analgesic, astringent, expectorant, laxative, thermogenic, hepatoprotective, relaxant, strangury, and wound healing properties.

Soil is one of the most significant factors in supporting plant growth. High ratio of soil pollution is caused by the presence of xenobiotics or other alteration in the natural soil environment. The most fascinating fact is that *Pergulariadaemia*acts as a bio-indicator of soil fertility. The folklore, people of Mali regions have the practice of cultivating *Pennisetumglaucum* along with *Pergulariadaemia* and found an increase in the grain weight of millet. Hence the objective of the study is to prove the novelty that *Pergulariadaemia* increases the soil fertility by showing plant growth as an indicator and can produce high quality crops at zero cost and thus also act as a phytoremediator.

Special effort has been made to prove that the addition of termite soil to *Pergulariadaemia* also improves the soil fertility thus making it a two-fold increase. Termites are a group of soil dwelling insects. They increase the soil fertility by increasing the levels of N, P, K, Ca and Mg. Hence this study also reveals the effects of termite activity on soil profile development, soil physio-chemical parameters, soil microbiology and plant growth thus proving that the effects of termite activity on plant production generally indicates a positive influence. For this reason, "Termites are called as the world's best bio-converters," and great compost producers of the modern era.

Keywords: Termite soil; phytoremediatior; soil fertility.

Synthesis of Schiff bases as corrosion inhibitors

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The current study generated two Schiff bases, namely, (2E,2'E)-2,2'-(pyridine-2,3-diylbis-(azanylylidene))bis(1,2-diphenylethanol) (**BPA),** (E)-2-((2-hydroxy-1,2-diphenylethylidene)-amino)phenol (**BAP**), were employed as highly efficient inhibitor of mild steel corrosion by corrosive acid. Inhibition efficiencies were estimated based on weight loss method. Moreover, scanning electron microscopy was used to investigate the inhibition mechanism. The synthesised Schiff bases were characterised by FTIR, NMR, Mass, and Micro-elemental analysis. The inhibition efficiencies depend on four factors the amount of nitrogen in the inhibitor, the inhibitor concentration, molecular mass, and conjugation of the double bond. Inhibition efficiencies of 98 and 94% were achieved with BPA and BAP, respectively, at the maximum tested concentration.

Keywords: Schiff bases; Corrosion inhibitor; FT-IR; NMR.

Atom-bond sum connectivity index of fuzzy graphs

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The study of graph connectivity has long been an essential part of mathematical graph theory. Recently, the concept of fuzzy graphs, which involve membership values for edges and vertices, has emerged as a significant extension of classical graph theory. In this paper, we introduce the atom bond sum connectivity (ABS) of fuzzy graphs, a measure that aims to capture the connectivity of a fuzzy graph based on a weighted approach that incorporates the interaction of atoms (vertices) and bonds (edges). We define and explore the properties of ABS, investigate its relationships with classical connectivity measures.

Keywords Fuzzy graphs; atom bond sum connectivity; graph theory; connectivity measures; fuzzy set theory; weighted connectivity

POSTER PRESENTATIONS

Semi-synthetic PTP1B inhibitor from *Cassia auriculata* linn. by *in silico* method for diabetes management

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The n-butanol extract from the flowers of *Cassia auriculata* Linn. contains a compound, propanoic acid 2-[3-acetoxy-4,4,14-trimethyl androst-8en-17-yl] which inhibits protein tyrosine phosphatase 1B(PTP1B)**.** PTP1B down regulates insulin and leptin signalling by dephosphorylating insulin receptors, contributing to insulin resistance in type 2 diabetes. By inhibiting PTP1B, this compound could enhance insulin sensitivity, improving glucose metabolism and potentially aiding in the management of diabetes. The objective of this study is to enhance the aqueous solubility of the compound and improve the binding affinity of the compound to the target protein Also to minimize the toxicity of compound. The working methodology of this study is through an Advanced computer-aided drug design tools. The SWISS ADME software was utilized to optimize the compound's properties. The modified molecule was applied for Molecular docking studies with SWISS DOCK evaluated the binding affinity of both the original and modified compounds to PTP1B. Additionally, computational toxicological assessments conducted via ProTox-3.0 compared the toxicity profiles of the original and modified compounds. As a result of this the structural modifications, specifically converting the acetoxy and acidic groups at the 3- and 17-positions into an acid and an amide, respectively, resulted in several key improvements. The new modified molecule improved its aqueous solubility, the Log S value increased from -6.19 to -5.54, as calculated using SWISS ADME. The Molecular docking via SWISS DOCK revealed a threefold enhancement in binding affinity, with the AC score improving significantly from -5.45 to -18.55. When studying the toxicological profile of both molecules by ProTox-3.0 analysis the modified compound demonstrated significantly reduced toxicity and avoided interactions with unintended receptors outside the specified targets. While the original compound exhibited respiratory toxicity, cardio toxicity, immunotoxicity, carcinogenicity and interacting with androgen receptors (AR), gamma-amino butyric acid receptors (GABAR), pregnane X receptors (PXR). These findings indicate that the modified compound is superior in solubility, binding affinity, and safety compared to the original, making it a promising candidate for further development. This work will provide an excellent outcome than existing synthetic PTP1B inhibitor such as Ertiprotafib have encountered challenges in clinical trials. This natural semi-synthetic inhibitor offers a promising alternative for managing type 2 diabetes. It’s enhanced pharmacokinetic and safety profile positions it as a strong candidate for improved clinical trial outcomes.

Keywords: *Cassia auriculata* Linn.; PTP1B inhibitor; SWISS ADME; SWISS DOCK; PROTOX-3.0; Computational toxicological; solubility; antidiabetic activity.

Exploring the role of revolutionizing the potential of explainable AI in drug discovery

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Artificial intelligence (AI) has the potential to revolutionize the drug discovery process, offering improved efficacy, accuracy and speed. However, it depends on the availability of high quality of data. Physical applications include the following robot assisted surgery, AI-enhanced prosthetics, real time patient monitoring and automated laboratory process. For example, AI in robot assisted surgery can provide medical professionals with relevant information to assist them in making more informed decisions. While AI cannot replace human doctors, it can enhance their capabilities and improve patient care. Thus, AI powered surgical robots enable surgeons to perform complex procedures with greater precision and control. These robots can reduce the risk of complications, minimize invasions, and shorten recovery times, and lead to better surgical outcomes. On other hand AI-driven prosthetics are developed to adapt to the user's movements and respond to their natural signals. These advance prosthetics significantly improve the quality of life for amputees, and allowing them to perform complex task with greater ease and naturalness. AI based monitoring system continuously analyze patient data such as their vital signs and electronic health records, to identify the potential signs of deterioration or complications. This enables healthcare providers to intervene on time and avert adverse events. Studies have also shown that AI- based algorithms can outperform human doctors in certain diagnostic tasks, such as detecting certain types of cancer or interpreting pulmonary function tests. In some automated laboratory process, include sample analysis, sorting and preparation this reduces the workload of laboratory staff and minimize the risk of human errors, ensuring more accurate results. Quantitative structure-activity relationship (QSAR) has served as a valuable predictive tool in drug designing and developing. QSAR methods have been applied in the development of relationship between properties of chemical substance and their biological activity to obtain a reliable statistical model for prediction of the activities of new chemical entities and they can help in identify the candidate compounds with specific biological activities, and optimize a balance of potency, selectivity and other parameters to develop safe and effective drugs. Classical QSAR studies include ligand with their binding site, inhibition constants, rate constants and other biological end points and in addition to molecular properties such as lipophilicity, polarizability, electronic and stearic properties or with certain structural features. 3D QSAR has emerged as natural extension to the classical Hansch and Free-Wilson approaches, which exploit the three-dimensional properties of the ligand to predict their biological activities using the robust chemo metric techniques such as PLS, G/PLS and ANN. Computer-aided drug design (CADD) have become powerful tool in development of drug discovery. These methods include structure-based design such as molecular docking and dynamics and ligand-based design such as QSAR and pharmacophore modeling. In addition, the increasing number of X-rays, NMR and electron microscopy structures of biological target, along with fast and inexpensive hardware, have led to the development of more accurate computational methods that accelerated the discovery of novel chemical entities.

Keywords: AI enhanced automated laboratory process; QSAR studies; CADD; NMR and electronic microscopy.

Molecular dynamics simulations of phytochemicals from *Citrullus colocynthis* and *Pulicaria crispa* for anti-cancer potentials

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Cancer is a disease characterized by uncontrolled cell growth that can spread throughout the body. Factors such as genetics, tobacco use, and exposure to carcinogens can trigger it. Breast cancer, one of the most common types among women, occurs when abnormal cells develop in breast tissue. In 2020, over 2.3 million new cases were reported globally. Despite treatment advancements, it remains a leading cause of cancer-related deaths, highlighting the need for early detection and continued research.

We investigated two medicinal plants with promising potential against breast cancer targets: *Citrullus colocynthis* (bitter apple) and *Pulicaria crispa*. *Citrullus colocynthis*, from the Cucurbitaceae family, and *Pulicaria crispa*, from the Asteraceae family, are known for their strong antioxidant and anticancer properties. Given the role of growth factors in cancer progression, there is a need for developing effective drug candidates. This study focuses on revealing the anti-cancer potentials of various chemical components from both plants through docking studies.

In this study, we used Glide Schrodinger to perform *in silico* docking analysis of plant phytoconstituents against breast cancer targets such as ER alpha and HER-2. Molecular dynamics simulation studies were performed using Desmond Schrodinger to validate the docking results.

The selected phytoconstituents demonstrated significant interaction with the breast cancer targets. After the docking process, the number of interactions formed with the specific amino acids was observed. The docking study of various phytochemicals with the HER2 kinase domain highlights their binding affinities and key interactions. Epicatechin (-8.054) forms hydrogen bonding and pi-pi stacking with ASN 135, TYR 137, and TYR 217. Caffeic acid (-7.562) binds hydrogen with ASN 135, ARG 175, GLN 39, and ASN 72. Kaempferol (-7.468) also forms hydrogen bonds and pi-pi stacking with SER 40, ASN 135, and TYR 137, while Gallic acid (-7.142) interacts through hydrogen bonds with ASN 135 and THR 94. ASN 135 is commonly involved in all interactions, highlighting its importance in binding to the HER2 kinase domain. The docking study of various phytochemicals with the ER alpha protein reveals their binding parameter. Apigenin (-10.374) forms hydrogen bonds with LEU 346 and GLY 420, while Quercetin (-10.352) binds through hydrogen bonds with ASP 351, GLU 353, and ARG 394. Kaempferol (-7.585) interacts via hydrogen bonds with ASP 351. In contrast, Beta-caryophyllene (-8.161) and Caryophyllene oxide (-8.139) do not show specified interactions in this analysis. In this phytoconstituent, Apigenin exhibits the highest docking score of -10.374 with the amino acids LEU 346 and GLY 420. Molecular dynamics simulations confirmed the stability of phytoconstituents from *Citrullus colocynthis* and *Pulicaria crispa* in breast cancer target complexes. This computational study will lead the development of natural complexes from medicinal plants as anti-cancer agents

Keywords: Molecular dynamics simulations; phytochemicals; *Citrullus colocynthis; Pulicaria crispa*; breast cancer targets.

Molecular dynamics study of afimetoran using Desmond: Insights into structural dynamics and binding interactions

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Afimetoran, a novel immunomodulatory compound, has garnered significant attention for its therapeutic potential in managing inflammatory and autoimmune disorders. To unravel the molecular intricacies of its activity, we employed molecular dynamics (MD) simulations using the state-of-the-art Desmond software. This study delves into the structural behavior, binding interactions, and stability of afimetoran in complex with its target receptor, providing a detailed molecular perspective on its mode of action. The computational workflow involved meticulous preparation of the afimetoran-receptor system. The structure was solvated using a TIP3P explicit water model and neutralized with counterions, ensuring a physiologically relevant environment. Periodic boundary conditions were applied, and energy minimization was conducted to eliminate steric clashes and stabilize the initial configuration. Following system equilibration under NVT and NPT ensembles, a 100-nanosecond production run was performed, employing a 2-femtosecond time step. Long-range electrostatic interactions were handled via the particle mesh Ewald (PME) method, with the OPLS4 force field providing high-fidelity parameterization. Key findings from the simulations revealed afimetoran's remarkable structural stability and strong binding affinity. Root mean square deviation (RMSD) analysis indicated that the system stabilized within the initial 10 ns of simulation, with deviations consistently below 2.5 Å, demonstrating robust convergence. Root mean square fluctuation (RMSF) data highlighted flexible regions within the protein, primarily localized in distal loop regions, suggesting minimal perturbation to the overall protein structure upon ligand binding. Binding interactions were extensively analyzed, unveiling a network of persistent hydrogen bonds, hydrophobic interactions, and π-stacking phenomena critical to afimetoran's affinity. Residues within the binding site demonstrated consistent engagement with the ligand throughout the simulation. Free energy calculations using the molecular mechanics generalized Born surface area (MM-GBSA) method underscored a favorable thermodynamic profile, reinforcing the stability of the afimetoran-receptor complex. Further insights were gained through solvent-accessible surface area (SASA) analysis, which revealed conformational adjustments at the binding site upon ligand binding, shedding light on the adaptive nature of the interaction. Principal component analysis (PCA) captured dominant motions within the receptor, emphasizing dynamic features crucial for afimetoran's functional engagement. This comprehensive study highlights afimetoran's structural resilience and high binding affinity, providing a molecular foundation for its therapeutic efficacy. Beyond its immediate findings, this work exemplifies the power of Desmond simulations in deciphering complex molecular behaviors with exceptional precision. The results pave the way for future investigations into afimetoran's interactions with additional targets, as well as opportunities for optimizing its pharmacological properties through rational drug design. In conclusion, the molecular insights garnered from this study not only enhance our understanding of afimetoran's mechanism of action but also serve as a vital resource for advancing its development as a potent therapeutic agent.

Keywords: Molecular dynamics; afimetoran; desmond; autoimmune disorder; TIP3P.

Quantum mechanical analysis of the conformational and structural properties of clopidogrel bisulfate in the gas phase

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This study presents a comprehensive theoretical investigation of Methyl (+)-(S)-O-(2-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridine-5(4H)-acetate hydrogen sulfate, commonly known as Clopidogrel bisulfate ($CPG.H_2SO_4$), an antiplatelet agent. Unlike previous Density Functional Theory (DFT) studies that examined clopidogrel base and sulfuric acid individually, our research focuses on the combined bisulfate molecule. Employing the B3LYP method with the 6-311+G (d, p) basis set, we analysed the molecule's molecular structure, vibrational properties, thermodynamic characteristics, and Frontier Molecular Orbitals (FMO). The HOMO-LUMO analysis revealed critical information on charge transfer potential, band gap, and pharmacological relevance. The C3 conformer emerged as the most stable structure with the lowest energy, exhibiting notable electron-withdrawing behaviour. Electrostatic potential (ESP) analysis provided valuable insights into electron distribution and potential reactive sites. These findings contribute to a deeper understanding of $CPG.H_2SO_4$'s drug-receptor interactions and its pharmacological profile.

Keywords: Clopidogrel bisulfate; Density Functional Theory (DFT); B3LYP; vibrational analysis; electrostatic potential (ESP).

Identification of new chemical entities targeting glycogen synthase kinase-3 protein using *in silico* through artificial intelligence having indirubin as reference molecule

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Glycogen synthase kinase-3 is a highly preferred protein serine/threonine kinase plays a central role in wide variety of cellular processes concerned with catabolic and anabolic pathways. Designing active molecules acting on GSK3, with suitable characteristics like minimal toxicity, high bioavailability, cost effective is required in current scenario as the existing GSK3 inhibitors show cardiac toxicity. To achieve this Indirubin is taken as a basic analogue. This study is aimed to obtain indirubin derivatives inhibiting Glycogen synthase kinase 3 (GSK3) by AI driven pharmacophore modelling followed by virtual screening.

Creation of drugs using computers is benefiting medical chemistry which leads to early scepticism related to the use of AI in pharmaceutical discovery. Pharmacophore based virtual screening will be carried out using web-based tools. The pharmacophore (Ligand based) was generated from compound libraries known for their affinity data (IC_{50}) against Alzheimer's disease. Subsequently, the validated pharmacophore will be the query input for virtual screening in the molecular libraries containing indirubin derivatives. The molecules closer to the structure of indirubin are modified. To curate a focused library of indirubin derivatives for this investigation, we initiated a structure similarity search within the PubChem database, utilizing indirubin as the reference molecule for compound identification. The search criteria were anchored on the Tanimoto coefficient, a measure of chemical similarity, with a threshold set at≥0.85 to ensure a high degree of structural resemblance to the indirubin scaffold. This stringent threshold was deliberately chosen to maintain structural integrity, and upon application, yielded an initial list of compounds exceeding our target number. Using AI tool Github the new molecules are generated which are isoforms of indirubin which are less toxic than indirubin. Pharmacophore based virtual screening and molecular docking are done AI platform. Final Validation of compounds was done using Schrodinger. ADME-Tox prediction was carried out to filter the toxic and compounds do not show desired pharmacokinetics properties. The molecules closer to the structure of indirubin were selected for virtual screening. Pharmacophore modelling based on the 3D structure of Alzheimer's disease drug targets done in this study.

The AI aided pharmacophore modelling based virtual screening was done this study. For practical considerations related to computational and experimental manageability, we constrained our selection to the first 1000 compounds ranking their Tanimoto scores. It is important to note that while a Tanimoto threshold of 0.85 to meet our numerical goal. The Ligand based three to five featured pharmacophore model was obtained when indirubin dataset was subjected to pharmacophore modelling. As an initial screening around thousand molecules were retrieved. The docking results were validated by conventional docking studies and

molecular dynamic studies. The dynamic studies demonstrate compounds having important interactions with the target.

An AI driven pharmacophore modelling and virtual screening against prepared library was employed to retrieve possible GSK3 inhibitors from pool of indirubin analogues. This study, in its endeavour, meticulously analysed the interaction profiles of select indirubin derivatives with GSK2β, drawing parallels with the established reference inhibitor.

Understanding the intricate mechanisms of protein–ligand interactions is crucial in the complicated field of molecular interactions in order to fully recognize and utilize the therapeutic potential of molecular entities.

Keywords: Glycogen synthase kinase-3 (GSK); indirubin; AI driven pharmacophore modeling.

Integrative in silico framework for evaluating meridine analogues: Toxicity, QSAR, and molecular dynamics insight

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Marine ecosystem harbours a wealth of bioactive compounds with potent anticancer properties. Among these, meridine, a marine-derived alkaloid, holds promise as a novel therapeutic agent. This compound has significant attention for targeting oncogenic pathways, particularly DNA topoisomerase 1, a critical enzyme in cancer proliferation. Leveraging advances in computational drug design, meridine analogues can be synthetically generated and analysed to enhance therapeutic efficacy.

This study aims to perform an in-silico approach to determine the organ-specific toxicity and lethal dose (LD_{50}) of the generated SMILES, Quantitative Structure-Activity Relationship (QSAR) studies, Molecular Dynamics (MD) simulation, and the comparative study with the toxicological profile of standard anticancer drugs Paclitaxel (Plant derived) and Doxorubicin (synthetic) are evaluated alongside meridine analogues.

Recurrent neural network (RNN) based generation of nearly more than 50 analogues of meridine are generated targeting DNA topoisomerase 1, a critical enzyme in cancer cell proliferation. Organ-specific toxicity prediction tools (Pro-Tox) are employed to evaluate the safety profile and lethal dose of the analogues. The structural features of the analogues are correlated with their pharmacological efficacy and safety using QSAR modelling software (QSAR Toolbox and ADMET Predictor). Molecular dynamic simulations are performed with the software (GROMACS), which provide insights into the stability and binding mechanism of the analogue. The efficacy-to-toxicity ratios and therapeutic windows of meridine analogues are compared with those of Paclitaxel and Doxorubicin.

The integration of in-silico toxicity prediction, QSAR modelling, and MD simulation offers a cost-effective framework for screening RNN generated meridine analogues as potential anticancer agents. The research targets the safety, efficacy, and therapeutic advantage of meridine analogues over conventional drugs, paving the way for further preclinical studies and clinical applications.

Keywords: Analogues; Recurrent Neural Network (RNN); SMILES; simulation; lethal dose (LD_{50}).

Medicinal mushrooms in cancer treatment

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Medicinal mushrooms have indeed been a staple in Asian traditional medicine for centuries, revered for their potential health benefits. Recent research has shown promising results in the context of cancer treatment. Compounds isolated from mushrooms, such as polysaccharides and triterpenoids, have demonstrated anti-cancer properties. Polysaccharides can stimulate the immune system to target and kill cancer cells, while triterpenoids may inhibit tumor growth and possess anti-inflammatory effects. Mushrooms like Reishi and Cordyceps are known to enhance immune cell activity against cancer. However, it's crucial to note that further studies are needed to confirm their effectiveness and safety in treating cancer. Therefore, mushrooms should be considered as alternatives to conventional cancer treatments.

Keywords: Immunity; mushroom; cancer; medicine.

Application of machine learning in drug discovery

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Drug discovery and development pipelines are long, complex and depend on numerous factors. Machine learning (ML) approaches provide a set of tools that can improve discovery and decision making for well-specified questions with abundant, high-quality data. Opportunities to apply ML occur in all stages of drug discovery. Examples include target validation, identification of prognostic biomarkers and analysis of digital pathology data in clinical trials. Applications have ranged in context and methodology, with some approaches yielding accurate predictions and insights. The challenges of applying ML lie primarily with the lack of interpretability and repeatability of ML-generated results, which may limit their application. In all areas, systematic and comprehensive high-dimensional data still need to be generated. With ongoing efforts to tackle these issues, as well as increasing awareness of the factors needed to validate ML approaches, the application of ML can promote data-driven decision making and has the potential to speed up the process and reduce failure rates in drug discovery

Keywords: Machine learning (ML); systematic; biomarkers.

AI and ML in drug discovery

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Drug discovery is a multifaceted field that combines advanced scientific methodologies, computational tools, and innovative technologies to develop effective and safe therapeutic agents. This process involves identifying potential drug candidates, optimizing their chemical properties, and evaluating their efficacy and safety profiles. Recent advancements in computational biology, artificial intelligence (AI), and machine learning have revolutionized drug discovery, enabling rapid screening of vast molecular libraries and prediction of drug-target interactions. High-throughput screening, molecular docking, and structure-based drug design are critical tools that have expedited the development of novel therapeutics.

Furthermore, the integration of omics technologies—such as genomics, proteomics, and metabolomics—has facilitated a deeper understanding of disease mechanisms, aiding in the identification of new drug targets. Techniques like CRISPR-Cas9 and other gene-editing tools have further expanded the scope of drug discovery by offering precision-targeted therapies. Despite these advancements, challenges such as high costs, extended timelines, and regulatory hurdles persist. Addressing these challenges through collaborative efforts and continued innovation is essential to transform the landscape of healthcare and meet the growing demand for personalized medicine.

This presentation outlines the evolving methodologies and applications in drug discovery, highlighting the potential to revolutionize treatment paradigms and improve patient outcomes.

Zero maintenance system for production of biofuels

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The quest for sustainable production of renewable and cheap biofuels has triggered an intensive search for domestication of the next generation of bioenergy crops. Aquatic plants which can rapidly colonize wetlands are attracting attention because of their ability to grow in wastewaters and produce large amounts of biomass. Representatives of Azolla species are some of the fastest growing plants, producing substantial biomass when growing in contaminated water and natural ecosystems. Together with their evolutional symbiont, the cyanobacterium *Anabaena azollae,* Azolla biomass has a unique chemical composition accumulating in each leaf including three major types of bioenergy molecules: cellulose/hemicellulose, starch and lipids, resembling combinations of terrestrial bioenergy crops and microalgae. A limited number of investigations has been reported for the production of biodiesel from microalgae like *Spirulina mazxima*. In the last two decades, numerous microorganisms have been engineered to selectively produce ethanol. Recently, the CRISPR has emerged as a novel technology for targeted genomic engineering. This genetic machinery seems to be a ground-breaking discovery to engineer the microbial genomes for desired traits such as enhancing the biofuel tolerance, inhibitor tolerance and thermotolerance as well as modifying the cellulases and hemicelluloses enzymes. The high productivity, the ability to grow on wastewaters and unique chemical composition make Azolla species the most attractive, sustainable and universal feedstock for low cost, low energy demanding, near zero maintenance system to produce a wide spectrum of renewable biofuels.

Keywords: Biofuel; renewable; sustainable; symbiont; spirulina; azolla.