SRI VENKATESWARA INTERNSHIP PROGRAM FOR RESEARCH IN ACADEMICS (SRI-VIPRA)

SRI-VIPRA

Project Report of 2024: SVP-2450

"QSAR studies on medicinally important plant-based metabolites"

IQAC
Sri Venkateswara College
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SRIVIPRA PROJECT 2024

Title : QSAR studies on medicinally important plant-based metabolites

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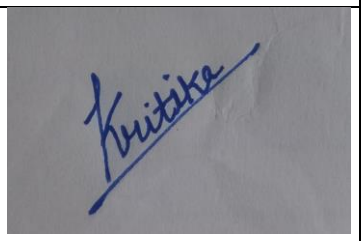
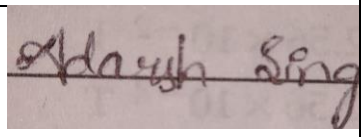
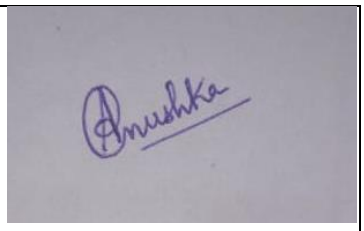
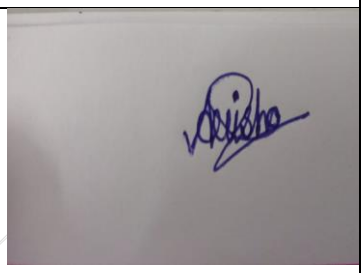
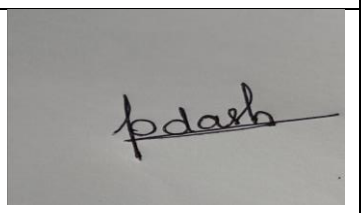
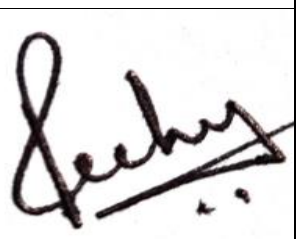
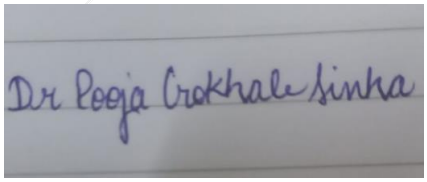
1		Kritika	1422047	BSc (H) Botany	
2		Adarsh singh	1323066	BSc (H) Biological sciences ences	

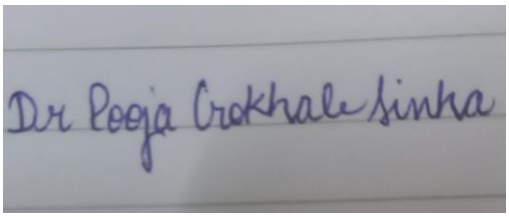
3		Anushka Singh	1122015	Bsc(P) Life sciences	
4		Arisha Siddiqui	1322013	BSc (H) Biological Sciences	
5		Prasanti dash	1122037	Bsc(P) Life sciences	
6		Peehu Chouksey	1222020	B.Sc. (H) Biochemistry	



Signature of Mentors

Certificate of Originality

This is to certify that the aforementioned students from Sri Venkateswara College have participated in the summer project SVP-2450 titled "**QSAR studies on medicinally important plant-based metabolites"**. The participants have carried out the research project work under our guidance and supervision from 1st July, 2024 to 30th September 2024. The work carried out is original and carried out in an online/offline/hybrid mode.



Signature of Mentors

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1. INTRODUCTION

Quantitative structure-activity relationship (QSAR) and quantitative structure-property relationship (QSPR) studies are important in silico methods in rational drug design. The aim of these methods is to optimize the existing leads in order to improve their biological activities and physico-chemical properties. Also, to predict the biological activities of untested and sometimes yet unavailable compounds. QSAR models are now regarded as a scientifically credible tool for predicting and classifying the biological activities of untested compounds, drug resistance, toxicity prediction and physicochemical properties prediction.

QSAR equations have been used to describe thousands of biological activities within different series of drugs and drug candidates. Especially enzyme inhibition data have been successfully correlated with physicochemical properties of the ligands.

Molecular descriptors used for study of QSAR:

- **SCF energy** represents the total electronic energy of the molecule in its most stable configuration. Lower SCF energy correlates with the stability of the molecule.
- **Heat of formation** reflects the thermodynamic stability of the compound. Compare the heat of formation with biological activity.
- **Electrostatic Potential (ESP) maps** provide insight into the charge distribution of the molecule, highlighting reactive sites (nucleophilic/electrophilic regions). ESP map helps in understanding interactions with biological targets.

2. Medicinal Plants and their Importance:

Nature has been a source of medicinal products for millennia, with many useful drugs developed from plant sources. The World Health Organization (WHO) estimated in 1985 that approximately 65% of the population of the world predominately relied on plant-derived traditional medicines for their primary health care, while plant products also play an important, though more indirect role in the health care systems of the remaining population who mainly reside in developed countries.

A medicinal plant is defined as any plant which has compounds that can be used for the therapeutic purpose or which contain precursors of chemo pharmaceutical synthesis. Throughout the world, plants are used traditionally to treat many ailments, particularly infectious diseases, such as diarrhea, fever, cold as well as

for birth control and dental hygiene. Also, many psychoactive substances used in traditional medicine are of plant origin. Traditionally used medicinal plants produce a variety of known therapeutic properties.
As part of their regular metabolic activities, all plants produce some chemical compounds known as phytochemicals. They may be categorized into:
(1) primary metabolites comprising carbohydrates, lipids, and proteins, which are found in all plants having essential roles associated with photosynthesis, respiration, growth, and development; and
(2) secondary metabolites comprising compounds found in a smaller range of plants, serving a more specific function and accumulating in high concentrations in some species.

Medicinal plants have been used for centuries to treat various ailments due to their natural bioactive compounds. Modern drug discovery increasingly looks to these plants as sources of potential therapeutic agents. QSAR studies play an essential role in screening and optimizing these bioactive compounds, predicting their activity based on molecular structure. These medicinal with secondary metabolites have significant role in drug and designing and manufacturing.

3. Plants investigated:

1. Andrographis is a genus within the Acanthaceae family, consisting of approximately 40 species, many of which are valued in traditional medicine. Notably, Andrographis paniculata Nees is renowned for its diverse therapeutic uses, including as an antidote for snake bites and insect stings, and in treating conditions such as dyspepsia, influenza, dysentery, malaria, and respiratory infections. It is also recognized for its properties as a heat-clearing, antipyretic, detoxifying, anti-inflammatory, swelling-reducing, fever-reducing, and pain-relieving agent, making it effective in treating acute infections of the gastrointestinal tract, respiratory system, and urinary tract. Andrographis paniculata (Burm. f.) Nees (Acanthaceae) (A. paniculata, Chuanxinlian), native to Taiwan, Mainland China and India, is a medicinal herb with an extremely bitter taste used to treat liver disorders, bowel complaints of children, colic pain, common cold and upper respiratory tract infection. The aerial part of A. paniculata is commonly used in Chinese medicine. According to Chinese medicine theory, A. paniculata 'cools' and relieves internal heat, inflammation and pain and is used for detoxication.

2. *C. roseus* is a plant belonging to Apocynaceae family and the name *Catharanthus* comes from Greek word which means 'pure flower'. *C. roseus* is a perennial plant that commonly grows in tropical countries and *Catharanthus* is more known as Madagascar periwinkle *C. roseus* has long been cultivated for herbal medicine and also as an ornamental plant. In Indian and Chinese traditional medicine, the extracts have been used against numerous diseases such as malaria, diabetes and Hodgkin's disease. It has been reported that *C. roseus* contain more than 70 different types of chemical constituents such as indole type of alkaloids, ajmalicine, serpentine and reserpine (Kabesh et al., 2015). The *Catharanthus* alkaloids provide protection against microbial infection, abiotic environmental stresses such as UV irradiation and are wide importance in clinical medicine due to the anti-hypertensive and antispasmodic properties (Sain and Sharma, 2013; Nejat et al., 2015) The *Catharanthus* alkaloids, vincristine and vinblastine which found abundantly in the leaves part of the plant inhibited the growth of tumour and hence contribute the anticancer property of *C. roseus* (Das and Sharangi, 2017). Vinblastine and vincristine were the first natural drugs used in cancer therapy and still among the most valuable agents used in cancer treatment (Costa et al., 2008). Vinblastine and vincristine are able to inhibit the cell mitotic and widely used medically to treat different kinds of cancers such as breast cancer, Hodgkin's lymphoma and leukemia. Vinblastine and vincristine bind to tubulin which is a structural protein that can be found in the cytoplasm, thereby inhibit the assembly of microtubule structures.

3. Curcuma longa L., commonly known as turmeric, is a member of the ginger family (Zingiberaceae), native to Southwest India with its rhizomes being the source of a bright yellow spice and dye. The use of the yellow color of turmeric rhizome and other plant derivatives as dyes is on the increase toward replacing synthetic additives with natural compounds. This yellow color is due to the presence of three main curcuminoids in the rhizome namely, curcumin, demethoxycurcumin, and bis-demethoxycurcumin. Rhizomes of C. longa are part of numerous traditional medicines used as stomachic, stimulant, and blood purifier, and to treat liver complaints, biliousness, and jaundice, for arthritic, muscular disorders, biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism and sinusitis. Mixed with warm milk, they are used to cure common cold, bronchitis, and asthma. Juice from fresh rhizomes is applied against many skin infections, whereas a decoction is effective against eye infections. It has promising pharmaceutical activity against cancer, dermatitis, AIDS, inflammation, high cholesterol levels, and dyspeptic conditions). C. longa also

has insecticidal, fungicidal, and nematicidal properties. In Madagascar, ground rhizomes are mixed with grains to protect them from storage pests. One of the curcuminoids in the rhizome, curcumin, has demonstrated a number of pharmacological activities including antioxidant, antineoplastic, antiviral, antiinflammatory, antibacterial, antifungal, antidiabetic, anticoagulant, antifertility, cardiovascular protective, hepatoprotective, and immunostimulant activity in Animals and therefore could be one of the constituents responsible for bioactivities of the rhizome of this plant. C. longa can act as antidiabetic, hepatoprotective, and antioxidant in diabetes especially type 1 diabetes. They showed that administration of methanolic extract of this plant to alloxan-induced diabetic rabbits significantly improved the levels of serum glucose, serum transaminases, and antioxidant activity.

4. The drumstick tree (*Moringa oleifera*) member of the Moringaceae family is widely spread from India to Africa and numerous other tropical and arid countries, mainly utilized as food and medicine . Its drought resistance properties, i.e., water-logging of roots, make this plant grow well in drier regions. Moringa plants can grow on different soil types, but well-drained loamy and sandy soil with a pH of 5–9 is best suited for its growth . Moringa oleifera is viewed as a most valuable plant because all parts can be utilized for food, medication, and other industrial and household purposes . The leaves, in particular, may be consumed as a salad, roasted, or stored as dried powder for a long period without losing nutritious content. Besides utilizing its leaves for food and feed, because of inborn phytochemicals like phenolic acids, flavonoids, carotenoids, and glucosinolates, they also have potential applications as functional foods nutraceuticals . Crypto-chlorogenic acid, isoquercetin, and astragalin are the significant phytochemicals present in moringa leaves which are attributed to the antioxidant, anti-hypertension and anti-inflammation activities . The medicinal functions and biological activity of these plants extract have been predominantly upheld by various in vitro assays based upon the bioactive components and their antioxidant activity . Its high phenolic content is primarily responsible for its antioxidant effects. Different pharmaceutical products from this plant have been manufactured and sold in both the Indian and worldwide markets due to these medicinal advantages . Moringa oleifera is also called “Miracle Tree” or “Tree of life”, owing to its excellent health, nutritional and environmental effects. Traditionally, moringa leaves are used as medicine in India to cure conjunctivitis and also to remove intestinal worms from the abdomen . The fresh moringa leaves also improve the milk production of pregnant and lactating mothers and are used to treat anemia . Diabetic patients can also use moringa leaves juice to control blood

pressure and blood glucose levels. Moringa processing may sometimes alter the bioaccessibility of moringa nutrients and polyphenols. Therefore, new approaches are needed to increase polyphenol retention when moringa leaves are processed and stored. Recently, the usage of herbal medicine has been increased exponentially. Developing countries depend basically on therapeutic plants for their wellbeing needs. Consequently, moringa leaves are a suitable option in developing nations looking for quality health services that offer inexpensive and easily accessible treatment in places not accessible to Western medicine. The proper dietary consumption knowledge by medical science experts helps in slowing the growth of many diseases. Since no aggregated data on moringa leaves are available revealing the vital bioactive components, bioaccessibility and health benefits, this review intends to fill a void in the scientific literature.

5. *Mentha piperita* (Peppermint) is known for its complex chemical composition, which includes a variety of essential oils, flavonoids, and phenolic compounds. These phytochemicals are responsible for the plant's diverse biological activities.*Mentha piperita* has been extensively used in traditional medicine for its antispasmodic, anti-inflammatory, antimicrobial, and antioxidant properties. Its wide range of therapeutic effects makes it a valuable subject for QSAR studies. The compounds derived from *Mentha piperita* have shown potential in treating various ailments, including gastrointestinal disorders, respiratory issues (like bronchitis, sinusitis, tuberculosis, and the common cold), and skin conditions.*Mentha piperita* is one of the most researched medicinal plants, with a wealth of literature available on its chemical constituents and biological activities. This existing knowledge base provides a strong foundation for conducting QSAR studies and ensures the reliability of the results.As a widely cultivated herb, *Mentha piperita* is economically important in the pharmaceutical and cosmetic industries. *Mentha piperita* is easy to cultivate and widely available, making it a practical choice for experimental studies. Its accessibility ensures a steady supply of plant material for ongoing research.

6. Rosemary (Rosmarinus officinalis) due to the significant health benefits conferred by its secondary metabolites, which play a vital role in the pharmaceutical industry. Rosemary is renowned for its rich profile of bioactive compounds, including rosmarinic acid, carnosic acid, and various essential oils, which have been extensively studied for their therapeutic properties. In medicinal aspects, Lamiaceae is a very important family of the plant kingdom and also recognized as mint family.

Their capability to produce essential oils allows most of the members of this family to survive high temperatures of the Mediterranean countries. The rosemary (Rosmarinus officinalis L.), representative of Lamiaceae family, has been reckoned as a perennial herb. R. officinalis L. have shown numerous pharmacological effects, i.e. antioxidant, anticancer, hepatoprotective, antidiabetic, antispasmodic, antiseptic and sedative properties. R. officinalis L. is known to exert potent antioxidant activity and inhibits genotoxicity as well as protects from carcinogens or toxic agents (González-Vallinas et al. 2015). Moreover, the most fundamental characteristics of carcinoma cells are their excessive proliferation rates accompanied by retarded apoptosis (Hanahan and Weinberg 2011). Polyphenols, from R. officinalis L., have been found to regulate cell growth and differentiation thereby reducing rates of tumorigenesis.

The secondary metabolites we have chosen to study in detail include caffeic acid, rosmarinic acid, carnosol, and carnosic acid. We aim to analyze their chemical structures and, through quantitative structure-activity relationship (QSAR) modeling, explore the relationships between their structural characteristics and biological activities.

4. Concept and Methodology

Students first learnt the basics of QSAR Modelling, how to use the Argus Lab software, how to do geometry optimization and how to calculate the properties of a molecule. QSAR (Quantitative Structure-Activity Relationship) modelling is a computational method used to correlate chemical structure with biological activity. The core concept involves developing mathematical models that relate chemical properties (descriptors) to biological or pharmacological activity. These models are used to predict the activity of new compounds, thus aiding in drug discovery and development.

How QSAR Models Correlate Structure with Activity: QSAR models are built on the principle that the biological activity of a chemical compound can be predicted b8ased on its chemical structure. This is achieved by quantifying chemical features (such as electronic, steric, and hydrophobic properties) and correlating them with the observed biological activity. Common steps in QSAR modeling include:

Data Collection: Gathering experimental activity data for a series of compounds.

Descriptor Calculation: Calculating molecular descriptors that represent various chemical properties.

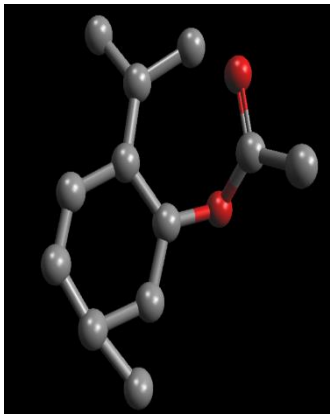
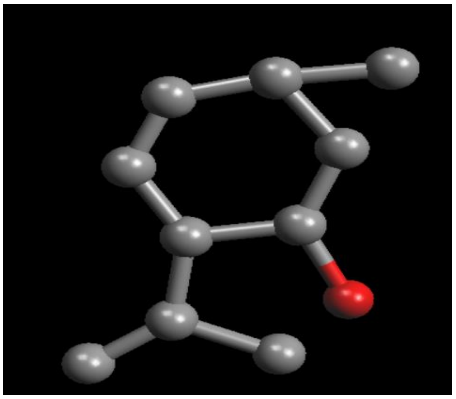
Model Building: Using statistical or machine learning methods to build a model that relates descriptors to activity.

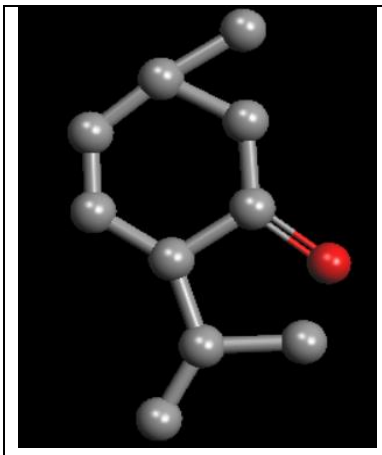
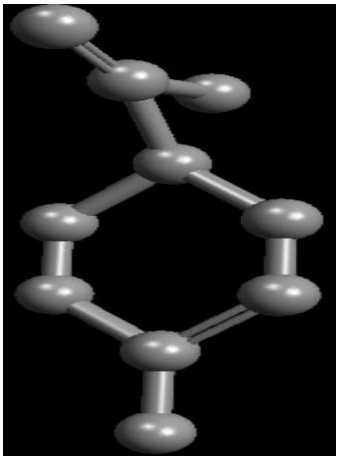
Validation: Assessing the model's predictive performance and generalizability.

5. Result And Observation

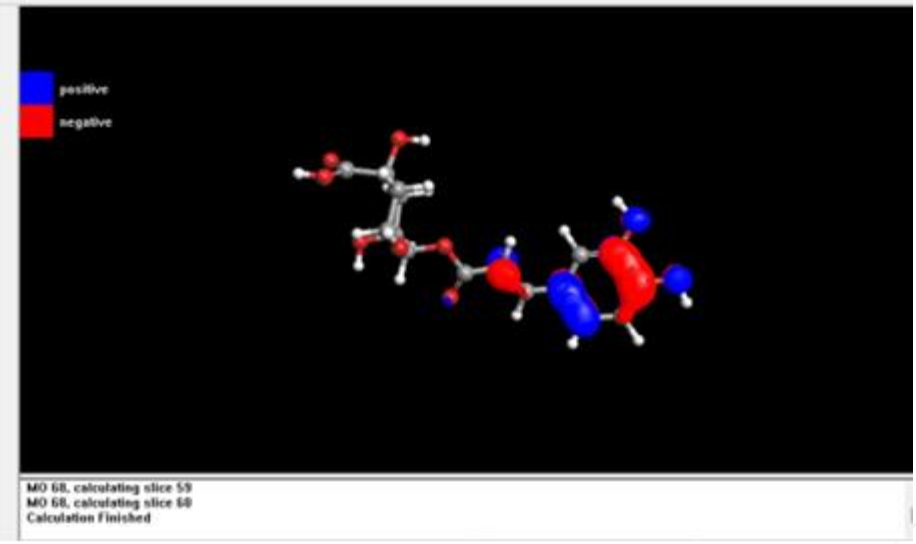
All the above listed biologically important molecules were investigated using computational studies. Some of the results are mentioned in the table below:

Molecule	**SCF Energy**	**Enthalpy**	**Bond Length**

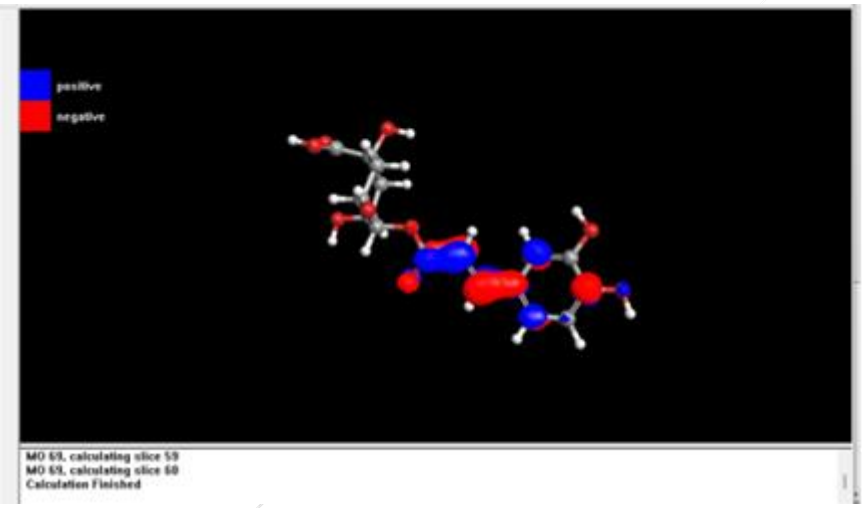
Isomenthyl acetate 	-72.9589 au -45782.4 kcal/mol	511.4028 kcal/mol	1.4116 Å 1.3886 Å
Menthol 	-53.646 au -33663.55 kcal/mol	426.8199 kcal/mol	1.3807 Å 1.4213 Å
Menthone	-58.091 au -36453.29 kcal/mol	464.6186 kcal/mol	1.3596 Å 1.4211 Å

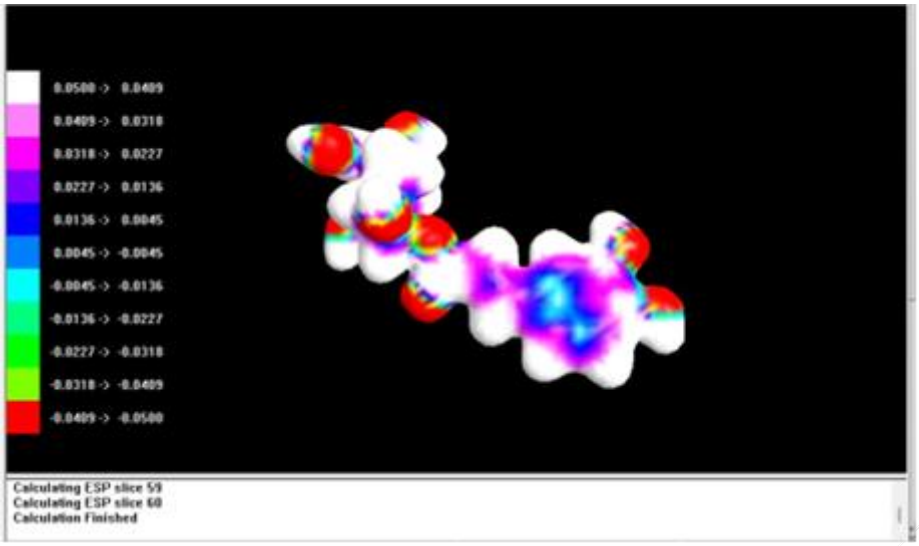
			
Limonene 	-42.671 au -26776.48 kcal/mol	582.0919 kcal/mol	1.4541 Å 1.4783 Å

The figures below give a glimpse of some 3D optimised structure of medicinally important molecules as obtained from Arguslab



The HOMO-LUMO obtained from Arguslab





Electrostatic Potential (ESP) map obtained from Arguslab

6. Conclusions

Through this project, we explored the capabilities of Arguslab software to generate geometrically optimized molecular models. This experience provided us with valuable knowledge to design and evaluate new molecules, including those derived from medicinal plants. Arguslab was instrumental in achieving optimized structures, accompanied by relevant energy calculations such as the heat of formation, SCF (Self-Consistent Field) energy, and geometrical energy. These computed data are straightforward and insightful, aiding in the assessment of the molecule's properties for specific applications, particularly in the context of bioactive compounds from medicinal plants.

Medicinal plants have long been recognized for their therapeutic properties, and computational chemistry tools like Arguslab can expedite the exploration of these properties. By modelling plant-derived compounds, we can predict their potential biological activities, which supports the discovery of new drugs and natural remedies. One of the key benefits of computational chemistry, exemplified by Arguslab, is its efficiency. Any discrepancies or adjustments needed can be addressed without undergoing time-consuming and complex experimental testing. Additionally, the software's ESP (Electrostatic Potential) density mapping provides a clear representation of charge distribution within molecules. This is crucial for understanding the reactivity of plant-derived molecules toward nucleophiles and electrophiles, guiding us in selecting appropriate solvents and reagents for further reactions and testing.

In summary, Arguslab not only enhances our understanding of molecular structures but also plays a pivotal role in advancing the study of medicinal plants, potentially leading to the discovery of new therapeutic agents.

REFRENCES

1. Roy, K., Kar, S., & Das, R. N. (2015). Understanding the Basics of QSAR for Applications in Pharmaceutical Sciences and Risk Assessment. Academic Press
2. Verma, J., Khedkar, V. M., & Coutinho, E. C. (2010). 3D-QSAR in drug design–Areview. Current Topics in Medicinal Chemistry, 10(1), 95-115.
3. Applications of QSAR Study in Drug Design International Journal of Engineering Research & Technology (IJERT) ISSN: 2278-0181
4. Cragg, G.M.; Newman, D.J. Natural products: A continuing source of novel drug leads. Biochim. Et Biophys. Acta (BBA)-Gen. Subj. 2013, 1830, 3670–3695.
5. Farnsworth NR, Akerele RO, Bingel AS, Soejarto DD, Guo Z. Medicinal plants in therapy. Bull World Health Org. 1985;63:965–981.
6. Chopra and Ananda S: Āyurveda In Selin, Helaine. Medicine across cultures: history and practice of medicine in non-western cultures. Norwell, A: Kluwer Academic Publishers 2003; 75-83.
7. Lim, C. M., G. C. L. Ee, M. Rahmani, and C. F. J. Bong. 2009. Alkaloids from Piper nigrum and Piper bettle Pertanika. Journal of Science and Technology
8. Silva, R. M., Rodrigues, S. M., & Santana, J. D. (2020). Rosmarinic acid: Neuroprotection through modulation of neuroinflammation. *Frontiers in Neuroscience*, 14, 578933.
9. Lee, C. H., Kim, S. Y., & Lee, J. H. (2013). Neuroprotective effects of carnosic acid in a mouse model of Alzheimer's disease. *Journal of Agricultural and Food Chemistry*, 61(47), 11343-11350.
10. Kwon, S. Y., Kim, H. J., & Kim, J. S. (2019). Carnosic acid protects against neurotoxic damage in a cellular model of Alzheimer's disease. *Neurotoxicity Research*, 36(3), 531-545.