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Review Article

A Chemo-Informatic and HR-LCMS Approach to Uncover Anticonvulsant Constituents in Malvastrum Coromandelianum Stem Extract

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ABSTRACT

Malvastrum coromandelianum, a plant from the Malvaceae family, has demonstrated a wide array of medicinal properties, including anti-inflammatory, analgesic, anti-diabetic, and anti-microbial activities. This study aims to explore its anticonvulsant potential through a combined chemo-informatic and High-Resolution Liquid Chromatography-Mass Spectrometry (HR-LCMS) approach. Phytochemical analysis revealed the presence of key bioactive compounds such as alkaloids, flavonoids, and terpenes, which are implicated in the plant's therapeutic effects. Using in-silico drug discovery methods, molecular docking, and ADMET predictions, we identified promising anticonvulsant candidates. HR-LC/MS further enabled the precise identification and structural elucidation of these compounds, offering a comprehensive understanding of their pharmacological properties. This integrated methodology bridges the gap between traditional herbal use and modern drug discovery, providing a targeted approach for the development of novel anticonvulsant therapies derived from Malvastrum coromandelianum.

INTRODUCTION

Herbal medicines have garnered increased attention recently due to their diverse therapeutic applications, favorable safety profiles and generally well-tolerated nature compared to conventional pharmaceuticals. *Malvastrum coromandelianum* a member of Malvaceae family has long been recognized for its medicinal attributes. The presence of alkaloids, essential oils and phenolic glycosides in plant of this family is associated with their established anti-bacterial and anti-fungal activities. Phytochemical analysis of extract from *Malvastrum coromandelianum* has confirmed the presence of alkaloids, saponins,

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flavonoids, triterpenes, tannins and steroids. Numerous prior investigations underscore the pharmacological potential of the species. Specifically, the plant has been evaluated for its anti-fungal, anti-microbial, hepatoprotective and anti-dysenteric properties.

1.1) Herbal Therapy: A Timeless Approach To Healthcare:

Herbal therapy, an ancient form of medicine, utilizes whole plants or specific plant components to manage various debilitating diseases and promote overall well-being. A wide array of herbal formulations exists, demonstrating efficacy in alleviating symptoms across a spectrum of conditions, from clinical depression to across respiratory infections like common cold and influenza.

The World Health Organization (WHO) has established specific criteria for evaluating the safety, potency and quality of herbal remedies. It's estimated that approximately 80% of the global population currently incorporates herbal formulation as a primary healthcare system. This trend is experiencing a significant increase, largely attributed to concerns regarding the toxicity and adverse reactions associated with conventional allopathic pharmaceuticals, leading to a rapid rise in herbal drug manufacturers.

Herbal products have garnered widespread acceptance as a valuable therapeutic agents, exhibiting a diverse range of pharmacological activities including:

Antimicrobial properties, Anti-fertility effects, Anti-diabetic actions, Anti-arthritic effects, Anti-aging properties, Antidepressant effects, Sedative properties, Antispasmodic effects, Anxiolytic actions, Anti-inflammatory effects, Analgesic properties, Vasodilatory effects, Anti-HIV activity, Hepatoprotective effects, treatment for liver cirrhosis, management of acne vulgaris, Asthma management , Menopausal symptom relief, Erectile dysfunction treatment, Gallstone management, Migraine prophylaxis/treatment, Management of Alzheimer's disease, Treatment of chronic fatigue syndrome, Cognitive enhancement.



Fig (1). Herbal Medicine

1.2) Evolution Of Traditional Medicine System:

Historically, natural botanical remedies have been extensively employed for the therapeutic management and prevention of various ailments. The ongoing evaluation of their benefits and limitations has led to the development of novel herbal remedies, design to promote health with minimal or no adverse effects. This extensive body of knowledge concerning natural products has progressively evolved into various structured medical systems, including:

- Traditional Indian Medicine (Ayurveda)
- European Traditional Medicine
- Japanese Kampo Medicine
- Traditional Chinese Medicine
- Traditional Arabic and Islamic Medicine
- Ethnomedical practices (Folk Medicine)

These systems encompass not only phytotherapy (herbal treatments) but also pharmaceuticals derived from minerals and metals (e.g., purified mercury, elemental sulfur, gold, silver and animal products (e.g., ivory, deer antler, animal horns). Furthermore, they often incorporate physical therapeutic procedure (e.g., Panchakarma in Ayurveda).

1.3) Future Prospects of Herbal Medicine:

Our understanding of herbal medicine indicates that approximately 121 pharmaceutical drugs have been developed from natural sources within the last decade. It's estimated that at least 25% currently available medications including well-known drugs like aspirin and picrotoxin, along with many synthetically produced equivalents derived from plant-based molecules, originate from botanical sources. The increasing acceptance and integration of plant-based therapeutics are expected to accelerate the future expansion of plant utilization as sources for medicinal agents. This trend has significantly boosted the export of herbal remedies and attracted numerous pharmaceutical companies, including multinational corporations. The World Health Organization's (WHO) initiatives to document the use of medicinal botanicals by various ethnic communities have led to increased scientific validation for their applications. Consequently, this provides individuals with enhanced information regarding the safety and efficacy of these treatments. While the regulation of herbal products has contributed to their improvement, further refinements are necessary to promote and advance high-quality research in this field.

1.4) Global Adaptation Of Traditional And Complementary Medicine:

Conventional medicinal systems have gained widespread global acceptance, driven by public interest in herbal remedies and their notable perceived efficacy, often with minimal to no adverse effects, against various challenging health conditions. Currently, 60% of the world's population relies on herbal or conventional treatments for managing malaria-related fevers. Furthermore, a significant portion of individuals in various regions opt for herbal or alternative treatments as their initial approach to managing diverse diseases : 80% of Africans, 30-50% of Chinese, 48% of Australians, 70% of Canadians, 80% of Germans, 42% of Americans, 39% Belgians, 76% of French individuals.

In Urban centers such as San Francisco, London and the Republic of Africa, 75% of individuals with HIV/AIDS incorporate herbal medicines into their treatment regimens. Countries like

Malaysia despite the availability of healthcare providers and affordability concerns are allocating more resources towards costly prescription medications compared to allopathic ones, even as a herbal medicine continue to grow in popularity.

Projections indicate that a large proportion of people in low-income and developing countries primarily access healthcare through traditional medicines. Herbal products and remedies are highly valued as integral components of their cultural heritage. The use of herbal remedies is also extensive in many developed nations, with increasing recognition and importance in regions such as the European Union, North America, Australia and the United Kingdom.

2. Epilepsy

Epilepsy is a chronic neurological disorder affecting over 50million individuals globally characterized by recurrent, unprovoked seizures. The etiology of most epilepsy cases remains idiopathic, though some are attributable to brain

injury, cerebrovascular accident (stroke), neoplasm, infections and congenital anomalies. A subset of cases is linked to genetic mutations. Seizures arise from an imbalance in neuronal excitability, specifically neurotransmitter dysregulation, leading to synchronized neuronal firing within the brain.

2.1) Classification Of Epileptic Seizures:

Table (1). Classification of Epilepsy

Types	Description
❖ Partial Seizures (seizures begin locally)	➢ Simple (Cortical focal epilepsy; without impairment of consciousness) A. With motor manifestations. B. With special sensory or somatosensory manifestations. C. With psychic phenomena. ➢ Complex (with impairment of consciousness) A. Simple partial onset followed by impairment of consciousness with or without automatisms. B. Impaired consciousness at onset with or without automatisms. ➢ Secondarily Generalized (partial onset evolving to generalized tonic clonic seizures)
❖ Generalized Seizures (bilaterally symmetrical and without local onset)	➢ Characterized by immediate loss or diminution of consciousness, lasting 3-30secs. This often refers to absence seizures, which typically involve brief lapses of awareness.
❖ Unclassified Seizures	➢ Special syndromes encompass conditions such as febrile seizures, where seizures are precipitated by specific situations (e.g., fever).
❖ Status Epilepticus	➢ Status epilepticus is prolonged or repeated seizures over 30 minutes needing treatment, most commonly tonic-clonic.

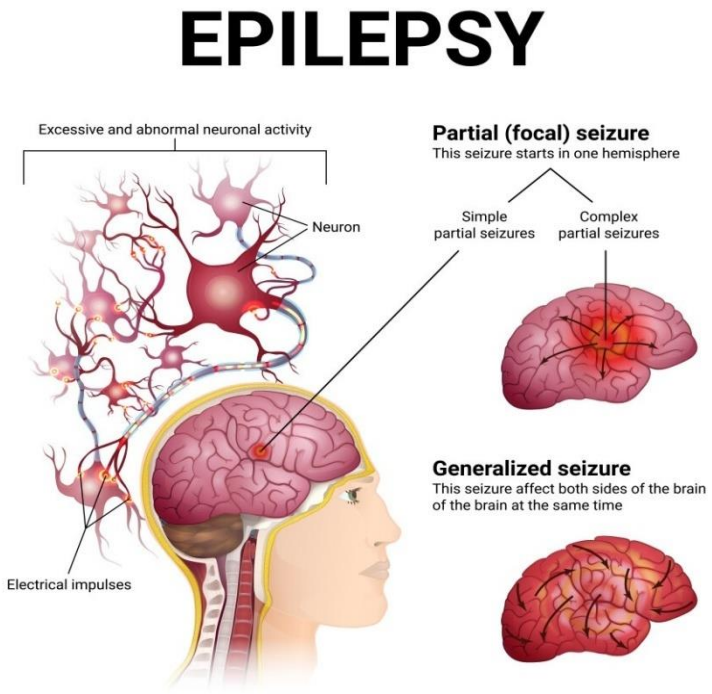


Fig (2). Epilepsy

2.2) Etiology Of Epilepsy Across Age Groups:

There are several causes of epilepsy are common to different age groups:

- In the neonatal and early childhood : The most prevale causes include hypoxic-ischemic encephalopathy , central nervous system (CNS) infection, head trauma, congenital CNS malformations and metabolic disorders.
- At the end of the toddlerhood and geezer hood: Febrile convulsions are most common infections that can be caused by trauma and central nervous system.
- Childhood: Various epileptic syndromes are commonly observed in this age group.
- In Adolescence and Adulthood: Seizures are more likely to be secondary to structural lesions of Central Nervous System (e.g., tumors, vascular malformations, remote head injury).
- In the elderly: Cerebrovascular disease (e.g., stroke) is the predominant cause. Other contributing factors include CNS neoplasm, head trauma and neurodegenerative disorder such as dementia.

Epileptic Seizure occurs when a group of neurons discharges excessively and consistently. All epileptic syndromes share a rise in neuronal excitability. Currently, a definitive cure for epilepsy remains elusive, as its precise mechanisms are not yet fully elucidated. The primary treatment involves administration of anticonvulsants, also called antiepileptic or anti-seizure drugs, which aims to manage and mitigate seizure symptoms.

2.3) Neurochemistry And Targets To Treat Epilepsy:

The neurochemical underpinnings of seizure disorders are intricate and not fully elucidated. Nevertheless, Acetylcholine (Ach) and Dopamine (DA) are recognized as key neurotransmitters influencing epileptic seizures. Ach function as an Excitatory neurotransmitter, while DA is considered an Inhibitory neurotransmitter in the context of seizure activity. Evidence supporting DA's inhibitory role includes:

- Pretreatment with d-amphetamine has been observed to mitigate the occurrence of epileptic episodes in audiogenic mice.
- Conversely, while amphetamine exacerbates audiogenic seizures, levodopa (L-DOPA), a dopamine precursor, has been used to counteract d-amphetamine effects.
- Dopaminergic receptor agonists induce a delay in audiogenic seizures in murine models and a comparable delay in photogenic seizure in *Papio papio.*

Epilepsy may result from enduring neural plasticity, impacting various neurochemical and structural facets of the brain. These encompass alteration in neurotransmitter efflux and uptake, modification in receptor and ion-channel properties, dysregulation of gene expression, synaptic reorganization and aberrant astroglial activity. Initially, ion channel dysfunctions were posited as the primary instigators of the paroxysmal depolarizing shifts that trigger epileptic activity. However, contemporary investigations into synaptic and non-synaptic transmission, ion channel interactomes, intracellular signal transduction pathways and glial-neuronal signaling suggests that numerous neurochemical pathways contribute significantly to seizure initiation, perpetuation and cessation.

3. Anticonvulsants

Anticonvulsants are expanding class of pharmacological agents that exert their therapeutic effect through diverse mechanisms to control seizure activity. Acute antiepileptic drug toxicity commonly manifests as triad of symptoms: CNS depression, ataxia and nystagmus. However, various antiepileptic agents are associated with more specific adverse effects, including paradoxical seizure exacerbation, of which clinicians must be cognizant.

Antiepileptic drugs (AED's) exert their therapeutic actions via diverse mechanisms, including:

a) Modulation of excitatory and inhibitory neurotransmission through effects on voltage-gated ion channels, GABA (A) receptors and Glutamate-mediated excitatory neurotransmission.

b) Restoration of biochemical and morphological homeostasis is critical for optimal neuronal network function. This includes addressing increased presynaptic neuronal excitability, calcium influx, activation of phosphatases or protein kinases, phosphorylation and dephosphorylation of receptors, ion channels and other proteins, and cytoskeletal remodeling and the mobilization of receptors and ion channels.

c) Potentiating of GABAergic neurotransmission via calcineurin (protein phosphatase 2B)

d) Attenuation of extra synaptic N-methyl- D-aspartate (NMDA) receptor activation.

e) Inhibition of the extracellular signal-regulated kinase (ERK) and p38 α mitogen-activated protein kinase (MAPK) pathways.

4. Plant Profile: *Malvastrum coromandelianum*

4.1) Tribe:

Malveae

4.2) Synonyms:

Malva coromandeliana L., Malva domingensis Spreng exDC., Malvastrum carpinifolium (Medik)

4.3) COMMON NAMES:

False mallows, Prickly malvastrum, sai kui (China), sonchal buti (India), taw pilaw (Myanmar).

4.4) Vernacular Names:

Table (2). Vernacular Names

Hindi	Kharenti
Bhilli	Bairara
Thai	Daikat

4.5) Taxonomical Classification:

Division : Angiosperms

Clade : Eudicots

Clade : Core eudicots

Clade : Superrosids

Clade : Rosids

Clade : Malvids

Order : Malvales

Family : Malvaceae

Genus : *Malvastrum*

Species : *Malvastrum coromandelianum*



Fig (3). *Malvastrum coromandelianum*

4.6) Botanical Description:

It is a herb which grows to 1m tall in the wastelands and by the roadsides in tropical Asia and Pacific. The stems are hairy and somewhat stiff. The leaves are simple, spiral and stipulate. The stipules are lanceolate and up to 7mm long. The petiole is upto 3cm long, somewhat reddish and hairy. The blade is broadly lanceolate, 3-7cm x 1-4cm, hairy, round to cuneate at base, serate at margin and acute to obtuse apex. The flowers are axillary and solitary. The calyx is five lobed, the lobes are ovate, hairy and about 1cm long. The corolla comprises five petals which are yellowish, veined 1cm long, obovate and somewhat asymmetrical and irregular. The androecium includes numerous stamens joined partially in a tube which is about 6mm long. The fruit is discoid.

4.7) Distribution And Ecology:

Distributed throughout the world tropics and extending into temperate regions of North and South America, this species widely occurs in Peninsular India. It is successful colonizer of degraded and disturbed area right from the sea-coast to the foot-hills of Western Ghats and also as a weed in agricultural lands. It flowers almost throughout the year. The autogamous flowers open at about 2.00pm and close before 5.00pm under Indian conditions.

4.8) *Malvastrum coromandelianum*- Ethnomedical Uses:

The entire plant of *Malvastrum coromandelianum* is recognized for its emollient, resolvent and bechic properties. A decoction of the plant is traditionally administered for the management of dysentery. This botanical is also utilized in traditional medicine as an anti-inflammatory and analgesic agent and for the treatment of jaundice, ulcers and abdominal pain. The flowers are specifically employed for alleviating cough, thoracic diseases and pulmonary ailments. Various parts of this species contribute to numerous herbal formulations used for treating otitis, neoplasms, rheumatic arthralgia, gout and laying hen salpingtis, in addition to being components in herbicidal compositions and medicinal wines.

Pharmacological investigations of *Malvastrum coromandelianum* have substantiated a broad spectrum of biological activities. Specifically, the aqueous extract of its leaves has demonstrated significant anti-diabetic and anti-hyperlipidemic effects. The aqueous extract of the whole plant exhibited inhibition of carrageenan-induced inflammation and formalin-induced nociception. The crude extract from the aerial parts displayed anti-bacterial activity against methicillin-resistant *Staphylococcus aureus* strains. Furthermore, chloroform and acetone extracts possess notable anti-nociceptive activity. The ethanolic extract from this species has demonstrated wound healing and immune-modulatory properties.

Extracts derived from the roots, stem and leaves of the plant has shown a hypertensive effect. The leaf powder exhibits larvicidal activity in a dose-dependent manner, with LC_{50} value of 0.62 in acetone. It also effectively retards larval development of *Aedes albopictus*, a known vector for 33 fungi toxicity against damping-off fungi, exhibiting 92.31% inhibition against *Pythium aphanidermatum*, 82.22% against *Pythium dedaryanum,* and 72.22% against *Rhizoctonia solani.* Notably, a flavonoid-rich extract from the plant has been utilized for the management of prostatic diseases, particularly benign and prostatic hyperplasia (BPH), prostate cancer and non-bacterial prostatitis.

4.9) Phytochemical Investigations:

Phytochemical screening has identified the presence of alkaloids, tannins, proteins, carbohydrates and ascorbic acid (vitamin-C) in roots and leaves. The phytoconstituents reported from the aerial parts of the plant include β-phenyl ethylamine, dotriacontane, dotriacontanol, β-sitosterol, stigmasterol, campesterol, lutein, N-methyl-β-phenyl ethylamine, indole alkaloids and a steroidal saponins, 3-O-β-D-glucopyranosyl (1,2)-β-D-glucopyranosyl (1,4)- β -D-galactopyranoside 25R, 5α-spirostane-2α,3 β-diol having antithyroidal activity. Additionally, a long-alkyl-side chain lactone, malvastrone, has been isolated from the leaves. The seed oil from a *Malvastrum coromandelianum* is a source of unusual cyclopropenoid fatty acids comprising palmitic acid 22.7%, palmitoleic acid 2.4%, stearic acid 2.7%, oleic acid 14.6%, linoleic acid 37%, malvalic acid 10.5% and sterculic acid 10.1%.

Since no data on its Pharmacognostical and Phytochemical aspects have been reported so far, the present study was undertaken to explore the Anti-Convulsant activity of *Malvastrum coromandelianum.*

5. Extraction (Soxhlet Extraction)

5.1) Introduction:

Soxhlet extraction, a widely recognized standard technique for extracting analytes from solid samples, is a preferred method over alternative

leaching techniques due to its superior extractive efficiency. However it remains a labor-intensive process. Recent advancements in the original Soxhlet design aims to optimize process parameters to decrease extraction duration and solvent consumption and to integrate automation or semi-automation. These technological enhancements encompass the application of elevated thermal and pressure conditions, microwave irradiation, ultrasound and others, each presenting its unique operational advantages and disadvantages, such as cost. It is a continuous solid/ liquid extraction. The solid material which is to be extracted is placed in thimble which is made of a material such that it contains solids but allows only liquids to pass through it (It acts as a filter paper).The thimble is then placed in the extractor body. An Organic solvent is subjected to thermal energy within a reflux system, initiating vaporization. The resulting solvent vapors ascend and undergo condensation in a condenser unit, subsequently flowing into and filling the thimble. This process is repeated until the complete transfer of target constituents from the solid materials is achieved.

A typical Soxhlet Extractor system comprises the following instrumentation:

1) Soxhlet Extractor Assembly

2) Electric Heating Mantle (for controlled thermal input)

3) Water- Cooled Condenser (for vapor liquefaction)

4) Flash Evaporator (for solvent recovery post-extraction)

5.2) Collection & Procedure

5.2.1) Collection & Drying of *Malvastrum coromandelianum*:

The *Malvastrum coromandelianum* stems were collected, cleaned with distilled water and dried under shade for consecutive days. The dried stems were then crushed into coarse powder using blender. Later on, the obtained powder was subjected to solvent extraction using Soxhlet apparatus.

5.2.2) Preparation Of *Malvastrum Coromandelianum* Stem Extracts:

Soxhlet extraction method will be performed for the preparation of crude extract from the stem of *Malvastrum coromandelianum.* For preparation of the alcoholic extract of stem of *Malvastrum coromandelianum*, 100gm of stems should be dried at room temperature in dark and then crushed into coarse powder. The powder material is then soaked in 100ml of 80% ethanol overnight and then exhaustively extracted with 80% ethanol (100ml X2) in a Soxhlet apparatus at 80ºC for 72hrs. The crude extract is filtered and evaporated to dryness on a water bath set at 100ºC. The dried residue of crude extract was cooled in desiccators for 30mins, then filtered via disc of filter paper and accurately weighed for analysis. The crude extract will be used for further Analytical purpose.

6. HR-LC/MS Analysis

6.1) Introduction:

High-Resolution Liquid Chromatography-Mass Spectrometry (HR-LC/MS) is a powerful analytical technique that combines the separation power of Liquid Chromatography (LC) with the High resolution and High-Mass accuracy capabilities of Mass Spectrometry (MS).This hyphenated technique is a cornerstone of Modern Analytical Science, allowing for the sensitive and selective identification and quantification of a vast range of compounds in complex mixtures. The “High-Resolution” aspect is critical, as it allows

for the precise determination of compounds elemental composition, which is often impossible with conventional low-resolution mass spectrometry.

6.2) Principles Of Operation:

The HR-LC/MS System can be broken down into two main components.

- The Liquid Chromatograph
- High-Resolution Mass Spectrometer

Liquid Chromatography (LC):

The LC units primary function is to physically separate the different components of a sample mixture.

- Stationary Phase: The sample is injected into a column packed with a solid material, such as Silica, known as the Stationary phase.
- Mobile Phase: A liquid solvent (mobile phase) is pumped through the column.
- Separation: Compounds in the sample interact with the stationary phase to varying degrees. Compounds that interact more strongly moves slower, while those that interact less moves faster. This difference in migration speed causes the individual components to elute from the column at different times, which are called retention time. This separation is first layer of specificity in the analysis.

High-Resolution Mass Spectrometry (HRMS):

After the components are separated by the LC, they are introduced into the Mass Spectrometer. This process involves several stages:

- Interface: This is a crucial step that bridges Liquid phase LC with the high vacuum environment of the MS. Common Ionization Techniques and interface include Electrospray ionization (ESI) and Atmospheric Pressure Chemical Ionization (APCI).ESI is ideal for polar and non-volatile compounds, while APCI is better suited for less polar or volatile compounds. These interfaces convert the liquid eluent into gas-phase ions.
- Ionization: The separated molecules are ionized, which means they are converted into charged ions.
- Mass Analysis: The ions are then sorted based on their mass-to-charge ratio (m/z). The high resolution capability of the mass analyzer (e.g., Time-of-Flight (TOF), Orbitrap, or Fourier Transform Ion Cyclotron Resonance (FT-ICR)) allows it to distinguish between ions with extremely similar masses. This is what provides the High Mass Accuracy.
- Detection: The separated ions strike a detector, which measures their abundance. The result is a Mass Spectrum, a plot of ion abundance versus m/z.

6.3) Workflow And Data Analysis:

- Sample Preparation: The sample is prepared to isolate and concentrate the analytes of interest, while removing interference substances.
- LC-MS Acquisition: The prepared sample is injected into the HR-LC/MS system. The instrument acquires data, generating a series of Mass Spectra over time.
- Data Processing: Specialized software is used to process the raw data. This involves peak picking (identifying signals), deconvolution (separating overlapping signals) and peak alignment (matching peaks across different samples).

- Compound Identification: This is the core of the analysis. The high mass accuracy of the measured ions is used to propose an elemental formula. This formula, along with retention time and fragmentation data (from MS/MS), is then searched against chemical databases and spectral libraries for confident compound identification.

- Interpretation and Reporting: The final step involves interpreting the results; performing statistical analysis is necessary and generating comprehensive report.

6.4) Application In *Malvastrum coromandelianum*:

✓ Phytochemical Profiling: HR-LC/MS enables comprehensive phytochemical profiling of *Malvastrum coromandelianum* extracts. This means researchers can identify a wide range of compounds, including alkaloids, flavonoids, terpenes, fatty acids and other secondary metabolites that may be responsible for plant's medicinal properties.

✓ Targeted vs. Untargeted Analysis:

- Targeted Analysis: If a specific Anti-Convulsant compound is suspected to be present, HR-LC/MS can be used for targeted analysis to confirm its presence and quantify its concentration.

- Untargeted Analysis (Metabolomics): For a more exploratory approach, Untargeted Metabolomics using HR-LC/MS can be employed. This involves analyzing all detectable compounds in the extract without prior knowledge. The data can then be used to compare the chemical profiles of different plant parts or extracts and to identify potential new bioactive compounds.

✓ Identification of Anti-Convulsant Candidates:

- *Malvastrum coromandelianum* is traditionally used for various ailments and some studies have reported its pharmacological activities, including Anti-Inflammatory, Analgesic and Anti-Oxidant effects. HR-LC/MS could be used to specifically investigate extracts that are shown promising Anti-Convulsant activity in bioassays.

- By analyzing the active fractions using HR-LC/MS and comparing their chemical profiles less active fractions, researchers can pinpoint the compounds that are unique to or more abundant in the active fractions. This process helps to narrow down the potential Anti-Convulsant constituents.

✓ Structure Elucidation: Once potential Anti-Convulsant compounds are identified, HR-LC/MS, particularly with MS^2 and higher-order fragmentation (MS^n), can be used for their structural elucidation. This involves determining the exact structure of the molecule, which is critical step in Drug Discovery.

In Summary, HR-LC/MS is an indispensable tool in natural product research. Its ability to provide high-resolution separation, accurate mass measurements and detailed structural information through fragmentation makes it ideal for the complex task of identifying and characterizing the Anti-Convulsant constituent from the plant *Malvastrum coromandelianum.* It allows for a systematic and comprehensive approach to linking the plants traditional medicinal use to its specific chemical components.

7. In-Silico Drug Discovery in Natural Products

7.1) Evolution Of Drug Discovery Methods:

In recent years, In-silico techniques have emerged as a transformative approach in drug discovery, offering computational stimulation to predict the behavior, efficacy and safety of molecules before experimental validation. These methods play a crucial role in minimizing time, cost and attrition rates in early-phase drug development.

7.2) What Is In-Silico Drug Discovery?

The term 'in-silico' refers to the use of computational models and simulations to perform biological and chemical analysis. Unlike *in-vitro* (in the lab) or *in-vivo* (in organisms) studies, in-silico studies utilize software programs, algorithms and molecular data to predict drug-likeness, target binding affinity, absorption, toxicity and other pharmacokinetic and pharmacodynamic properties.

Key in-silico techniques include:

1. Molecular Docking
2. Pharmacophore modeling
3. Virtual Screening
4. Molecular dynamics simulations
5. Quantitative structure-activity relationship (QSAR) modeling
6. ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) prediction.

These tools are often applied in sequential or integrated manner to screen thousands of compounds and prioritize potential leads.

7.3) In-Silico Tools In The Context Of Natural Products:

Natural products, including phytochemicals from medicinal plants, are a rich source of structurally diverse and biologically active compounds. However, their complex structure often poses challenges in traditional high throughput screening. In-silico tools provide a solution by enabling virtual screening of natural compound libraries against specific molecular targets involved in disease pathophysiology. This allows researchers to focus only on compounds with the highest binding affinity or favorable ADMET properties. When study plant-derived Anti-Convulsant agents such as flavonoids from *Malvastrum coromandelianum,* In-silico techniques can predict their interaction with epilepsy-related targets, such as GABA receptors, Sodium channels or Glutamate transporters.

7.4) Overview Of Core In-Silico Techniques:

❖ **Molecular Docking**

Molecular docking simulates the interaction between small molecules (ligand) and a target protein, predicting binding orientation, affinity and energy. It helps identify how well a Phytochemical fits into the active site of protein relevant to epilepsy. Software like AutoDock, Molecular Operating Environment (MOE) and Schrodinger Glide are widely used.

❖ **Pharmacophore Modeling**

Pharmacophore represents the spatial arrangement of functional groups in a molecule that are necessary for biological activity. Pharmacophore-based screening allows researchers to filter plant compounds based on whether they contain the key chemical features required to interact with a neurological target.

❖ QSAR (Quantitative Structure-Activity Relationship)

QSAR models statistically correlate with chemical structure with biological activity using descriptors such as molecular weight, hydrophobicity and hydrogen-bonding potential. It is particularly useful for predicting the efficacy of untested plant-derived compounds.

❖ ADMET Prediction

Even if a compound shows strong binding affinity, it may fail due to poor pharmacokinetics or toxicity. Tools like SwissADME, pkCSM, and admetSAR predict absorption, blood brain barrier permeability, hepatic metabolism and potential for toxicity, which are crucial for CNS-targeted drugs.

❖ Advantages of In-silico Approaches in Drug Development

In-silico methods offer numerous advantages, especially in natural product research

- ✓ Time Efficiency: Reduces the number of wet-lab experiments required, significantly cutting development timelines.
- ✓ Cost-Effective: Eliminates the need for expensive synthesis and animal testing at early stages.
- ✓ Predictive power: Helps forecast binding affinity, toxicity and pharmacokinetics before compound isolation.
- ✓ Data-Driven Decisions: Supports rational drug design based on biological targets and structure-activity relationships.

❖ Application to Anti-Convulsant Discovery

Epilepsy is a complex neurological disorder involving multiple molecular pathways. In-silico methods allow the identification of Phytochemicals that may act on:

- ➢ GABA-A receptors (modulators of inhibitory neurotransmission)
- ➢ Voltage-gated Sodium and Calcium channels
- ➢ AMPA and NMDA glutamate receptors

By virtually docking compounds from *Malvastrum coromandelianum* against these targets, researchers can prioritize those with potential Anti-Convulsant activity for further *in-vitro* and *in-vivo* testing. Quercetin and other flavonoids identified in this plant have previously shown neuroprotective and anti-oxidant activities, making them excellent candidates for In-silico evaluation.

❖ Limitations and Considerations

While powerful, In-silico techniques are not without limitations. Their accuracy depends heavily on the quality of input data, such as protein structures (often derived from crystallography or homology modeling) and chemical descriptors. Additionally, false positives can occur due to oversimplified scoring functions. Hence, computational predictions must be validated experimentally.

Despite these constraints, In-silico screening remains a vital first step in the multi-stage drug discovery process.

❖ Relevance to this Study

Given the growing interest in alternative and plant-based therapies for epilepsy, this study focuses on applying In-silico techniques to evaluate the anticonvulsant potential of phytochemicals from *Malvastrum coromandelianum.* By employing a computational pipeline involving molecular

docking, ADMET prediction and pharmacokinetic modeling, this work aims to identify bioactive constituents that warrant further pharmacological investigation.

8. CONCLUSION

The integrated chemo-informatics and HR-LC/MS approach offers a highly efficient and targeted strategy for identifying potential Anti-Convulsant agents in *Malvastrum coromandelianum.* Chemo-informatics, utilizing molecular docking and network pharmacology, predicts compounds with high binding affinity to neurological targets. HR-LC/MS then provides high-resolution structural elucidation and confirmation of these compounds, bridging the gap between In-silico predictions and in-vitro presence. This synergistic methodology accelerates the dereplication of known compounds and the identification of novel constituents with potential therapeutic relevance for seizure disorders, thereby streamlining the natural product drug discovery pipeline.

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