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Review Article

# *Lantana Camara* Linn: Unveiling a reservoir of novel antiepileptic compounds through systematic review

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## Abstract

Epilepsy affects approximately 52.5 million people worldwide, with one-third experiencing treatment-resistant seizures despite available antiepileptic drugs (AEDs), while *Lantana camara*, traditionally regarded as an invasive weed, has emerged as a compelling candidate for epilepsy treatment based on traditional knowledge and scientific investigations. This structured review comprehensively analyzes current knowledge of *Lantana camara's* anticonvulsant properties, examining its phytochemical composition, mechanisms of action, and therapeutic potential as a novel antiepileptic agent. A systematic literature search was conducted following PRISMA 2020 guidelines across Google Scholar, PubMed, Science Direct, and Web of Science databases using relevant search terms to identify research on *L. camara's* anticonvulsant properties. Key findings include isolation of ursolic acid stearoyl glucoside (UASG) by Kazmi et al. (2012), which demonstrated anticonvulsant activity in seizure models, while recent studies revealed *L. camara's* multifaceted therapeutic mechanisms involving GABAergic modulation, antioxidant properties, neuroinflammatory regulation, and ferroptosis inhibition. These investigations collectively demonstrate the plant's ability to modulate multiple pathways in seizure generation and propagation, establishing its potential as a multi-target therapeutic agent. *L. camara* exhibits promising potential for developing novel antiepileptic medications, particularly for drug-resistant cases, with potentially better safety profiles than conventional AEDs, however, critical gaps remain including comprehensive toxicological studies, standardization of active compounds, and clinical translation requiring future research focus.

**Keywords:** Epilepsy, *Lantana camara*, Anticonvulsant activity, Ursolic acid stearoyl glucoside (UASG), Ferroptosis

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## Introduction

Epilepsy remains as one of the most significant illnesses in modern neurology, impacting approximately 52.5 million people globally. (1) As a neurological disorder marked by unpredictable and recurrent seizures, it creates substantial burdens for both patients and healthcare systems globally. The condition's impact extends well beyond its physical manifestations, affecting patients' psychological well-being, social relationships, and professional capabilities. Despite the availability of numerous antiepileptic drugs (AEDs), the therapeutic landscape faces considerable challenges. Most notably, around one-third of patients continue experiencing seizures despite treatment, categorizing them as having treatment-resistant or refractory epilepsy. (2, 3) This treatment gap represents more than just statistics; it reflects a critical unmet medical need affecting millions globally. The persistence of seizures in these cases highlights current treatment limitations and emphasizes the urgent requirement for innovative therapeutic approaches.

The challenges associated with existing AED treatments are further complicated by their side effects, which significantly impact patients' quality of life. These adverse effects range from mild cognitive impairments affecting daily activities to potentially life-threatening systemic reactions. (4) Common cognitive symptoms include memory difficulties, attention deficits, and reduced processing speed, while physical manifestations include dizziness, fatigue, and coordination problems. More severe complications can involve hepatic dysfunction, hematological disorders, and serious dermatological reactions. The cumulative effect of these side effects often necessitates difficult decisions between seizure control and life quality. This challenging therapeutic landscape has sparked intensive research into alternative treatment approaches, with natural products emerging as a particularly promising avenue. (5, 6) This invigorated interest in natural compounds represents more than a return to traditional medicine; it combines ancient wisdom with modern scientific methodologies, leveraging centuries of ethno-medicinal knowledge while employing cutting-edge research techniques.

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The historical significance of natural compounds in epilepsy treatment provides compelling precedent for this research direction. Early anticonvulsant medications, including bromide and phenobarbital, trace their origins to natural sources, establishing a foundation for nature-derived therapeutic agents in epilepsy management. (7, 8) Modern research has revolutionized this field through advanced screening technologies, sophisticated analytical chemistry techniques, and improved understanding of molecular mechanisms. These contemporary approaches enable researchers to identify and characterize bioactive compounds with unprecedented precision, (9) opening new possibilities for drug discovery.

In light of these credible needs for novel antiepileptic agents and the promising potential of natural products, this systematic review aims to comprehensively evaluate *Lantana camara*. Linn as a potential source of novel antiepileptic compounds and assess its therapeutic potential in epilepsy management. Precisely, this review seeks to examine existing literature on the antiepileptic properties of the plant and identify bioactive compounds with anticonvulsant activity, analyze the mechanisms of action through which these compounds exert their antiepileptic effects, evaluate the therapeutic efficacy of the derived compounds in preclinical and clinical studies, and identify research gaps while providing recommendations for future investigations into *Lantana camara* as an antiepileptic agent.

## Materials and Methods

This methodical review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure methodological rigor and transparent reporting.

**Inclusion Criteria:** Studies were eligible for inclusion if they investigated the anticonvulsant or antiepileptic effects of *L. camara* extracts or isolated compounds using established animal seizure models (maximal electroshock seizure [MES], pentylenetetrazol [PTZ], kainate, picrotoxin, or strychnine). Only peer-reviewed articles published in English up to December 2024 that reported quantitative seizure outcomes were included.

**Exclusion Criteria:** Studies were excluded if they were review articles without original experimental data, conference abstracts without full-text availability, or studies lacking sufficient methodological detail for data extraction. Additionally, studies that did not specifically investigate seizure or epilepsy outcomes were excluded.

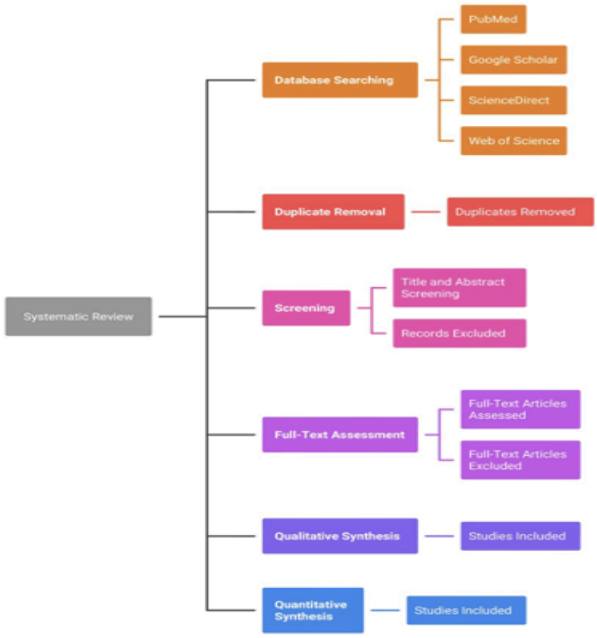
### Information Sources and Search Strategy

A comprehensive systematic literature search was conducted across major electronic databases: Google Scholar, Pub-Med, Science-Direct, and Web of Science, to identify and evaluate existing research on the anticonvulsant properties of *Lantana camara*. The search strategy employed a combination of relevant keywords and Medical Subject Headings (MeSH) terms, including primary terms such as "*Lantana camara*", "anticonvulsant", "antiepileptic", "seizure", and "epilepsy". The search focused on research that specifically investigated the anticonvulsant or antiepileptic activity of *L. camara* extracts or isolated compounds.

### Study Selection

Titles and Abstracts of all retrieved records were independently screened followed by full-text evaluation of potentially eligible studies. The selection process was documented using a PRISMA flow diagram.

**Figure 1: Flowchart of the articles satisfying inclusion/ exclusion criteria**




### Data Collection Process

A database search identified 778 records across PubMed (156), Google Scholar (423), Science Direct (187), and Web of Science (12). After removing 184 duplicates, 594 records remained for screening. Title and abstract screening excluded 571 records that did not meet inclusion criteria, leaving 23 records for full-text assessment. During full-text evaluation, 16 articles were excluded due to insufficient seizure data (8), different plant species (4), or lack of original data (4), resulting in 7 studies spanning 2012-2024 being included in the qualitative synthesis. Data extraction used standardized forms to capture study characteristics, intervention details, outcomes, and risk factors, including author information, publication year, study location, animal models, sample sizes, *L. camara* preparation details, seizure models, outcomes, and proposed mechanisms.

### Risk of Bias Assessment

Study quality was assessed using adapted criteria for preclinical animal studies, evaluating randomization, blinding, selective outcome reporting, sample size adequacy, and statistical analysis appropriateness.

## Results

### Study Selection

The systematic search strategy identified records across the targeted databases. Following duplicate removal and screening processes, seven studies met the final inclusion criteria and were included in the qualitative synthesis.

### Study Characteristics

The included studies, spanning from 2012 to 2024, were conducted across multiple countries including India and Cameroon. All studies employed animal models with various seizure induction methods, providing comprehensive evaluation of *L. camara's* anticonvulsant properties.

**Table 1: Summary of *Lantana camara's* Anticonvulsant Studies**

| Study Authors | Country | Animal Model (n) | Extract/ Compound Type | Dosage | Treatment Duration | Route | Seizure Models | Key Findings | Proposed Mechanisms |
|---|---|---|---|---|---|---|---|---|---|
| Kazmi et al. (32) | India | Mice (n=60) | Ursolic acid stearoyl glucoside (UASG) | 5, 10, 20 mg/kg | Single dose, 30 min before induction | IP | MES, PTZ | Prevented hind limb tonic extension; Delayed seizure onset; Reduced seizure severity; Showed antidepressant properties | Increased GABA levels; Decreased glutamate levels |
| Chinnala et al. (34) | India | Rats (n=36) | Ethanol extract | 200, 400 mg/kg | Single dose, 1 hour before induction | Oral | MES, PTZ | Reduced tonic hind limb extension duration; Provided protection from electrically-triggered seizures | GABAergic modulation (inferred) |
| Pathan et al. (35) | India | Wistar albino rats (n=48) | Ethanolic and aqueous extracts (stems and flowers) | 200, 400 mg/kg | Single dose, 1 hour before induction | Oral | MES, PTZ | Reduced seizure duration; Reduced mortality rates; Ethanolic extracts showed superior efficacy | Not specified |
| Bora & Singh (36) | India | Swiss albino mice (n=72) | Multiple extracts (petroleum ether, chloroform, ethanol, water) from dried flowers | 100, 200, 400 mg/ kg | Single dose, 60 min before induction | Oral | MES, PTZ, picrotoxin, strychnine | Dose-dependent seizure protection; Lengthened time before seizure onset; Decreased seizure duration | GABAergic system modulation |
| Kandeda et al. (37) | Cameroon | Mice (n=45) | Aqueous extracts | 100, 200, 300 mg/ kg | Single dose, 1 hour before induction | Oral | Kainate-induced | Reduced seizure severity by 40-60%; Increased seizure latency by 15-30 minutes; Optimal dosage: 200-300 mg/kg | Elevated GABA by 25-35%; Increased antioxidant enzymes by 30-50%; Reduced inflammatory markers by 20-40%; Increased anti-inflammatory IL-10 by 30-50% |
| Talom et al. (38) | Cameroon | Male Swiss mice (n=54) | Ethanolic and aqueous extracts (leaves) | Ethanolic: 230, 460, 920 mg/ kg; Aqueous: 460 mg/ kg | 14 days treatment after 19-day epileptogenic period | Oral | Kainate-induced | Reduced seizure number and duration by 70-90%; Improved anxiety-like behavior; Increased GABA levels by 50-180%; Decreased iron and ferritin levels; Increased GSH levels; Reduced neuronal degeneration | Ferroptosis inhibition; GABAergic modulation; Iron homeostasis regulation; Antioxidant mechanisms (GSH/MDA modulation) |

**Synthesis of Findings**

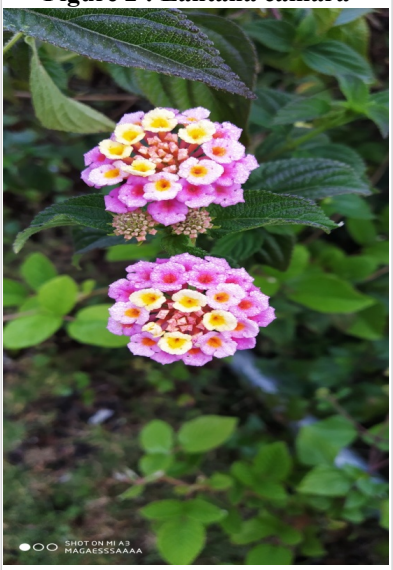
All seven included studies demonstrated significant anticonvulsant effects of *L. camara* preparations across diverse seizure models. The evidence consistently supports dose-dependent protection against seizures, with optimal dosages ranging from 200-400 mg/kg for crude extracts and 5-20 mg/kg for isolated compounds. Ethanolic extracts consistently outperformed aqueous preparations in studies that compared both extraction methods. The anticonvulsant effects were observed across multiple seizure types, including generalized tonic-clonic seizures (MES model), absence seizures (PTZ model), and complex partial seizures (kainate model).

## Discussion

### *Lantana camara*: An Emerging Candidate for Epilepsy Research

Scientific studies highlight *Lantana camara* (Fig.2) (10) as a potent focus in epilepsy research. This Verbenaceae family member, commonly known as wild sage or lantana, represents an interesting contradiction in medicinal botany. (11) Despite originating in the Americas and spreading worldwide as an invasive species, its broad geographical presence has enabled comprehensive scientific studies revealing medical research potential.

**Figure 2 : Lantana camara**



### Historical Perspective and Early Studies

Sharma et al.'s 1988 study (12) created a detailed analytical framework examining both environmental impact and medical applications, tracking worldwide spread while considering animal health interactions. Verma and Verma's 2006 investigation (13) conducted in-depth chemical analysis of *L. camara var. aculeata* leaves, identifying complex compound interactions and effectiveness against termites using methodical extraction and analytical techniques. Barceloux's 2008 toxicology study (14) positioned *L. camara* within the broader medicinal plant spectrum, establishing specific safety assessment methods and medical usage guidelines. Sathish et al.'s 2011 research (15) examined *L. camara's* impact on digestive system conditions, finding significant ulcer-prevention effects in rat models at varying concentrations.

### Phytochemical Profile and Mechanisms of Action

*L. camara* exhibits remarkable chemical diversity with numerous distinct compounds across multiple classes. (16-20) Triterpenes show notable structural variations and biological effects ranging from inflammation reduction to neuroprotection. Flavonoids demonstrate strong antioxidant effects with potential neural protective benefits; their blood-brain barrier penetration makes them particularly promising for neurological treatments. Phenolic compounds show significant biological activity including inflammation reduction and antioxidant properties, with combined effects potentially enhancing overall therapeutic effectiveness. Essential oils constitute another key group showing varied biological effects and therapeutic potential. (21)

### Flavonoids as Therapeutic Agents for Epilepsy

Flavonoids enhance cellular antioxidant defenses through modulation of key enzymes and influence of PI3K/AKT and Nrf2 pathways, providing comprehensive neuroprotective effects. Methanol flower extracts demonstrated highest flavonoid concentration (13.58 mg/g via RP-HPLC) and superior antioxidant activity in DPPH assays, with additional bioactive compounds including carbohydrates, cardiac glycosides, oxalates, and saponins providing synergistic effects. (22) Flavonoids demonstrate significant potential as therapeutic agents for drug-resistant epilepsy patients through multiple complementary mechanisms targeting key pathophysiological processes. They exert anti-inflammatory and antioxidant effects by modulating critical signaling pathways including NF-κB, MAPK, JNK, and JAK for neuronal protection. (23)

At the molecular level, flavonoids modulate neurotransmitter systems and ion channels to inhibit abnormal neuronal depolarization, thereby suppressing seizure activity while directly addressing molecular pathways contributing to epileptogenesis and reducing cognitive deficits. (24) Preclinical studies demonstrate robust neuroprotective capabilities in various epilepsy models, supporting therapeutic potential. Combination of flavonoids with conventional antiepileptic drugs represents a promising therapeutic strategy enhancing overall efficacy while potentially reducing drug resistance and minimizing adverse effects. (25, 26) However, clinical translation faces challenges regarding bioavailability limitations, with current research exploring nanotechnology and chemical modifications to enhance therapeutic efficacy. (23)

### Animal Models in *L. camara* Epilepsy Research

Only Swiss albino mice and rats have served as primary animal models for *L. camara* research, with testing and development of epilepsy treatments depending critically on advanced animal testing methods that effectively replicate various aspects of the condition. (27) Models for studying acute seizures have been instrumental in initial screening of potential anticonvulsant compounds, (28) including chemically-induced seizures using pentylenetetrazole and kainic acid providing rapid, reproducible results. The maximal electroshock method has emerged as a standard approach in antiepileptic drug development, proving particularly effective for evaluating treatments for generalized convulsive seizures. Long-term epilepsy models provide comprehensive insights into chronic epileptic conditions, with pilocarpine-induced status epilepticus successfully reproducing key features of temporal lobe epilepsy including spontaneous recurring seizures. Kindling models help researchers understand gradual epilepsy development and drug resistance emergence, while genetic models serve as effective tools for studying inherited epilepsy forms. (29-31).

### GABAergic Mechanisms and Neurochemical Modulation by UASG

UASG (ursolic acid stearoyl glucoside), a compound found exclusively in *L. camara*, provides the first direct evidence of GABAergic mechanism in epilepsy treatment. (32) This study demonstrated methodologically significant findings showing increased brain GABA levels alongside decreased glutamate concentrations, establishing favorable excitatory-inhibitory balance for seizure suppression. (33) The concurrent discovery of UASG's antidepressant properties highlighted the compound's dual therapeutic potential for addressing epilepsy's psychiatric comorbidities, representing a promising advancement in

comprehensive treatment strategies for drug-resistant epilepsy patients

## Conclusion

This methodical review provides conclusive evidence for *Lantana camara's* anticonvulsant potential through multiple complementary mechanisms. The progression from single-compound studies to comprehensive extract evaluations demonstrates the plant's therapeutic complexity and multi-target efficacy , the consistent dose-dependent effects and broad-spectrum activity across all included studies support *L. camara's* development as a source of novel antiepileptic compounds. The plant's ability to simultaneously modulate GABAergic transmission, reduce oxidative stress, control neuroinflammation, and inhibit ferroptosis suggests a comprehensive therapeutic strategy that addresses epilepsy's multifaceted pathophysiology. This multi-target profile may offer advantages over conventional single-target interventions, particularly for treatment-resistant cases. With significant gaps remain in translating these promising preclinical findings to clinical applications. Future research must prioritize comprehensive toxicological evaluation, pharmacokinetic profiling, standardization studies, and progression to appropriately designed clinical trials across different model organisms like, zebrafish, genetic epilepsy models, chronic seizure models and non-human primate models.

*L. camara* stands at the intersection of traditional knowledge and modern scientific inquiry, emerging as a valuable natural source for innovative antiepileptic therapeutics. The systematic evidence presented provides a solid foundation for future clinical development programs. Paradoxically, this research highlights the therapeutic potential of a species widely regarded as one of the world's most problematic invasive weeds, demonstrating nature's capacity to conceal medicinal treasures within ecologically disruptive plants. Currently classified as a noxious weed across multiple continents due to its aggressive colonization and ecological disruption, *L. camara* presents a unique opportunity to transform environmental liability into pharmaceutical asset. Successful clinical translation could fundamentally shift the paradigm from costly eradication efforts to sustainable approach, creating economic incentives that align conservation goals with therapeutic innovation. This transformation from ecological burden to neurological therapy exemplifies how comprehensive phytochemical research can reveal hidden value in the most unlikely botanical candidates, potentially converting widespread invasive species into sources of life-changing medicines for patients with treatment-resistant epilepsy in near future.

This review addresses the critical treatment gap affecting one-third of epilepsy patients worldwide who remain treatment-resistant. Expanding Therapeutic Applications beyond epilepsy could establish *L. camara* as a multi-indication agent for anxiety disorders, neurodegenerative diseases, and psychiatric comorbidities.

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**Conflict of interest**

The Author's declare no Conflict of Interest

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