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The Double- Edged Sword of Lantana Camara : Toxicological Risk And Therapeutic Potential

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ABSTRACT:

One of the most remarkable contradictions in the plant kingdom is embodied by the Verbenaceae family's prolific flowering shrub, Lantana camara L. Although it is well acknowledged as a devastating invasive species and a strong hepatotoxin to cattle, it also has a long history in ethnobotanical medicine on many continents. This thorough review explores this dichotomy in great detail, methodically looking at L. camara's toxicological and ecological risks as well as its potential pharmacotherapeutic uses. The structure-activity relationships of the hepatotoxic triterpenoids (lantadenes) and the diverse bioactive compounds (flavonoids, phenolics, essential oils) that support its antimicrobial, anti-inflammatory, anticancer, and other therapeutic properties are the main focus of our in-depth examination of viewpoint by combining historical background, mechanistic toxicity, and contemporary pharmacological research. While promoting thorough scientific research to responsibly harness its latent therapeutic value and turn a biological threat into a biomedical resource, it also emphasises the urgent need for coordinated strategies to control its ecological spread and mitigate its toxicological risks.

Keyword : lantana camara , toxicology, Therapeutic potential , invasive species , Hepatotoxicity , Allelopathy .

1.Introduction

Lantana camara, also referred to as tickberry, red sage, or wild sage, is a fascinating story of molecular intricacy, ecological upheaval, and human intervention. Originally from Central and South America's tropical regions, it was introduced as an ornamental plant to more than 60 nations, which led to its inclusion in the list of the top ten worst invasive species worldwide [1]. The plant actively outcompetes natural flora to create thickets that are impenetrable and monotypic, which drastically reduces biodiversity and changes the dynamics of ecosystems. From an agricultural perspective, L. camara is notorious for causing ruminant hepatotoxicity that is acute and frequently lethal, which leads to significant financial losses, especially in pastoral communities in Asia, Africa, and Australia [2]. its On the other hand, a review of traditional medical practices from both its natural range and the areas it has infiltrated reveals a highly esteemed plant. Its leaves, stems, and flowers have been used in decoctions, poultices, and infusions to cure a wide range of ailments, including as dermatitis, cuts and wounds, fevers, coughs, asthma, rheumatism, and even as an antiseptic for leprosy lesions [3]. Its extensive and varied phytochemical composition is the basis for this striking difference between its harmful and advantageous functions. The goal of this review is to provide a thorough synthesis of the scientific literature that is currently accessible on both aspects of L. camara, including a description of its pharmacology, toxicity, and the chemical components that determine its dual nature.

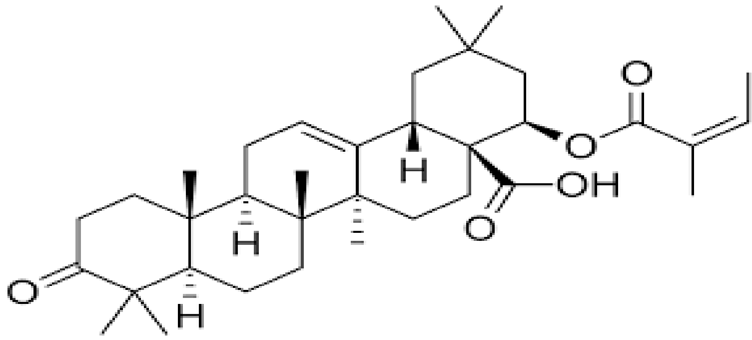
fig.1 L.camara leaves & Flowers Fig.2 L.camara fruits

2. The Toxicological Edge: A Multifaceted Threat

2.1. Phytochemistry of Toxicity

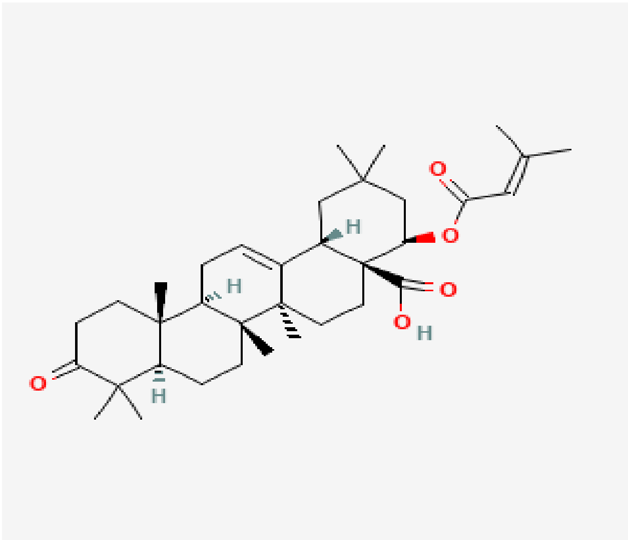
The lantadenes, a group of pentacyclic triterpenoids, are the main substances that cause L. camara's toxicity.Lantadene A and Lantadene B are the most prevalent and highly hepatotoxic of these [4].These substances are produced and stored all over the plant, but concentrations are highest in the green, unripe berries, which makes them especially appetising and harmful to grazing animals.

- **Lantadene A:** ((22β)-22-{[(2E)-3,3-Dimethyloxiran-2-yl]carbonyl}oxy-3-oxoolean-12-en-28-oic acid) features an oleanane core with a ketone group at the C-3 position and a characteristic epoxylated isobutyryl ester moiety at C-22.



Sturture 1: lantadene A

- **Lantadene B:** (3-Oxo-22-{[(2Z)-2,4,5-trimethyl-2,5-dihydrofuran-3-yl]carbonyl}oxyolean-12-en-28-oic acid) is structurally similar but possesses a rearranged furan-containing ester group at C-22.



Strture 2 : lantadene B

The specific structural features of these esters are critical for their toxicity, influencing their absorption, metabolism, and interaction with hepatic cells.

2.2. Mechanistic Pathways of Hepatotoxicity

The pathophysiology of lantana poisoning is a well-studied, multi-step process centered on the liver. 1. Ingestion and Absorption: When other food is limited, ruminants, notably sheep and cattle, graze on the plant. During ruminal fermentation, the lantadenes are released and taken up by the portal circulation. 2. Hepatic Insult and Cholestasis: The lantadenes are carried to the liver, where they directly damage the bile duct epithelium and the canalicular membrane of hepatocytes. The condition known as intrahepatic cholestasis, a functional stoppage of bile flow from the liver to the duodenum, is caused by this injury, which interferes with the active secretion of bile [5]. 3. Photosensitisation: A photodynamic substance known as phylloerythrin is not excreted when bile flow is stopped. Chlorophyll is broken down by bacteria in the rumen to produce phylloerythrin. Normally, the liver effectively eliminates it and excretes it as bile. It builds up in the peripheral circulation when lantana poisoning occurs. When it gets to the skin, its excited state produces reactive oxygen species when exposed to sunlight, especially UV radiation, which leads to severe photodermatitis. Hepatogenous (or secondary) photosensitisation is the term used to describe this [6].

2.3. Pathology and Clinical Presentation

After intake, clinical symptoms appear 24 to 48 hours later. Hepatogenous photosensitisation is the most noticeable and distinctive symptom, which manifests as:

• Severe skin irritation and pruritus.

• Oedema, especially in the eyelids, muzzle, and ears.

• Skin sloughing and necrosis, particularly in regions with scant hair and lack of pigmentation.

Additional systemic symptoms include:

Jaundice:

Hyperbilirubinemia-induced yellowing of the sclera and mucous membranes.

• Gastrointestinal Stasis:

ruminal atony, constipation, and anorexia, most likely brought on by a failure to expel bile salts required for fat digestion and gut motility.

• Weakness and Dehydration: As the illness worsens, animals experience weakness, depression, and dehydration. Additionally, tubular damage from circulating toxins may result in renal failure.

Post-mortem examinations consistently show signs of epidermal necrosis, a dilated gall bladder, and an enlarged yellow-orange, friable liver, a distended gall bladder, and evidence of skin necrosis [2, 5].

2.4. Allelopathy and Ecological Impact

L. camara is an aggressive ecosystem engineer in addition to being directly hazardous to wildlife. A number of characteristics are responsible for its invasion success:

• Prolific Seed Production and Fast Growth:

It generates large amounts of seeds, which are spread by animals like birds.

• Allelopathy: Through leaf leachate and root exudates, L. camara releases a variety of allelochemicals into the soil, including as phenolics, flavonoids, and terpenoids. These substances promote the establishment of monospecific stands by preventing the germination and development of rival native plant species [7].

• Modified Fire Regimes: Because it is frequently more resistive to wildfires than native vegetation, the dense, dry thickets it develops can intensify and increase their frequency, further solidifying its control.

3. The Therapeutic Edge: An Ethnobotanical Treasure Trove

3.1. Traditional and Historical Applications

Many societies have long included L. camara's medical usage in their pharmacopoeias. Leaf infusions are used to treat bronchitis, influenza, and fever in Brazilian traditional medicine. It is used to treat malaria, rheumatism, and tetanus in India. The leaves are used to make poultices that are administered to wounds, ulcers, and skin diseases in Africa in order to avoid sepsis [3, 8]. The original motivation for scientific research into its bioactive qualities came from this extensive traditional usage.

3.2. Phytochemistry of Therapeutics

A wide range of secondary metabolites that are different from or coexist with the lantadenes are thought to be responsible for L. camara's medicinal potential. Important classes consist of:

• Flavonoids: A significant portion of the plant's antioxidant action is attributed to this broad class of polyphenolics. Important delegates consist of:

o Lutein: A flavone with strong antioxidant, anti-inflammatory, and anti-cancer effects.

o Quercetin: A common flavonol having potent anticancer, cardioprotective, and free-radical scavenging properties.

• Phenolic Acids: These substances greatly enhance the antioxidant and antibacterial characteristics of the plant. Gallic acid, ferulic acid, and caffeic acid are a few examples.

• Essential Oils: Although L. camara's volatile oil is complex and chemotypically variable, sesquiterpenes like germacrene-D and β-caryophyllene (which have anti-inflammatory and antibacterial properties) and monoterpenes like 1,8-cineole (eucalyptol) are typically the most abundant [9] . • Benign Triterpenoids: Not every plant has poisonous triterpenoids. Well-known pentacyclic triterpenoids ursolic acid and oleanolic acid have been shown to have anti-inflammatory, hepatoprotective, and anticancer properties, demonstrating how minor structural variations can significantly change biological consequences.

3.3. Comprehensive Pharmacological Studies

• Antimicrobial Activity:

The traditional usage of L. camara treating infections has been confirmed by a number of in vitro investigations. The leaves' methanolic and ethanolic extracts have demonstrated broad-spectrum efficacy against both Gram-negative (like Escherichia coli and Pseudomonas aeruginosa) and Gram-positive (like Staphylococcus aureus and Bacillus subtilis) bacteria. There have also been repeated reports of antifungal action against dermatophytes and Candida albicans [10]. The activity is ascribed to the combinatorial action of essential oils, flavonoids, and tannins, which can hinder energy metabolism and damage microbial cell membranes. • Anti-inflammatory and Analgesic Properties: These effects have been strongly supported by preclinical research conducted in rodent models. Extracts of L. camara dramatically decreased inflammation in animals like as formaldehyde-induced arthritis and carrageenan-induced paw oedema. The suppression of pro-inflammatory mediators such as prostaglandins, leukotrienes, and cytokines (TNF-α, IL-6) is one of the suggested mechanisms [11]. Triterpenes (ursolic acid) and flavonoids (luteolin, quercetin) are strong inhibitors of enzymes that are important in the inflammatory cascade, such as lipoxygenase (LOX) and cyclooxygenase-2 (COX-2). The acetic-acid writhing and hot-plate tests showed analgesic effects, which are probably the result of this anti-inflammatory action.

• Cytotoxic and Anticancer Potential:

This is one of the most exciting study topics. A variety of human cancer cell lines have shown cytotoxic responses to crude extracts and identified components from L. camara. For example, research has demonstrated that human promyelocytic leukaemia (HL-60), lung carcinoma (A-549), and breast adenocarcinoma (MCF-7) cells exhibit growth suppression and apoptosis induction [12]. The mechanisms are complex and consist of:

o Apoptosis induction: downregulation of anti-apoptotic proteins (Bcl-2) and upregulation of pro-apoptotic proteins (Bax, caspase-3).
o Cell Cycle Arrest: Stopping the growth of cancer cells at particular checkpoints, such as the G2/M phase.
o Antioxidant and Pro-oxidant Effects: Although flavonoids are often antioxidants, they can also function as pro-oxidants in the high-stress, high-metabolic environment of cancer cells, producing reactive oxygen species that set off apoptotic pathways.

o Inhibition of Angiogenesis and Metastasis: It has been demonstrated that substances such as ursolic acid block pathways essential for the blood supply and dissemination of tumours.

• Additional Pharmacological Actions:

o Wound Healing: Its traditional usage in wound management is attributed to its antibacterial and anti-inflammatory qualities as well as certain chemicals' purported fibroblast-proliferating activities.

o Antidiabetic: In animal models of diabetes, some research reports hypoglycemic effects, possibly as a result of increased peripheral glucose uptake or insulin secretion.

The essential oil and extracts have demonstrated effectiveness against mosquito larvae (such as Aedes aegypti) and other insect pests, suggesting that they may be used for vector control [13].

4. Handling the Duality:

:From Issue to Opportunity

The main obstacle in managing L. camara is the overlap of its hazardous and therapeutic components in terms of both space and chemistry. To overcome this, advanced strategies are needed:

1. Advanced Extraction and Fractionation: The hazardous lantadenes can be physically separated from the advantageous flavonoids and essential oils using methods such as preparative HPLC, column chromatography, and bio-guided fractionation. Desired compound classes can be extracted selectively by using particular solvent polarity.

2. Phytochemical Engineering and Synthesis: Investigating the synthesis of lantadene analogues using medicinal chemistry may result in derivatives that have less hepatotoxicity but still have the same or improved bioactivity for use in anticancer leads, among other applications [4]. 3. Toxicokinetic Studies: The creation of protective agents or antidotes may benefit from a better knowledge of the absorption, distribution, metabolism, and excretion (ADME) of lantadenes in various species.

4. Utilisation and Management: From an ecological perspective, identifying profitable applications for the biomass, including composting, biofuel generation, or as a source of phytochemicals, could encourage its collection and management, transforming a waste issue into a useful good.

5. Prospects for the Future

The future requires an interdisciplinary approach. To lessen its negative effects on the environment, ecologists and farmers must keep up their efforts. At the same time, medicinal chemists, pharmacologists, and phytochemists need to step up their research to:

Clearly define the precise molecular mechanisms of action for its poisons and treatments. Describe its phytochemical profile in detail, including any minor compounds.

• Perform thorough in vivo pharmacological and toxicological investigations to determine the safety and effectiveness profiles of possible therapeutic uses.
• Create standardised extracts devoid of toxins for use in therapeutic development.
Humanity can strive to become proficient with the dual strategy of Lantana camara, efficiently neutralising its menacing edge while deftly using its healing one.

5. Conclusion

A botanical Jekyll and Hyde is Lantana camara. Its status as a deadly poison and destructive invasive species is indisputable, necessitating ongoing management through mechanical and biological control as well as public awareness. But to see it only in this way is to miss its vast untapped potential. Its intricate chemistry, which has been shaped by evolution as a defence mechanism, is a priceless collection of bioactive compounds that are just waiting to be completely understood.

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