Review Article

Pharmacological Potentials and Formulation Strategies of *Euphorbia hirta*

Abstract

Euphorbia hirta, commonly known as asthma weed or garden spurge, has a rich history in folk medicine, particularly in tropical and subtropical regions. Its diverse pharmacological properties, stemming from a rich composition of bioactive substances such as alkaloids, flavonoids, tannins, saponins, and phenolic acids, have attracted significant attention within the scientific community. Various extraction methods, including solvent extraction, steam distillation, and chromatography, have been used to isolate these compounds, leading to the creation of formulations with significant antimicrobial, anti-inflammatory, antioxidant, and antidiabetic effects. This review explores the chemical makeup, traditional applications, and pharmacological prospects of Euphorbia hirta, with a focus on the latest advances in extraction techniques and formulation approaches. It also emphasizes the need for continued research on the plant, suggesting that further studies could lead to the development of new therapeutic agents from this versatile species.

Keywords: Traditional medicine, phytochemistry, pharmacological activities, formulation strategies.

Introduction

The Euphorbia family, also known as Euphorbiaceae, is a large and diverse group of plants that includes over 2,000 species, ranging from small herbs to large trees, many of which are known for their unique milky sap and various medicinal properties. Medicinal plants have been the cornerstone of traditional medicine systems for millennia, offering therapeutic solutions for many health conditions. *Euphorbia hirta* Linn, commonly known as the asthma plant, is a member of the Euphorbiaceae family and is one of the most prominent species used in traditional medicine across Asia, Africa, and Latin America. The plant is distinguished by its hairy stems, reddish-purple coloration, and milky latex, which has been utilized for its medicinal properties in folk medicine.In traditional systems, *Euphorbia hirta* has been employed to treat various conditions, such as asthma, bronchitis, dysentery, fever, and gastrointestinal disorders.[1]

The broad spectrum of its pharmacological activities can be attributed to its diverse chemical composition, which includes alkaloids, glycosides, flavonoids, tannins, terpenoids, and phenolic acids.[2] These bioactive compounds have been shown to exhibit significant therapeutic effects, making *Euphorbia hirta* a valuable resource for the development of new pharmacological agents.[2,3]

The global burden of diseases such as diabetes, cardiovascular disorders, and microbial infections has spurred interest in discovering new therapeutic agents from natural sources. *Euphorbia hirta* has garnered attention in this regard due to its potent bioactive properties. Moreover, the growing resistance to conventional antibiotics and the rising incidence of chronic diseases highlight the need for alternative treatments, where plants like *Euphorbia hirta* could play a crucial role.[3,4,5]

This review aims to provide a comprehensive overview of *Euphorbia hirta's* chemical composition, traditional uses, and pharmacological properties.[3,4,5] Additionally, it will explore the advances in extraction and formulation techniques developed to harness this plant's medicinal potential. By examining traditional and modern perspectives, this paper highlights the importance of *Euphorbia hirta* in contemporary medicine and its potential role in addressing global health challenges.[6,7] This study seeks to provide an updated review of the chemical composition and applications of *Euphorbia hirta*, aiming to identify existing research gaps and limitations in the current body of knowledge.

Historical Background and Traditional Uses

The Euphorbia family, or Euphorbiaceae, boasts a rich history that dates back to ancient times, with records indicating its use in traditional medicine and cultural practices across various civilizations. This large and diverse plant family, which includes over 2,000 species, has been utilized for its unique characteristics, such as its distinctive milky sap and wide range of biological activities. Members of the Euphorbia family have been documented in ancient texts for their medicinal properties, with different species being used to treat various ailments, from skin conditions to digestive disorders.

Euphorbia hirta has been used for centuries in traditional medicine systems such as Ayurveda, Traditional Chinese Medicine (TCM), and African traditional medicine**(Plate 1)**. In Ayurveda, *Euphorbia hirta* is known as "Dudhali" and is used to treat conditions such as asthma, bronchitis, and cough. The plant's latex is applied topically to treat warts, skin infections, and boils. In TCM, *Euphorbia hirta* is used as an anti-inflammatory agent, and its decoction is employed to treat respiratory ailments and gastrointestinal disturbances. African traditional medicine utilizes *Euphorbia hirta* for its antimicrobial and anti-inflammatory properties, particularly in treating malaria, diarrhea, and skin infections.[6,7]

Euphorbia hirta has a well-documented history as a remedy for asthma, a fact that is reflected in its common name, "asthma weed." Traditionally, the leaves and stem of the plant are boiled to create tea or decoction and consumed to alleviate symptoms of asthma, bronchitis, and other respiratory ailments. Additionally, the plant has been used to treat gastrointestinal problems like dysentery and diarrhea. The latex of *Euphorbia hirta* is applied to warts, boils, and other skin lesions to promote healing and reduce inflammation.[7,8]

In the Philippines, *Euphorbia hirta* is known as "tawa-tawa" and is traditionally used to treat dengue fever. The plant is believed to increase platelet counts and reduce the severity of the disease, although

scientific evidence supporting this use is limited. Nonetheless, *Euphorbia hirta* remains a popular remedy in rural areas where access to conventional medical treatment is limited.[8,9,10]

In West Africa, *Euphorbia hirta* is a galactagogue to promote milk production in lactating women. The plant is also employed as an anthelmintic to expel intestinal worms and as a diuretic to increase urine output. In Nigeria, the plant treats diabetes, hypertension, and various infections, reflecting its broad spectrum of medicinal applications.[8,9,10]

Plate 1:*Euphorbia hirta*(Source: Wikipedia)

Botanical Description and Phytochemistry

Euphorbia hirta is a small, erect annual herb that typically grows to a height of 30 to 60 cm. The plant is characterized by its hairy stem, which is reddish or purplish, and its leaves, which are opposite, elliptical, and serrated.[8,9] The leaves are typically 1 to 3 cm long and 0.5 to 1.5 cm wide, with a dark green coloration on the upper surface and a pale green underside. The plant produces small, yellowish-green flowers that are clustered in axillary cymes. The fruits are small, three-lobed capsules that contain numerous seeds.[10,29]The taxonomical classification for it is provided in **Table 1**.

Table 1: Taxonomical Classifications: [8,29,30]

Sr. No.	**Taxa**	**Scientific name**
1.	Kingdom	Plantae
2.	Subkingdom	Viridiplantae
3.	Division	Tracheophyta
4.	Subdivision	Spermatophytina
5.	Class	Magnoliopsida
6.	Order	Malpighiales
7.	Family	Euphorbiaceae
8.	Genus	*Euphorbia*
9.	Species	*Euphorbia hirta*

The phytochemical profile of *Euphorbia hirta* is diverse, with several classes of bioactive compounds identified in different parts of the plant. These include alkaloids, flavonoids, tannins, saponins, terpenoids, and phenolic acids, responsible for the plant's wide range of pharmacological activities**(Figure 1)**.[29,30]

Alkaloids: Alkaloids are a class of nitrogen-containing compounds with significant biological activity. In *Euphorbia hirta*, alkaloids such as euphorbin, a toxic alkaloid, have been identified. Alkaloids in the plant are known for their antimicrobial, anti-inflammatory, and analgesic properties.[10,11,12,13]

Flavonoids: Flavonoids are a group of polyphenolic compounds widely distributed in the plant kingdom. They are known for their antioxidant, anti-inflammatory, and anti-cancer properties. In *Euphorbia hirta*, flavonoids such as quercitrin, rutin, and myricetin have been identified. These compounds contribute to the plant's ability to scavenge free radicals and reduce oxidative stress.[10,11,12,13]

Tannins: Tannins are polyphenolic compounds that have astringent properties. They are known for their antimicrobial, anti-inflammatory, and antioxidant activities. *Euphorbia hirta* contains hydrolyzable tannins such as ellagitannins and gallotannins, which contribute to the plant's antimicrobial and wound-healing properties.[10,11,12,13]

Saponins: Saponins are glycosides that have surfactant properties. They are known for lowering cholesterol levels, boosting the immune system, and exhibiting anti-cancer activity. *Euphorbia hirta* contains saponins that have been shown to exhibit significant biological activity, including anti-inflammatory and antimicrobial effects.[13,14,15]

Terpenoids: Terpenoids are a large and diverse class of organic compounds derived from five-carbon isoprene units. They are known for their wide range of biological activities, including anti-inflammatory, antimicrobial, and anti-cancer properties. In *Euphorbia hirta*, terpenoids such as euphorbia and taraxerol have been identified.[10,11,12,13]

Phenolic Acids: Phenolic acids are a type of polyphenol known for their antioxidant and anti-inflammatory properties. *Euphorbia hirta* contains phenolic acids such as gallic acid, chlorogenic acid, and caffeic acid, contributing to the plant's ability to reduce oxidative stress and inflammation.

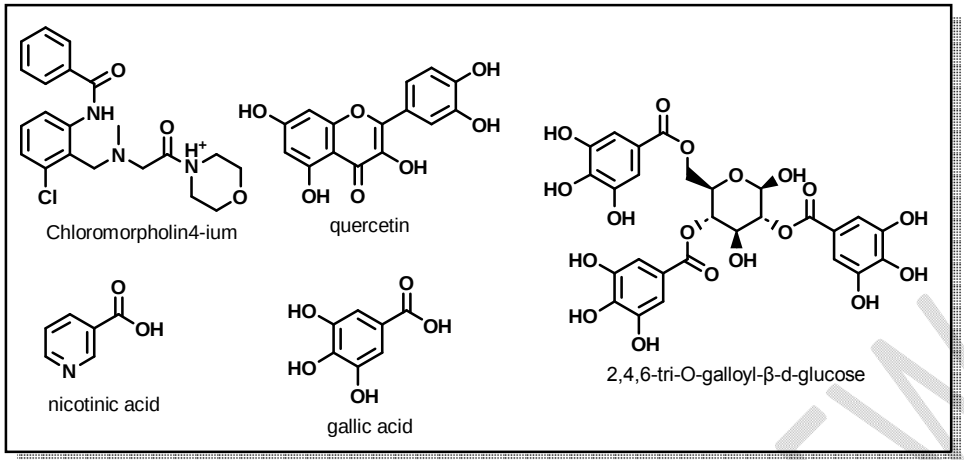

Figure 1: Main compounds isolated from *Euphorbia hirta*[10,11]

Combining these bioactive compounds in *Euphorbia hirta* results in a plant with a broad spectrum of pharmacological activities. The diversity of compounds also presents an opportunity to develop new drugs and therapeutic agents based on the chemical constituents of *Euphorbia hirta*.

Evaluation Parameters for Formulations

Skin spreadability:"A 10% ointment, in a hydrophilic base, of a 95% ethanolic extract of the whole plant of *E. hirta* was topically applied once daily". [15,16]

Oral administration:"10% w/v suspension of 95% ethanolic extract of whole plant of *Euphorbia hirta* in 2% tragacanth was given orally, once daily, 200 mg/kg BW"[15,16,29]

Pharmacological Properties

Antibacterial Activity

The antibacterial properties of *Euphorbia hirta* have been extensively studied, with several studies demonstrating its effectiveness against a wide range of bacterial pathogens. Methanolic and ethanolic extracts of the plant have shown significant antibacterial activity against Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Bacillus subtilis*.[21,22,23]

A studyinvestigated the antibacterial activity of methanolic extracts of *Euphorbia hirta* against dysentery-causing *Shigella*species. The results showed that the extract exhibited significant antibacterial activity, with a minimum inhibitory concentration (MIC) of 0.78 mg/mL against *Shigelladysenteriae*.[23,25,26] The study concluded that *Euphorbia hirta* has the potential to be developed into a natural antibacterial agent for the treatment of dysentery and other bacterial infections.The antibacterial activity of *Euphorbia hirta* is believed to be due to the presence of flavonoids, tannins, and phenolic acids in the plant. These compounds have been shown to inhibit bacteria's growth by disrupting the bacterial cell membrane, inhibiting protein synthesis, and interfering with nucleic acid replication.[24,25,26]

Antifungal Activity

Euphorbia hirta has also exhibited antifungal activity against various fungal pathogens. Studies have demonstrated the effectiveness of the plant's extracts against fungal species such as *Candida albicans*, *Aspergillus niger*, and *Trichophytonrubrum*.[27] The antifungal activity of *E.hirta* is attributed to the presence of saponins, tannins, and terpenoids, which have been shown to disrupt the cell membrane of fungi and inhibit their growth.The antifungal properties of *Euphorbia hirta*extract against *Candida albicans*, a common fungal pathogen responsible for opportunistic infections in immunocompromised individuals.[1] The results showed that the methanolic extract of *E.hirta* exhibited significant antifungal activity, with a MIC of 1.56 mg/mL. The study concluded that *E.hirta*could be developed into a natural antifungal agent to treat fungal infections.[26,28]

Antioxidant Activity

Oxidative stress is a significant contributing factor to the development of chronic diseases such as cancer, cardiovascular disorders, and neurodegenerative diseases. Antioxidants are crucial in protecting the body against oxidative damage by neutralizing free radicals and reducing reactive oxygen species (ROS) levels. *Euphorbia hirta* has been shown to possess significant antioxidant activity due to its high flavonoid content, phenolic acids, and tannins.[22,23,24]

A further study in the literature evaluated the antioxidant activity of *Euphorbia hirta* extracts using in vitro assays, such as the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assay and the ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation decolorization assay. The results showed that the methanolic extract of *Euphorbia hirta* exhibited potent antioxidant activity, with an IC_{50} value of 12.5 µg/mL in the DPPH assay. The study concluded that *Euphorbia hirta* has the potential to be developed into a natural antioxidant agent for the prevention and treatment of oxidative stress-related diseases.[2]The antioxidant activity of *Euphorbia hirta* is believed to be due to the presence of flavonoids such as quercitrin, rutin, and myricetin, as well as phenolic acids such as gallic acid and chlorogenic acid. These compounds have been shown to scavenge free radicals, inhibit lipid peroxidation, and reduce oxidative damage to DNA and proteins.[23,26,27]

Anti-inflammatory Activity

Inflammation is the body's protective response to injury or infection, but chronic inflammation can develop diseases such as arthritis, cancer, and cardiovascular disorders. *Euphorbia hirta* has been shown to possess significant anti-inflammatory activity, which is attributed to its high content of flavonoids, tannins, and terpenoids.[2,29]

A study investigated the anti-inflammatory properties of *E.hirta* extract in animal models of inflammation. The results showed that the methanolic extract of *Euphorbia hirta* significantly reduced the levels of pro-inflammatory cytokines such as TNF-α and IL-6 in rats with induced paw edema. The study

concluded that *Euphorbia hirta* has the potential to be developed into a natural anti-inflammatory agent for the treatment of inflammatory diseases.[21,24]

The anti-inflammatory activity of *Euphorbia hirta* is believed to be due to the presence of flavonoids such as quercitrin and myricetin, which have been shown to inhibit the production of pro-inflammatory cytokines and reduce the expression of inflammatory enzymes such as Cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS).[25]

Antidiabetic Activity

Diabetes is a chronic metabolic disorder characterized by hyperglycemia, insulin resistance, and impaired glucose tolerance. *Euphorbia hirta* has been traditionally used to treat diabetes in various cultures, and recent studies have provided scientific evidence to support its antidiabetic properties.

They investigated the antidiabetic and hypolipidemic activities of *Euphorbia hirta* in streptozotocin-induced diabetic rats. The results showed that the methanolic extract of *Euphorbia hirta* significantly reduced blood glucose levels, improved insulin sensitivity, and decreased serum cholesterol and triglyceride levels in diabetic rats.[1,4,21] The study concluded that *Euphorbia hirta* has the potential to be developed into a natural antidiabetic agent for the treatment of diabetes and its associated complications.The antidiabetic activity of *Euphorbia hirta* is believed to be due to the presence of flavonoids and phenolic acids. These compounds have been shown to inhibit the activity of enzymes involved in carbohydrate metabolism, such as α-glucosidase and α-amylase. These compounds also enhance insulin secretion and improve glucose uptake in peripheral tissues.[23,24]

Antiasthmatic Activity

Asthma is a chronic respiratory disorder characterized by airway inflammation, bronchoconstriction, and increased mucus production. *Euphorbia hirta* has been traditionally used to treat asthma, and recent studies have provided scientific evidence to support its antiasthmatic properties and investigated the antiasthmatic activity of *Euphorbia hirta* in animal models of asthma.[21,22] The results showed that the methanolic extract of *Euphorbia hirta* significantly reduced airway inflammation, decreased bronchoconstriction, and improved lung function in asthmatic rats.[25,28] The study concluded that *Euphorbia hirta* has the potential to be developed into a natural antiasthmatic agent for the treatment of asthma and other respiratory disorders.The antiasthmatic activity of *Euphorbia hirta* is believed to be due to the presence of flavonoids such as quercitrin and rutin. These compounds have been shown to inhibit the release of histamine and other inflammatory mediators from mast cells. These compounds also relax bronchial smooth muscle and reduce airway resistance.[5,6,24]

Formulation Strategies and Applications

The therapeutic potential of *Euphorbia hirta* has led to the development of various formulations for its use in modern medicine. These formulations include extracts, tinctures, ointments, and capsules designed to deliver the bioactive compounds of *Euphorbia hirta* in a standardized and effective manner.[22,27,28]

"The powdered aerial parts of each drug (100 g) were extracted in the Soxhlet apparatus for 24 h with ethanol, then concentrated and dried under reduced pressure. The extracts were weighed, and percentage yields were calculated in w/w. (*E. hirta* 7.44%, E. alba 6.5%, and *Tridax procumbens* 6.22%)".[15,16]"The semisolid masses of extracts obtained were used as ingredients for 10% ointment preparation. About 10 g of semisolid extract of aerial parts of *E. hirta* was incorporated into 100 g of simple ointment base, and 3.33 g of each of semisolid extracts of *E. hirta, E. alba*, and *Tridax procumbens* were incorporated into 100 g of simple ointment base. A simple ointment base was used as a placebo in the control group. Extract ointments were used twice daily to treat different groups of animals".[12]

Mouthwash Formulation:"As much as 100 ml of mouthwash was produced for each formulation with *Euphorbia hirta*L. extract as the active substance. The formulations of *Euphorbia hirta* L. mouthwash contained Propylene glycol, which was added to the *Euphorbia hirta*L. extract and placed in a glass beaker".[15,16]

"It was then raised to 60 C, stirred with a magnetic stirrer at 300 rpm, Tween 80, and added sorbitol and distilled water. Benzoic acid and sodium benzoate were dissolved in distilled water, added to the solution, and stirred with a magnetic stirrer until homogeneous. Subsequently, 100 ml of the sorbitol and distilled waterwere stirred until the solution became clear, and Oleum menthaepiperitae was added".[13]

Extracts and Tinctures

Extracts and tinctures of *Euphorbia hirta* are widely used in traditional medicine and have been adapted for use in modern herbal medicine. These formulations are typically prepared by macerating the plant material in solvents such as ethanol, methanol, or water to extract the bioactive compounds.[12,14] The resulting extract is then concentrated and standardized to ensure consistent potency and efficacy.A study investigated the chemical composition of the methanolic extract of *Euphorbia hirta* and its pharmacological properties.[12]The results showed that the extract contained significant amounts of flavonoids, tannins, and phenolic acids, contributing to its antioxidant, antimicrobial, and anti-inflammatory activities. The study concluded that *Euphorbia hirta* extract could be developed into a standardized herbal formulation for treating various diseases.[15,16,26]

Ointments and Creams

Ointments and creams containing *Euphorbia hirta* extract are used for the topical treatment of skin infections, wounds, and inflammatory conditions. These formulations are designed to deliver bioactive compounds directly to the affected area, providing localized relief from symptoms such as pain, swelling, and infection.This study formulated and evaluated an herbal ointment containing *Euphorbia hirta* for its

antimicrobial activity. The results showed that the ointment exhibited significant antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*, with a zone of inhibition comparable to standard antibiotics. The study concluded that *Euphorbia hirta* ointment could be developed into a natural antimicrobial agent for treating skin infections.[2]

Capsules and Tablets

Capsules and tablets containing *Euphorbia hirta* extract are used for the oral treatment of various diseases, including diabetes, hypertension, and respiratory disorders. These formulations are designed to deliver bioactive compounds systemically, providing therapeutic effects throughout the body.Thedevelopment of jaina topical formulation of *Euphorbia hirta* for its antimicrobial activity.[1] The results showed that the formulation exhibited significant antimicrobial activity against various bacterial and fungal pathogens, with an MIC comparable to standard antibiotics. The study concluded that *Euphorbia hirta* could be developed into a natural antimicrobial agent to treat various infections.[27,28]

Conclusion

Euphorbia hirta is a versatile medicinal plant with various pharmacological activities, including antimicrobial, anti-inflammatory, antioxidant, and antidiabetic properties. The plant has been used for centuries in traditional medicine and has garnered significant attention in modern scientific research. The bioactive compounds in *Euphorbia hirta*, such as flavonoids, tannins, saponins, and phenolic acids, contribute to its therapeutic potential and make it a valuable resource for developing new drugs and formulations.

The advances in extraction and formulation techniques have allowed for the development of standardized herbal products that harness the medicinal properties of *Euphorbia hirta*. These formulations, including extracts, ointments, and capsules, offer a natural alternative to conventional pharmaceuticals and have the potential to address global health challenges such as antibiotic resistance and chronic diseases.Further research is needed to fully elucidate the mechanisms of action of the bioactive compounds in *Euphorbia hirta* and to explore its potential in clinical applications. Nonetheless, the current evidence supports using*Euphorbia hirta* as a safe and effective medicinal plant with broad therapeutic potential.

Data availability statement

The data supporting this study's findings are available in Google Scholar at https://scholar.google.com/.

Because this work is a review, the data supporting the findings of this study are available online, as various manuscripts about the *Euphorbia* genus and its applications have been reported. All references (Doi) are noted in the references section. The dataset that supports the findings of this review is included in the article.

Availability of data and materials

The data was collected from various websites and search engines, such as Science Direct, Taylor and Francis, Google Scholar, ResearchGateetc.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

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