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Review Article

Exploring Modern Insights into Phytochemistry, Pharmacological, Toxicology, and Industrial Potential of *Euphorbia tirucalli* Linn.

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ABSTRACT

Medicinal plant often referred as phytomedicine or botanical medicine or plant medicine. For thousands of years, traditional healthcare systems throughout the world have relied heavily on herbal medicines. In addition to reflecting the knowledge of past societies these natural cures nevertheless have an impact on contemporary medical procedures. Herbal therapy is now prized for its cost, accessibility and all-encompassing approach to health. The goal of this narrative review summarizes the available literature on the phytochemistry, pharmacological properties, toxicological profile, industrial potential and current information on the phytochemical compositions and therapeutic uses of different portions of *Euphorbia tirucalli*. This plant is known for a variety of medicinal applications *E. tirucalli* is the family of *Euphorbiaceae* which is also known as 'pencil tree' or 'Barki Tohar'. Despite being native to Americas, the species has effectively adapted and is now widely distributed throughout India, where it is acknowledged as a commonly used medicinal herb. Both the milky latex and the stem bark are used in traditional methods. The latex has dose dependent effects in little amounts, it functions as a moderate purgative, but in greater doses, it becomes bitter, counter irritating and emetic. Pharmacological studies *in-vitro* and *in-vivo* have shown that the latex and bark exhibit a variety of biological activities, such as antimutagenic, antibacterial and antihyperthermic qualities. It's interesting to note that the latex has both cocarcinogenic and anticarcinogenic capabilities. Its ethnomedical significance across culture is further demonstrated by the traditional use of it as a folk treatment against syphilis in northeastern Brazil. The phytochemistry, taxonomical distribution, morphology, and other pharmacological characteristics of *E. tirucalli* are highlighted in this paper, which may encourage a thorough assessment of the plant as a therapeutic agent.

INTRODUCTION

The current value of herbs has long been acknowledged by ancient medical systems, including Traditional Chinese Medicine, Ayurveda and African traditional medicine, with documented evidence going back to 3000 BCE. The efficacy and safety of many plant-based treatments have not been thoroughly evaluated using standardized research methodologies, making the scientific validation of herbal medicine. Despite of its long history a crucial challenge in contemporary healthcare. Increasing worries about the plant adverse effects of synthetic medications, increased instances of antibiotic resistances, and the growing need for natural and holistic healthcare

solutions have all contributed to a resistance of interest in herbal therapy in recent years. Conferring to the WHO, estimates that almost 80% population of world would be contingent on herbaceous remedies being primary source of healthcare, particularly in regions where access to modern pharmaceuticals remains limited. While this reliance underscores the cultural and therapeutic importance of medicinal plants, their integration into formal healthcare systems requires rigorous scientific validation. Establishing pharmacological efficacy, clarifying mechanisms of action and ensuring well-defined safety profiles are essential steps to bridge traditional

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practices with evidence-based medicine and to promote their acceptance in mainstream clinical use.^[1]

Euphorbia is considered with 2000 species; it is regarded as the second biggest genus in angiosperms. Trees, succulents, and the herbaceous plants are all members of the *Euphorbiaceae* family. Numerous species can be found growing in the wild or as cultivated plants in homes and gardens all around the world. The family of booming plants includes a vast range of vegetative forms, some of which are quite significant. *Euphorbia* in structural way is very small tree or woody plant that is originating from humid tropical regions and gets its colloquial name 'pencil tree' from its pencil like branches. Because its shoots and twigs (branches) stay green throughout the year and are rarely consumed by animals. It is typically evergreen. It has white, toxic latex, which could explain its therapeutic qualities and low herbivore pressure. Because of *E. tirucalli* generates a hydrocarbon compound that resembles petrol, it is known as a petroleum plant. Harvesting entire plants is valuable from an energy perspective, with rubber, petroleum and alcohol serving as energy produces and resins that might be utilized in the leather, oil, skin, and linoleum industries. Gun powder can be made from the charcoal that is produced there.^[2]

Its taxonomy and chemistry have recently attracted attention perhaps due to the diverse range of chemical compositions among its members, many of which are toxic but beneficial. The family's global spread exposes its members to a wide range of environments to which they naturally adapted to that is resulting in production of several compounds that are used for defence and survival. The milky sap is a common characteristic of *Euphorbiaceae*. There are around 322 genera and 8910 species in the family, many of which are valuable economically and add to the floral riches of tropical and subtropical nations worldwide. There are several widespread and endangered taxonomic groups in the family. Most of the traditional medicine has documented the majority of its therapeutic properties, but there is little scientific or laboratory evidence to support these claims.^[3]

The common name pencil tree was inspired by the slender, pencil shaped branches. In tropical areas, *Euphorbia tirucalli* grows as a shrub or small tree. It is known as the 'pencil tree' because of its thin, tree. The plant is rarely grazed by herbivores and is mostly evergreen, with stems and branches staying green all year round. Its toxic white latex, which may account for both its decreased herbivore induced stress and its recognized therapeutic value, is responsible for this resilience.^[2,4]

Phytoconstituents

The chemicals were isolated from *E. tirucalli* are euphol, euph-8-enol, gallic acid, methyl gallate and rutin by using phytochemical analysis. Numerous studies have been conducted on the chemical components of different

portions of the plant. Citric acid, malonic acid and succinic acid make up nearly 7.4% of *E. tirucalli*. Flavonoids, tannins, diterpenes, steroids, alkaloids and other phytochemicals have been supplied by this plant. Terpenes, tirucallol, taxasterol, cycloeuphorenol, beta-sitosterol, terpenic alcohol^[5] and their reported activities are shown in Table 1 and some important phytochemical structures are shown in Table 2. When damaged or cut, euphorbia plants secrete a milky white latex that makes them easy to identify. The plant's lactified organ created this latex.

Additionally preliminary research indicates that latex contains proteolytic enzymes, which could account for its vesicant and rubefacient properties which are mentioned in the Table 1. The biochemical foundation for the plant's ethnomedical uses and contemporary pharmaceutical interest is formed by these phytoconstituents taken together.^[13]

Traditional Uses

Traditional medicine has long used *Euphorbia tirucalli* latex to treat rheumatism, asthma, earaches, cough and toothaches. It is also used as a treatment for syphilis in traditional ways. In addition to this use, the sap is employed as a laxative in traditional medicine and to manage parasitic organisms of the intestine. It is also used to treat moles, epitheliomas, sarcomas, and other membrane tumors in north eastern Brazil. Traditional and Modern uses are shown in the Table 3.

Euphorbia tirucalli stem has long been used to treat spleen infections, asthma, whooping cough, and blood diseases. It has been used to treat various ailments like dyspepsia, gonorrhea, leprosy, neuralgia. It is considered a carminative, purgative and stomachic. The plant's bark is also prized in traditional medicine, especially for treating asthma, whooping cough, blood problems, colic and spleen infections. Conversely, the roots are primarily used to treat colic.

Leaves of *E. tirucalli* are traditionally boiled in some parts of East Africa, and the resulting extract is given to women to treat infertility. The herb is also used in African ethnomedicine to cure warts, syphilis, snakebite, sexual dysfunction, hemorrhoids, and fractured bones. In Brazil it is used to treat spasmodic disorders, cancer, asthma, and scorpion stings. Furthermore, plant has been investigated to have emmenagogic and abortifacient qualities in the Ayurvedic medical system.^[13]

Although its caustic nature necessitates careful handling, the latex has also been administered externally as a vesicant and rubefacient. In addition to its therapeutic uses. The plant has been used for fencing boundary marking, and windbreak in semi-arid areas.

Although they can be cultivated on lawns, potted plants are typically found in homes and work places. Due to its attractive evergreen pencil like branches and ease of maintenance, it has become more popular internationally

Table 1: Phytochemical classes of *Euphorbia tirucalli* with their Reported Biological activities

Class	Representative compound	Source (plant part)	Reported activities	References
Sterols	Lanosterol, cycloeuphornol, α -euforbol	Latex, stem	Immunomodulatory, antiviral	[6]
Phenolics	Gallic acid, methyl gallate	Aerial parts	Hepatoprotective, Antioxidant	[7]
Diterpenes	Ingenol derivatives, 12-deoxyphorbol esters	Latex	Tumor-promoting/anticancer (dose dependent)	[8]
Proteolytic enzymes	Amino acid chains, serine, cysteine, threonine and aspartic acid.	Latex	Vesicant, rubefacient, proteolytic activity	[9]
Alkaloids & tannins	Reported in root extracts	Roots	Anti-inflammatory, Anti-arthritis	[10]
Flavonoids	Rutin, Quercetin	Aerial parts	Antioxidant, hepatoprotective	[11]
Triterpenes	Euphol, β amyryl, taraxerol, tirucallol	Latex, stem bark	Anticancer, antimicrobial, anti-inflammatory	[12]

and is now widely distributed in places where it was not indigenous. According to a statement from the 17th conference of the resolution on International Trade in Endangered Species of Wild Fauna and Flora (CITES) plants agency, which took place in Geneva, Switzerland, from April 15-19, 2006 the trade in *E. tirucalli* is flourishing. The same report lists as an endangered species that needs to be preserved perhaps for a similar reason.^[14]

Van Damne and the Belgian CITES board associates, however, contested the latter decision. *E. tirucalli* is currently included in the minimum disturbed grouping of the international Union for conservation of Nature's (IUCN) 2010 red list of threatened species most likely in recognition of this difficulty.^[14]

Reported Pharmacological Activities

In vivo studies

Anti-Arthritic Action

The *Euphorbia* plant biopolymeric fraction (BET). The fraction showed both in vivo immunomodulatory potential a crucial component in the prevention of arthritis and dose dependent antiarthritic efficacy based on flow cytometry. It reduced intracellular interleukin-2 (IL-2) and interferon-gamma (IFN- γ) and decreased CD4⁺/CD8⁺ T-lymphocytes. Rats treated with the plant's BET fraction in adjuvant-induced arthritis models showed concentration-dependent reduction of paw oedema. Oral doses of 100-200 mg/kg exhibit the greatest therapeutic results in which activity that prevents arthritis.^[23]

Anthelmintic Activity

It has been demonstrated that plant latex extracts prepared with petroleum ether and dichloromethane – methanol can drive out helminth parasite worms from the body. At ten unique concentrations (0.1-1.0%), the extract obtained using a dichloromethane- methanol extract was found to be efficient in contradiction of *Pheretima postuma* earthworm. According to the study when earthworm is treated with dichloromethane, methanol, petroleum ether,

ethyl acetate extract, their life span or time to paralysis and death decreases.^[24]

Analgesic Activity

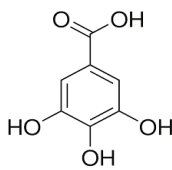
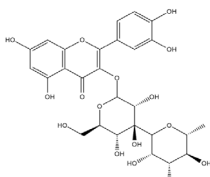
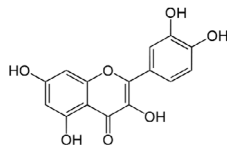
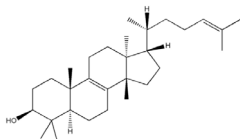
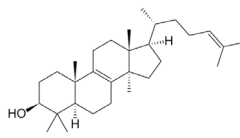
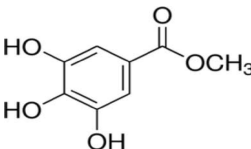
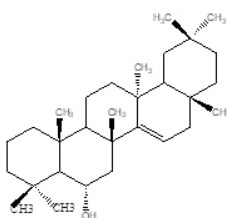
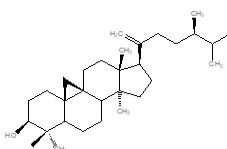
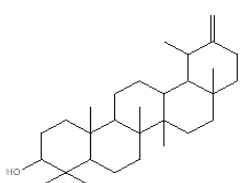
Euphorbia tirucalli's analgesic potential has been investigated in both experimental pharmacology and ethnomedicinal contexts; data suggests that its latex and stem extracts have pain-relieving qualities. The presence of triterpenes, flavonoids, and diterpenes which are known to regulate inflammatory pathways and nociceptive responses is responsible for this function, according to phytochemical studies. Methanolic extracts of the stem given in animal models at doses between 100 and 400 mg/kg showed significant inhibition of formalin-induced paw licking and acetic acid-induced writhing in mice, indicating peripheral and central analgesic effects. The latex, which is rich in phorbol esters, has also shown activity in reducing pain perception, although its irritant nature limits direct clinical application. Comparative studies show that higher doses (>400 mg/kg may be toxic. Due to *E. tirucalli*'s long-standing medicinal value, traditional medical systems have used diluted formulations of the plant to treat inflammatory diseases and rheumatic pain. However, thorough pharmacological validation is required prior to translation into clinical practice due to the tight margin between hazardous concentrations and effective analgesic levels.^[25]

Oxytocic Activity

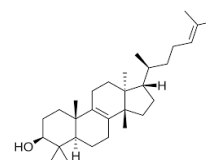
The plant latex components, particularly phorbol esters and diterpenes, which stimulate uterine smooth muscle, have been identified as the main source of its oxytocic potential. With effective doses reported in the range of 50–200 μ g/mL, experimental pharmacological studies have shown that crude latex extracts cause dose-dependent uterine contractions in isolated rat and guinea pig uterine strips. Higher dosages (>200 μ g/mL) caused tissue necrosis and prolonged spasms, highlighting the limited therapeutic margin. At lower levels, the extracts produced rhythmic contractions similar to those induced



Table 2: Chemical Structures of following Bioactive compound

Compounds	Structure
Gallic acid	
Rutin	
Quercetin	
Euphol	
Lanosterol	
Methyl gallate	
Euphorginol	
Cyclotirucanenol	
Taxaserol	

Tirucallos



by oxytocin. The presence of 12-O-tetradecanoylphorbol-13-acetate and related diterpenes, which are known for their irritating and tumor-promoting qualities but also linked to smooth muscle stimulation, is confirmed by phytochemical tests. This plant's exhibited potent oxytotoxic action against gravid rat uterus strips. ^[1]

Hepatoprotective Action

The hepatoprotective effect of *E. tirucalli* aqueous extract against CCl_4 induced liver injury in rat was investigated systemically and scientifically. The degree of reversal of elevated biochemical indicators of hepatitis, serum glutamate pyruvate transaminase (SGPT), alkaline phosphate (ALP), bilirubin, cholesterol and triglycerides as well as tissue glutathione (GSH) stages and the degree of muscle phospholipid peroxidation reduction, were measured to determine the hepatoprotective property. Similarly, *E. tirucalli* aqueous extract at 125 and 250 mg/kg significantly reduced serum enzymes, bilirubin, cholesterol, triglycerides and tissue lipid peroxidation while significantly raising tissue GSH levels in a dose dependent manner. ^[26]

Anti-inflammatory Action

Euphol, which is derived from the latex of *Euphorbia tirucalli*, was shown to have anti-inflammatory qualities in TPA- induced skin irritation in mice. The study came to the conclusion that euphol's anti-inflammatory qualities are linked to its capacity to stop edema and leukocyte infiltration, upregulation of COX-2 and chemokines, and activation of ERK, PKca and PKcd. ^[27]

Molluscicide Activity

On *Biomphalaria glabrata*, an aqueous solution of *E. tirucalli* latex collected in locations with lots of sunlight demonstrated molluscicide effect, LD_{50} was found at a concentration of 28.0 ppm and LD_{90} at a concentration of 85.0 ppm. The product's harmfulness to fish was comparable to that of copper sulphate and bayluscide. However, 'avelos' is a promising agent in the control of schistosomiasis due to the plant's widespread distribution, ease of cultivation and straightforward process for extracting the biodegradable active ingredient. ^[28]

Immunomodulatory Activity

In tumor-bearing mice, myelo suppression was seen concurrently with elevated spleen CFU-GM levels. When these animals were treated with *E. tirucalli* (125, 250 and 500 mg/kg). The formation of spleen colonies was decreased and marrow myelopoiesis was increased,

Cont...

Table 3: Traditional and Modern uses

Category	Uses	References
Traditional medicine	Treatment of warts, asthma, rheumatism, toothache, leprosy, jaundice, colic, tumors	[15,16]
Ethnoveterinary	Purgative, anti-helminthic, wound healing	[17]
Household/folk uses	Boundary demarcation, live fencing, windbreak	[16]
Antimicrobial	Euphol, gallic acid, methyl gallate, active against resistant klebsiella	[18]
Anticancer	Igenol derivatives, phorbol esters (cytotoxicity)	[19]
Antioxidant/anti inflammatory	Rutin, quercetin, gallic acid	[20]
Immunomodulatory/antiviral	Sterols, triterpenoids	[21]
Industrial	Biofuel, adhesives, resins	[22]

there were no variations in dose responses effects across the three doses. The *E tirucalli* therapy corrected the alterations in total and differential marrow cell counts caused by the tumour bearers. *E.t* dramatically increased survival while simultaneously slowing the growth of tumours in the peritoneal cavity. [29]

CNS Depressant/Neuropathic pain

The potential of euphol to stop neuropathic pain brought on by sciatic nerve ligation has been studied. Euphol's antinociceptive effects were considerably diminished by pretreatment with CB₁R and CB₂R genes, suggesting that it has potential as a therapeutic agent for the treatment of neuropathic diseases. Additionally, using an actophotometer and chlorpromazine as the reference medication. The Locomotor behavior analysis was employed to investigate the CNS depressant effects of petroleum ether, dichloromethane-methanol, and aqueous fractions of *E. tirucalli* latex, all of which demonstrated inhibitory activity. These effects are probably caused by elevated GABA levels in brain. [30]

Larvicidal/Ovicidal

Euphorginol, which was extracted from the plant's stem or bark, was found to have larvicidal properties against the schistosomiasis-causing *lymnaea mollusca acuminata* and *Biomphalaria glabrata*. When dilutions made which is obtained from the latex of the plant after then tested in counter to *B. glabrata*, the results showed LD₅₀ at 28 ppm and LD₉₀ at 85 ppm using fresh latex from *Euphorbia tirucalli* in various dilutions, Larvicidal efficacy was observed against *Anopheles funestus* and *A.gambae*. It is best to use the greatest dilution (1:250) to avoid latex overdose. [31]

Myelopoeisis

Increased spleen CFU GM was a sign of myelosuppression in tumor-bearing animals. Animals treated with *Euphorbia tirucalli* extract had decreased spleen colony development and increased marrow myelopoiesis. Consequently, the

extract greatly increased survival rates and inhibited the formation of tumors. [29]

Genotoxic mutagenic

The inductest, Ame's test, and Chromotest were used to assess the genome damaging and capable of inducing mutations and potential of latex and phytoconstituents therapeutic re-solutions made from *Euphorbia tirucalli*. The inductest results indicated and increased in the lysogenic cycle and no decrease in bacterial survival. Likewise, there was no indication of mutagenic or genotoxic effects in the Ames and Chromotest. [32]

In vitro studies

Antiviral Activity

At a concentration of 150 ppm, the extracts made using comparative analysis demonstrated that petroleum ether extract achieved 80% resistance whereas dichloromethane-methanol extract achieved 81% resistance against tomato mosaic virus, highlighting their near equivalent protective potential. The MTT colorimetric test and the End point Titration Technique (EPTT) have been used to measure the amount of pretreatment needed to attenuate the membrane disruption action of the reduction in cell viability was observed in both infected and clean cultures upon treatment with HSV-2. The strongest antiviral activity is found in the aqueous and methanolic extracts organized from the leaves and stems of 10 *Euphorbia* species were evaluated for antiviral activity. The therapeutic index of active extracts was determined by calculating the ratio of CC₅₀ (50% cytotoxic concentration) to IC₅₀ (50% inhibitory concentration of viral action). The *E. tirucalli* leaf/stem water methanol showed the maximum activity. [23]

Antimicrobial Activity

The plant's antimicrobial, antibacterial, and antifungal properties were investigated using plant extracts in a variety of solvents, including petroleum ether, ethyl



acetate, ethanol, dichloromethanol, chloroform, acetone and hexane. *Candida tropicalis*, *Pseudomonas aeruginosa*, *Streptomyces aureus*, *Bacillus subtilis*, *E. coli*, *Candida albicans*, *Salmonella enteritidis*, *klebsiella pneumoniae*, *A. flavus*, *Aspergillus niger*, *A. fumigatus* and well diffusion assay were among the gram-positive and gram-negative bacteria that were successfully extracted from *Euphorbia tirucalli*'s leaves and stem. *Euphorbia tirucalli* stem acetone extracts shown significant sensitivity against *Escherichia coli* and considerable antibacterial action. Furthermore, with minimum inhibitory concentrations (MICs) of 500 µg, 750 µg, and 750 µg, respectively, they prevented the growth of *Candida albicans*, *Aspergillus niger*, and *A. fumigatus*. With MIC values of 750 µg/mL, 250 µg/mL, 500 µg/mL, 500 µg/mL, 1000 µg/mL and 750 µg/mL, respectively, chloroform extracts were effective against *Bacillus subtilis*, *Proteus vulgaris*, *Staphylococcus aureus*, *E. coli*, *A. niger* and *Candida albicans*.^[33] Significant action against *B. subtilis*, *S. aureus*, *E. coli*, *Candida albicans*, and *Enterococcus faecalis* was shown by methanolic extracts. *B. subtilis* and *E. faecalis* needed 750 µg, *C. albicans* shown inhibition at 1000 µg, while *S. aureus* and *E. coli* had MICs of 500 µg. Methanol extracts showed the strongest antibacterial activity among the studied solvents, especially against some fungal strains and gram-positive bacteria.^[34]

Antioxidant Activity

Antioxidant capacity was evaluated using a version of the ABTS (2,2-azino-bis(3-ethyl-benzothiazoline-6-sulfonic acid)) test technique. Equal quantities of 2.6 mM K2S2O8 and 7.4 mM ABTS solution were combined to create the stock solution, which was then incubated for more than 15 hours at room temperature in the dark. In order to produce at 734 nm, the UV is spectrophotometer registered an optical density of 1.10 ± 0.02 , reflecting consistent antioxidant activity, an aliquot of the stock solution was diluted roughly 1:60 with methanol to create a working solution. After that, 200 µL of the sample was added to 3.8 mL of the ABTS•+ working solution, and the mixture was incubated for two hours at room temperature in the dark. Next, absorbance was measured at 734 nm (in relation to the occupied solution).^[35-36]

Antiherpetic Activity

Experimental validation was performed by using in-vitro the end point titration technique (ETT) along with a calorimetric assay which shows *E. tirucalli* antiherpetic potential. The water methanol extract showed the highest action, with viral inhibition exceeding 65% according to the therapeutic index, which was computed as the ratio of CC₅₀ (50% cytotoxic concentration) to IC (50% inhibitory concentration of viral impact). These results imply the *E. tirucalli* contains bioactive chemicals that can inhibit HSV-2 proliferation, validating its ethnomedical use and calling for additional pharmacological investigation.^[37] Figure 1

E. tirucalli represents medicinal uses and pharmacological activities as shown below.

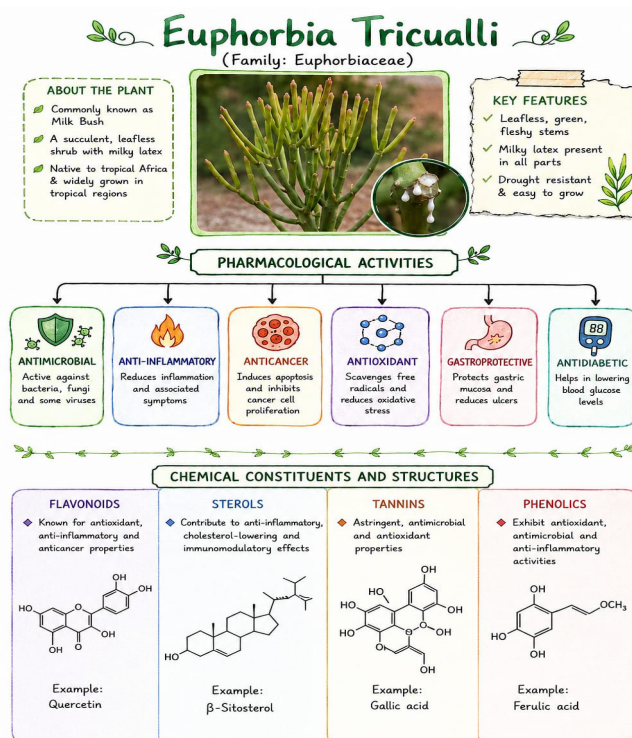


Fig. 1: *E. tirucalli* medicinal uses and pharmacological activities

Toxicological Profile

Evaluation of the aqueous latex solution of *E. tirucalli* revealed no inhibitory effects on embryonic tuberin growth or implantation events, indicating minimal interference with early developmental stages. Interestingly, while embryonic development remained unaffected, notable alterations were observed in placental morphology, suggesting that the latex may exert selective effects on reproductive tissues. This highlights the plant's complex bioactivity, where certain physiological processes are preserved while others are modulated.^[38] Further investigations are expanded the understanding of its systemic effects. In their study, animals treated with *E. tirucalli* latex exhibited a statistically significant increase in food consumption ($p < 0.05$), yet this did not translate into corresponding weight gain. This paradoxical outcome points toward possible metabolic modulation, where nutrient intake is enhanced but energy utilization or storage is altered. Such findings raise intriguing questions about the latex's influence on metabolic pathways, appetite regulation, and nutrient absorption.^[39]

Chemical constituents responsible for toxicity

Euphol, diterpenes, phorbol esters and other irritant compounds. Euphol, various diterpenes, and phorbol esters, which have strong irritant and tumor-promoting effects, are the main components of *Euphorbia tirucalli*'s toxicological profile. Phorbol esters, especially 12,13-diester, activate

protein kinase C, starting inflammatory cascades and carcinogenic pathways. Experimental studies show that the latex exhibits dose-dependent toxicity, with lethal concentrations (LC_{50}) against *Lymnaea acuminata* at 0.92 mg/L at 24 hours and 0.55 mg/L at 96 hours against *Indoplanorbis exustus*.^[40]

Local Toxic Effects

Skin irritation, vesicant properties, conjunctivitis, mucosal damage. Due to its phorbol ester-rich diterpenes and irritating triterpenes like euphol, *Euphorbia tirucalli* latex has strong local toxic effects. While ocular exposure causes conjunctivitis, keratoconjunctivitis, corneal epithelial destruction, and excruciating pain, dermal contact frequently causes skin irritation, erythema, vesicant responses, and blister formation. Burning sensations, ulceration, and mucosal erosion are caused by mucosal contact, especially when it involves the oral cavity or gastrointestinal tract.^[41]

Systematic Toxicity

Gastrointestinal disturbances, mutagenic potential, hepatotoxicity, carcinogenicity *Euphorbia tirucalli* latex exhibits substantial systemic toxicity in addition to its local irritating effects, including hepatotoxicity, carcinogenicity, gastrointestinal disorders, and mutagenic potential. Doses exceeding 200–400 mg/kg body weight have been proven to cause significant gastrointestinal discomfort, including nausea, vomiting, diarrhea, and mucosal bleeding, when taken orally in animal models. At dosages higher than 500 mg/kg, hepatotoxic effects, including increased liver enzymes and histological alterations, have been documented in rats, suggesting dose-dependent hepatic stress. The carcinogenic potential of latex extracts is confirmed by *in vitro* tests, which show that 1–10% concentrations cause chromosomal abnormalities and breaks in DNA strands in human leukocytes.^[42]

Experimental and Clinical Evidence

In vitro cytotoxicity studies case reports in human rat's models. Both laboratory tests and clinical case reports have confirmed *Euphorbia tirucalli*'s toxicity potential. The genotoxic activity of phorbol esters and diterpenes has been confirmed by *in vitro* cytotoxicity experiments, which show that hydroalcoholic latex extracts at concentrations of 1–10% cause considerable DNA damage, oxidative stress, and apoptosis in human leukocytes. These results are corroborated by animal models: in rats, oral latex extract treatment at dosages greater than 200 mg/kg body weight resulted in systemic toxicity, hepatic stress, and gastrointestinal irritation, whereas lower levels caused moderate inflammatory reactions.^[43]

Dose Dependent Responses and Safe Limits

Threshold levels, toxic doses, variability across species. *Euphorbia tirucalli* latex's toxicological profile shows

distinct dose-dependent reactions, with thresholds differing greatly between species. Lethal concentrations (LC_{50}) of 0.5–1.4 mg DWL^{-1} are obtained in 24–96 hours in aquatic invertebrates such *Lymnaea acuminata* and *Indoplanorbis exustus*, indicating severe sensitivity caused by acetylcholinesterase inhibition. In comparison to snails, fish models, such as *Channa punctatus*, require significantly greater dosages; mortality was detected at around 9 mg DWL^{-1} (24h). Studies on mammals show that systemic toxicity occurs at oral dosages greater than 200–400 mg/kg body weight, causing gastrointestinal discomfort, while hepatotoxicity manifests in rats at ≥ 500 mg/kg, resulting in increased liver enzymes and histological damage.^[44–45]

Traditional Handling and safety practices

Folk medicine of detoxification, ethnomedical precautions. *Euphorbia tirucalli* has long been used in folk medicine for detoxification, especially as a purgative or cleansing agent, but because of its extremely irritating latex, ethnomedical traditions constantly stress the need for stringent safety measures. Because pure latex can result in severe mucosal injury, gastrointestinal bleeding, and skin vesicant reactions, traditional healers usually administer the latex in extremely diluted quantities, often blended with other herbs or boiled to diminish its potency. It is customary to urge vulnerable populations, like children, pregnant women, and the elderly, to completely avoid its use. To reduce toxicity while maintaining therapeutic benefit, ritual precautions such as regulated dose regimens and preparing techniques are essential.^[46]

Industrial and Agriculture Applications

Euphorbia tirucalli has become a significant industrial and agricultural resource in addition to its medical use. The creation of renewable energy is one of its most promising uses. The plant is a potential source of biofuel and biogas since the hydrocarbon-rich latex contains substances that can be transformed into liquid fuels. Its appeal as a sustainable energy crop is further enhanced by its capacity to flourish on marginal soils with low water requirements. Because of its drought resistance, quick growth, and capacity to serve as a living fence, the plant is also used in agroforestry systems. *E. tirucalli* is commonly used by farmers as a hedge plant to prevent soil erosion and grazing animals. Additionally, the latex has insecticidal and pesticidal qualities, providing prospects for the creation of ecologically friendly pest control methods.^[47] Applications in industry include carbon sequestration, biomass generation, rubber alternatives, and environmental restoration initiatives. The species is useful for ecological restoration and climate-resilient agricultural methods because of its exceptional adaptation to damaged and dry areas. However, enhanced farming methods, processing innovations, and evaluations of economic viability are necessary for large-scale commercialization.^[1]



Complications Associated with *Euphorbia tirucalli*

Difficulties after acquaintance (exposure) to stem latex are infrequent, although unadorned consequences together with impaired vision have been observed. Worries are infrequent following dermal contact; However, the affected areas are at risk for subsequent bacterial infection. Individuals who have corneal epithelial abnormalities contagious impurity. Individuals who have corneal epithelial abnormalities are more susceptible to bacterial eye infections. Without therapy, corneal scarring anterior staphyloma, corneal neovascularisation, and blindness may follow. [48-49]

Limitations, Challenges and Future Perspectives

Limitations of Existing Studies

Most studies on *Euphorbia tirucalli* are limited to in vitro experiments and animal models. The extraction methods, doses and experimental protocols vary considerably among studies, making direct comparison difficult. In addition, many investigations use crude extracts rather than purified bioactive compounds, and sample sizes are often small. [50]

Safety and Toxicity

Although *Euphorbia tirucalli* possesses promising pharmacological activities, its milky latex contains irritating diterpene esters that may cause skin irritation, eye injury, gastrointestinal toxicity, and allergic reactions. Comprehensive acute, sub-chronic, and chronic toxicity studies are still limited, and safe therapeutic dosage ranges have not been established. [51]

Pharmacokinetics

There is limited information regarding the absorption, distribution, metabolism and excretion (ADME) of the major bioactive constituents of *Euphorbia tirucalli*. The bioavailability and tissue distribution of these compounds remain poorly understood, which limits their clinical development.

Herb-Drug Interactions

Potential interactions between *Euphorbia tirucalli* extracts and conventional medicines have not been adequately investigated. Since phytochemicals may influence drug-metabolizing enzymes and transporters further studies are required before co-administration with prescription medications can be considered safe. [52]

CHALLENGES

Clinical translational is also limited by the absence of standardized extract preparation, quality-control guidelines, dosage recommendations and regulatory approval. Standardizations of bioactive constituents and compliance with international quality standards are essential before therapeutic use. [53]

FUTURE PERSPECTIVES

Future research should focus on standardized extraction procedures, isolation of active compounds, pharmacokinetics evaluation, comprehensive toxicity studies, well-designed animal experiments, and randomized clinical trials to validate the safety and efficacy of *Euphorbia tirucalli* in humans.

CONCLUSION

Euphorbia tirucalli is a multipurpose industrial and medicinal plant with a wide range of biological activity and bioactive chemicals. The species antibacterial, anticancer, anti-inflammatory, antioxidant, immunomodulatory, and hepatoprotective qualities are attributed to terpenoids, triterpenoids, flavonoids, phenolics, sterols, and other secondary metabolites. Its therapeutic benefits have long been acknowledged by traditional medical systems, and contemporary scientific research has produced mounting evidence to support a number of ethnomedical claims.

E. tirucalli has significant promise as a natural insecticide, renewable energy source, agroforestry component, and environmental restoration species in addition to its pharmacological relevance. However, its extensive therapeutic use is still restricted by worries about toxicity, insufficient clinical validation, and a lack of standardized formulations.

Comprehensive toxicological evaluation, clinical research, phytochemical standardization, molecular mechanism investigations, and sustainable industrial development should be the main focus of future studies. By addressing these issues, *Euphorbia tirucalli*'s scientific foundation will be strengthened and its incorporation into contemporary industry, agriculture, and medicine will be made easier.

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