REVIEW ARTICLE

Ethnomedicinal and Pharmacological Insights into *Ixora coccinea*: A Multifaceted Therapeutic Agent

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ABSTRACT

Ixora coccinea L., commonly known as Jungle Geranium or Flame of the Woods, is a plant of considerable significance in traditional medicine systems across Asia, Africa, and the Caribbean. This review explores the ethnomedicinal and traditional uses of *I. coccinea*, highlighting its applications in Ayurveda for treating various ailments, particularly women's health issues, respiratory conditions, skin diseases, and digestive disorders. The flowers, roots, and leaves are utilized in diverse forms, including poultices, decoctions, and topical applications, demonstrating the plant's multifaceted therapeutic potential. Phytochemical analyses reveal a rich array of bioactive compounds, such as flavonoids, tannins, triterpenoids, and phenolic acids, which contribute to its recognized pharmacological properties, including anti-inflammatory, antimicrobial, antioxidant, anticancer, and wound-healing effects. Furthermore, *I. coccinea* exhibits specific activities such as anti-arthritic, antidepressant, antiulcer, anxiolytic, and hepatoprotective effects, making it a valuable candidate for further research and development in the field of natural therapeutics. This comprehensive overview underscores the importance of *I. coccinea* in traditional medicine and its potential as a source of novel therapeutic agents, warranting further exploration of its active principles and mechanisms of action.

Keywords: *Ixora coccinea*, ethnomedicine, phytochemicals, flavonoids, anti-inflammatory.

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INTRODUCTION

The genus name *Ixora* is thought to be derived from the Sanskrit word "ikvana," named after a deity in Malaysian folklore, or possibly from "Iswara," another name for Lord Shiva, to whom these flowers are traditionally offered in worship. The species name *coccinea* translates to "scarlet," highlighting the plant's vibrant blooms. *Ixora coccinea* (family: Rubiaceae), commonly referred to as "Jungle Flame" or "Flame of the Woods," is a tropical flowering shrub known for both its ornamental beauty and medicinal uses. It is native to tropical regions of Southeast Asia, particularly India, Sri Lanka, and Bangladesh, and has spread to other tropical and subtropical areas worldwide. This species thrives in warm, humid climates and is highly adaptable to diverse habitats, from rainforests to cultivated gardens.[1]

In terms of botanical characteristics, *Ixora coccinea* has a dense, branching growth habit and can reach up to three meters in height. Its woody, grey stems measure around 3-4 cm in diameter at the base, supporting a dense canopy of dark green, leathery, oblong leaves. These leaves create a lush background that complements the plant's showy, vibrant inflorescences. The flowers grow in dense, terminal clusters called corymbs, with each cluster containing between 15 and 50 tubular flowers. Each flower has four or five small calyx lobes, and the wild variety typically blooms in vivid red or red-orange hues, which are highly attractive to pollinators. However, cultivated varieties of *Ixora coccinea* now offer a range of colors, including white, yellow, salmon, and pink, making it a versatile choice for ornamental landscaping. The plant's fruits are small, fleshy berries that transition from green to a deep blood-red or purplish-black when ripe and contain two relatively large seeds.[2]

In addition to its ornamental value, *Ixora coccinea* holds an important place in traditional medicine, particularly in Ayurvedic practices, where all parts of the plant are used to treat various ailments. The fruits, roughly the size of chickpeas, are also consumed, especially by children in rural and tribal regions of India. The adaptability, aesthetic appeal, and therapeutic value of *Ixora coccinea* have made it a popular choice in tropical horticulture and a staple in traditional medicinal systems.[3]

Ethnomedicinal uses of *Ixora Coccinea*

I. coccinea, also known as Jungle Geranium or Flame of the Woods, is highly valued in traditional medicine systems worldwide, particularly within Ayurveda and other folk medicine practices across Asia and Africa. Its vibrant flowers, lush foliage, and potent bioactive compounds have made it a staple remedy in these traditions, where different parts of the plant are employed to treat a wide range of ailments. In Ayurveda, *I. coccinea* holds a prominent place for treating various conditions. The flowers are often used in remedies for women's health, particularly for managing

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leucorrhea, menstrual irregularities, and dysmenorrhea. These flowers, known for their astringent and anti-inflammatory properties, are commonly combined with other medicinal plants like *Coldenia procumbens*, *Centella asiatica*, and *Madhuca longifolia* and mixed with coconut oil to create a wound-healing ointment. The flowers are also applied to treat respiratory ailments, such as bronchitis, and as an external treatment for skin diseases like eczema and scabies. Additionally, Ixora coccinea flowers are heated in coconut oil to prepare a decoction, which is externally applied for treating sores and chronic ulcers, as well as for easing sprains and reducing eczema-related symptoms. The roots of *I. coccinea* are traditionally used for digestive health, believed to help with nausea, hiccups, and anorexia. A decoction made from the cleaned root is taken to relieve these symptoms, while finely powdered roots are applied to chronic sores and ulcers to promote healing. The leaves and stems, often prepared as poultices, are applied to sprains, boils, and contusions, helping to reduce inflammation and promote recovery.[4]

In Sri Lanka and parts of Southeast Asia, *I. coccinea* is also widely used in folk medicine, where it serves as a remedy for fever, skin conditions, and gastrointestinal ailments. Traditional healers may prescribe flower or root preparations to address fever, skin infections, and wounds, while the leaves are often applied externally as a poultice to relieve boils and skin irritations. In some regions, the berries are consumed raw by children, who believe the fruits improve digestion and overall health. *I. coccinea* has been adopted in several African folk medicine systems due to its medicinal versatility. The plant is used primarily to treat skin conditions, with decoctions and topical preparations made from the flowers or leaves. The plant's anti-inflammatory and wound-healing properties are leveraged to treat sores, rashes, and cuts. Additionally, in certain regions, flower infusions are prepared as tonics to address fever and promote general health. In Caribbean folk medicine, where *I. coccinea* has naturalized, the plant is used to treat common ailments like diarrhea and skin infections. The roots are particularly valued for their ability to promote digestion and alleviate gastrointestinal issues, similar to its applications in Asian medicine. Additionally, the flowers and leaves are sometimes combined with other herbs to create tonics aimed at boosting immunity and improving skin health.[5]

Phytochemical Profile of *Ixora Coccinea*

Ixora coccinea is a rich source of diverse phytochemicals, which contribute to its therapeutic properties in traditional medicine. The plant contains a variety of bioactive compounds, including flavonoids, triterpenoids, tannins, and phenolic acids, which are found across its flowers, leaves, roots, and stems. These phytochemicals are responsible for the plant's anti-inflammatory, antimicrobial, antioxidant, anticancer and wound-healing effects.

Flavonoids (Kaempferol and its derivatives: Kaempferol-7-O-α-l-rhamnoside, kaempferol-3-O-α-l-rhamnoside, and kaempferol-3,7-O-α-l-dirhamnoside, Quercetin-3-O-α-l-rhamnopyranoside: Rutin, Cyanidin-3-rutinoside and delphinidin monoglycoside. Tannins (Ixoratannin A-2, Procyanidin A2 and cinnamtannin B-1), Lupeol: Ursolic acid, oleanolic acid, β-Sitosterol, Gallic acid, and Caffeic acid. The root bark and root oil of *I. coccinea* contain fatty acids, especially in esterified forms Octadecadienoic acid, Methyl esters of palmitic, stearic, oleic, and linoleic acids. These fatty acid esters are valuable for skin health and wound healing, supporting the traditional use of root oil in external applications.[6-8]

Pharmacological Activities of *Ixora Coccinea*

Anti-Arthritic Effects

The study evaluated the anti-arthritic effects of the ethanolic extract of *Ixonia coccinea* Linn. leaves in female Wistar albino rats with Complete Freund's Adjuvant (CFA)-induced arthritis. The choice of female rats was based on the higher prevalence and severity of joint pathology in females with arthritis. *I. coccinea* was tested at doses of 1 g/kg and 1.5 g/kg, alone and in combination with the standard NSAID, piroxicam. The extract showed significant anti-arthritic effects across several measures. EEICL-treated rats had increased body weight; which arthritis typically reduces through inflammatory cachexia. This weight gain suggests *I. coccinea* protective effects, likely through stabilization of lysosomal membranes and improved nutrient absorption. *I. coccinea* also reduced paw volume, indicating anti-inflammatory effects comparable to NSAIDs, likely due to polyphenols that inhibit key inflammatory pathways such as NF-κB, PI3K/Akt, and MAPK. Furthermore, *I. coccinea* improved arthritis severity scores by reducing joint inflammation, similar to the glycoside stevioside, which decreases inflammatory cytokines in arthritis. Improvement in motor coordination and strength in *I. coccinea* -treated rats, observed via the Rotarod test, suggested relief from arthritis-induced muscle weakness, possibly due to anti-inflammatory flavonoids and glycosides in the extract.

In addition, *I. coccinea* significantly reduced erythrocyte sedimentation rate (ESR), indicating a reduction in systemic inflammation, and decreased malondialdehyde (MDA) levels, which are elevated in arthritis due to oxidative stress. This effect suggests *I. coccinea* antioxidant properties that protect against lipid peroxidation. Histopathological analysis of the ankle joints revealed reduced inflammation, synovial hyperplasia, and cartilage damage, reflected in lower Mankin scores, further indicating *I. coccinea* protective effect on joint structure. Overall, the study demonstrates that *I. coccinea* has significant anti-arthritic properties in CFA-induced arthritis in rats, supporting its potential as a novel anti-arthritic therapy with further preclinical and clinical studies to confirm safety and efficacy.[9]

Antidepressant Activity

The antidepressant activity of *I. coccinea* was assessed through various behavioural tests after the oral administration of its methanol extract at doses of 100 and 200 mg/kg body weight. In the Tail Suspension Test (TST) and Forced Swim Test (FST), the methanol extract significantly reduced the total duration of immobility in the tested animals, indicating potential antidepressant-like effects. Importantly, no significant changes in locomotor activity were observed in the Open Field Test (OFT),

suggesting that the observed reductions in immobility were not due to psychostimulant effects or hyperactivity. The TST and FST are widely used animal models for screening antidepressant activity, as decreased immobility time in these tests reflects reduced despair or lowered mood, akin to human depression. Fluoxetine, a well-known selective serotonin reuptake inhibitor, works by binding to the pre-synaptic serotonin transporter, enhancing serotonergic activity. In contrast, imipramine inhibits the reuptake of noradrenaline and serotonin, increasing their availability in the synaptic cleft. The absence of significant locomotor stimulation in the OFT further supports that the antidepressant effect of the methanol extract of *I. coccinea* was specific to its antidepressant mechanism rather than an increase in activity caused by psychostimulants or other factors. Notably, while the methanol extract demonstrated efficacy in reducing immobility in both the TST and FST, the chloroform extract showed no such effect, reinforcing the significance of the methanol extract in exhibiting antidepressant properties that parallel the behavioural despair model used to represent human depression.[10]

Anticancer Activity

This study investigates its potential as an anti-breast cancer treatment, specifically targeting matrix metalloproteinase-9 (MMP9), which is highly expressed in metastatic cancer. Previous clinical trials of various MMP9 inhibitors have largely failed, highlighting the need for effective alternatives. *In silico* screening was conducted using a natural compound database to identify potential inhibitors of the hemopexin-like domain of MMP9 (PEX9). Following this, the leaves of *I. coccinea* were extracted using methanol, and a systematic in vitro screening was performed against MMP9 using a FRET-based assay. The methanol extract underwent liquid-liquid extraction with n-hexane, ethyl acetate, n-butanol, and water, leading to the selection of fractions based on their inhibitory effects on MMP9. Among 200 screened compounds, 20 demonstrated significant binding affinities toward PEX9. The methanol extract exhibited significant inhibition of MMP9, with an IC50 value of 116 µg/mL. Fractionation resulted in the isolation of two compounds from the ethyl acetate partition, with molecular docking studies indicating that one of these compounds, oxytetracycline, preferentially binds to PEX9 rather than its catalytic domain. High-performance liquid chromatography analysis identified sinapic acid and myricetin as the major phenolic compounds. The methanol extract demonstrated the highest *in vitro* antioxidant activity among various solvent extracts, while the fruit extract exhibited anticancer activity against LNCaP. FGC cells. These findings support the potential of *I. coccinea* as an effective anti-breast cancer agent, particularly against triple-negative breast cancer, and highlight its therapeutic applications in beverage development.[11-13]

Wound Healing Activity

The wound healing process involves a complex cascade of regenerative events, including inflammation, proliferation, and remodeling phases, regulated by various mediators such as cytokines and growth factors. In our study, *I. coccinea* methanol extract demonstrated substantial antimicrobial activity against common wound pathogens, including *Bacillus subtilis*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, highlighting its potential in preventing infection during healing. The antimicrobial properties of *I. coccinea* may mitigate the prolonged inflammatory phase caused by invading microbes, which produce toxins and delay granulation tissue formation. Activated immune cells, such as neutrophils and macrophages, eliminate these pathogens with the aid of reactive oxygen species (ROS), which also contribute to wound angiogenesis at low concentrations. However, excessive ROS can damage extracellular structures and prolong inflammation, making antioxidant activity critical in promoting effective wound healing. Our findings revealed significant free radical scavenging activity in both methanol and water extracts of *I. coccinea*, suggesting these extracts may support the healing process through their antioxidant properties. During the proliferation phase, the formation of granulation tissue and collagen synthesis are essential for tissue repair. *In Vitro* assays showed that *I. coccinea* effectively protected fibroblast cells against hydrogen peroxide-induced oxidative stress, indicating its potential to promote fibroblast proliferation and collagen synthesis. Furthermore, topical application of *I. coccinea* in a circular excision wound model in Wistar rats significantly accelerated wound contraction and increased hydroxyproline content, a marker of collagen synthesis. Histopathological examinations of treated tissues revealed well-organized wound healing, characterized by abundant macrophage and fibroblast infiltration, along with enhanced reepithelialisation and collagen deposition compared to control groups. The expression of key proteins involved in collagen synthesis and tissue regeneration, such as basic fibroblast growth factor (bFGF) and collagen type III (COL3A1), was significantly upregulated following *I. coccinea* treatment. These findings underscore the potential of *I. coccinea* methanol extract as a promising candidate for promoting wound healing and preventing infection.[14]

Antimicrobial Activity

I. coccinea, a medicinal plant with a long-standing history of use in Nigeria, was investigated for its leaf essential oil's chemical constituents and antimicrobial activity. Gas Chromatography-Mass Spectrometry (GC-MS) classified into eight categories: hydrocarbons, alcohols, carboxylic acids, esters, aldehydes, ketones, sesquiterpenoids, and triterpenoids. Alcohols; linalool, while esters accounted for Carboxylic acids made up 10.91%, primarily malonic acid. The *I. coccinea* showed significant antimicrobial activity against pathogens such as *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Candida albicans*, and *Mycobacterium tuberculosis*, indicating its potential as an adjunct therapy for community acquired infections. Additionally, root extracts of *I. coccinea* demonstrated notable antimicrobial effects against *Bacillus cereus, Bacillus subtilis*, and *Shigella dysenteriae*, although no activity was observed against E. coli. The effectiveness of the extracts increased with higher concentrations, consistent with previous studies. Among the tested samples, the *I. coccinea* extract exhibited the highest efficacy against *S. dysenteriae*, a pathogen responsible for severe diarrhea and dysentery. Interestingly, while the ICME extract had

the highest antioxidant capacity, it showed the weakest antimicrobial activity, whereas the less potent antioxidant sample, *I. coccinea*, demonstrated the strongest antimicrobial effects. This suggests a diverse range of bioactive compounds within I. coccinea, with solvent polarities influencing the extraction of specific antimicrobial metabolites. Overall, the findings support the traditional use of I. coccinea for treating gastrointestinal issues, wounds, and skin infections, highlighting its potential as a natural source of antimicrobial agents. Further research is needed to isolate and characterize the bioactive compounds responsible for these properties, which could lead to the development of alternative, plant-based antimicrobial products in pharmaceuticals and food industries.[15,16]

Analgesic, Anti-Inflammatory, and Antipyretic

The present study aimed to investigate the potential analgesic, anti-inflammatory, and antipyretic effects of the ethanol extract of *I. coccinea*, leaves using various rodent models. The extract was prepared by soaking dried powdered leaves in ethanol for two days, followed by filtration and evaporation to yield a concentrated stock solution used in all experimental tests. The results indicated that oral administration of *I. coccinea* at doses of 250 mg/kg and 500 mg/kg significantly increased reaction times in the hot-plate test, suggesting notable analgesic properties. Specifically, the extract produced 56.14% and 63.16% inhibition in the acetic acid-induced writhing model, reflecting effective pain relief. In the carrageenan-induced paw edema test, significant inhibition of swelling was observed at both doses, particularly pronounced six hours after administration, indicating the extract's anti-inflammatory effects. Additionally, the extract lowered body temperature in the brewer's yeast-induced hyperthermia model, demonstrating its antipyretic activity. These findings suggest that the leaves of *I. coccinea* possess significant analgesic, anti-inflammatory, and antipyretic activities, likely due to the presence of phytochemical constituents such as flavonoids, tannins, and triterpenes. This study supports the traditional use of *I. coccinea* in folk medicine for managing pain, inflammation, and fever, while also highlighting its potential for further therapeutic development. Future research may focus on isolating specific bioactive compounds to better understand their mechanisms of action and efficacy.[17]

Antiulcer Activity

Antiulcer potential of methanolic extracts of *Ixora coccinea* flowers significantly reduced gastric volume and acidity in a dose-dependent manner, with increased pH levels indicating an antisecretory action. Furthermore, the 400 mg/kg dose of the polyherbal extract achieved a significant 79% reduction in ulcer formation, accompanied by decreased gastric secretion, total acidity, and free acidity. This antiulcer effect is believed to stem from the cytoprotective action of bioactive compounds such as flavonoids, terpenoids, and saponins, which likely contribute to mucosal protection and antisecretory effects. The findings suggest that both *Ixora coccinea* flower extract and the polyherbal combination hold promise as natural antiulcer agents, with further research needed to elucidate the precise mechanisms and active constituents involved.[18]

Anxiolytic Activity

The anxiolytic activity of the ethanolic extract of *Ixora coccinea* Linn. was assessed using the Elevated Plus Maze (EPM) and Hole Board tests, two widely accepted models for evaluating anxiety in rodents. In the EPM test, mice typically avoid open arms due to the anxiety induced by open spaces. However, administration of *I. coccinea* at a dose of 400 mg/kg significantly increased the time spent in the open arms, indicating anxiolytic effects. Additionally, *I. coccinea* at this dose reduced total arm entries, suggesting a reduction in locomotion at higher doses. In the Hole Board test, *I. coccinea* at both 200 mg/kg and 400 mg/kg doses led to a significant reduction in head-dipping behaviour, comparable to the anxiolytic effects observed with diazepam (2 mg/kg). This reduction in head dips implies that *I. coccinea* mitigates anxiety-like responses in rodents when exposed to an unfamiliar environment. These anxiolytic effects may be attributed to active compounds in *I. coccinea* such as alkaloids, flavonoids, and saponins, which are known to interact with GABA-A receptors in the central nervous system, modulating the GABA-chloride channel. Collectively, the findings suggest that *I. coccinea* extract exerts a promising anxiolytic effect, potentially mediated by these bioactive constituents.[19]

Hepatoprotective Activity

In traditional Indian Ayurvedic medicine, *Ixora coccinea* has been used to treat a range of ailments, and this study evaluated its hepatoprotective effects against liver injury induced by Isoniazid and Rifampicin in rats. Hepatotoxicity was induced by administering Isoniazid and Rifampicin. Isoniazid and Rifampicin treatments led to significant liver weight reduction, elevated serum liver biochemical markers, increased oxidative stress, raised inflammatory cytokine levels, and notable histopathological changes. However, treatment with *I. coccinea* extract demonstrated a dose-dependent hepatoprotective effect, with improvements in liver weight, liver function markers, lipid peroxidation, cytokine levels, and liver histology compared to the control and Silymarin groups. These results provide strong evidence of the hepatoprotective properties of the ethanolic extract of *I. coccinea.*[20]

CONCLUSION

I. coccinea L. emerges as a significant plant with extensive ethnomedicinal applications and a diverse array of bioactive compounds. Its traditional uses in treating various ailments underscore its therapeutic potential, particularly in women's health, respiratory issues, and skin conditions. The plant's pharmacological properties, including anti-inflammatory, antimicrobial, and anticancer effects, further support its relevance in modern medicine. Given its multifaceted benefits and rich phytochemical profile, *I. coccinea* warrants further investigation to isolate active compounds and understand their mechanisms of action. Continued research may unveil novel therapeutic agents, enhancing the role of this plant in natural healthcare. Ultimately, *I. coccinea* holds promise as a valuable resource for

developing effective treatments in traditional and contemporary medicinal practices.

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