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A COMPREHENSIVE REVIEW ON MEDICINAL APPLICATIONS AND PHARMACOLOGICAL ACTIVITIES OF TRIDEX PROCUMBENS

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ABSTRACT

Tridax procumbens Linn, a widely distributed medicinal plant, has garnered significant attention due to its diverse medicinal properties. This review aims to comprehensively evaluate its medicinal importance based on scientific literature and traditional knowledge. Tridax procumbens exhibits a plethora of pharmacological activities, including anti-inflammatory, antioxidant, antimicrobial, antidiabetic, and wound healing effects. Additionally, it shows promise in the management of various ailments such as arthritis, malaria, dysentery, and skin disorders. The plant's therapeutic efficacy can be attributed to its rich phytochemical profile, which includes flavonoids, alkaloids, phenolics, and terpenoids. Furthermore, studies have elucidated the underlying mechanisms of action for many of its bioactive compounds. Despite its promising medicinal properties, further research is needed to fully understand the pharmacological mechanisms and optimize its therapeutic applications. Tridax procumbens holds immense potential as a valuable source of natural remedies and warrants continued investigation for its integration into modern medicine.

I. INTRODUCTION

Tridax procumbens Linn., a member of the Compositae family, is commonly referred to as `Ghamra' in local parlance and colloquially known as `coat buttons' in English due to the appearance of its flowers. It has been widely utilized in the Ayurvedic system of medicine for treating various ailments. Some Ayurvedic practitioners also dispense it as "Bhringraj," a renowned remedy for liver disorders.[1]This plant, originating from Central America, is an annual or perennial weed widely distributed in India, notably in regions such as Maharashtra, Madhya Pradesh, and Chhattisgarh. It frequently roots at nodes and features solitary, long-stalked, yellow composite flowers that are heterogamous and bisexual, with white flowering heads. Its leaves, which are very hairy and coarsely toothed, are petiolate and ovate or lanceolate in shape. The entire aerial part of the plant holds medicinal value, with the leaves exhibiting properties such as wound healing, insecticidal effects, antisecretory action, and hypotensive properties, while the seeds are employed for controlling bleeding.[2] This review aims to present an overview of the morphology, traditional uses, phytochemistry, and pharmaceutical activities of T. procumbens, including discussions on structures, yields, in vitro and in vivo models, and MIC/MFC controls. By consolidating past and current research findings, the article seeks to offer insights for future directions in the development and commercialization of this plant. India boasts a rich legacy of traditional medicine, with its materia medica offering abundant insights into folklore practices and traditional dimensions of crucial natural products for therapeutic purposes. Indian traditional medicine draws from diverse systems such as Ayurveda, Siddha, and Unani. The assessment of these medicinal substances primarily relies on:

- Pharmacognostical scrutiny
- Phytochemical analysis
- > Pharmacological examination

Scientific Classification of Tridex Procumbens Linn



Figure 1: Whole Plant of Tridex Procumbens Linn @International Research Journal of Modernization in Engineering, Technology and Science [391]



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• Kindom	- Plantae-Plants		
 Sub kingdom 	- Tracheobionta -Vas	cular plants	
Division	- Spermatophyta		
Subdivision	- Magnoliophyta-Flow	wering plants	
• Class	- Magnoliopsida -Dicc	otyledons	
Subclass	- Asteridae		
• Order	- Asterales		
• Family	- Asteraceae-Aster fai	mily	
• Genus	- Tridax LTridax		
 Species 	- Tridax procumbens	LCoat buttons	

• Species

Synonyms:

- Hindi : Khal muriya, Tal muriya, Ghamra
- Sanskrit : Jayanti Veda •
- English : Coat buttons, Tridax Daisy, Wild daisy •
- Oriya : Dagadi pala •
- Marathi : Gaddi Chemanthi •
- Tamil : Vettukaya thalai, Thatha •
- Telugu : Gayapu aku, Gaddi chamanthy, or Palakaaku •

Plant Morphology:

Tridax procumbens can reach heights of 40 cm or more, and it is an herbaceous perennial plant with a spreading basal portion.

1. Stem & Root :

The stems are cylindrical and covered with multi-cellular hairs, measuring millimeters in length. The base root features tuberculation and possesses a robust taproot system. The plant stem ascends to a height of 30-50 cm, branching sparsely, and featuring root formation at nodes. (Figure 2)



Figure 2: Stem & Root

2. Leaf:

The leaves exhibit irregular toothed margins and typically have an arrowhead shape. They are simple, ovate, opposite, exstipulate, and lanceolate, measuring 3-7 cm in length. With a wedge-shape base, the leaves are shortly petioled and hairy on both surfaces. (Figure 3)



Figure 3: Leaf



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3. Flower/Inflorescence:

The plant's flowers resemble daisies, featuring tubular structures with yellow-centered white or yellow petals, each adorned with three toothed ray florets. The inflorescence takes the form of a capitulum, containing two types of flowers: ray florets and disc florets with basal placentation. Occasionally, the flowers may have three lobes and appear on long, penduncled heads. The achenes are black, narrowly obconical, measuring 2.0-2.5 mm in length, and are accompanied by feathery pappus. Flowering and fruiting occur throughout the year. (Figure 4)



Figure 4: Flower

4. Calyx: It is represented by scales or reduced to pappus.

5. Fruits :

The fruits are achenes, ranging in color from dark brown to black, oblong in shape, and measuring 0.08 inches (2 mm) in length. Each achene is topped with a head of pappus bristles, which can vary from 0.12-0.24 inches (3-6 mm) in length. The fruit itself is a hard achene covered with stiff hairs and featuring a feathery, plume-like white pappus at one end. The plant is invasive partly due to its prolific production of achenes, and each achene's ability to catch the wind in its pappus allows for dispersal over considerable distances.

6. Seeds:

Tridax procumbens seeds germinate more readily at higher temperatures (35/25 and 30/20) when exposed to 58 to 78% light intensity. However, their germination is highly sensitive to salt concentration and water stress. The chromosome count is 36 (diploid) and 18 (haploid) in gametes. Reproduction primarily occurs through the spreading of stems and seed production. (figure 5.)



Figure 5: Seeds
II. DESCRIPTION

The plant produces daisy-like flowers with yellow centers and white or yellow ray florets that have three teeth. Its leaves are typically toothed and arrowhead-shaped. The fruit is a tough achene covered in stiff hairs, featuring a feathery, plume-like white pappus at one end. The calyx is either represented by scales or reduced to pappus. This plant exhibits invasive tendencies partly due to its prolific production of achenes, with up to 1500 per plant, and each achene's ability to be carried by the wind over some distance thanks to its pappus.T. procumbens is categorized as a harmful weed in Alabama, Florida, Minnesota, North and South Carolina, and Vermont. It is under quarantine in California and Oregon and is prohibited in Massachusetts according to the U.S. Department of Agriculture. In Guatemala, T. procumbens is considered a weed with extensive growth potential, thriving in both dry and moist soils, typically on previously cultivated land, ranging from sea level up to 2300 m (Po?ll, 2005).



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Traditional Use:

In Nigeria, various parts of the Tridax plant are utilized in treating ailments such as typhoid fever, cough, fever, stomachache, backache, diarrhea, and epilepsy. Across Africa, farmers employ the plant for livestock treatment; for instance, Tridax, when ground along with Vigna parkeri and mixed with salt and water, is used to address chronic mastitis in livestock. Studies have investigated the antibacterial properties of Tridax against mastitis-causing bacteria, revealing significant activity in ethanolic extracts against Staphylococcus aureus. However, aqueous extracts showed minimal to no activity against Streptococcus uberis and Klebsiella pneumoniae, especially when compared to extracts from Spathodea campanulata. In Benin, breeders incorporate Tridax into the feed of rabbits and other livestock alongside other plants, although rabbits tend to consume it less compared to other fodder, likely due to its lower palatability.[3] Research conducted in Chiquimula, Guatemala, revealed that lactating pregnant women suffering from anemia could alleviate their symptoms by using Tridax (Calder¢n, unpublished findings). Additionally, this species is employed in treating gastrointestinal and respiratory infections, hypertension, and diabetes (Po?ll, 2005; Giovannini et al., 2016; Pardeshi and Bhiungade, 2016). In Guatemala, the entire plant is utilized in the treatment of protozoal infections, including malaria, leishmaniasis, and dysentery (Caceres et al., 1998; Berger et al., 1998; Mart;n-Quintal et al., 2009; Gamboa-Leon et al., 2014; Ebiloma et al., 2017).[4,5]

Phytochemical review:

The phytochemical analysis indicated the existence of alkaloids, carotenoids, flavonoids (including catechins and flavones), and tannins. The plant is notably abundant in carotenoids and saponins. In terms of its proximate composition, it exhibits high levels of sodium, potassium, and calcium.[6]The leaf of Tridax primarily comprises crude proteins (26%), crude fiber (17%), soluble carbohydrates (39%), and calcium oxide (5%). Its flowers have been found to contain compounds such as luteolin, glucoluteolin, quercetin, and isoquercetin. Additionally, the plant has been reported to contain fumaric acid, ?-sitosterol, and tannins.[7]Jude CI et al. conducted an assessment of the phytochemical and mineral proximate composition of Tridax procumbens. Their phytochemical analysis revealed the presence of flavonoids (including catechins and flavones), alkaloids, tannins, saponins, and carotenoids.[8]Several compounds, such as betulinic acid, esculetin, puerarin, oleanolic acid, and newly discovered flavones named 6,8,three-trihydroxy-three,7,4-trimethoxyflavone,8,threedihydroxy-three,7,4-trimethoxy-6-O--D-glucopyranosyl flavone, have been isolated from various parts of the plant.[9]From the leaves of Tridax procumbens Linn, two water-soluble polysaccharide fractions were purified: WSTP-IA (containing approximately 1:3 molar proportions of l-Araf and d-Galp) and WSTP-IB (predominantly composed of d-Galp as the main sugar component).[10]The essential oil obtained from hydro distillation of Tridax procumbens contains 1,8-cineole, p-cymen-7-ol, Biformene, Trans--caryophyllene, and Dibutyl phthalate as the main compounds. Additionally, minor compounds present include 9,12,15-octadecatrienoic acid, Z--trans Bergamotol, -Elemene, 2--pinene, Tricosane, -Selinine, -Amyrin, Caryophyllene oxide, -humulene, Eicosane, Quercetin 7,3',4'-trimethyl, and tau-cadinol.[11]Two novel flavones, namely, 8,3'-dihydroxy-3,7,4'-trimethoxy-6-0--D-glucopyranosyl flavone and 6,8,3'-trihydroxy-3,7,4'-trimethoxyflavone, were discovered in Tridax procumbens Linn. Additionally, four known compounds-puerarin, esculetin, oleanolic acid, and betulinic acidwere also isolated from the plant. Tridax procumbens is commonly found in disturbed areas, lawns, and roadside areas with tropical or subtropical climates.[12]

Pharmacological review:

Tridax procumbens exhibits a range of potential therapeutic properties, including antimicrobial, antioxidant, antibiotic effectiveness, wound healing, insecticidal, anti-inflammatory, diarrhea, and dysentery activities. The juice from its leaves is applied to fresh wounds to promote healing and stop bleeding, and it is also used as a hair tonic. In India, Tridax procumbens is primarily utilized for wound healing, as an anticoagulant, antifungal agent, and insect repellent. In traditional folk medicine, leaf extracts are used to treat infectious skin ailments.[13]

1. Antimicrobial Activity:

The entire Tridax plant has been documented for its antimicrobial effects against various bacterial strains. To obtain the juice, the entire plant is squeezed between the palms of the hands. Fresh plant juice is then applied twice daily for 3-4 days to treat cuts and wounds. The extract derived from the entire Tridax plant exhibited



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antibacterial properties specifically against Pseudomonas aeruginosa.[14] The chloroform extracts exhibited antibacterial activity against B. faecalis, B. subtilis, E. coli, and Pseudomonas aeruginosa. However, the experiments require improved controls and detailed procedure descriptions. Extracts from T. procumbens contain alpha and beta pinenes, which, when used in small quantities, may aid in the treatment of bacterial and fungal infections. There are conflicting results regarding the antimicrobial activity of this species. Some studies did not show significant biological activity compared to the antibiotic control, but there is evidence supporting the potential antimicrobial properties of this species, necessitating further research in this area.[15]

2. Antiobesity Activity :

In the model of obesity induced by an atherogenic diet, rats treated with Tridax procumbent exhibited notable decreases in total cholesterol, triglycerides, total protein, and free fatty acids, along with an increase in high-density lipoprotein cholesterol. Tridax procumbens demonstrated significant anti-obesity effects in this study.[16] During the research study, the animal treated with the plant decoctions displayed a notable decrease in total cholesterol, triglycerides, total protein, and free fatty acids, alongside an increase in high-density lipoprotein cholesterol levels.[17]

3. Antidiabetic Activity :

The alcohol and water extracts of Tridax procumbens Linn. leaves exhibit significant antidiabetic activity, leading to a notable decrease in blood glucose levels. This activity was evaluated in a rat model of alloxaninduced diabetes. Administration of a 50% methanol extract of Tridax procumbens orally, both in acute and subchronic doses, resulted in reduced fasting blood glucose levels in diabetic rats. Notably, this plant material did not affect blood sugar levels in normal rats.[13] The hypoglycemic effects of dried alcoholic, petroleum ether, and aqueous (60-80°C) leaf extracts of Tridax procumbens were assessed in rats with alloxan-induced diabetes. Both alcoholic and aqueous extracts demonstrated a notable reduction in blood glucose levels at a dosage of 200 mg/kg, while the petroleum ether extract exhibited minimal hypoglycemic activity.[18]

4. Anticancer Activity:

The anti-cancer potential of traditional Tridax procumbens flower extracts, both crude aqueous and acetone, was investigated on PC3 prostate epithelial cancer cells using the MTT assay to assess cell viability. This assay involves the conversion of the soluble yellow tetrazolium salt MTT (3-(4,5-dimethyl-thiazole-2-yl)-2,5-diphenyl tetrazolium bromide) to a blue formazan by mitochondrial succinate dehydrogenase. The assay relies on the ability of viable cell mitochondria to reduce MTT to formazan, which is measured spectrophotometrically at 570nm. Results indicated that the crude flower extract exhibited anti-cancer activity.[19]

5. Antioxidant Activity :

Tridax procumbens, with a total phenol content expressed as Gallic Acid Equivalent (GAE), demonstrates a high phenolic content of 12 mg/g GAE. This finding suggests a correlation between phenol content in medicinal plants and antioxidant activity, as supported by previous studies. Secondary metabolites such as flavonoids, tannins, catechins, and other phenolic compounds are known to exhibit significant antioxidant properties. These bioactive compounds play a preventive role in conditions like cancer, heart disease, and age-related illnesses.Reduced absorbance in the reaction mixture suggests increased free radical scavenging activity. The ability to scavenge DPPH radicals was determined using the equation: Scavenging Effect (%) = [1 - Absorbance of Sample/Absorbance of Control] x 100. The antioxidant activity of the fractions was quantified as IC50, representing the concentration (in µg/ml) of methanolic extract fractions necessary to scavenge 50% of DPPH radicals.[20]

6. Anti Inflammatory :

The ethanol extract of Tridax procumbens leaves was evaluated for its anti-inflammatory effects using a carrageenan-induced mice model. Parameters such as histopathology and inflammatory edema were observed and compared with those of a control group. In the treated groups, improved histology and a notable reduction in paw inflammation in mice were observed after 24 hours. Molecular activity was assessed by examining cyclooxygenase (COX2) and Tumor necrosis factor (TNF α) gene expression levels at the inflammatory site using reverse transcription quantitative polymerase chain reaction (qPCR) and polymerase chain reaction (PCR) analysis. The PCR and relative quantity (RQ) values decreased with increasing doses in the test groups. Significant reductions in band density were observed in the real-time polymerase chain reaction (RT-PCR)



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results for COX2 and TNF-α gene expression levels in the treated group, indicating anti-inflammatory activity of Tridax procumbens at the molecular level.[21] Rats were orally administered with varying doses of watersoluble powder derived from Tridax leaf extract. The findings indicated the presence of analgesic properties in the extract. Tridax procumbens L. dose led to a reduction in abdominal writhing. Additionally, the alcoholic and hydroalcoholic extracts of Tridax exhibited anti-inflammatory activity in the rat-paw edema assay, resulting in edema inhibition percentages of 10.82%, 16.80%, and 11.39%.[13]

7. Analgesic Activity:

Lyophilized decoctions of Tridax procumbens leaves were utilized to assess analgesic activity in rats through various tests: the Acetic Acid-induced Writhing test, Formalin-induced persistent pain test, and Complete Freund's Adjuvant (CFA)-induced hyperalgesia test. A notable and dose-dependent reduction in abdominal writhing was observed in the Acetic Acid-induced abdominal constriction test upon extract administration. Additionally, the extract significantly suppressed the late phase of moderate pain in the Formalin test. Furthermore, a significant decrease in mechanical hyperalgesia was noted in CFA-injected rats treated orally with the extract. These findings underscore the analgesic properties of Tridax procumbens, which may involve both centrally and peripherally mediated mechanisms.[22]

8. Wound Healing Activity:

The process of wound healing encompasses a intricate interplay among epidermal and dermal cells, the extracellular matrix, regulated angiogenesis, and plasma-derived proteins, all orchestrated by a variety of cytokines and growth factors.[23] n the incision wound model, tensile strength was assessed, revealing significant outcomes in wound index, epithelization period, and wound contraction in animals treated with 5% and 2.5%w/w EETP. Both diabetic and non-diabetic groups exhibited potent wound healing activity when treated with a 5% w/w simple ointment base of Tridax procumbens ethanolic extract. Notably, compared to the diabetic group, the non-diabetic group showed a highly noticeable and remarkable wound healing activity with the 5% w/w T. procumbens ointment.[24] The plant not only enhances lysyl oxidase activity but also increases protein and nucleic acid content in the granulation tissue, likely attributed to the rise in glycosaminoglycan levels. The wound healing potential of Tridax procumbens aqueous and ethanol extracts of the whole plant was assessed using animal models. Both excision and incision wounds were treated with the plant extracts in this study. Incision wounds were treated with the extract for 14 days, and on the 14th day, wound healing capacity was evaluated using tensiometer. A section of the incised skin was subjected to histopathological examination to assess reepithelialization and collagen formation. Excision wounds were treated with the plant extract for 15 days, and changes in wound area were monitored every three days. The wound area was measured using graph paper. Tridax procumbens exhibited a significant increase in hydroxyproline, collagen, and hexosamine content, indicating its effective wound healing action.[13]

9. Antidiarrhoeal Activity :

Extracts from various parts of 31 indigenous medicinal plants of India, including alcohol, hexane, chloroform, butanol, and aqueous extracts, were evaluated for their ability to inhibit secretion against E. coli. Among these extracts, the T. procumbens extract exhibited notably high antisecretory activity.[2] In the prostaglandin-E2 induced diarrheal model, the lower dose of petroleum ether extract exhibited superior anti-diarrheal activity compared to the higher dose, effectively reducing the volume of intestinal fluid. Additionally, all extracts of Tridax procumbens demonstrated dose-dependent anti-diarrheal effects in the gastrointestinal motility test model, as evidenced by decreased propulsion of charcoal meal. Furthermore, in the castor oil-induced diarrheal model, these extracts reduced the frequency of defecation and the total weight of wet diarrhea compared to the control group.[25]

10. Anti-malarial Activity :

This study extracted essential oil from Tridax procumbens L leaves using the steam distillation method. The antimalarial activity of the essential oil was assessed in mosquito cages against Anopheles stephensi, the malaria vector. Tridax procumbens essential oil was tested at three concentrations (2%, 4%, and 6%). A notably significant repellent effect was observed at the 6% concentration, with protection lasting over 300 minutes.[26]



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11. Immunomodulatory Effects :

The ethanolic extracts derived from Tridax leaves exhibit an immunomodulatory effect on albino rats administered with Pseudomonas aeruginosa, while also inhibiting the proliferation of the same.[27] Furthermore, a notable rise in the phagocytic index, leukocyte count, and splenic antibody-secreting cells was documented with the ethanol-insoluble fraction of the aqueous extract of Tridax. Additionally, an enhancement in the humoral immune response was observed, accompanied by an increase in hemagglutination antibody titer. Moreover, an increase in the humoral immune response, accompanied by an augmentation of the hemagglutination antibody titer, was observed. Notable data regarding the activation of the cellular immune system was documented, notably through an enhanced type IV (delayed) hypersensitivity reaction. Tridax procumbens ethanol-insoluble fraction (TPEIF) also promotes activation of both the cell-mediated and humoral immune systems. Consequently, it facilitates the generation of an amplified antibody response to specific clinical antigens.[28]

12. Antibacterial Activity :

The antibacterial activity of ethanolic and aqueous extracts from Tridax procumbens leaves was evaluated using the agar well diffusion technique against various bacteria, clinical isolates, and standard strains. While the aqueous extract did not demonstrate any antibacterial activity, the alcoholic extract exhibited notable antibacterial activity at a concentration of 5 mg/ml against Pseudomonas aeruginosa. Furthermore, compared to several antibiotics including augmentin, cefotaxime, and ciprofloxacin, the ethanolic extract displayed significant activity against nosocomial strains of Pseudomonas.[29]

13. Hepatoprotective Activity:

The hepatoprotective effect of the aerial components of Tridax demonstrates significant efficacy in mitigating D-Galactosamine/Lipopolysaccharide (D-GalN/LPS) induced hepatocellular injury. D-GalN/LPS is suggested to induce hepatotoxicity by damaging liver cells. The multifocal necrosis triggered by D-GalN resembles the lesions observed in viral hepatitis in humans. This amino sugar selectively inhibits transcription and indirectly impacts hepatic protein synthesis. Consequently, it leads to fulminant hepatitis within 8 hours of administration due to endotoxin toxicity.[30]

14. Anti-arthritic Activity :

The ethanolic extract of the entire Tridax procumbens plant exhibited noteworthy anti-arthritic effects against Freund's Complete Adjuvant (FCA)-induced arthritis in female Sprague Dawley (SD) rats at doses of 250 and 500mg/kg. This was confirmed by a reduction in paw volume. Control animals with arthritis showed a significant decrease in body weight compared to control animals without arthritis. Treatment with Tridax procumbens helped restore body weight in a dose-dependent manner. The anti-arthritic activity of Tridax procumbens extract was compared to the standard drug indomethacin. Furthermore, the hematological and biochemical changes induced by FCA were significantly modified by Tridax procumbens extract.[31]

15. Anti-ulcer Activity:

At a dosage of 400 mg/kg, the ethanolic leaf extract of Tridax procumbens demonstrated dose-dependent inhibition of ulcer lesion index and alterations in gastric pH and volume in rats with ethanol-induced ulcers. Additionally, the extract contributed to the restoration of large fibroblast cells and decreased levels of glutathione (GSH), catalase, and superoxide dismutase (SOD) in the rat stomach. These findings highlight the therapeutic potential of Tridax procumbens.[32]

16. Antiparasitic Activity :

T. procumbens has been investigated for its efficacy in treating diseases caused by protozoal infections such as malaria, dysentery, colic, and vaginitis through bioassay-guided fractionation using a methanol extract to isolate an active compound, (3,S)-16,17-Didehydrofalcarinol, an oxylipin. Additionally, crude extracts from the entire plant showed potential anti-leishmanial activity. In a study conducted in Ghana, the antiplasmodial effects of aqueous, chloroform, ethyl acetate, and ethanolic extracts from the flowers, leaves, and stem of T. procumbens were evaluated. Evidence suggests that aqueous and ethanolic extracts from the plant species possess antiplasmodial properties. A study utilizing the tetrazolium-based colorimetric assay demonstrated that T. procumbens helps protect red blood cells from damage caused by P. falciparum. Tridax shows promising



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potential in combating a disease that claims millions of lives worldwide.[33]

III. **CONCLUSION**

Tridax procumbens Linn holds significant medicinal importance due to its diverse therapeutic properties. Through various scientific studies and traditional uses, it has been identified as a valuable source of bioactive compounds with potential health benefits. The plant exhibits a wide range of pharmacological activities, including anti-inflammatory, antioxidant, antimicrobial, antidiabetic, and wound healing properties. Additionally, it shows promise in the management of conditions such as arthritis, malaria, dysentery, and skin disorders. Further research and exploration into its phytochemical constituents and mechanisms of action are warranted to fully harness its therapeutic potential and promote its integration into modern medicine.

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