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## From pest to remedy: The untapped therapeutic potential of a Devil weed, *Chromolaena odorata* (L.) R.M. King & H. Rob

N.S. Disha and B.S Ashok Kumar♦

R.L. Jalappa College of Pharmacy, Sri Devaraj Urs Academy of Higher Education and Research (A Deemed To Be University), Tamaka, Kolar-563103, Karnataka, India

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### Abstract

Devil weed is scientifically known as *Chromolaena odorata* (L.) R.M. King & H. Rob, is a perennial shrub of the Asteraceae family recognized for its therapeutic potential. Despite its invasive nature, the plant has gained attention for its diverse medicinal applications due to its rich phytochemical composition, including phenols and flavonoids. Traditionally, it has been used in ethnomedicine to treat burns, wounds, skin infections, diabetes, and malaria. The leaves and flowers, known for their characteristic pungent odour, are particularly effective in wound healing, disinfection, and managing ailments such as dysentery, fever, and urinary tract infections. Scientific studies sourced from Scopus, PubMed, and Google scholar support these traditional uses, highlighting its antimicrobial, anti-inflammatory, antidiabetic, wound-healing, and anticancer properties. Devil weed exhibits broad-spectrum antimicrobial activity against bacterial and fungal pathogens, including multidrug-resistant strains. Phytochemicals such as sinensetin and germacrene-D contribute significantly to these pharmacological effects. Research emphasizes its ability to disinfect wounds, reduce blood loss, and accelerate healing, making it a promising alternative therapeutic agent. While its invasive nature presents ecological concerns, further research on standardizing its bioactive compounds could enhance its integration into modern medicine. Sustainable utilization of its medicinal properties is essential for balancing ecological management with pharmaceutical advancements.

### 1. Introduction

Devil weed is scientifically known as *Chromolaena odorata* (L.) R.M. King & H. Rob (Figure 1), belongs to the family Asteraceae, native to Central and South America, it has spread to tropical and subtropical regions across Asia, Africa, and Australia, thriving in diverse habitats. Despite its classification as an invasive species capable of disrupting local ecosystems, this plant has garnered significant attention for its medicinal properties and applications in traditional medicine. The leaves and flowers emit a distinct pungent odour when crushed, and the plant's bioactive profile includes secondary metabolites such as phenols and flavonoids, which contribute to its pharmacological efficacy (Gautier, 1992; Kriticos *et al.*, 2005).

Traditionally, Devil weed has been extensively used in various regions for its therapeutic properties. In India, the plant is utilized to treat burns, skin infections, diabetes mellitus, and infectious wounds. In African countries like Nigeria, it is employed as a local antiseptic and for managing conditions such as dysentery, fever, urinary tract infections, cervical pain, and postpartum wounds. In Southeast Asia, particularly among communities in Aceh Besar and Nepal, the leaves are used to address diabetes, diarrhoea, malaria, and soft tissue

wounds. The plant has been widely recognized for its wound-healing potential, as it can disinfect wounds, prevent blood loss, and accelerate healing, making it a preferred choice in folklore and ethno medicine for external treatments (Bamisaye *et al* 2014; Omokhua *et al* 2016). Additionally, it is used for treating inflammation, abdominal pain, and skin diseases, further validating its significance in traditional medicine. Research supports its role as an alternative treatment for malaria, and its rich phytochemical composition enhances its efficacy against infectious diseases and inflammatory conditions. Despite its invasive nature, Devil weed serves as a valuable resource in traditional healthcare systems, emphasizing the need for further studies to explore its bioactive compounds and therapeutic potential (Layek *et al.*, 2022; Bhargava *et al.*, 2013; Elebiyo *et al.*, 2023).



Figure 1: Devil weed.

Corresponding author: B.S. Ashok Kumar

Professor, Department of Pharmacognosy, R.L. Jalappa College of Pharmacy, SDUAHER Tamaka, Kolar-563103, Karnataka, India

E-mail: [ashok4vani@gmail.com](mailto:ashok4vani@gmail.com)

Tel.: +91-7019794075

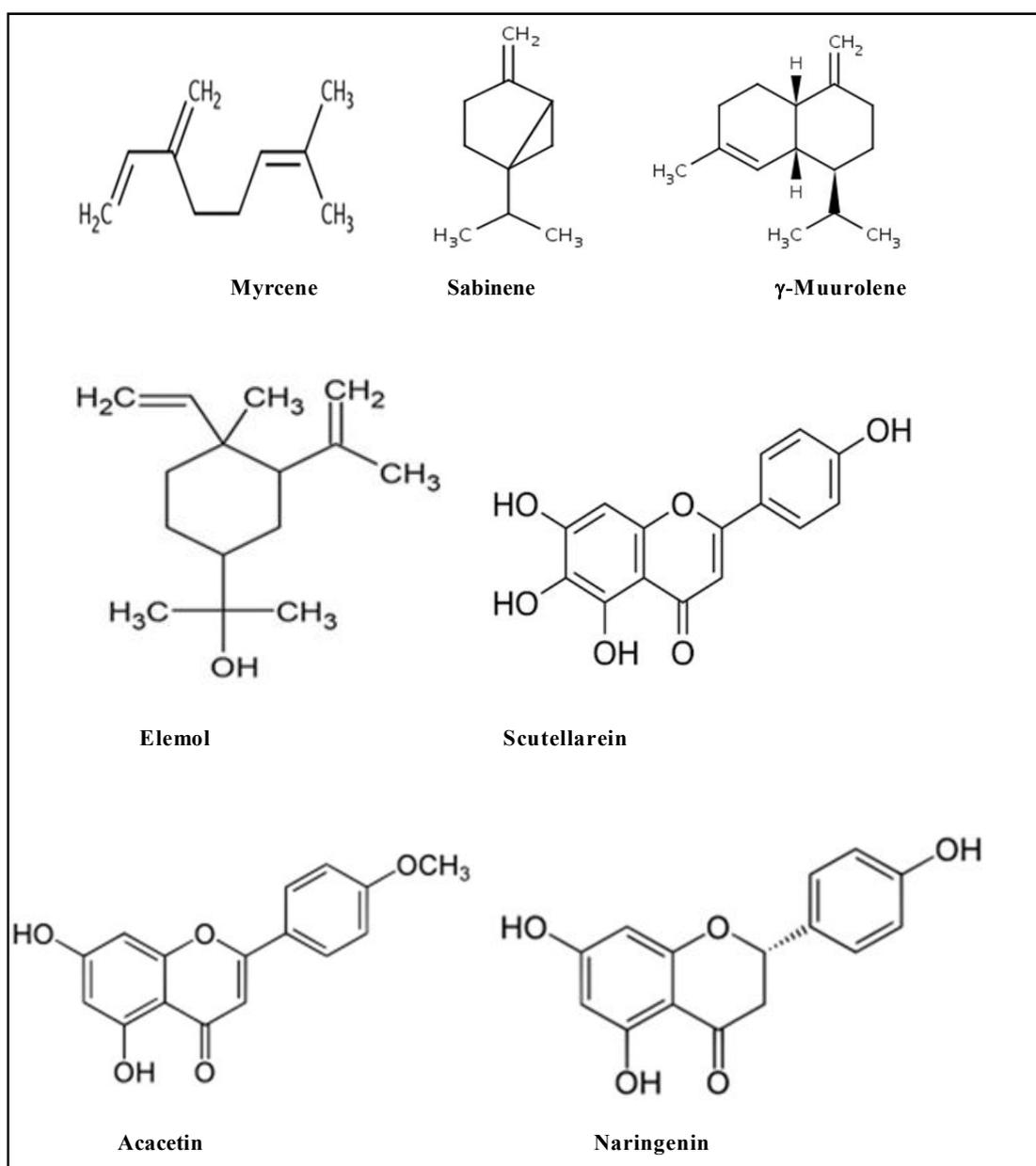
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## 2. Bioactive compounds

Devil weed is a medicinally significant plant known for its diverse array of bioactive compounds that contribute to its extensive pharmacological properties. The plant is abundant in phenolic compounds and flavonoids, including kaempferol, quercetin, naringenin, isosakuranetin, acacetin, salvigenin, and chromomoric acid, which are recognized for their powerful antioxidant and anti-inflammatory activities strategies (Dat *et al* 2009; Hung *et al* 2011; Park *et al* 2019). These compounds play a vital role in neutralizing free radicals and preventing oxidative damage, which is pivotal for managing inflammatory and degenerative diseases. Additionally, Devil weed contains a variety of terpenoids, such as  $\alpha$ -pinene,  $\beta$ -pinene, caryophyllene, germacrene D, and D-cadinene. These terpenoids are known for their anti-inflammatory, antimicrobial, and insecticidal properties, making the plant a valuable resource in managing infections

and protecting against pests. The plant also includes significant levels of alkaloids, coumarins, and essential oils. Alkaloids contribute to its antimicrobial and therapeutic efficacy, while coumarins like scutellarein tetramethyl ether exhibit anticoagulant and antioxidant activities (Pitapawasutthi *et al.*, 2016; Omonije *et al.*, 201). The essential oils, including myrcene, sabinene,  $\gamma$ -muurolene, and elemol, enhance the plant's pharmacological potential due to their aromatic and anti-inflammatory effects. Furthermore, Devil weed features a range of chalcones, flavanones, and derivatives like 4-hydroxybenzoic acid, 5-hydroxy-7,4'-dimethoxyflavanone, and 6-methoxyacacetin, which have shown antimicrobial, anticancer, and anti-inflammatory properties. This rich chemical composition not only underpins its traditional medicinal uses but also highlights its potential for further exploration and application in modern therapeutic (Heisse *et al* 2014; Pandith *et al.*, 2013; Prabhi and Ravi 2012; Omokhua Uvi *et al.*, 2020).



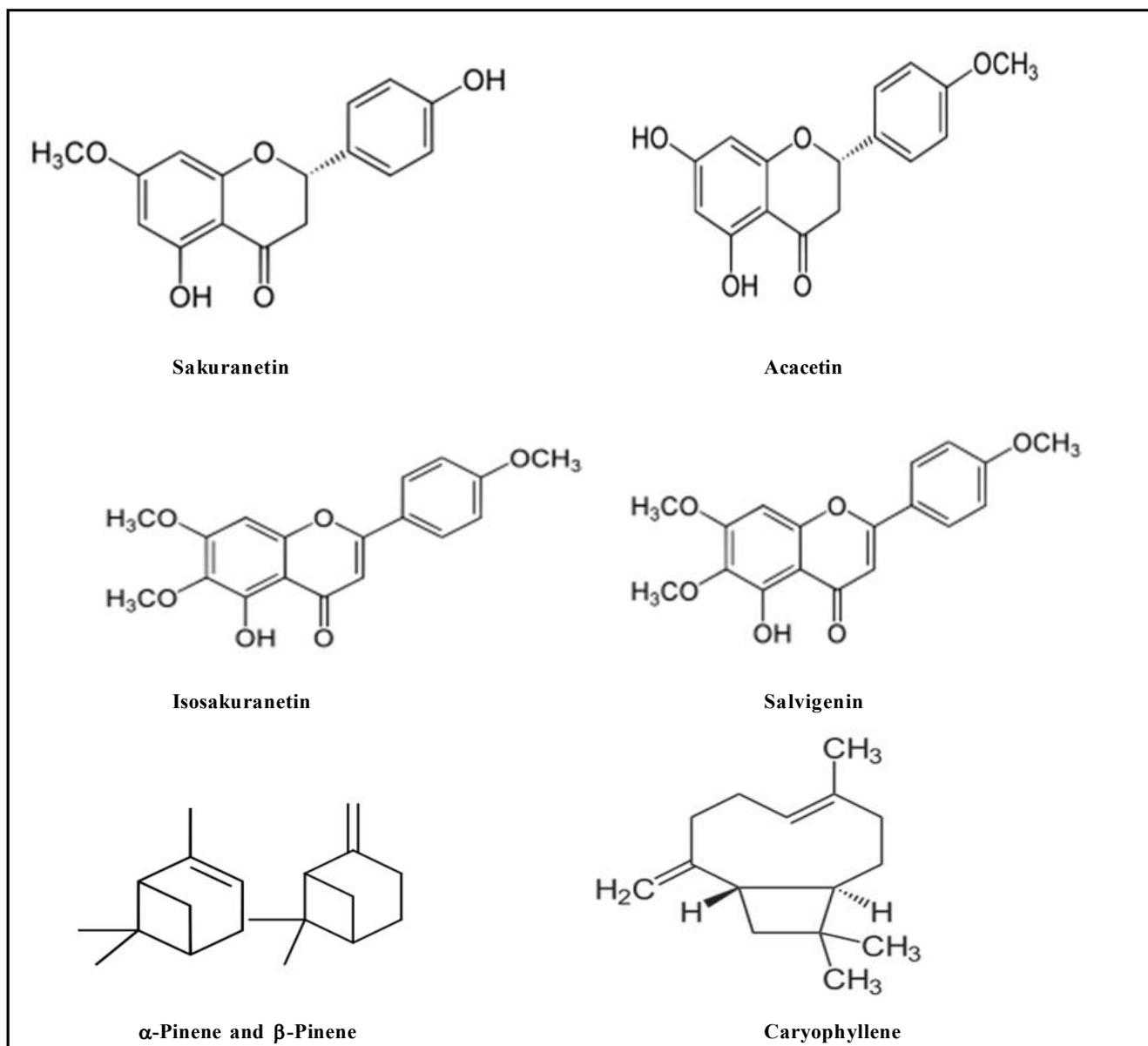


Figure 2: Bioactive compounds.

### 3. Pharmacological properties

#### 3.1 Wound healing activity

Wound healing is a critical physiological process involving coagulation, inflammation, proliferation, and tissue remodelling. Factors such as age and pathological conditions can delay or impair wound healing, potentially leading to complications like hypertrophic scars and keloids. Devil weed has been extensively studied for its wound-healing potential, with traditional applications in treating burns, cuts, and other soft tissue injuries. Its bioactive compounds, including phenols, flavonoids, and specific metabolites like eupolin, have demonstrated significant efficacy in accelerating tissue repair. Eupolin has even been approved in Vietnam as a treatment for soft tissue burns and wounds. The haemostatic properties of Devil weed play a crucial role in wound healing. The plant stimulates

vasoconstriction and promotes blood coagulation by upregulating thromboxane synthase activity, which aids in the formation of fibrin clots that act as protective barriers (Ukwueze *et al.*, 2013; Vijayaraghavan *et al.*, 2017). Studies have shown that extracts of *C. odorata* reduce blood clotting time and enhance platelet aggregation, largely due to compounds like tetramethoxyflavone, scutellarein, and stigmasterol. In the inflammation stage, *C. odorata* exhibits antimicrobial activity through its alkaloids and flavonoids, which combat bacterial and fungal infections. The plant also mitigates oxidative stress by scavenging reactive oxygen species (ROS) with its potent antioxidants, including protocatechuic acid and vanillic acid. These antioxidants protect keratinocytes and fibroblasts from oxidative damage, thereby reducing inflammation (Aja *et al.*, 2023). Devil weed also enhances fibroblast proliferation and collagen synthesis, essential for tissue regeneration and angiogenesis. By

promoting cell adhesion and upregulating key molecules like laminin and fibronectin, the plant facilitates re-epithelialization and tissue remodelling. Its ability to regulate growth factors and prevent excessive matrix protein formation further underscores its role in preventing keloid formation. Overall, Devil weed accelerates the wound-healing process through its haemostatic, anti-inflammatory, and tissue-regenerative properties, making it a promising candidate for therapeutic applications (Phan *et al.*, 2001; Sirinthipaporn and Jiraungkoorskul 2017).

### 3.2 Anticancer potential

Devil weed has demonstrated notable anticancer activity against a variety of cancer cell lines, including breast, colorectal, cervical, hepatocellular carcinoma, and leukaemia cells. The ethyl acetate extract of Devil weed showed cytotoxic effects on breast cancer cell lines Michigan Cancer Foundation-7 (MCF-7) and T47D, with  $IC_{50}$  values of 218.78  $\mu\text{g/ml}$  and 307.61  $\mu\text{g/ml}$ , respectively. The extract selectively targeted cancer cells while exerting minimal effects on normal Vero cells, highlighting its safety profile compared to conventional chemotherapy agents like doxorubicin. Apoptosis assays confirmed that Devil weed induced necrosis in MCF-7 and T47D cells, making it a promising candidate for safer breast cancer treatment. Furthermore, Devil weed exhibited over 80% cytotoxicity at higher concentrations (500  $\mu\text{g/ml}$ ) against high tumor burden (HTB) and 4T1 breast cancer cells, reinforcing its efficacy. In colorectal cancer, Devil weed exhibited moderate activity against human colon carcinoma cell line (WiDr) colon cancer cells, achieving significant cytotoxicity above 50% at 500  $\mu\text{g/ml}$ . These findings suggest its potential role in colorectal cancer prevention and management (Yusuf *et al.*, 2021, 2023).

For hepatocellular carcinoma (HepG2) cells, the ethanolic extract of Devil weed leaves exhibited potent anticancer activity. The crude ethanolic extract had the lowest  $IC_{50}$  value (23.44  $\mu\text{g/ml}$ ), outperforming fractions like n-hexane (84.52  $\mu\text{g/ml}$ ), ethyl acetate (88.51  $\mu\text{g/ml}$ ), and other ethanolic fractions (167.49  $\mu\text{g/ml}$ ). The efficacy of the crude extract is attributed to its diverse phytochemical content, including compounds such as 1-Carboethoxy- $\beta$ -carboline and Canthin-6-one, which are known to target cancer cells through various biochemical pathways (Yusuf *et al.*, 2022). Additionally, the soluble ethyl acetate extract of Devil weed leaves exhibited significant cytotoxicity against HeLa cervical cancer cells, with an  $IC_{50}$  value of  $82.41 \pm 6.73$   $\mu\text{g/ml}$ . Apoptosis analysis showed dose-dependent morphological changes in HeLa cells, with more than 97% cell death observed at  $IC_{50}$  and  $2 \times IC_{50}$  concentrations ( $p < 0.05$ ). Proliferation assays revealed a significant reduction in HeLa cell growth at doses of  $\frac{1}{2} IC_{50}$ ,  $IC_{50}$ , and  $2 \times IC_{50}$  within the first 24 h ( $p < 0.05$ ). The n-hexane fraction of *C. odorata* demonstrated antiproliferative activity against breast cancer cell lines such as MCF-7, MDAMB-468, and CAL51, while the ethanol extract inhibited the growth of Lewis lung carcinoma (LLC) and HL-60 human leukaemia cells. Essential oils derived from the plant, containing pentacyclic triterpenoids, reduced a human hepatoma (liver cancer) cell line (HepG2) cell viability by 90% with an  $IC_{50}$  value of 206  $\mu\text{g/ml}$  (Mutalib *et al.*, 2023; Elekofehinti *et al.*, 2023). These findings collectively underscore the broad-spectrum anticancer potential of *C. odorata*. Its selective cytotoxicity, ability to induce apoptosis, and inhibitory effects on cell proliferation position it as a promising candidate for developing novel cancer therapies. Further research, including clinical trials, is needed to validate its mechanisms of action and therapeutic applications.

### 3.3 Antidiabetic potential

Devil weed, a medicinal plant widely used in traditional remedies, has shown promising antidiabetic properties in various experimental studies. Extracts of Devil weed leaves have demonstrated the ability to regulate blood glucose levels, improve insulin secretion, and support pancreatic beta-cell regeneration (Elebiyo *et al.*, 2021). These effects are believed to stem from the plant's rich phytochemical composition, including phenols, flavonoids, alkaloids, tannins, and saponins. In diabetic animal models, Devil weed extracts significantly reduced blood glucose levels and increased insulin secretion in a dose-dependent manner. Higher doses of the extract exhibited hypoglycemic effects comparable to glibenclamide, a standard antidiabetic drug. The plant's extract also mitigated muscle wasting associated with hyperglycemia, leading to improvements in body weight and metabolic activity (Elekofehinti *et al.*, 2023; Yusuf *et al.*, 2020).

At the molecular level, Devil weed enhanced the expression of key genes involved in glucose metabolism and oxidative stress regulation, such as Glut2, glucokinase, and Nrf2, while suppressing the expression of Keap1. This gene modulation contributes to its protective effects on the liver and other tissues affected by diabetes. In vitro studies have supported these findings, with Devil weed extracts inhibiting enzymes like  $\alpha$ -amylase and glycosylated haemoglobin, further corroborating its role in glycaemic control. Additionally, the plant's extracts have shown the potential to restore biochemical parameters, such as liver function markers and protein levels, which are often disrupted in diabetes. Overall, Devil weed holds significant promise as a natural antidiabetic agent with multiple mechanisms of action, including enhancing insulin secretion, reducing glucose production and absorption, and supporting beta-cell regeneration. Further studies are needed to isolate and identify the bioactive compounds responsible for these effects and to explore their potential for therapeutic applications (Salsabila *et al.*, 2021; Omonijeet *et al.*, 2019; Marianne *et al.*, 2014).

### 3.4 Antihypertensive and cardioprotective activities

The aqueous extract of Devil weed leaves exhibits significant antihypertensive and cardioprotective properties, as demonstrated in experimental models. Studies on salt-loaded rats revealed that the extract, administered at doses of 100 and 200 mg/kg body weight, effectively reduced systolic, diastolic, pulse, and mean arterial pressures in a dose-dependent manner. These effects were accompanied by modulation of plasma sodium and potassium levels, suggesting the involvement of electrolyte balance in its antihypertensive action.

Gas chromatographic analysis identified several bioactive components in the extract, including flavonoids such as kaempferol, quercetin, and apigenin, as well as carotenoids like  $\alpha$ -carotene and lycopene. These compounds are known for their antioxidant and vascular-protective effects, which may contribute to blood pressure regulation. Additionally, the extract contained hydroxycinnamic acid derivatives like p-coumaric and caffeic acids, and phytosterols such as sitosterol, further supporting its cardiovascular benefits. In lipid profile studies, the extract significantly lowered plasma levels of total cholesterol, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and non-HDL cholesterol while increasing high-density lipoprotein (HDL) cholesterol levels. It also improved atherogenic indices, including the cardiac risk ratio, atherogenic

coefficient, and atherogenic index of plasma, indicating its potential to prevent dyslipidemia-induced cardiovascular complications. Moreover, the extract demonstrated cardioprotective effects by reducing heart size and mitigating hypertension-induced cardiac remodelling. The observed reduction in plasma triglycerides and improvement in lipid metabolism suggest additional mechanisms through which the extract supports heart health. These findings highlight the potential of Devil weed leaves as a natural remedy for hypertension and related cardiovascular conditions, warranting further investigation into its active compounds and therapeutic applications (Ikewuchi *et al.*, 2011, 2012, 2014, 2014a).

### 3.5 Antiallergic properties

Devil weed exhibits promising antiallergic properties due to its diverse phytochemical constituents, including alkaloids, flavonoids, phenolic compounds, glycosides, saponins, and tannins. These bioactive compounds are known to suppress allergic responses by modulating inflammatory pathways and reducing the activity of immune cells such as eosinophils, basophils, and neutrophils. In experimental studies, ethanol extract ointment derived from Devil weed leaves demonstrated a significant reduction in allergen-induced inflammatory responses when applied to the nasal mucosa of rabbits, although the one-way ANOVA showed no significant differences in individual inflammatory cell counts ( $p > 0.05$ ), the Kruskal-Wallis test revealed a strong dose-dependent relationship between the extract concentration and the reduction of inflammatory cells ( $p < 0.05$ ;  $r = 0.907$ ). This suggests that the extract effectively mitigates allergic inflammation. Further research highlights the plant's anti-inflammatory and antihistamine effects, making it particularly effective in managing allergic rhinitis. The topical application of Devil weed extract has been shown to alleviate symptoms by reducing eosinophilia and basophilic infiltration, which are key mediators of hypersensitivity reactions. Overall, the antiallergic potential of Devil weed supports its use in traditional medicine for the management of allergies and inflammation, offering a natural alternative to conventional antiallergic drugs (Teuku Husni *et al.*, 2022; Ehi-omosun *et al.*, 2024).

### 3.6 Anti-inflammatory and analgesic properties

Devil weed has been extensively studied for its anti-inflammatory and analgesic properties, which are supported by both traditional usage and experimental evidence. Research demonstrates that Devil weed exerts significant anti-inflammatory effects in both acute and chronic inflammation models. In studies using carrageenan-induced paw oedema, cotton pellet-induced granuloma, and formaldehyde-induced oedema models in Wistar rats, the aqueous and methanol extracts of Devil weed were shown to attenuate inflammation. For example, methanol extract at doses of 50, 100, and 200 mg/kg inhibited oedema formation by 40.7%, 64.0%, and 59.3%, respectively, in the carrageenan model. The reduction in inflammation is comparable to that achieved by indomethacin (65.1%), a standard anti-inflammatory drug. The mechanism of action is attributed to the inhibition of pro-inflammatory mediators such as prostaglandins, which are synthesized through the cyclooxygenase-2 (COX-2) pathway. Studies have shown that Devil weed suppresses COX-2 expression and inhibits nitric oxide (NO) production by downregulating inducible nitric oxide synthase (iNOS) and nuclear factor kappa B (NF- $\kappa$ B) activity. Furthermore, compounds such as chalcones and fatty acids identified in the plant act synergistically to block inflammatory pathways. In

lipopolysaccharide (LPS)-induced inflammation models, the ethyl acetate extract of Devil weed downregulate the expression of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-1 beta (IL-1 $\beta$ ), thereby reducing inflammation. This highlights its potential as a therapeutic agent for managing inflammatory conditions. Devil weed also exhibits analgesic effects, demonstrated in models of acute and chronic pain. The plant's aqueous extracts (400 and 800 mg/kg) significantly reduced pain induced by acetic acid, formaldehyde, and pressure-based methods in rodent models. These findings suggest both central and peripheral analgesic activity. The analgesic mechanism of Devil weed involves the inhibition of arachidonic acid peroxidation, leading to reduced prostaglandin synthesis, which mediates pain. Flavonoids, saponins, and alkaloids present in the plant are believed to contribute to its pain-relieving effects. Flavonoids suppress pain perception by reducing prostaglandin levels, while saponins may bind to sensory nerve terminals to attenuate pain stimuli. The effectiveness of Devil weed in inhibiting nociceptive pain is similar to that of nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids, making it a promising natural alternative for managing pain. The anti-inflammatory and analgesic properties of Devil weed are supported by its ability to modulate key inflammatory and pain-related pathways. Its bioactive compounds, including flavonoids, chalcones, and fatty acids, act through mechanisms such as COX-2 inhibition, cytokine suppression, and nociceptor modulation. These findings validate its traditional use and suggest its potential for developing novel therapeutic agents for inflammation and pain management (Elion Itou *et al.*, 2017; Taiwo *et al.*, 2000; Owoyele *et al.*, 2008).

### 3.7 Antipyretic activity

Traditionally, aqueous decoctions of Devil weed leaves and roots have been used to alleviate febrile conditions, including rheumatic fever. Experimental studies support this traditional use, highlighting the plant's significant antipyretic activity. In a study by Taiwo *et al.* (2000), the methanolic extract of Devil weed leaves was found to significantly reduce yeast suspension-induced hyperthermia in rats. Although the specific bioactive compounds responsible for this activity were not identified, the authors suggested that flavonoids such as isosakuranetin, quercetin, and sakuranetin, which are abundant in the plant, may play a role. This was further supported by findings from (Owoyele *et al.*, 2008) where flavonoid-rich fractions (dichloromethane and n-butanol fractions) of Devil weed significantly lowered rectal temperatures in febrile rats. The antipyretic mechanism of Devil weed is likely related to its ability to inhibit prostaglandin E2 (PGE2) synthesis, a key mediator of fever in the preoptic region of the anterior hypothalamus. This effect may be achieved through the downregulation of pro-inflammatory proteins, such as COX-2 and iNOS, which are known to influence PGE2 production. While the precise bioactive compounds and pathways involved remain unclear, these findings suggest that Devil weed exerts its antipyretic effects through flavonoid-mediated modulation of inflammatory and pyretic responses. Further studies are required to fully elucidate the underlying mechanisms and identify the specific compounds responsible for its antipyretic activity (Oko *et al.*, 2024).

### 3.8 Antimicrobial activity

Devil weed is widely recognized for its potent antimicrobial activity, making it a promising source for the development of novel antimicrobial agents. Numerous studies have highlighted its

effectiveness against a broad spectrum of microorganisms responsible for various infections, including diarrhoea, skin infections, wound infections, urinary tract infections, and food spoilage. Methanolic and ethanolic leaf extracts have consistently demonstrated significant antibacterial activity against both Gram-positive and Gram-negative bacteria. Key pathogens such as *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* have been shown to be highly susceptible to these extracts, with minimum inhibitory concentrations (MIC) as low as 12.5 mg/ml for urinary tract pathogens and 0.25 mg/ml for multidrug-resistant strains (Stanley *et al.*, 2014; Sukanya *et al.*, 2011). The antimicrobial activity of Devil weed extends to fungal pathogens. Ethanolic extracts, in particular, have exhibited strong antifungal properties against species such as *Candida albicans*, *Aspergillus flavus*, *Candida tropicalis*, and *Trichophyton rubrum*. In one study, complete inhibition of *Neurospora crassa* was achieved within 24 h using leaf extracts, showcasing its potent fungicidal capacity. Comparative analyses of solvent extracts revealed that ethyl acetate and ethanol extracts consistently outperformed aqueous extracts, suggesting that non-polar solvents are better suited for extracting the bioactive phytochemicals responsible for the antimicrobial effects. Several studies have also explored the antimicrobial potential of specific phytochemicals within Devil weed (Odutayo *et al.*, 2017; Vital and Rivera, 2009). Compounds such as sinensetin, scutellarein-tetramethyl ether, and trimethoxyflavanones have demonstrated significant inhibitory activity against bacterial strains like *Klebsiella oxytoca*, *Salmonella enterica*, and *Shigella sonnei*. Methanolic extracts, characterized by high phenolic and flavonoid content, have shown a strong correlation between phytochemical concentration and antimicrobial efficacy. These findings underline the importance of bioassay-guided fractionation for isolating and identifying the most active compounds within the plant. The antimicrobial activity of Devil weed is influenced by several factors, including the plant part used, the extraction method, and environmental conditions. Leaf extracts have consistently shown greater efficacy compared to other parts of the plant, likely due to the higher concentration of bioactive compounds. Variations in geographical and environmental conditions, such as altitude, soil pH, and climate, also play a role. For instance, plants grown in high-altitude regions with harsher climates have been shown to produce more bioactive phytochemicals, resulting in enhanced antimicrobial activity. Overall, Devil weed demonstrates substantial potential as a source of antimicrobial agents, particularly against antibiotic-resistant pathogens (Stanley *et al.*, 2014). It is broad-spectrum activity, coupled with the ability to inhibit multidrug-resistant bacteria and fungi, highlights its significance in addressing the global challenge of microbial resistance. Further research into the standardization of extraction methods and the development of pharmaceutical formulations could pave the way for its incorporation into modern medicine (Thophon *et al.*, 2016; Alabi *et al.*, 2019).

#### 4. Conclusion

Devil weed, despite its invasive nature, holds immense potential as a therapeutic agent due to its rich phytochemical profile and proven pharmacological properties. Its broad-spectrum antimicrobial, anti-inflammatory, and wound-healing activities make it a valuable resource for combating infections and inflammatory disorders. The plant's potential for drug development is significant, especially in addressing multidrug-resistant pathogens. Sustainable exploration and standardization of its bioactive compounds can bridge the gap between

traditional medicine and modern therapeutics, fostering ecological balance alongside pharmaceutical innovation.

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#### Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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