



REVIEW ARTICLE

# Traditional uses of *Ageratum conyzoides* L. (Asteraceae) and its scientific evidence for therapeutic efficacy: A review

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## Abstract

*Ageratum conyzoides* L. (Asteraceae) is a medicinal plant widely distributed in tropical and subtropical regions. It is an integral part of traditional medicine in Africa, Asia and South America, where it is used to treat a wide range of diseases, such as diabetes, skin diseases, respiratory disorders, inflammation, burns, wounds, diarrhea, fever, muscle pain, reproductive problems, leprosy and other ailments. This review aimed to consolidate and critically analyze scientific studies on *A. conyzoides* to assess its therapeutic potential and safety. A narrative literature review was carried out using databases such as Google Scholar, Scopus and PubMed, covering the period from 2023 to 2025. Keywords related to the plant's traditional uses, phytochemistry, pharmacological properties and toxicology were used. Only studies providing experimental or ethnobotanical data in English were included. Results show that *A. conyzoides* contains diverse bioactive compounds such as flavonoids, alkaloids, terpenes, chromenes and phenolic acids. These are associated with anti-inflammatory, antimicrobial, antidiabetic, anticancer, antioxidant and wound-healing activities. In particular, flavonoids and chromenes contribute to the plant's antioxidant and anti-inflammatory effects, while pyrrolizidine alkaloids may cause hepatotoxicity at high doses. Overall, the available data corroborate many of the traditional uses of this plant. However, the lack of standardized extraction methods and the limited nature of preclinical and clinical data justify further studies to validate its efficacy and ensure the safety of its therapeutic use.

**Keywords:** *Ageratum conyzoides*; bioactive compounds; medicinal plants; pharmacological activities; pyrrolizidine alkaloids

## Introduction

Plants have been used to treat illness since ancient times and play an essential role in the health systems of many cultures around the world (1). Studies have shown that the use of plants for medicinal purposes is a practice that has been handed down from generation to generation in many civilizations. Thus, from traditional African and Chinese medicine to Ayurveda and native American remedies, plants have always been at the centre of healing practices and well-being (2). Today, the World Health Organization (WHO) estimates that 80 % of the population in developing countries rely on traditional medicine for their primary healthcare needs, largely due to its accessibility and its affordability (3). The WHO therefore encourages the integration of traditional medicine practices into modern health systems. This widespread reliance highlights the importance of understanding the therapeutic potential of medicinal plants, both to preserve traditional knowledge and to discover new treatments (2).

*Ageratum conyzoides* is one of the medicinal plants that arouses considerable interest because of its multiple therapeutic virtues and its use in traditional medicines in various parts of the world (4). Commonly known as billy goat weed in English, *A. conyzoides* is a plant of the Asteraceae family native to tropical and subtropical regions of America. It has spread to Africa, Asia and Australia, becoming an integral part of local pharmacopoeias (5). The whole plant or its various parts such as leaves, stems and roots are used in folk medicine. In African countries such as Nigeria, Benin, Togo, Ghana, Guinea and Cameroon, it is used to treat diabetes, headaches, dyspnea, skin diseases, rheumatism, fever, colic, intestinal parasitosis and wounds from burns. In Kenya, it is used as an antiasthmatic, antispasmodic and for its haemostatic effects. It is also used for treating dyspepsia, eye problems, uterine disorders and pneumonia (1). In India, *A. conyzoides* is regarded as a wound-healing agent and is used to treat respiratory disorders, leprosy, ophthalmic diseases and dandruff. Additional applications include the management of diarrhea and dysentery (3). In South America,

particularly Brazil, the leaves are used for their anti-inflammatory, analgesic and anti-diarrheal properties, while in Vietnam the plant is prized for treating ulcers, skin ailments and gynaecological diseases (6). The wide range of these applications demonstrates its importance in traditional medicine worldwide (6).

The therapeutic virtues of *A. conyzoides* are largely attributed to its rich composition in bioactive compounds, notably terpenes, flavonoids, alkaloids and essential oils. These compounds have attracted renewed scientific interest, leading to numerous studies exploring and confirming the plant's medicinal properties (7). For example, ethanolic extracts of *A. conyzoides* have demonstrated antidiabetic effects in both normoglycemic and diabetic rats (8). *In vitro* evaluation of different types of extracts of the plant showed antimicrobial activity against both Gram-positive and Gram-negative bacteria validating its traditional use in infection treatment (9). In many studies, *A. conyzoides* extracts have shown anticancer effects even if more research is required to fully elucidate its anticancer mechanisms and potential therapeutic applications (4). The plant's anti-inflammatory activity has also been demonstrated in a number of experimental conditions. In addition, studies have also reported its antioxidant potential, which could make it a good candidate for the development of treatments to combat oxidative stress, implicated in many chronic diseases (10, 11).

However, despite the abundance of traditional uses and promising scientific findings, there remains a lack of consolidated information linking these uses with mechanistic evidence and toxicity data. This review therefore critically evaluates the phytochemistry, pharmacological activities and safety profile of *A. conyzoides* to identify existing research gaps and highlight its therapeutic potential for possible integration into modern medicine.

### Review methodology

For this review, a structured narrative approach was adopted to collect and analyze data on the traditional uses, phytochemistry and pharmacological activities of *A. conyzoides*. The following steps were followed:

**Literature search:** A comprehensive literature search was carried out using electronic databases like PubMed, Scopus and Google Scholar. The search covered the period October 2023 to June 2025 to ensure inclusion of both classical and recent studies. The following search terms and Boolean combinations were used: “*Ageratum conyzoides*” AND (“traditional uses” OR “ethnomedicine” OR “phytochemical composition” OR “pharmacological activities” OR “toxicology” OR “therapeutic efficacy”). Reference lists of selected articles were also screened to identify additional relevant publications.

**Inclusion and exclusion criteria:** Studies were included if they were peer-reviewed articles, theses or reports written in English and contained empirical or experimental data on the phytochemistry, pharmacological properties or ethnomedicinal uses of *A. conyzoides*. Eligible study types included experimental *in vitro* and *in vivo* studies, clinical trials and ethnobotanical surveys. Reviews were considered when they provided original synthesis or comparative analysis. Studies focusing on other *Ageratum* species, non-empirical reports or publications lacking detailed data were excluded.

**Data extraction and analysis:** For each selected study, the following key information was extracted: publication year, country of study, plant part used, extraction solvent, identified compounds, biological activity tested, models used and main outcomes. Data

were then organized by geographical region and pharmacological category (anti-inflammatory, antidiabetic, antimicrobial, antioxidant, anticancer).

**Synthesis and critical appraisal:** The collected information was synthesized to provide a comprehensive overview of the traditional applications, phytochemical constituents and scientific evidence supporting the therapeutic efficacy of *A. conyzoides*. A critical appraisal of the studies was conducted to identify methodological limitations, variations in experimental design and research gaps requiring further investigation.

## Results and Discussion

### Taxonomical classification of *Ageratum conyzoides*

*Ageratum conyzoides* is a flowering plant belonging to the Asteraceae family, which comprises numerous species known for their medicinal value. The plant is found in various countries around the world, where it is known by several local names. Its taxonomic classification is presented in Table 1. The nomenclature of the *Ageratum* genus goes back to ancient Greek, where “a geras” means “stay young”, referring to the plant's longevity. The specific epithet, *conyzoides*, is attributed to it because of its resemblance to the *Inula helenium* plant known as “konyz” in Greek (12).

### Description of the plant

*Ageratum conyzoides* is an annual herb with shallow and fibrous roots. It generally grows between 30 and 80 cm in height but can sometimes reach up to 1 m depending on environmental conditions (Fig. 1). The stem, quadrangular in cross-section, is erect, branched and covered with fine white hairs. In some instances, the stems may root where the bases touch the ground, becoming cylindrical and strong, even woody with age. The leaves are opposite and simple, ranging from oval to lanceolate with toothed margins and a rounded to wedge-shaped base. They measure between 2 and 10 cm in length and 5 to 50 mm in width, with hairy petioles 5-75 mm long. Both leaf surfaces are sparsely hairy and rough with prominent veins, giving the plant a slightly downy appearance. When crushed, the leaves emit a characteristic odour reminiscent of a male goat, hence the English name “goat weed”. The inflorescences are small blue-purple flower heads, sometimes white or pink, grouped in dense corymbs at the ends of the stems, either terminal or axillary. Each inflorescence bears 4-18 flower heads arranged in showy, flat-topped clusters. Individual flower heads measure 5 to 8 mm in diameter, each composed of 60-75 bisexual tubular flowers. The flower head is surrounded by two or three rows of oblong bracts, which are green with pale or reddish-violet tops, measuring 3-5 mm high and 0.5-1.75 mm wide. These bracts are sparsely hairy, with evenly toothed upper parts and an abruptly acuminate, acute tip. The fruits are ribbed or angled, black or brown achenes that are linear and slightly flattened, measuring about 1.25 to 2 mm long, roughly hairy and topped by a small apex bearing 5 to 6 rough bristles. These bristles are white to cream-coloured, 1.5-3 mm long, with upward-turning spines, which facilitate wind dispersal (14, 15). A voucher specimen (YH 788/HNB) of *A. conyzoides* has been deposited at the National Herbarium of Benin, University of Abomey-Calavi, to authenticate the plant material used for reference and study.

### Biology and reproduction

*Ageratum conyzoides* reproduces mainly by sexual means through

**Table 1.** Taxonomic tree and some vernacular names of *A. conyzoides* (13, 14)

Domain	Eukaryota
Kingdom	Plantae
Subkingdom	Angiospermae
Class	Eudicots
Order	Asterales
Family	Asteraceae
Genus	<i>Ageratum</i>
Species	<i>conyzoides</i>
Binomial name	<i>Ageratum conyzoides</i> Linn.
EPPO code	AGECO
<b>International common names</b>	
English	Billy goat weed, Appa grass, Tropical ageratum
French	Herbe aux sorciers, Herbe à bouc, Baume blanc
Spanish	Barba de chivo, Catinga de bode, Hierba del perro
Chinese	Huò xiāng jì
<b>Local common names</b>	
Nigeria	Imi esu (Yoruba), Ula ujula (Igbo), Ahenhen (Hausa)
Benin	Awovitakinman (Fon and Goun), Kourotoko (Bariba), Ewe arougbo or ollokopè (Yoruba)
Ivory Coast	Kondrè, koudrè (Baoulé), Zanouin (Guéré), Douzi, Doussouo (Yacouba), Bonwo (Bété)
Ghana	Guakro, Efoe momoe
Cameroon	Nyada elog (Ewondo), Mhéguefa, Tchounamo (Bamileke)
Guinea	Mamakhoyi fikhè (Sousou), Kikalapouri (Pular), Koumbenin (Malinké)
Burundi	Akarura (Kirundi)
East Africa	Adwolo, Gathenge (Kikuyu), Kimavi cha kuku (Kiswahili)
South Africa	Mutungwi (Tshivenda)
India	Jangli pudina, Visadodi, Kubhi (Hindi), Visamusti (Sanskrit)
Brazil	Catinga de barao, Camará apeba

**Fig. 1.** *Ageratum conyzoides* in its natural habitat.

the production of a large number of seeds. Each plant can produce several thousand seeds, allowing wide dispersal and rapid propagation under diverse environmental conditions. The seeds are primarily dispersed by wind, water or animals. Germination generally occurs under warm and humid conditions, favouring rapid colonization of disturbed soils (16).

In addition to sexual reproduction, the plant has a limited capacity for vegetative propagation through the rooting of stems at the nodes, particularly under humid conditions. This mixed reproductive capacity contributes to the species' persistence in varied environments, making the plant highly adaptable and sometimes invasive in certain regions (16).

#### Origin and distribution

*Ageratum conyzoides* is native to the tropical and subtropical regions of Central America, particularly Mexico (17). However, due to its remarkable ability to adapt to a wide range of soils and climates, it has spread throughout the world and has become naturalized

across many tropical and subtropical regions of Africa, Asia and South America. In Africa, the plant is found in numerous countries such as Nigeria, Benin, Cameroon, Zimbabwe, Mauritius, Angola, Ethiopia, Kenya, Liberia, Uganda, the Democratic Republic of Congo, Egypt, Ghana, Côte d'Ivoire, Tanzania and South Africa. In Asia, it is commonly found in India, China, Thailand, Japan, Indonesia, Malaysia, the Philippines, Cambodia, Vietnam, Bangladesh, Pakistan and Sri Lanka (14, 16). The species is also present in Australia, New Caledonia and several Latin American countries such as Brazil, Peru and Colombia. Its wide distribution is facilitated by its tolerance to different soil types, including poor soils and by its ability to rapidly colonize disturbed land such as wastelands, roadsides and cultivated fields (16). In addition to its ecological role, *A. conyzoides* is known for its impact as a weed in agricultural systems, where it can compete with cultivated crops for nutrients and light. Nevertheless, its extensive traditional medicinal applications make it a plant of significant interest in many cultures around the world (17).

#### Use of *Ageratum conyzoides* in traditional medicine across different regions

*Ageratum conyzoides* is a medicinal plant widely used throughout Africa, Asia and Latin America, with applications varying from region to region (Table 2). In Africa, the plant plays a central role in traditional medicine across many countries. In West Africa, notably Nigeria, Ghana and Benin, *A. conyzoides* is used to treat headaches, mental illness, skin diseases, diabetes, diarrhoea and abdominal pain in children. It is also applied to accelerate wound healing, treat infectious diseases and manage conditions such as HIV/AIDS (18, 19). Other uses include the management of pneumonia, snake-venom antitoxin, typhoid fever, malaria, sore throat and candidiasis. The roots are employed in the treatment of tumours, lithiasis and diarrhoea in infants. The plant is also used to relieve itching, insomnia, cough, intestinal worms, and as a tonic, as well as for treating pathologies affecting the female genital tract, such as painful periods, blocked fallopian tubes, and cysts (4, 7). In Togo, it is used against measles and snake bites, whereas in Kenya, it serves as an antiasthmatic and antispasmodic (4, 20). In Cameroon and

**Table 2:** Some recipes of traditional uses of *A. conyzoides* in different cultures

Condition	Parts used	Recipes/mode of administration	Countries	References
Pneumonia	Leaves	Press the leaves onto the patient's chest	Most of the African countries where it is found	(1, 4, 7)
Wounds	Fresh leaves	The leaves are crushed, pressed or pulverized and applied topically in various forms to sanitize burns, sores and fresh wounds	Most of the African countries where it is found	(24)
	Stems	The leaf juice is applied into the eye	Ethiopia most of the African countries where it is found	(6)
Eye diseases	Leaves	The fresh leaves of <i>A. conyzoides</i> are crushed along with the leaves of <i>Dichrocephala integrifolia</i> ; the resulting juice is extracted and used as eye drops	Tanzania	(25)
Cough	Leaves	Juice	Democratic Republic of Congo, Nigeria	(26)
	Roots	Decoction or infusion	Tanzania	(25)
	Stem bark	A combination of the leaves with <i>Ocimum</i> and bush pepper is employed as a remedy for stomach ailments	Nigeria	(26)
Stomach disorders	Leaves			
	Aerial parts	The fresh roots are masticated as a remedy for indigestion.	Tanzania	(25)
Skin diseases	Fresh roots		Mauritius and most of the African countries where it is found	(1)
	Whole plant	Decoction	Most of the African countries where it is found	(6,7)
	Leaves	Juice	Most of the African countries where it is found	(6,7)
Diarrhoea		Poultice	Nigeria	(26)
		Infusion		
		Consume decoction of the mixture of the whole plant with <i>Annona senegalensis</i> stem bark, three times a day	Nigeria, Benin and most of the African countries where it is found	(9, 24)
Female infertility		Decoction of the plant alone can also be consumed		
	Whole plant	A maceration of <i>A. conyzoides</i> , <i>Stachytarpheta indica</i> and <i>Sorghum guineensis</i> is taken twice daily	Nigeria	(6, 24)
		Maceration of the plant is taken in a glass cup once daily.		
HIV/AIDS	Leaves	Decoction of the plant with <i>Cassia occidentalis</i> and <i>Newbouldia laevis</i> taking twice a day	Nigeria	(26)
	Whole plant	Prepare the whole plant with water or palm wine and take it.	Cameroon	(27)
Diseases of the urogenital system in women (vaginal infections, cysts, fibroids, myomas, painful periods, etc.)		A decoction or maceration is consumed three times daily	Nigeria	(19)
	Leaves or whole plant	Decoction or maceration for intimate cleansing and/or oral consumption. Sometimes other plants are combined with it.	Benin, Nigeria, Uganda	(6, 9)
Bronchitis	Roots	Boil the root and breath the resulting vapour.	Kenya	(6, 7)
Ear pain	Leaves	Put leaf exudates in droplet form into the ear.	Nigeria	(1)
Anti-emetic	Whole plant	Infusion	Some parts of African countries	(6)
		Juice extract with water	Nigeria	(6)
Snake bite	Fresh leaves or whole plant	The decoction of a whole plant alone or with <i>D. integrifolia</i> is used as a bath and/or take orally	Cameroon, Nigeria, Benin	(6, 9)
		Take orally the decoction of the plant and combination with <i>D. integrifolia</i> and <i>Citrus limon</i>		
Repellent		Triturate or grind the leaves alone or with <i>Elaeis guineensis</i> and rub on the body for friction.		
	Leaves	Crushed <i>A. conyzoides</i> leaves, alone or in combination with <i>Diodia scandens</i> leaves.	Nigeria, Cameroon, Togo	(6, 15, 19)
Weakness in pregnancy		It is applied topically as a repellent for insects	Most of the African countries where it is found	(6, 7)
	Leaves	Grind and put in water, then use the mixture for bathing.	Uganda	(20)
Leprosy		Prepare lotion with the plant and use topically	India	(20)
	Whole plant/leaves			
Inflammation, pain and diarrhoeic diseases	Whole plant/leaves	Take decoction orally	Brazil	(20)
	Leaves	Maceration	Guinea	(13)

Uganda, it is valued for its haemostatic properties and is used to stop bleeding and treat “craw-craw,” a common skin condition (20). In Central Africa, the plant is used to treat pneumonia and, more commonly, wounds and burns. In Tanzania, it is used for its anti-inflammatory effects and in the management of cough and chest congestion (3, 15, 20). In North African countries such as Egypt, *A. conyzoides* is traditionally used in the treatment of bleeding-related disorders (21). An ethnobotanical survey conducted in Guinea also revealed its use in treating inflammatory diseases in Conakry and Dubreka (22).

In Asia, *A. conyzoides* is widely used in the Indian traditional system of remedies, Ayurveda. It is applied as a fomentation in the treatment of leprosy and pediculosis (15) and is used against purulent eye infections and as a hair lotion for dandruff. The plant is also valued for its purgative and febrifuge properties and is used to relieve colic and ulcers. It has been recognized as a traditional remedy for prostate and venereal diseases (3). In traditional Chinese medicine, *A. conyzoides* is prescribed for respiratory ailments, fevers and musculoskeletal inflammation. In Vietnam, it is prized for the treatment of gynaecological disorders. In Indonesia, it is used topically for joint pain, while in Bangladesh, it has been recognized for its antimicrobial and cytotoxic activities (17).

In Latin America, *A. conyzoides* has long been highly valued for its medicinal virtues. In countries such as Brazil and Colombia, it is traditionally used for its anti-inflammatory, antioxidant, analgesic, antidiarrheal and antifungal properties. In Mexico and Peru, it is used for its antidiarrheal and antidiabetic activities, as well as for treating respiratory problems, muscular pain and infection due to its antiseptic properties (15, 20, 23). Other reported uses include treatments for headaches, leucorrhoea, sleeping sickness, cough, lice infestation and insect control, as well as use as a mouthwash for toothache. The entire plant produces a volatile oil with a strong aroma, which is associated with several biological activities (20). Beyond its medicinal applications, *A. conyzoides* also plays a role in agriculture as an organic amendment to improve soil fertility. It can be used as a selective weed or as a substrate for oyster mushroom cultivation, helping to increase protein content and reduce production time (16). In addition to its medicinal and agricultural uses, *A. conyzoides* holds cultural and mystical significance in many societies. In Côte d'Ivoire, it is believed to protect followers of snake cults from bites and to ward off evil spirits when combined with other plants. Among Yoruba communities in western Nigeria, the plant's distinctive smell is believed to repel witches and neutralize harmful “bad medicine” (20). In Benin, it is used in potions against witchcraft and to attract good fortune. In Gabon, it plays a role in ritualistic sorcery, while in Congo, its leaf sap is thought to bring luck to card players when applied to their hands (3). Another Congolese belief holds that if the sap is rubbed on a person's hand and they are pricked with a needle during a trial, pain will be felt only if they are guilty (6).

These diverse uses highlight the importance of *A. conyzoides* not only as a medicinal resource but also as a plant with deep cultural and spiritual significance across different regions especially in Africa. Numerous studies have also established a correlation between its traditional use in the treatment of disease and the presence of biologically active secondary metabolites in the plant.

#### Phytochemical composition of *Ageratum conyzoides*

*Ageratum conyzoides* is a plant recognized for its high content of phytochemicals, which are responsible for its many medicinal

properties (15). These bioactive compounds include flavonoids, alkaloids, terpenes, coumarins, phenolic acids, chromenes and essential oils (Table 3), all of which have been extensively studied for their pharmacological properties (7).

#### Flavonoids

Flavonoids are phenolic compounds widely present in the plant kingdom and play a crucial role in the medicinal properties of many plants. They represent one of the major groups of phytochemicals present in *A. conyzoides* (28). Over 21 flavonoids have been isolated from *A. conyzoides* to date, most of which are polyoxygenated flavonoids (7, 15). These include quercetin, kaempferol, luteolin, apigenin, sinensetin and others. These compounds exhibit important antioxidant, anti-inflammatory and anticancer properties. They protect cells by neutralizing free radicals, reduce inflammation through the inhibition of pro-inflammatory enzymes and suppress cancer cell proliferation by inducing apoptosis (28). An important feature of *A. conyzoides* phytochemistry is the presence of tricin derivatives, a type of 3,4,5-oxygenated flavone rare in nature but of high pharmacological importance. These tricin derivatives include 5'-methoxynobiletin, linderflavone B, 5,6,7,3',4',5'-hexamethoxyflavone, eupalestin and hexamethoxyflavone. Additionally, the plant contains polyhydroxyflavones such as scutellarein (5,6,7,4'-tetrahydroxyflavone), kaempferol-3-rhamnopyranoside and kaempferol-3,7-diglucopyranoside, along with several isoflavones, all contributing to its diverse pharmacological potential (7, 15).

#### Alkaloids

Alkaloids are nitrogenous organic compounds known for their potent biological activities. Several classes of alkaloids have been identified in *A. conyzoides*, mainly pyrrolizidine alkaloids (PAs). The most common PAs found in the plant are lycopsamine and its isomer echinatine, which possess anti-inflammatory, analgesic, antimicrobial, antitumour and immunomodulatory properties (7). However, despite these beneficial effects, PAs are also associated with hepatotoxicity, requiring careful toxicological evaluation (29).

#### Chromenes, chromones, benzofurans and coumarins

Chromenes, a class of compounds characterized by a benzopyran structure, are significant constituents of *A. conyzoides* essential oil. Notably, precocene I (7-methoxy-2,2-dimethylchromene) and precocene II (6,7-dimethoxy-2,2-dimethyl-2H-chromene or ageratochromene) are reported as the main constituents of the leaf oil (15). Gas chromatography–mass spectrometry (GC–MS) analysis of flower oil revealed that precocene II is the most abundant compound, accounting for 59.5 % of the total oil (30). Other related compounds identified include encecalin (7), 6-vinyl-7-methoxy-2,2-dimethylchromene, dihydrodemethoxyencecalin, demethylenececalin and 2-(1-oxo-2' -methylpropyl)-2-methyl-6,7-dimethoxychromene (31). A dimeric form of precocene II has also been isolated from the plant's essential oil. Moreover, ethanol extracts of the whole yielded additional chromenes such as chromene, 2,2-dimethylchromene-7-methoxy-6-O-beta-D-glucopyranoside (32). The hexane extract of the aerial parts revealed further derivatives, including 2,2-dimethylchromene-7-O-β-glucopyranoside, 6-(1-methoxyethyl)-7-methoxy-2,2-dimethylchromene, 6-angeloyloxy-7-methoxy-2,2-dimethylchromene and mixtures of encecanescins (7). These chromenes are of pharmacological interest for their structural uniqueness and biological activities, such as anti-inflammatory, anticancer, antimicrobial, antiprotozoal and insecticidal effects, which justify the plant's use in pest control (7, 32).

**Table 3.** Some common compounds with their pharmacological activities isolated from *A. conyzoides*

Compound	Part used	Molecular formula	Structure	Pharmacological effects	Method of characterization	References
<b>Flavonoids</b>						
Quercetin	Leaves	C <sub>15</sub> H <sub>10</sub> O <sub>7</sub>		Antimicrobial, anti-inflammatory, antioxidant, antiviral, anticancer, antifungal and hepatoprotective	UPLC-PDA-ESI-QToF-MS	(15, 35)
Rutin	Leaves	C <sub>27</sub> H <sub>30</sub> O <sub>16</sub>		Antioxidant, antimicrobial, antifungal, anti-allergic, anticancer, anti-diabetic, anti-ulcer, antiasthmatic, antitussive, diuretic, analgesic, anti-arthritis and anti-hypertensive	UPLC-PDA-ESI-QToF-MS	(35)
Nobiletin	Leaves	C <sub>21</sub> H <sub>22</sub> O <sub>8</sub>		Anticancer and anti-hepatitis	UPLC-PDA-ESI-QToF-MS	(35)
(2S)-7,3',4'-trimethoxyflavone	Whole plant	C <sub>18</sub> H <sub>18</sub> O <sub>5</sub>			2D NMR, ESI-TOFMS	(36)
(2S)-7-methoxy-3',4'-methylenedioxyflavan	Whole plant	C <sub>17</sub> H <sub>16</sub> O <sub>4</sub>			2D NMR, ESI-TOFMS	(36)
Eupalestin	Aerial parts/leaves	C <sub>21</sub> H <sub>20</sub> O <sub>9</sub>		Antiprotozoal and anti-inflammatory	UV, NMR/ UPLC-PDA-ESI-QToF-MS	(35)
Kaempferol-3-rutinoside	Leaves	C <sub>27</sub> H <sub>30</sub> O <sub>15</sub>		Antioxidant, anticancer, antidiabetic, anti-inflammatory, antibacterial, antifungal, antiprotozoal and anti-hepatitis	UPLC-PDA-ESI-QToF-MS	(35)
Sinensetin	Leaves	C <sub>20</sub> H <sub>20</sub> O <sub>7</sub>		Anti-inflammatory, antioxidant, anticancer, neuroprotective, anti-obesity and antidiabetic	UPLC-PDA-ESI-QToF-MS	(35)
<b>Pyrrolizidine alkaloids</b>						
Lycopsamine	Leaves Whole plant	C <sub>15</sub> H <sub>25</sub> NO <sub>5</sub>		Hepatotoxic, anticancer, antimicrobial and anti-inflammatory	MS, COSY, NMR UPLC-PDA-ESI-QToF-MS	(35)
Echinatine		C <sub>15</sub> H <sub>25</sub> NO <sub>5</sub>		Hepatotoxic, anticancer, antimicrobial and anti-inflammatory	MS, COSY, NMR UPLC-PDA-ESI-QToF-MS	(35)

Sterols						
Stigmasterol	Aerial parts	C <sub>29</sub> H <sub>48</sub> O		Immunomodulatory, antiparasitic, antifungal, antibacterial, anticancer, anti-osteoarthritis, anti-inflammatory, anti-diabetic, antioxidant and neuroprotective	IR, GC-MS and NMR	(37)
β-sitosterol	Aerial parts	C <sub>29</sub> H <sub>50</sub> O		Anticancer, anti-arthritis, antitubercular, antinociceptive	IR, GC-MS and NMR	(37)
Terpenes						
Phytol	Leaves	C <sub>20</sub> H <sub>40</sub> O		Anxiolytic, anticancer, antioxidant, antinociceptive, anti-inflammatory, immunomodulatory and antimicrobial	GC-MS	(6, 15)
Triterpenoids						
Lupeol	Stem bark	C <sub>30</sub> H <sub>50</sub> O		Anti-inflammatory, Anti-angiogenic, antioxidant, antitumour, hepatoprotective, antidiabetic and cardioprotective	NMR, FTIR and MS	(34)
Sesquiterpene						
β-caryophyllene	Flowers and stems	C <sub>15</sub> H <sub>24</sub>		Antioxidant, anti-inflammatory, antimicrobial, cardioprotective, hepatoprotective, gastroprotective, neuroprotective, nephroprotective, immunomodulatory, anticancer and analgesic	Gas chromatography - Mass spectroscopy	(30, 33)
Fatty acids						
Hexadecanoic acid	Stem	C <sub>16</sub> H <sub>32</sub> O <sub>2</sub>		Antibacterial	GC-MS	(33)
Chromenes						
Precocene I	Flowers, leaves and oil	C <sub>12</sub> H <sub>14</sub> O <sub>2</sub>		Insecticidal, antimicrobial, antifungal, anticancer, anti-inflammatory, antioxidant	GC-MS	(15, 30, 32)
Precocene II	Flowers, leaves and oil	C <sub>13</sub> H <sub>16</sub> O <sub>3</sub>		Insecticidal, antimicrobial; antifungal, anticancer, anti-inflammatory, antioxidant	GC-MS, MS, IR, NMR	(15, 30, 32)

Chromones, another important group of compounds found in *A. conyzoides* are associated with antioxidant and anti-inflammatory activities (33). Chromone derivatives such as 3-(2'-methylpropyl)-2-methyl-6,8-dimethoxychroman-4-one and 2-(2'-methylprop-2-enyl)-2-methyl-6,7-dimethoxychroman-4-one have been identified (31). Benzofurans, consisting of fused benzene and furan rings, have also been isolated, notably 2-(2'-methylethyl)-5,6-dimethoxybenzofuran and 14-hydroxy-2H-β,3-dihydroeuparone (31). These exhibit antimicrobial and antioxidant properties. Furthermore, *A. conyzoides* essential oil contains coumarin and its derivatives (1.24 %), known for their anticoagulant activity and potential in managing of cardiovascular diseases (7).

#### Monoterpene and sesquiterpenes

Terpenic compounds are a diverse class of plants metabolites with various pharmacological effects. Monoterpene and sesquiterpenes

are among the major constituents of *A. conyzoides* essential oil (23). Gas chromatography-mass spectrometry analyses have revealed numerous mono- and sesquiterpenes from samples collected in different countries. In a Nigerian sample, 51 constituents were reported, including 20 monoterpenes (6.4 % of the oil) and 20 sesquiterpenes (5.1 % of the oil) (23). Among the monoterpenes, sabinene and β-pinene were found at about 1 %, β-phellandrene at 1.6 % and limonene at 2.9 %. Terpinen-4-ol and α-terpineol were present at 0.6 % and 0.5 % respectively. Ocimene, found only in trace amounts in the Nigerian sample, accounted for 5.3 % of the Indian plant oil, which also contained α-pinene (6.6 %), eugenol (4.4 %) and methyleugenol (1.8 %). Among the sesquiterpenes, β-caryophyllene was the major component constituting 1.9 % of the oil in the Nigerian sample, 10.5 % in the oil from Cameroon and 14–17 % in the oil from Pakistan. δ-Cadinene was present at about 4.3 % in the Indian sample, while sesquiphellandrene and caryophyllene epoxide were detected

at 1.2% and 0.5% respectively. These compounds are known for their anti-inflammatory, antimicrobial, antioxidant, anticancer, analgesic and insecticidal activities (7, 15, 30).

### Triterpenes and steroids

Triterpenes are a class of terpenoids composed of six isoprene units, with diverse biological activities. In *A. conyzoides*, friedelin has been identified as a major triterpene (6), while lupeol, a pentacyclic triterpenoid, has also been reported (34). Sterols, another key class of compounds, contribute significantly to the plant's pharmacological profile.  $\beta$ -sitosterol and stigmasterol are the main sterols isolated, along with minor constituents such as brassicasterol, dihydrobrassicasterol, spinasterol and dihydrospinasterol (6, 15).

### Phenolic acids and other compounds

Studies indicate that *A. conyzoides* contains several phenolic acids, including caffeic acid, chlorogenic acid, coumaric acid and hydroxybenzoates, identified using advanced chromatographic techniques such as UPLC-ESI-QToF-MS (35). Other compounds detected include (+)-sesamine, fumaric acid, phytol, various hydrocarbons and 12,6-methyl-heptadecenoic acid, which has insecticidal properties. The seed oil is rich in fatty acids such as oleic, palmitic, stearic, linoleic and linolenic acids. The leaves, flowers and pollen also contain amino acids such as cystine, leucine and histidine, while the flowers additionally contain vitamins A and B (7, 15). Qualitative phytochemical screening of *A. conyzoides* demonstrates the presence of numerous secondary metabolites, including tannins, phenols, coumarins, alkaloids, carbohydrates, steroids, terpenoids, glycosides, saponins, anthraquinones and amino acid. Quantitatively, coumarins, tannins, alkaloids and phenols are most abundant in the leaves (18). These diverse compounds collectively contribute to the plant's traditional medicinal uses.

### Studies of the plant's bioactivity

Studies on the bioactivity of *A. conyzoides* extracts show that the plant possesses a wide range of therapeutic and pharmacological properties attributed to its rich chemical composition (Table 3) (6).

### Pharmacological studies

#### Antidiabetic activity

Diabetes and its complications remain a major global public health problem. Current treatments aim to regulate blood glucose levels, but their side effects and the increasing number of diabetes justify the search for safer and more effective therapeutic alternatives (38). *Ageratum conyzoides* has traditionally been used to treat diabetes and several studies have been conducted to verify its efficacy. Experimental studies have confirmed the antidiabetic effects of *A. conyzoides* in streptozotocin-induced diabetic rats. Aqueous extracts of the plant's leaves, particularly at doses of 200 and 300 mg/kg, showed significant reductions in blood glucose levels, with one study reporting a 21.3 % decrease after 4 hr of administration (39). Additionally, the extracts stimulated body weight gain, reduced food and water intake and decreased urine excretion in diabetic rats. At these doses, the extract also improved lipid profiles by increasing high-density lipoprotein (HDL) cholesterol and reducing low-density lipoprotein (LDL) cholesterol and triglycerides (40, 41). Furthermore, the extracts elevated serum insulin and total protein levels, which confirm the plant's hypoglycemic and antihyperglycemic activities (8). The mechanism of action is thought to involve enhancement of insulin secretion and improvement of glucose metabolism, as

evidenced by increased insulin production in treated animals (42). Similar findings have shown that both aqueous and methanol extracts exert significant antihyperglycemic effects in alloxan-induced diabetic models (43). These results suggest that *A. conyzoides* may contain multiple antihyperglycemic compounds with distinct mechanisms of action, possibly related to flavonoids and phenolic compounds known for improving glucose utilization.

#### Antibacterial effect

Scientific investigations have demonstrated significant antibacterial properties of *A. conyzoides*, particularly with its extracts and essential oils. Ethanol extracts at 300 mg/mL showed strong antibacterial activity, with inhibition zones of 24–27 mm against pathogens such as *Salmonella* sp., *Enterobacter* sp., *Escherichia coli* and *Pseudomonas aeruginosa* (44). The minimum inhibitory concentration (MIC) values for ethanol extracts range from 50–75 mg/mL, while aqueous extracts show activity at 100 mg/mL for different plant parts. The minimum bactericidal concentration (MBC) of ethanol extracts was 50 mg/mL for leaves and stems and 75 mg/mL for flowers and roots. For *Staphylococcus aureus* and *E. coli*, both MIC and MBC were 120 mg/mL, whereas for *P. aeruginosa* and *Shigella dysenteriae*, they reached 160 mg/mL and 200 mg/mL respectively (44, 45). Another study on various human and animal pathogenic bacteria revealed that methanolic and ether extracts of *A. conyzoides* were particularly effective against oxidase-positive Gram-positive bacteria, showing 53.4 % sensitivity, while Gram-negative bacteria displayed lower sensitivity (4.9 % for oxidase-negative strains) (46). Moreover, flavonoids in the plant act as serine protease inhibitors, disrupting bacterial protein synthesis (47). Additionally, triterpenoids and coumarins present in the extracts contribute to the overall antibacterial effects (33, 34). These bioactive compounds may act synergistically to enhance the antimicrobial potential of *A. conyzoides*, which confirm its traditional use against bacterial infections and its potential relevance in the context of rising antibiotic resistance.

#### Antifungal activity

Several studies have confirmed the antifungal activity of *A. conyzoides* to support its traditional use in the treatment of fungal infections. The plant's efficacy is attributed to its diverse secondary metabolites such as chromenes, terpenoids, flavonoids and coumarins (3).

One of its major compounds, precocene II, has shown strong fungicidal activity against human pathogenic fungi including *Fusarium* spp., *Candida albicans* and *Aspergillus* spp., which cause aspergillosis in immunocompromised patients. A study indicates that it inhibited aflatoxin production in *Aspergillus flavus*, demonstrating its dual role in limiting both fungal growth restriction and toxin production (48, 49). Other studies have shown that essential oils of *A. conyzoides* possess significant antifungal activity (50). Compounds such as eugenol and  $\beta$ -caryophyllene in these oils inhibited the growth of *Candida* species, responsible for common infections such as oral thrush and vaginal candidiasis. These compounds act by disrupting fungal cell membranes and inhibiting spore germination, ultimately leading to cell death (3).

#### Wound healing property

Studies have shown that crude extracts of *A. conyzoides* significantly accelerate wound healing. In one experiment, the plant extract reduced the healing time of burn wounds in rabbits from 14 days (control with vaseline gauze) to 7 days (51). A comparative study

between *A. conyzoides* methanolic leaf extracts and honey showed faster wound contraction and fewer inflammatory cells on day 10 in the plant-treated group compared with the honey and control groups. Wounds treated with *A. conyzoides* also exhibited more fibrosis and fewer fibroblasts, indicating improved tissue repair (52). Similarly, topical application of ethanolic extracts on excision wounds in rats resulted in faster wound closure than controls. The extract promoted cell proliferation, collagen synthesis and epithelialization, improving tensile strength by about 40 % (53). The plant's wound-healing ability may be linked to its antimicrobial and anti-inflammatory compounds, notably flavonoids, terpenoids and phenolic acids.

#### **Anti-inflammatory property**

Chronic inflammatory diseases are a major global health concern worldwide (10). Although nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed, their adverse effects have prompted the search for safer plant-based alternatives (54). *Ageratum conyzoides* has demonstrated significant anti-inflammatory activity in both *in vivo* and *in vitro* models. In a carrageenan-induced paw edema test in Wistar rats, extracts of the plant produced 50.23 % inhibition of edema at the 4<sup>th</sup> hr, comparable to diclofenac sodium (54). Thus, ethanol extracts at 400 mg/kg reduced carrageenan and histamine-induced paw edema in rats by more than 57 %, similar to indomethacin (10). Crude extract of aerial parts and their ethanol, hexane, ethyl acetate and dichloromethane fractions along with isolated compounds such as 5'-methoxy nobiletin, 1,2-benzopyrone and eupalestin demonstrated potent anti-inflammatory effects. These compounds significantly reduced leukocyte infiltration, exudate protein concentration, myeloperoxidase, adenosine deaminase, nitric oxide metabolites and pro-inflammatory cytokines (IL-17A, IL-6, TNF- $\alpha$ , IFN- $\gamma$ ), while increasing anti-inflammatory IL-10 levels. They also inhibited NF- $\kappa$ B and p38 MAPK pathways activation (55). In another study, silver nanoparticles synthesized using *A. conyzoides* extracts exhibited strong anti-inflammatory effects by suppressing NLRP3 inflammasome activation and reducing the release of pro-inflammatory cytokines such as IL-1 $\beta$ , IL-18, TNF- $\alpha$  and caspase-1 (56). Additionally, the water-soluble fraction inhibited neutrophil migration and carrageenan-induced edema, while methanolic leaf extracts showed strong anti-arthritis and membrane-stabilizing activities (57, 58). The anti-inflammatory activity of *A. conyzoides* is mainly attributed to its polyphenolic compounds. These include quercetin, kaempferol, glycosides, tannins and flavonoids (10). Collectively, these findings provide a scientific basis for the potential of the plant as a promising source of new anti-inflammatory agents, particularly for the treatment of chronic inflammatory diseases such as rheumatoid arthritis.

#### **Analgesic effect**

Studies on *A. conyzoides* have shown significant analgesic properties. Aqueous extracts of the whole plant demonstrated notable analgesic activity in experimental animal models, significantly increasing reaction times in albino rats during tail immersion and muscle torsion tests (59). In addition, alcoholic extracts of the plant exhibited dose-dependent pain inhibition, achieving efficacy at high doses comparable to that of diclofenac (11, 54). The analgesic effects are attributed to phytochemical compounds such as flavonoids and terpenoids, which inhibit prostaglandin synthesis and modulate the inflammatory response (4, 6). Precocene I and II, present in the plant's essential oil, have also

shown effective relief of neuropathic pain comparable to pregabalin. These compounds are believed to act through the modulation of acute pain pathways within the mammalian central nervous system (60). A clinical study conducted on arthritis patients using an aqueous extract of the whole plant reported that 66 % of participants experienced pain relief, along with a 24 % improvement in joint mobility, with no adverse effects (61). Additionally, alkaloids and flavonoids found in the plant's oil appear to inhibit pain perception (62). The effectiveness of *A. conyzoides* in both acute and chronic pain models highlights its potential as a natural alternative for pain management.

#### **Antioxidant activity**

Several studies have demonstrated the significant antioxidant activity of *A. conyzoides*. Methanol and ethanol extracts of the plant, particularly from the leaves, exhibit strong antioxidant effects in DPPH ((1,1-diphenyl-2-picrylhydrazyl) and FRAP (Ferric Reducing Antioxidant Power) assays, with the ethanol extracts showing an IC<sub>50</sub> value of 24.8  $\mu$ g/mL in DPPH radical scavenging (49, 63). Methanol extract have been found to contain higher total phenolic (61.4 mg GAE/g) and flavonoid (42.2 mg QE/g) content than aqueous extracts and to exhibit superior lipid peroxidation inhibition, with IC<sub>50</sub> values of 94.21  $\mu$ g/mL in the pancreas and 75.95  $\mu$ g/mL in penile tissues (64). The antioxidant activity of *A. conyzoides* is strongly correlated with its flavonoid content (65). *In vivo* studies in diabetic rats showed that aqueous extracts at doses of 100 and 200 mg/kg significantly reduced lipid hydroperoxide levels, improved glycemia and increased FRAP (66). These findings confirm the plant's potent antioxidant capacity, largely attributed to flavonoids such as quercetin, kaempferol and apigenin.

#### **Anticancer property**

The anticancer property of *A. conyzoides* has been demonstrated through various *in vitro* and *in vivo* studies, indicating both cytotoxic and antitumoural activities against several types of cancer. Flavonoids isolated from the plant's extracts significantly inhibited proliferation, migration, invasion and clonality of human cervical adenocarcinoma (HeLa) cells by inducing S-phase cell cycle arrest and apoptosis, while reducing intracellular reactive oxygen species (ROS) levels (28). Other studies reported cytotoxic effects against lung carcinoma (A-549), leukemia (Jurkat and P-388), breast carcinoma (MDA-MB-231) and colon adenocarcinoma (HT-29), with ethylacetate extracts exhibiting IC<sub>50</sub> values as low as 0.68  $\mu$ g/ml (67, 68). Mechanistic studies revealed that the plant induces apoptosis through mitochondrial pathway activation, involving the opening of the mitochondrial permeability transition pore, release of cytochrome C and activation of caspase 3 and 7 (69). Essential oils from *A. conyzoides* leaves, in which precocene is the major constituent, have demonstrated anticancer activity by inhibiting the growth of SF-767, LNCaP, PC-3 and SF-763 cancer cell lines (70). The plant's pronounced antioxidant activity also helps counter oxidative stress, a known contributor to cancer progression, suggesting that its free radical scavenging ability may contribute to cancer prevention and therapy (63).

#### **Antimalarial property**

Malaria remains a major public health concern, particularly in sub-Saharan Africa, where medicinal plants such as *A. conyzoides* are traditionally used to treat the disease (71). Scientific studies have confirmed its antimalarial activity through the suppression and treatment of *Plasmodium berghei* infections in mice (72, 73). Aqueous

and methanolic extracts of the plant showed significant, dose-dependent antiplasmodial activity, with parasitemia suppression rates of up to 83 % in prophylactic tests at 200 mg/kg (72, 73). Moreover, most malaria deaths in Africa are caused by *Plasmodium falciparum*, due to the emergence of strains resistant to conventional drugs. Dichloromethane extracts of *A. conyzoides* showed efficacy against both chloroquine-resistant and chloroquine-sensitive strains of *P. falciparum*, with low IC<sub>50</sub> values (71). Similarly, aqueous and ethanolic extracts from leaves and stem demonstrated potent effects against the K1 chloroquine-resistant *P. falciparum* strain, with the ethanolic leaf extract showing the highest activity (74). These studies underscore the plant's potential as a candidate for developing new antimalarial agents, particularly against drug-resistant *Plasmodium* strains, though further pharmacological and toxicological studies are needed to confirm its clinical safety and efficacy.

#### Insecticidal effect

The insecticidal activity of *A. conyzoides* is among its most notable biological properties. The plant is effective against various insects, including *Musca domestica*, *Sitophilus zeamais*, *Schistocerca gregaria* and larvae of disease-carrying mosquitoes such as *Anopheles stephensi*, *Aedes aegypti*, *Anopheles gambiae* and *Culex quinquefasciatus* (15). Terpenoids, particularly precocenes, are mainly responsible for this insecticidal activity due to their anti-juvenile hormonal effects (17). The essential oil of the plant contains (Z)-6-methyl-12-heptadecenoic acid, which exhibits insecticidal and growth-regulatory activity against the desert locust *S. gregaria* (75). In another study, the plant extracts demonstrated potent insecticidal effects on *Spodoptera litura* larvae, with a 95 % mortality rate at a 12 % concentration, LC<sub>50</sub> and LC<sub>80</sub> values ranging from 3.45 % to 8.18 % (76). *Ageratum conyzoides* extracts were also effective in reducing populations of *Sitophilus oryzae*, significantly inhibiting adult emergence and preventing seed weight loss during food storage (77). These findings suggest that *A. conyzoides* could serve as a safe, eco-friendly alternative to synthetic pesticides for agricultural and vector control applications.

#### Other biological activities

*Ageratum conyzoides* also exhibits several other pharmacological properties. Its antispasmodic effect helps relieve muscle spasms in the gastrointestinal and respiratory systems (78). In male mice, essential oil of the plant induced relaxation of vas deferens contractions triggered by potassium chloride, with stronger effects on the tonic phase (79). Extracts of the root and aerial parts also relaxed isolated rat trachea, inhibiting 86 % of histamine and 79 % of 5-hydroxytryptamine (5-HT) activity. In isolated rat uterus, the extract inhibited 5-HT-induced contractions without affecting acetylcholine-induced ones, confirming specific antiserotonergic activity (80). These spasmolytic properties make the plant useful in managing conditions such as colic, asthma, bronchial spasms and premature ejaculation (78–80). The plant also possesses hematopoietic activity, demonstrated by increased hemoglobin concentration and red blood cell counts in rats treated with ethanol extracts (81). Its antidiarrheal effects have been confirmed in rat models, supporting its traditional use for gastrointestinal discomfort. Additionally, *A. conyzoides* provided protective effects against spray-induced lung damage in Wistar rats, with efficacy inversely proportional to the administered doses, suggesting potential applications in pulmonary disorders (82). A study in female rats further revealed that *A. conyzoides* improved insulin sensitivity, reduced inflammation and balanced key reproductive hormones. It

can also enhance antioxidant activity and restore ovarian and uterine structures, proving its potential in the treatment of polycystic ovary syndrome (83). Overall, these findings highlight the multifaceted pharmacological potential of *A. conyzoides*, making it a valuable candidate for the development of galenic formulations with diverse clinical applications.

#### Safety evaluation

*Ageratum conyzoides*, owing to its wide range of medicinal uses, has been the subject of several toxicological studies aimed at assessing its potential adverse effects. The results vary depending on the administered dose, extract type and duration of exposure. A study on hydroalcoholic extract at doses of 500 and 1000 mg/kg revealed hepatic, renal and haematological alterations in rats. These included elevated levels of liver enzymes -alanine amino transferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) - along with increased creatinine and glucose concentrations, normocytic anemia and thrombocytosis (29). Another study reported that doses of 1000 and 1500 mg/kg reduced AST, ALP, Lactate dehydrogenase (LDH) and creatinine kinase levels, but caused hepatocellular necrosis (84). Interestingly, at lower doses, *A. conyzoides* demonstrated hepatoprotective effect in other experimental models (85). In contrast, ethanolic extracts administered orally at doses of 200 - 600 mg/kg for 21 days did not produce significant changes in ALT, AST or ALP levels, suggesting an absence of toxicity at these concentrations (86). Similarly, subchronic oral administration of hydroalcoholic extracts at 250 and 500 mg/kg for 90 days produced no overt hepatotoxicity, though a mild reduction in liver enzyme activity was observed at the highest dose (87). Acute toxicity studies showed no mortality or clinical signs of toxicity up to 2000 mg/kg/day, establishing this as the No Observed Adverse Effect Level (NOAEL) (88). Furthermore, the maximum tolerable dose (MTD) was reported to exceed 5000 mg/kg in both acute and subacute toxicity evaluations (89). Regarding the essential oil, acute and subchronic toxicity studies in rats revealed LD<sub>50</sub> values of 1247.88 mg/kg for females and 1674.57 mg/kg for males. Subchronic exposure caused mild toxic signs, particularly in males, including reduced kidney weight and haematological abnormalities (90). Nevertheless, precocene II, a major constituent of the essential oil, demonstrated hypoglycemic properties without toxicity to major organs (91). It is important to note that *A. conyzoides* contains PAs, compounds known for their hepatotoxic, carcinogenic, genotoxic, teratogenic and pneumotoxic effects. The toxic effects reported in some studies may therefore be associated with the presence of these alkaloids (29). Finally, while *A. conyzoides* exhibits promising therapeutic properties, its safety profile is dose and extract-dependent. Factors such as extraction method, plant part used, exposure duration and individual susceptibility influence toxicity outcomes. Further comprehensive toxicological investigations, particularly chronic and high-dose studies are needed to clarify its safety for medicinal use and to guide standardized dosage formulations.

#### Limitations and future research directions

Although numerous studies have demonstrated the pharmacological potential of *A. conyzoides*, several limitations still constrain its clinical application. The majority of existing data come from *in vitro* and animal studies, with few well-controlled clinical trials to confirm safety and efficacy in humans. In addition, the lack of standardized extraction methods, variability in chemical composition due to geographical and environmental factors and

inconsistent experimental protocols make it difficult to compare findings across studies. Furthermore, toxicological data remain incomplete, particularly concerning long-term exposure and the effects of PAs, which are known to have hepatotoxic and genotoxic properties. These limitations highlight the need for more rigorous, reproducible and translational research.

Further research on *A. conyzoides* should therefore focus on validating and optimizing its traditional medicinal uses to facilitate its integration into conventional medicine. Research priorities should take into account the following areas:

### Standardization of extracts

Variability in chemical composition according to geographical location, climate and extraction methods is a major challenge in the use of medicinal plants like *A. conyzoides* in conventional medicine. Future research should aim to standardize extraction techniques to ensure consistent concentrations of active compounds such as flavonoids, alkaloids, precocenes I and II and terpenes. This will ensure reproducibility and reliability in preclinical and clinical applications (92, 93).

### Extensive preclinical studies

Based on its phytochemical composition, extensive preclinical studies using well-designed experimental models are needed to assess the plant's efficacy in treating diseases such as diabetes, malaria, diarrhoea, inflammation, cancer, microbial infections, liver disorders and diseases for which it is traditionally used (4). For instance, future studies could specifically explore:

- **Phytchemical synergy:** Examine potential synergistic or antagonistic interactions among major bioactive compounds (flavonoids, terpenes, precocenes) to understand their combined pharmacological effects (15).
- **Pharmacokinetics and bioavailability:** Characterize the absorption, delivery, metabolism and excretion of major bioactive constituents to inform dosage and clinical formulation strategies (94).
- **Endocrine and metabolic effects:** While several studies have documented the anti-diabetic activity of *A. conyzoides* (40), its influence on lipid metabolism, hormone regulation and thyroid function remains underexplored.
- **Hepatoprotective and hepatotoxic effects:** Although *A. conyzoides* shows hepatoprotective activity (85), some studies report hepatic cell damage linked to PAs (29). Quantifying these alkaloids and developing selective extraction techniques to minimize their presence are key priorities. Comparative studies between crude and PA-free extracts could clarify the therapeutic window.
- **Cancer treatment:** Despite evidence of anticancer effects (67), little research has focused on its ability to target cancer stem cells, which are responsible for tumour relapses and metastasis. Future research could assess its potential against these resistant cell populations.
- **Neuroprotective effect:** Given its antioxidant and anti-inflammatory properties (55), *A. conyzoides* may offer neuroprotective benefits. Experimental models of neurodegenerative diseases, such as Parkinson's and Alzheimer's, could help validate this potential.

### Formulations

Several *A. conyzoides*-based formulations such as gels, emulsified concentrates and nanoemulgels, have shown strong wound-

healing, anti-inflammatory and antimicrobial properties. However, few standardized pharmaceutical preparations using whole plant extracts or isolated compounds have been developed (3). Future work should therefore focus on designing and optimizing dosage forms such as capsules, tablets, ointments, nanoparticles, gels or transdermal patches containing well-characterized bioactive extracts or purified compounds. These formulations could target specific conditions (wound healing, inflammation, diabetes) based on the proven pharmacological activities. Moreover, although some studies report low toxicity at therapeutic doses (88, 89), long-term toxicological and pharmacokinetic studies remain essential to assess cumulative effects, define maximum safe doses and establish clinical safety parameters.

### Conclusion

Several studies have been carried out to demonstrate the anti-inflammatory, antimicrobial, antifungal, antioxidant, antidiabetic, antimalarial, insecticidal, antiprotozoal, anti-parasitic, anticancer effects of *A. conyzoides*. These pharmacological properties of the plant have been attributed to its composition of bioactive compounds such as flavonoids, alkaloids and terpenes, which also validate its traditional medicinal uses. However, the presence of PAs raises concerns about the toxicity of the plant, particularly with long-term use. To fully exploit the medicinal potential of the plant and ensure its safety, future research should focus on standardized extraction methods, long-term toxicological evaluations and rigorous preclinical and clinical trials. With such rigorous scientific validation, *A. conyzoides* could contribute to the development of improved and safe therapeutic formulations, bridging traditional medicine and modern pharmacotherapy.

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### Authors' contributions

GR, MN, AOB, NAA designed the study, drafted the manuscript, participated in its revision and validated the work. PN participated in the revision and validation. IC, LWS contributed to the writing, revision and validation. LB-M, ME contributed to the conceptualization, supervision and validation. All authors read and approved the final manuscript.

### Compliance with ethical standards

**Conflict of interest:** Authors do not have any conflict of interests to declare.

**Ethical issues:** None

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