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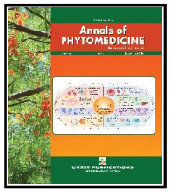

Review Article : Open Access

Phytochemical diversity, pharmacological activities and therapeutic potential of *Senna spectabilis* (DC.) H.S. Irwin and Barneby

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Abstract

Senna spectabilis (DC.) H.S. Irwin and Barneby (Fabaceae) is a tropical tree species widely recognised for its ethnomedicinal importance across South America, Africa, and Asia. For generations, different plant parts have been traditionally employed to manage infectious diseases, inflammatory conditions, parasitic infestations, neurological disorders and gastrointestinal disturbances. Growing scientific interest in this species is largely driven by the urgent need for alternative therapeutic agents capable of addressing antimicrobial resistance and neglected tropical diseases. Phytochemical investigations have demonstrated that *S. spectabilis* produces a diverse array of bioactive secondary metabolites. Piperidine alkaloids, particularly (-) cassine and (-) spectaline, are considered characteristic constituents of the species and serve as important chemotaxonomic markers. In addition, the plant contains anthraquinones, pentacyclic triterpenoids, flavonoids, phytosterols and structurally distinctive quinone methide triterpenoids. These compounds are associated with multiple experimentally validated biological activities, including antibacterial, antifungal, antileishmanial, antimalarial, anti-inflammatory, anticonvulsant, antioxidant and antiproliferative effects. Notably, quinone methide triterpenoids have demonstrated promising selectivity and potency against *Leishmania* species in preclinical models. Although, short-term toxicity studies suggest a favourable safety margin at therapeutic doses, comprehensive chronic toxicity, pharmacokinetic and controlled clinical studies remain limited. Further mechanistic and translational investigations are therefore essential to facilitate the development of standardised phytopharmaceutical formulations and novel drug leads from *S. spectabilis*.

1. Introduction

The accelerating emergence of antimicrobial resistance, the persistence of neglected tropical diseases, and the rising incidence of chronic inflammatory and neurological disorders have intensified global efforts to identify novel therapeutic agents. In this context, higher plants remain a crucial reservoir of structurally diverse and biologically active natural products. Historically, plant-derived compounds have played a central role in drug discovery, contributing to the development of widely used therapeutics such as anticancer, antimalarial, and analgesic agents. These successes highlight the continued relevance of phytochemical research in modern pharmacology and drug development (Atanasov *et al.,* 2015; Newman and Cragg, 2020). Moreover, plant-based medicines offer advantages including structural complexity, multi-target activity, and relatively lower toxicity, making them attractive candidates for addressing multifactorial diseases. Renewed scientific interest in medicinal plants is therefore both culturally rooted and strategically important, particularly in regions where traditional medicine remains a primary healthcare resource.

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The genus *Senna* (family Fabaceae) comprises over 350 species distributed across tropical and subtropical regions. Many species have long been utilised in traditional medicine for treating gastrointestinal, infectious, and inflammatory conditions. Their pharmacological importance is often attributed to the presence of anthraquinones, known for laxative effects, as well as other bioactive compounds with antimicrobial and anti-inflammatory properties (Lewis, 2016; Alshehri *et al.,* 2022). Among these, *S. spectabilis* have attracted increasing attention due to its extensive ethnomedicinal use and emerging pharmacological validation. *S. spectabilis* is widely used in traditional medicine for the treatment of fever, malaria, skin diseases, inflammation and gastrointestinal disorders, reflecting its broad ethnomedicinal relevance (Bargavi *et al*., 2025).

Native to tropical America and widely introduced into Africa and Asia, *S. spectabilis* is now naturalised across diverse ecological regions. Traditional systems of medicine report the use of it to manage constipation, fever, malaria, epilepsy, skin infections, inflammation, and gastrointestinal disorders (Nkantchoua *et al.,* 2018; Prameswari *et al.,* 2023). The recurrence of similar therapeutic applications across geographically distinct cultures suggests the presence of conserved bioactive constituents that merit systematic investigation.

Phytochemical studies reveal that *S. spectabilis* produces a diverse array of secondary metabolites. Piperidine alkaloids such as (–) cassine and (–) spectaline are considered characteristic compounds and serve as chemotaxonomic markers. Additional constituents include

anthraquinones, flavonoids, sterols, pentacyclic triterpenoids, and quinone methide triterpenoids, which exhibit notable antiprotozoal activity (Pivatto *et al.,* 2015; Monjane *et al.,* 2020). These compounds underpin a wide range of biological activities, including antimicrobial, antimalarial, anti-inflammatory, anticonvulsant, and antioxidant effects demonstrated in preclinical studies (Alshehri *et al.,* 2022).

Despite these promising findings, existing literature remains fragmented. Comprehensive understanding of its pharmacodynamics, molecular mechanisms, pharmacokinetics, long-term safety, and clinical efficacy is still limited. Therefore, this review aims to integrate current knowledge, critically evaluate available evidence, and identify research gaps to support future investigations and the development of standardised phytomedicinal products.

Unlike previous reviews that primarily focus on either ethnomedicinal applications or general pharmacological properties of *Senna* species, the present review integrates phytochemical diversity with experimentally validated pharmacological mechanisms and therapeutic implications. Particular emphasis is placed on correlating characteristic piperidine alkaloids and quinone methide triterpenoids with their biological activities, evaluating available toxicological evidence, and identifying barriers to clinical translation. This integrated approach provides a more comprehensive framework for understanding the medicinal value and drug-development potential of *S. spectabilis*.

2. Botanical description and distribution

2.1 Morphological characteristics

S. spectabilis is a fast-growing, deciduous tree reaching 5-20 m in height under favourable conditions, with trunk diameters up to 25-30 cm (Anoop *et al.,* 2025; Santos *et al.,* 2023). It may develop a single trunk or multiple stems, and its rapid canopy expansion enhances ecological adaptability, sometimes contributing to invasive behaviour (Suby and Santhoshkumar, 2024). The tree has a moderately straight bole and a broad, spreading crown that produces dense shade. The bark is smooth and greyish-brown in young plants but becomes rough and fissured with age. Leaves are alternate and paripinnate, measuring 30 to 40 cm long, with 4-15 pairs of opposite, elliptic to oblong leaflets (5-8 cm). The leaflets are glabrous with distinct venation and exhibit nyctinastic movement, folding at night. Seasonal leaf fall occurs during dry periods, confirming its deciduous nature (Santos *et al.,* 2023; Namirembe *et al.,* 2008). Flowering occurs in large terminal or axillary panicles (20-60 cm) bearing bright yellow, zygomorphic flowers. The androecium consists of seven fertile stamens and three staminodes, while the gynoecium has a superior ovary. Fruits are long cylindrical pods (15-40 cm) containing numerous hard-coated seeds with prolonged viability (García and Lima, 2008). Microscopically, leaves show anomocytic stomata, unicellular trichomes, calcium oxalate crystals, and lignified fibres, important pharmacognostic markers (Torey *et al.,* 2010).

2.2 Geographical distribution and ecology

S. spectabilis is native to the neotropical region, extending from southern Mexico and the Caribbean through Central America to South America, including Brazil, Bolivia, and Argentina (Lewis GP, 2016). It typically grows in seasonally dry tropical forests, moist deciduous forests, and open woodlands, showing adaptation to areas with distinct dry seasons and moderate rainfall. The species has been widely introduced as an ornamental and shade tree and is now naturalised across tropical Africa and Asia, including countries such as Nigeria, Kenya, India, Sri Lanka, and Thailand, as well as parts of northern Australia. Its rapid growth, abundant seed production, and environmental tolerance support its successful spread. Ecologically, *S. spectabilis* prefers well-drained soils and open, disturbed habitats such as roadsides, secondary forests, and degraded lands, growing up to 1,800 m elevation (García and Lima, 2008). Its aggressive colonisation and dense stand formation have led to its classification as an invasive species in regions like the Western Ghats of India (Suby and Santhoshkumar, 2024; Sudhabai, 2022).

3. Ethnomedicinal uses

S. spectabilis is widely used in traditional medicine across tropical regions, highlighting its ethnomedicinal significance. It is used as a traditional medicine in Southwestern Nigeria to manage fever, malaria, jaundice, and skin diseases (Soladoye *et al.,* 2012). Different plant parts-leaves, bark, roots, flowers, and pods are utilised to treat infectious, inflammatory, and gastrointestinal disorders. In South America, especially Brazil, leaf and flower decoctions are used as laxatives and purgatives due to their anthraquinone content (Viegas *et al.,* 2004). They are also used to manage fever, inflammation, and skin infections. In Colombia, bark and leaf infusions are used to treat diarrhoea and intestinal parasitic infections (de Gongora *et al.,* 1996).

In African countries such as Cameroon, Nigeria, Kenya, and Tanzania, *S. spectabilis* is used for epilepsy, insomnia, malaria, and gastrointestinal disorders (Bum *et al.,* 2010; Jiofack *et al.,* 2010; Njoroge and Bussmann, 2006). Leaf decoctions are administered for febrile illnesses, while crushed leaves are applied to treat fungal infections like ringworm (Chhabra *et al.,* 1984). In Mozambique, root and leaf extracts are used for diarrhoea, stomach pain, and respiratory conditions (Bruschi *et al.,* 2011).

In South and Southeast Asia, including India and Thailand, the plant is used for constipation, inflammation, and dermatological infections (Duraipandiyan *et al.,* 2006; Chuakul and Boonpleng, 2003; Gonfa *et al.,* 2023). The consistency of these uses across regions suggests the presence of bioactive compounds, supporting further pharmacological research (Jothy *et al.,* 2012; Alshehri *et al.,* 2022). WHO monographs also have reports that Senna species have stimulant laxative compounds due to their anthraquinone content; these compounds promote intestinal motility and are commonly employed in the management of constipation (WHO, 1999) (Table 1).

4. Chemical diversity and bioactive constituents

Phytochemical investigations of *S. spectabilis* have revealed a structurally diverse array of secondary metabolites distributed across different plant organs. Studies conducted over several decades indicate that the species is particularly rich in alkaloids, along with anthraquinones, terpenoids, sterols and phenolic compounds. This chemical heterogeneity provides a biochemical basis for its broad pharmacological profile. *S. spectabilis* exhibits remarkable chemical diversity, characterized by the presence of piperidine alkaloids, anthraquinones, flavonoids, phenolic compounds, terpenoids, and glycosides. These secondary metabolites are distributed across different plant parts, including leaves, flowers, seeds, bark, and roots, contributing to the species' broad spectrum of biological activities.

The structural diversity of these phytochemicals enhances their pharmacological potential and supports the utilisation of *S. spectabilis* in traditional and modern medicine. The rich phytochemical profile of tropical medicinal plants underscores their importance as valuable sources of bioactive compounds for therapeutic applications (Kabinesh *et al*., 2025).

Table 1: Region-wise utility of *S. spectabilis*

Region	Community/system	Plant part	Preparation and administration	Ailments treated	References
South America					
Brazil	Folk medicine, Afro-Brazilian	Leaves, flowers, pods	Decoction (oral), poultice (topical)	Constipation, purgative, malaria, flu, fever, headache, inflammation, skin infections	Viegas *et al.,* 2004
Colombia	Traditional healers	Bark, leaves	Infusion, maceration	Fever, diarrhoea, intestinal parasites	Góngora *et al.,* 1996
Africa					
Cameroon	Baka pygmies, folk medicine	Leaves, root, bark	Decoction (oral), crushed paste (topical)	Epilepsy, insomnia, anxiety, malaria, cough, wounds	Bum *et al.,* 2010; Jiofack *et al.,* 2010
Mozambique	Local communities	Roots, leaves	Decoction (oral)	Diarrhoea, stomach-ache, tuberculosis, asthma, and general pain	Bruschi *et al.,* 2011
Nigeria (Southwest)	Yoruba traditional medicine	Leaves	Infusion (oral), bath	Fever, malaria, jaundice, and skin diseases	Soladoye *et al.,* 2012
Kenya	Kamba community	Root, bark	Decoction (oral)	Stomach disorders, venereal diseases	Njoroge and Bussmann, 2006
Tanzania	Traditional healers	Leaves	Crushed juice (topical)	Ringworm, fungal skin infections	Chhabra *et al.,* 1984
Asia					
India (Tamil Nadu)	Paliyar tribe	Leaves, bark	Paste (topical), powder (oral with honey)	Skin diseases, wounds, ulcers, microbial infections	Duraipandiyan *et al.,* 2006
Thailand	Folk medicine	Leaves, flowers	Decoction (oral), steam bath	Ringworm, itching, inflammation, detoxification	Gonfa *et al.,* 2023; Chuakul and Boonpleng, 2003
Malaysia	Traditional Malay medicine	Leaves	Poultice, wash	Antimicrobial, antifungal, postpartum care	Ong and Norzalina, 1999
General Uses	Various	Seeds, pods	Powder, infusion	Laxative, purgative (common to many *Senna* species)	WHO Monographs, 1999

4.1 Piperidine alkaloids

Piperidine alkaloids represent the most characteristic and extensively studied class of metabolites in *S. spectabilis*. Early isolation studies identified (–) spectaline and (–) iso-6-cassine from the leaves, followed by the discovery of spectalinine and iso-6-carnavaline from seeds (Christofidis *et al.,* 1977a; 1977b). These compounds belong to the rare group of 2,6-dialkyl-3-hydroxypiperidine derivatives, typically bearing long aliphatic side chains that contribute to their biological activity.

Subsequent investigations expanded the alkaloid profile to include 3-O-acetylspectaline, 7-hydroxyspectaline and cassinicine in flowers, fruits and aerial parts (Viegas *et al.,* 2004). Advanced analytical techniques such as electrospray ionisation tandem mass spectrometry have facilitated rapid profiling and detection of additional alkaloid analogues, highlighting considerable chemical complexity within crude extracts (Pivatto *et al.,* 2005). These alkaloids are regarded as chemotaxonomic markers of the species and are largely responsible for its neuropharmacological and antiprotozoal activities.

4.2 Anthraquinones and related compounds

Although present in comparatively lower concentrations than alkaloids, anthraquinones constitute another important phytochemical group. Compounds such as emodin, chrysophanol and physcion have been identified in leaves and seeds (Silva *et al.,* 2012). Anthraquinones are widely recognised for their laxative effects through stimulation of intestinal peristalsis, as well as for antimicrobial and antioxidant properties. Their biological activity is often attributed to interference with microbial cell wall integrity, inhibition of nucleic acid synthesis and redox modulation.

4.3 Terpenoids and quinone methide triterpenoids

Pentacyclic triterpenoids, including friedelin, α-amyrin, β-amyrin, lupeol, ursolic acid, oleanolic acid and betulinic acid, have been reported from roots and bark (Silva *et al.,* 2012; Monjane *et al.,* 2020). These compounds are associated with anti-inflammatory, hepatoprotective and antimicrobial effects. Of particular significance is the isolation of the quinone methide triterpenoid 17 (methoxycarbonyl)-28-nor-isoiguesterin from the roots, which demonstrated

potent leishmanicidal activity (Monjane *et al.,* 2020). The occurrence of this structurally uncommon compound class enhances the chemotaxonomic and pharmacological relevance of the species.

4.4 Phenolics, flavonoids and sterols

Flavonoids such as quercetin and kaempferol, along with their glycosides, have been detected in leaves and flowers (Sangetha *et al.,* 2008). These compounds contribute to antioxidant and anti-inflammatory properties through free radical scavenging and modulation of cellular signalling pathways. Simple phenolics, including gallic acid and ellagic acid, as well as coumarins such as scopoletin, have also been reported (Monjane *et al.,* 2020). Additionally, phytosterols such as β-sitosterol and stigmasterol occur in aerial parts and may contribute to membrane-stabilising and anti-inflammatory effects (Silva *et al.,* 2012).

Overall, the phytochemical profile of *S. spectabilis* demonstrates considerable structural diversity, with alkaloids serving as signature constituents and terpenoids, anthraquinones and phenolics contributing to its multipronged pharmacological potential. Continued metabolomic and bioactivity-guided fractionation studies are warranted to identify novel derivatives and clarify structure activity relationships. Figures 1, 2, and 3 show the chemical structures of alkaloids.

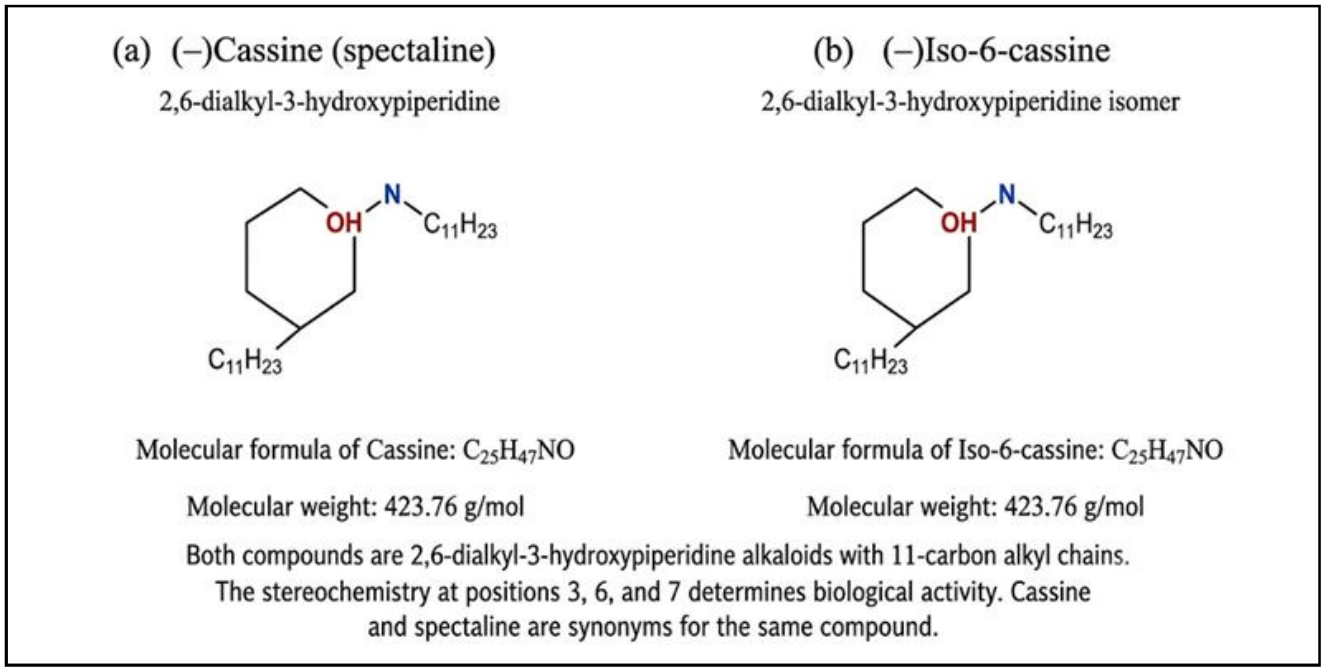

Figure 1: Molecular structures of (–) cassine and (–) spectaline, major piperidine alkaloids isolated from *S. spectabilis*. Adapted from Christofidis *et al.* (1977a, 1977b); Viegas *et al.* (2004).

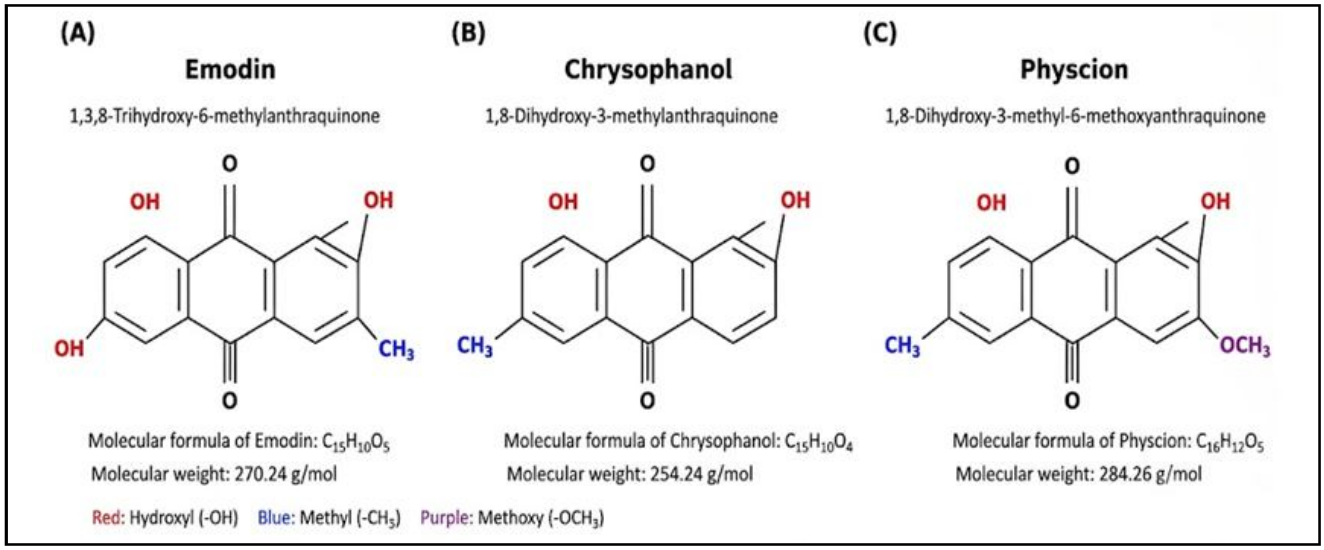

Figure 2: Chemical structures of representative anthraquinones (emodin, chrysophanol and physcion) reported in *S. spectabilis*. Adapted from Silva *et al.* (2012); Kim *et al.* (2004).

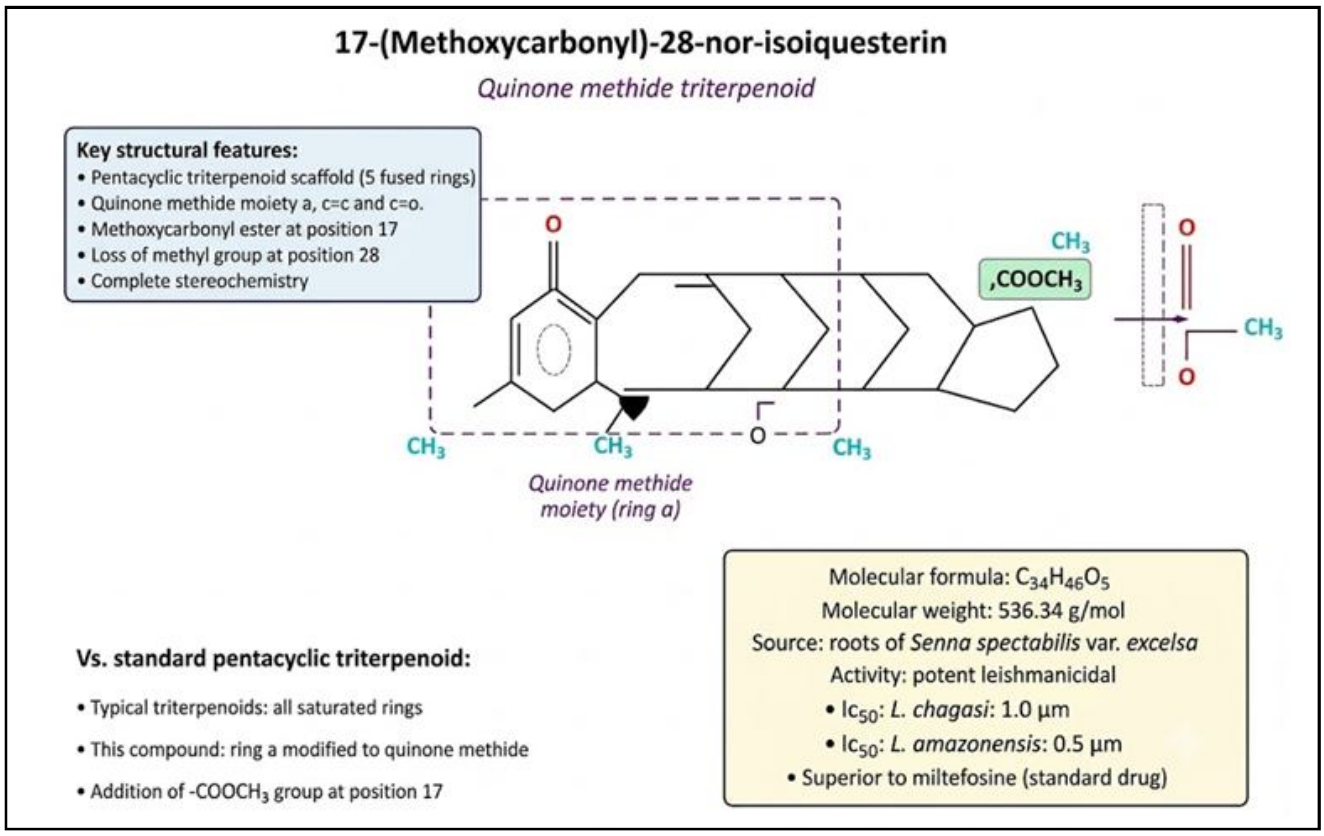

Figure 3: Chemical structure of the quinone methide triterpenoid 17-(methoxycarbonyl)-28-nor-isoiguesterin isolated from roots of *S. spectabilis*. Adapted from Monjane *et al.* (2020).

The biological activities reported for *S. spectabilis* are closely associated with its major phytochemical constituents. Piperidine alkaloids such as (–) cassine and (–) spectaline possess a hydroxylated piperidine nucleus and long aliphatic side chains that facilitate interactions with biological membranes and neuronal targets, contributing to anticonvulsant, antinociceptive and anti-inflammatory activities. Structural modifications, including hydroxylation and acetylation, may influence lipophilicity and receptor-binding affinity (Kumar *et al*., 2023). Similarly, quinone methide triterpenoids contain an electrophilic quinone methide moiety that can react with nucleophilic protein residues, thereby affecting parasite-specific enzymes involved in redox regulation and survival. Anthraquinones exert antimicrobial and laxative activities through redox cycling and stimulation of intestinal motility. At the same time, flavonoids contribute antioxidant and anti-inflammatory effects through free-radical scavenging and modulation of signalling pathways (Yang *et al*., 2025). These observations indicate that the pharmacological profile of *S. spectabilis* is strongly linked to its unique chemical architecture and support further structure activity relationship investigations (Kumar *et al*., 2023).

Table 2: Phytochemical constituents reported from different parts of *S. spectabilis*

Class	Compound name formula	Molecular	Plant part	References
Piperidine alkaloids	(–) Cassine (spectaline)	$C_{28}H_{57}NO$	Leaves, flowers, seeds	Christofidis *et al.,* 1977
	(–) Iso-6-Cassine	$C_{28}H_{57}NO$	Leaves, flowers	
	(–) Spectalinine	$C_{29}H_{59}NO_2$	Seeds	
	(–) Iso-6-Carnavaline	$C_{29}H_{59}NO_2$	Seeds	
	(–) 3-O-Acetylspectaline	$C_{30}H_{59}NO_2$	Flowers, fruits	Viegas *et al.,* 2004
	(–) 7-Hydroxyspectaline	$C_{28}H_{57}NO_2$	Flowers	Viegas *et al.,* 2004
	Iso-6-Spectaline	$C_{28}H_{57}NO_2$	Flowers	
	Cassinicine	$C_{20}H_{39}NO_2$	Leaves	

Anthraquinones	Emodin	$C_{15}H_{10}O_5$	Seeds, leaves	Kim *et al.,* 2004
	Chrysophanol	$C_{15}H_{10}O_4$	Seeds, leaves	Viegas *et al.,* 2004
Triterpenoids	Friedelin	$C_{30}H_{50}O$	Roots, bark	Monjane *et al.,* 2020
	β-Amyrin	$C_{30}H_{50}O$	Roots, leaves	Silva *et al.,* 2012
	α-Amyrin	$C_{30}H_{50}O$	Roots, leaves	
	Lupeol	$C_{30}H_{50}O$	Roots, bark	Monjane *et al.,* 2020
	Ursolic acid	$C_{30}H_{48}O_3$	Roots, leaves	Silva *et al.,* 2012
	Oleanolic acid	$C_{30}H_{48}O_3$	Roots, leaves	
	Betulinic acid	$C_{30}H_{48}O_3$	Leaves	
Quinone methide triterpenoid	17-(Methoxycarbonyl) -28-nor-isoiguesterin	$C_{29}H_{38}O_4$	Roots	Monjane *et al.,* 2020
Sterols	β-Sitosterol	$C_{29}H_{50}O$	Leaves, flowers	Viegas *et al.,* 2007
	Stigmasterol	$C_{29}H_{48}O$	Leaves, flowers	
Flavonoids	Quercetin	$C_{15}H_{10}O_7$	Leaves, flowers	Sangetha *et al.,* 2008
	Kaempferol	$C_{15}H_{10}O_6$	Leaves, flowers	
Others	Scopoletin (coumarin)	$C_{10}H_8O_4$	Roots	Monjane *et al.,* 2020
	Caffeine (purine alkaloid)	$C_8H_{10}N_4O_2$	Leaves	Silva *et al.,* 2012
	Octandronic acid	$C_8H_{16}O_4$	Roots	Monjane *et al.,* 2020

5. Pharmacological activities: Evidence-based validation

5.1 Antimicrobial activity

Extracts of *S. spectabilis* have demonstrated broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria, as well as selected fungal pathogens. Methanolic and ethanolic leaf extracts exhibit inhibitory effects against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Bacillus subtilis* in agar diffusion and broth microdilution assays (Krishnan *et al.,* 2010; Sangetha *et al.,* 2008). Reported activity varies depending on extract polarity and concentration, with moderate to strong inhibition observed in several studies.

The antimicrobial potential is primarily attributed to piperidine alkaloids, anthraquinones and flavonoids. Alkaloids such as (–) cassine and (–) spectaline may disrupt microbial membrane integrity and interfere with essential enzymatic pathways. Phenolic constituents contribute through membrane destabilisation and oxidative stress induction within microbial cells (Oladeji *et al.,* 2021). Alkaloid fractions of *S. spectabilis* have also demonstrated inhibitory activity against *Mycobacterium tuberculosis*, indicating potential antimycobacterial properties (Cantrell *et al.,* 2001)

In antifungal assays, leaf extracts have shown activity against dermatophytic fungi, including *Candida albicans* and *Aspergillus* species, supporting traditional use in treating cutaneous infections (Sangetha *et al.,* 2008). The observed effects are likely associated with phenolic-mediated membrane disruption and inhibition of fungal cell wall synthesis.

Although, *in vitro* findings are promising, most studies remain preliminary and lack standardised comparisons of minimum inhibitory concentration (MIC) values with those of conventional antibiotics. Future investigations should emphasise bioactivity-guided fractionation, elucidation of mechanisms, and studies of synergistic interactions with existing antimicrobial agents.

Table 3: Antimicrobial activity profile of *S. spectabilis* extracts against selected pathogens

Test organism	Plant part	Extract type	Key parameter (MIC/IZD)	References
Bacillus subtilis	Leaves	Acetone	0.625 mg/ml	Krishnan *et al.,* 2010
Staphylococcus aureus	Leaves	Methanol	1.25 mg/ml	
Escherichia coli	Leaves	Methanol	2.5 mg/ml	
Pseudomonas aeruginosa	Flowers	DCM fraction	IC_{50} : 0.6 µg/ml	Melo *et al.,* 2014
Candida albicans	Leaves	Methanol	6.25 mg/ml	Sangetha *et al.,* 2008
Aspergillus niger	Flowers	Methanol	12 mm IZD	
Mycobacterium tuberculosis	Not specified	Alkaloid fraction	Inhibitory at 50 µg/ml	Cantrell *et al.,* 2001

5.2 Antiparasitic and antiprotozoal activity

5.2.1 Leishmanicidal activity

Leishmanicidal activity represents one of the most promising therapeutic applications of *Senna spectabilis*, demonstrating significant efficacy against multiple *Leishmania* species through diverse mechanistic pathways. Dichloromethane fraction (FL-DCM) isolated from flowers exhibits remarkable potency against *Leishmania major* promastigotes with an IC_{50} value of 0.6 µg/ml, while purified alkaloid mixtures of (–) cassine and (–) spectaline demonstrate an IC_{50} of 24.9 µg/ml, both displaying favourable selectivity indices through negligible cytotoxicity to mammalian macrophages, indicating therapeutic safety margins essential for drug development (Melo *et al.,* 2014). Most notably, the quinone methide triterpenoid 17-(methoxycarbonyl)-28-nor-isoiguesterin isolated from roots demonstrates superior antiprotozoal activity against *L. amazonensis* and *L. braziliensis* with IC_{50} values of 9.6 and 6.3 µm, respectively, significantly outperforming miltefosine, the current standard antileishmanial chemotherapeutic agent (Monjane *et al.,* 2020). The proposed multitarget mechanism involves the quinone methide moiety functioning as a Michael acceptor, enabling nucleophilic addition reactions with critical cysteine residues in parasite thiol-dependent enzymes, thereby disrupting essential metabolic processes. Additional mechanistic pathways include induction of mitochondrial dysfunction through membrane potential dissipation, selective inhibition of trypanothione reductase, a unique antioxidant enzyme critical for trypanosomatids survival absent in mammalian hosts and perturbation of cellular redox homeostasis leading to accumulation of reactive oxygen species and subsequent parasite death, collectively establishing *S. spectabilis* as a promising natural source for developing novel antileishmanial therapeutics.

5.2.2 Antimalarial activity

S. spectabilis has a long history of traditional use in the treatment of malaria in several tropical regions, a practice that has gained scientific support through pharmacological studies. Crude extracts of the plant have demonstrated notable *in vitro* antiplasmodial activity against *Plasmodium falciparum*, validating its ethnomedicinal relevance (Tona *et al.,* 1999). This activity is largely attributed to the presence of piperidine alkaloids, which are believed to disrupt critical biochemical processes within the parasite. Proposed mechanisms include interference with hemozoin formation, leading to toxic heme accumulation, and inhibition of key metabolic pathways essential for parasite survival and replication.

5.3 Anti-inflammatory and analgesic activity

In vivo studies demonstrate significant analgesic and anti-inflammatory activities of the piperidine alkaloids (–) cassine and (–) spectaline from *Senna spectabilis*. In murine models, both compounds reduced acetic acid-induced writhing, indicating inhibition of peripheral nociception mediated by inflammatory mediators such as prostaglandins and bradykinin (Alexandre-Moreira *et al.,* 2007; Viegas *et al.,* 2008). They also suppressed pain behaviour in the late phase of the formalin test, suggesting effects on inflammatory pain and central sensitisation, while showing minimal impact on the early neurogenic phase.

Mechanistically, (–) cassine reduced exudate formation and leukocyte migration in carrageenan-induced pleurisy, along with decreased levels of Prostaglandin E2, Interleukin 1 beta, Interleukin 6, and Keratinocyte chemoattractant, indicating modulation of cyclo oxygenase and cytokine pathways (Da Silva *et al.,* 2012). Both alkaloids also inhibited lipid peroxidation, highlighting antioxidant activity that contributes to reduced oxidative stress and inflammation (Viegas *et al.,* 2007). These findings support their therapeutic potential as anti-inflammatory and analgesic agents.

5.4 Neuropharmacological activity: CNS depression

5.4.1 Anticonvulsant activity

Leaf extracts of *S. spectabilis* and the isolated piperidine alkaloid iso-6-cassine have demonstrated significant anticonvulsant activity in experimental animal models, providing pharmacological validation for the plant's traditional use in epilepsy management. *In vivo* studies showed effective protection of mice against seizures induced by pentylenetetrazol and maximal electroshock, two well-established models for evaluating antiepileptic potential (Bum *et al.,* 2010; Silva *et al.,* 2011). The observed effects suggest modulation of neuronal excitability, possibly through interaction with GABAergic neurotransmission or inhibition of seizure propagation pathways. These findings highlight the therapeutic promise of *S. spectabilis* alkaloids as leads for the development of novel anticonvulsant agents.

5.4.2 Sedative and anxiolytic activity

Administration of the extract significantly extended pentobarbital-induced sleep duration in experimental models and produced a marked decrease in locomotor and exploratory activity in both open-field and elevated plus-maze paradigms. These behavioural alterations suggest central nervous system depressant activity, consistent with sedative and potential anxiolytic properties (Bum *et al.,* 2010).

5.4.3 Mechanism

The anticonvulsant effect is likely mediated through modulation of the gamma-aminobutyric acid (GABAergic) system, reflecting the central role of GABA as the primary inhibitory neurotransmitter in the mammalian central nervous system. Enhancement of GABAergic neurotransmission reduces neuronal excitability by increasing chloride ion influx into neurons, resulting in membrane hyperpolarisation and stabilisation of neuronal firing. This suppresses the abnormal, synchronised electrical discharges that underlie epileptic seizures. Such a mechanism is shared by several clinically used anticonvulsant and sedative drugs, including benzodiazepines and barbiturates, which act by potentiating GABA receptor function.

5.5 Antioxidant activity

Methanolic extracts derived from the leaves, stems, and flowers of *S. spectabilis* have shown significant antioxidant potential *in vitro*, demonstrated through dose-dependent radical scavenging activity in 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,22 -azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) assays. These colorimetric assays are commonly employed to assess the capacity of phytochemicals to donate electrons or hydrogen atoms, thereby neutralising reactive oxygen species and stabilising free radicals. Recent phytochemical analyses indicate that the antioxidant capacity of *Senna* species is strongly correlated with total phenolic and flavonoid content, compounds recognised for their redox-modulating and chain-breaking antioxidant mechanisms (Alshehri *et al.,* 2022; Oladeji *et al.,* 2021).

Phenolic constituents such as flavonoids and related polyphenols act by interrupting radical propagation, chelating transition metals and enhancing endogenous antioxidant defences. Such mechanisms may contribute to the mitigation of oxidative stress-mediated cellular damage, which is implicated in inflammation, neurodegeneration and metabolic disorders (Xu *et al.,* 2017). The antioxidant activity observed in *S. spectabilis* extracts therefore provides a biochemical rationale for several of its experimentally reported pharmacological effects, particularly its anti-inflammatory and cytoprotective properties.

5.6 Cytotoxic and antiproliferative activity

Piperidine alkaloids isolated from the flowers exhibited selective cytotoxic activity against KB cells (nasopharyngeal carcinoma), indicating their potential as anticancer agents. Their positive response in a mutant yeast (*Saccharomyces cerevisiae*) assay suggests an ability to induce DNA damage, pointing toward a possible genotoxic mechanism of action (Bolzani *et al.,* 1995; Gonfa *et al.,* 2023). Such activity implies interference with cellular replication and repair pathways. However, these preliminary findings are largely based on *in vitro* and model-organism assays. Therefore, detailed testing in laboratory cell cultures and in living organisms is necessary to clearly understand how effective these compounds are, how selectively they act on cancer cells, and whether they are safe for use without causing harmful side effects.

5.7 Antihyperglycemic and hepatoprotective activity

Preliminary pharmacological studies suggest that *Senna spectabilis* possesses antihyperglycemic potential, lending scientific support to its traditional use in the management of metabolic disorders. Experimental investigations in animal models have reported a significant reduction in blood glucose levels following administration of plant extracts, indicating possible insulin-sensitising effects or enhanced peripheral glucose utilisation (Mazumder *et al.,* 2008). Although the precise mechanisms remain unclear, the activity may be associated with the presence of bioactive alkaloids, flavonoids, and phenolic compounds known to influence carbohydrate metabolism, inhibit intestinal glucose absorption, or modulate oxidative stress linked to diabetes. In addition, the hepatoprotective potential of *S. spectabilis* is an emerging area of interest. While direct evidence is limited, closely related species such as *Cassia fistula* have demonstrated marked protection against chemically induced liver damage, including normalisation of liver enzymes and histopathological recovery (Bhakta *et al.,* 1999). Given the shared phytochemical constituents, particularly flavonoids and triterpenoids, *S. spectabilis* warrants focused investigation as a promising candidate for hepatoprotective drug discovery.

6. Toxicological and safety assessment

Available toxicological studies indicate that *S. spectabilis* has a relatively favourable safety profile at tested doses. Acute oral toxicity studies following Organisation for Economic Co-operation and Development (OECD) guidelines show no mortality or major behavioural changes in rodents at doses up to 2000 mg/kg body weight, suggesting a Lethal Dose, 50% (LD_{50}) above this level and classifying the plant as practically non-toxic (Nkantchoua *et al.,* 2018; Alshehri *et al.,* 2022).

Subacute studies further report no significant alterations in body weight, organ weights, haematological parameters, or liver and kidney function markers within therapeutic ranges, indicating minimal cumulative toxicity during short-term exposure (Oladeji *et al.,* 2021; Alshehri *et al.,* 2022). Cytotoxicity studies show that crude extracts are generally low in toxicity, while isolated alkaloids such as (–) cassine and (–) spectaline exhibit selective antiproliferative effects against tumour cells with lower toxicity toward normal cells (Nascimento *et al.,* 2020; Franca *et al.,* 2022).

However, safety gaps remain, particularly regarding genotoxicity and long-term use. Anthraquinone-containing preparations may cause gastrointestinal irritation, electrolyte imbalance, and hypokalaemia with prolonged use, and use during pregnancy is contraindicated (Samavati *et al.,* 2017; Bernstein *et al.,* 2021). Further chronic and clinical studies are required.

In addition to acute and subacute toxicity assessments, a comprehensive toxicological evaluation should include chronic toxicity, reproductive toxicity, developmental toxicity, mutagenicity and carcinogenicity studies. Current evidence is insufficient to determine the safety of prolonged administration or repeated exposure to isolated alkaloids and quinone methide triterpenoids. Herb–drug interaction studies are also lacking despite the possibility that bioactive alkaloids may influence cytochrome P450-mediated drug metabolism. Furthermore, variability in phytochemical composition resulting from geographical origin, environmental conditions and extraction procedures may affect both efficacy and safety profiles. Establishment of acceptable daily intake limits and standardised safety parameters, therefore remains an important prerequisite for future clinical development (Latif and Nawaz., 2025).

7. Standardisation, quality control, and phytomedicine development

For reproducible efficacy and safety, standardisation of *S. spectabilis* preparations is required.

Marker compounds

(–) Cassine/spectaline (alkaloids) and/or emodin (anthraquinone) are the probable markers for standardisation.

Analytical methods

TLC/HPTLC for fingerprinting and semi-quantification (Torey *et al.,* 2010); HPLC-DAD/UV for precise quantification of marker compounds; GC-MS for profiling of volatile and alkaloid components (Pivatto *et al.,* 2005); Spectroscopic techniques, including Fourier-transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR) for chemical fingerprinting and authentication.

8. Translational significance and pharmaceutical prospects

The promising pharmacological activities of *S. spectabilis* position the species as a potential source of future phytopharmaceutical products and lead compounds. Piperidine alkaloids may serve as templates for the development of novel neuroactive and anti-inflammatory agents, whereas quinone methide triterpenoids represent attractive candidates for antileishmanial drug discovery. Nevertheless, translation from laboratory research to clinical application requires systematic pharmacokinetic characterisation, toxicity profiling, formulation optimisation and regulatory standardisation. Development of standardised extracts, identification

of validated biomarkers and implementation of good agricultural and collection practices (GACP) will be essential to ensure consistent quality and reproducibility. Collaboration among phytochemists, pharmacologists, toxicologists and clinical researchers will be necessary to advance promising compounds from preclinical evaluation to therapeutic use (Latif and Nawaz, 2025).

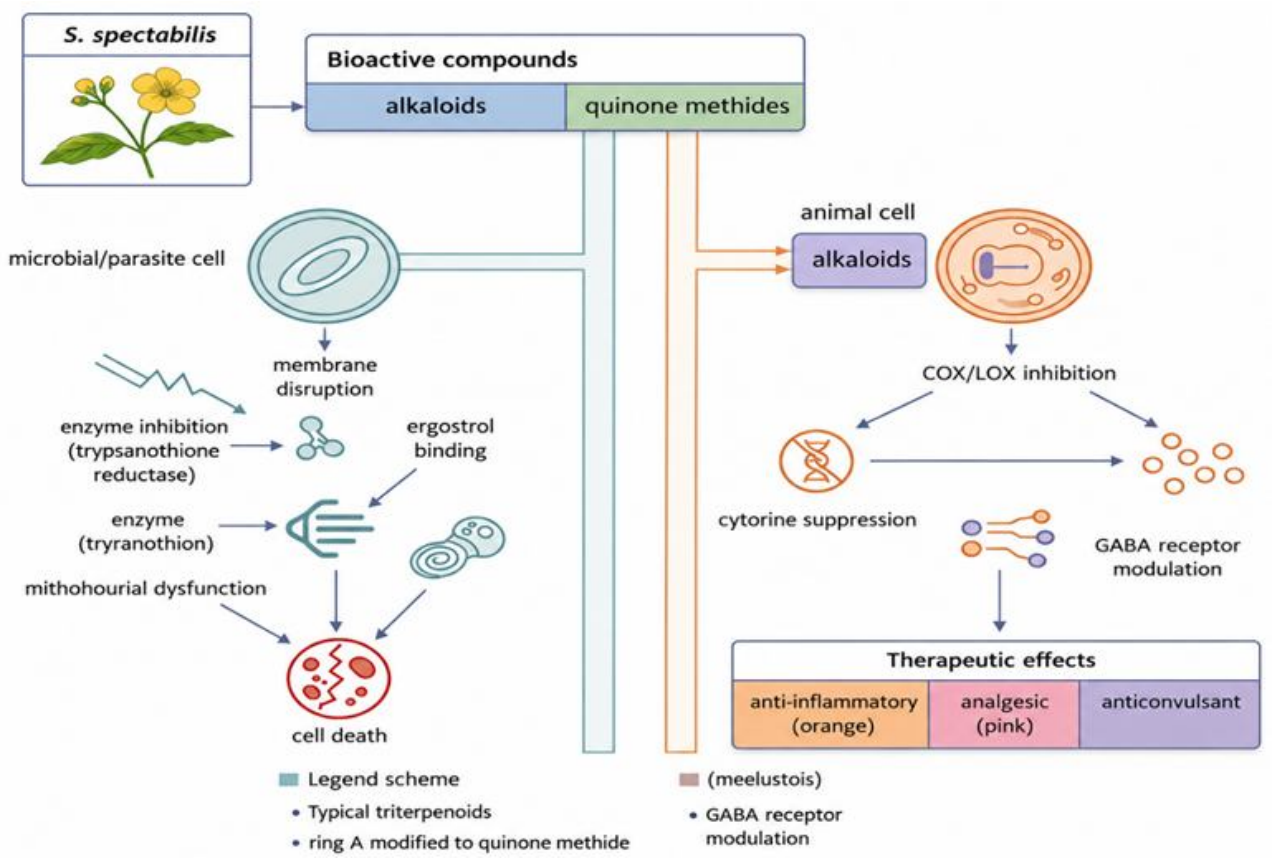

Figure 4: Proposed multitarget pharmacological mechanisms of major bioactive compounds from *S. spectabilis*.

9. Current research gaps and future perspectives

I. **Clinical trials:** A major gap. Conducting strict Phase I (safety) and Phase II (efficacy) trials for prioritised indications for neglected diseases, such as cutaneous leishmaniasis and fungal infections, is necessary.

II. **Mechanistic deep dive:** The specific molecular targets of major alkaloids and quinone methides need to be systematically identified. This can be achieved using integrated approaches such as proteomics and metabolomics to elucidate affected proteins and metabolic pathways, along with molecular docking studies to predict and validate compound-target interactions at the molecular level.

III. **Synergy studies:** More scientific studies must be carried out to find how phytochemicals from plants can work together with or enhance the effectiveness of standard antibiotics and antifungals to fight against infections that have become drug-resistant.

IV. **Pharmacokinetics and drug delivery:** ADME (absorption, distribution, metabolism, excretion) studies; development of new formulations such as nanoparticles and liposomes that enhance bioavailability.

V. **Sustainable sourcing:** Developing well defined agro techniques for systematic cultivation is crucial to provide long term sustainability and reproducible quality of plant material.

VI. **Endophyte exploration:** The endophytic fungus *Phomopsis cassiae* from this plant produces unique cadinane sesquiterpenes with antifungal activity, representing an untapped reservoir of novel chemistry (Silva *et al.,* 2006).

VII. **Broad-spectrum screening:** Testing for activity against other WHO-listed priority pathogens (ESKAPE pathogens, *Cryptococcus*).

10. Conclusion

S. spectabilis represent a pharmacologically promising medicinal tree supported by substantial ethnobotanical relevance and experimental validation. Accumulated evidence demonstrates that the species is a rich source of structurally diverse secondary metabolites, particularly piperidine alkaloids, anthraquinones, pentacyclic triterpenoids and quinone methide triterpenoids. These bioactive constituents underpin a broad spectrum of biological activities, including antimicrobial, antifungal, antiprotozoal, anti-inflammatory, analgesic, anticonvulsant and antioxidant effects validated through *in vitro* and *in vivo*

models. Among these activities, the leishmanicidal potential of quinone methide triterpenoids and the neuropharmacological properties of piperidine alkaloids emerge as particularly noteworthy. Toxicological investigations indicate a comparatively favourable safety margin at therapeutic doses; however, long-term toxicity, reproductive safety and herb-drug interaction studies remain insufficiently explored. Despite considerable phytochemical and pharmacological progress, translational advancement toward clinical application is limited by the absence of pharmacokinetic profiling, molecular target elucidation and controlled human trials. Future research should prioritise mechanistic studies, standardised extract development, ADME characterisation and well-designed clinical evaluations.

Additionally, sustainable cultivation strategies are essential to ensure reproducible phytochemical quality and conservation of natural populations. Even though there is encouraging pharmacological evidence, the majority of available studies remain preclinical, highlighting the need for greater methodological rigour and translational research. Future investigations should prioritise evidence-based validation through standardised experimental designs, mechanistic studies, pharmacokinetic assessment and controlled clinical trials. Addressing these limitations will facilitate the transformation of *S. spectabilis* from a traditionally utilised medicinal plant into a scientifically validated therapeutic resource. Overall, *S. spectabilis* holds significant potential as a source of standardised phytomedicines and novel therapeutic lead compounds. Strategic interdisciplinary research integrating phytochemistry, pharmacology and clinical sciences will be critical to realising its full medicinal value.

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Conflict of interest

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

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