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Review

Phytochemistry, pharmacological activities, and toxicological risks of *Heliotropium* species in Sub-Saharan Africa: A comprehensive review

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ABSTRACT

Medicinal plants remain vital resources for drug discovery, and *Heliotropium* species are recognized for their extensive ethnomedicinal use and diverse bioactive compounds. Despite their therapeutic potential, safety concerns related to pyrrolizidine alkaloids necessitate critical evaluation. This review synthesizes the literature on the taxonomy, ethnobotanical applications, phytochemistry, pharmacology, and toxicology of *Heliotropium* species. A systematic literature search was conducted following the principles of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Relevant publications were retrieved from major scientific databases, including Scopus, Web of Science, PubMed, Google Scholar, and ScienceDirect. Peer-reviewed articles, ethnopharmacological surveys, and toxicological studies published between 2000 and 2025 were screened and evaluated. After the removal of duplicates and the application of predefined inclusion criteria, relevant studies were selected for qualitative synthesis. More than 325 *Heliotropium* species are distributed worldwide, many of which are traditionally used to treat inflammatory conditions, infections, gastrointestinal disorders, and skin ailments. Phytochemical analyses reveal abundant secondary metabolites, including alkaloids, flavonoids, terpenoids, and phenolic acids. These compounds underpin diverse pharmacological effects, such as antioxidant, antimicrobial, anticancer, anti-ulcer, and anti-inflammatory activities. Essential oils from several species exhibit unique chemotypes with ecological and therapeutic significance. However, toxicological evidence indicates that pyrrolizidine alkaloids pose hepatotoxic and genotoxic risks, thereby limiting the safe clinical use of these plants. *Heliotropium* represents both an opportunity and a challenge: a valuable reservoir of novel bioactive compounds for drug discovery, yet one that requires cautious therapeutic application due to associated toxicity risks.

Keywords: *Heliotropium*, phytochemistry, ethnopharmacology, pyrrolizidine alkaloids, pharmacological activities, toxicology, natural product drug discovery.

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INTRODUCTION

Medicinal plants have played a fundamental role in the evolution of human civilization, shaping healthcare practices, cultural traditions, and the discovery of therapeutic agents. Since ancient times, communities worldwide have relied on plants as a primary defense against illness and disease (Refaz et al., 2017). Archaeological and historical evidence demonstrates the widespread use of plant-based remedies in ancient Egyptian, Chinese, Indian, Greek, and Mesopotamian societies, underscoring their universal importance in human health and survival. Rooted in traditional knowledge passed down through generations, these practices have laid the foundation for many modern medicines (Montinari et al., 2019).

Medicinal plants are widely regarded as reservoirs of bioactive compounds, particularly secondary metabolites such as alkaloids, flavonoids, terpenoids, phenolic acids, and saponins. These compounds are responsible for diverse biological activities, including antimicrobial, anti-inflammatory, antioxidant, anticancer, and antiviral effects

(Rafaz et al., 2017).

Background

Modern pharmacological research continues to validate the significance of medicinal plants, with many contemporary drugs, including aspirin, quinine, morphine, and artemisinin, tracing their origins to plant sources. This enduring link between traditional remedies and modern pharmacology highlights the continued relevance of plants as sources of novel therapeutic agents (Montinari et al., 2019). Beyond their medicinal roles, plants have historically served additional purposes, such as food preservation, flavor enhancement, and protection against epidemics, reflecting their multifunctional contributions to human societies (Rafaz et al., 2017).

Within this context, *Heliotropium* species are widely recognized in traditional and folk medicine for their therapeutic applications (Figure 1). In indigenous healing systems, different parts of these species, including leaves, roots, flowers, seeds, and whole plants, are used to prepare decoctions, infusions, poultices, and powders for managing ailments such as gout, inflammation, skin disorders, menstrual dysfunctions, rheumatism, and poisonous bites (Dash and Abdullah, 2013). Among the genus, *Heliotropium indicum* is one of the most extensively utilized species and is traditionally prescribed for fever, stomach aches, diarrhea, skin infections, menstrual irregularities, nervous disorders, and toxic bites (Kumar et al., 2007).

Recent scientific investigations have provided deeper insights into the phytochemistry and pharmacological basis of these traditional uses. Phytochemical screening of *H. indicum* has revealed the presence of alkaloids, triterpenes, sterols, amines, and volatile oils, supporting its broad spectrum of biological activities (Krishnaveni et al., 2024). Advanced GC–MS profiling has identified at least 29 compounds in ethanolic leaf extracts, several of which demonstrate potential anticancer properties, including activity against prostate cancer targets (Faleye et al., 2023). Similarly, phytochemical and fatty acid analyses have confirmed the antibacterial potential of *H. indicum*, supporting its ethnomedicinal use against infections (Idowu and Tolulope, 2023).

Other species also exhibit promising pharmacological activities. For instance, *Heliotropium crispum* has demonstrated significant anti-ulcer effects in vivo through metabolic profiling and animal studies (Fatima et al., 2022), while root extracts of *Heliotropium verdcourtii* have yielded bioactive phytochemicals with therapeutic potential (Tesfaye et al., 2024).

Taken together, both traditional knowledge and modern research affirm that *Heliotropium* species represent a valuable resource for drug discovery, effectively bridging ethnomedicine and contemporary pharmacology.

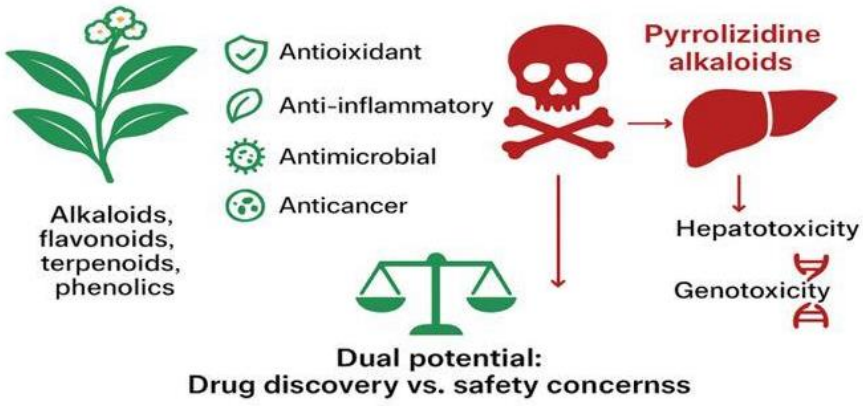

Figure 1. *Heliotropium*: Bioactive compounds, pharmacological promise and toxic risks. (Krishnaveni et al., 2024:Tesfaye et al., 2024).

Scope and objectives of this review

This review aims to provide a comprehensive synthesis of the taxonomy, ethnomedicinal uses, phytochemistry, pharmacological activities, and toxicological risks of *Heliotropium* species, with particular emphasis on their potential applications and relevance to Sub-Saharan Africa. Specifically, this article:

1. Documents the traditional uses of *Heliotropium* species across Sub-Saharan Africa, highlighting ethnomedicinal practices and cultural significance.
2. Reviews phytochemical profiles, emphasizing bioactive compounds responsible for therapeutic effects.
3. Evaluates pharmacological activities, including antioxidant, antimicrobial, anti-inflammatory, anticancer,

and other health-promoting properties.
4. Assesses toxicological risks, particularly hepatotoxicity and genotoxicity associated with pyrrolizidine alkaloids, to inform safe usage.
5. Identifies research gaps and opportunities, providing guidance for future studies and potential drug discovery efforts in the region.

Through this study, the review seeks to contribute to the discourse on sustainable medicinal plant utilization and drug discovery in Sub-Saharan Africa. By linking global technological advances with regional realities, it aims to position *Heliotropium* species as both a valuable resource for therapeutic development and a subject of informed, safe, and context-specific application in the region.

METHODOLOGY

Literature search strategy

This review was conducted following the principles of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) to ensure transparency, reproducibility, and systematic identification of relevant literature. A comprehensive search was performed across major electronic databases, including Scopus, Web of Science, PubMed, Google Scholar, and ScienceDirect.

Publications published between 2000 and 2025 were primarily considered; however, earlier foundational studies were included where necessary to provide historical context. The search strategy employed combinations of the following keywords: *Heliotropium* phytochemistry, *Heliotropium* pharmacological activity, *Heliotropium* medicinal uses, *Heliotropium* toxicity, *Heliotropium* secondary metabolites, pyrrolizidine alkaloids in *Heliotropium*, and *Heliotropium* species. Boolean operators (AND, OR, and NOT) were applied to refine the search and improve retrieval accuracy.

Study selection

The study selection process followed the PRISMA framework. The initial database search yielded approximately 420 articles related to *Heliotropium* phytochemistry, pharmacology, toxicology, and species diversity. After removing 95 duplicate records, 325 articles remained for title and abstract screening.

During this stage, 205 studies were excluded due to a lack of direct relevance to the phytochemistry, biological activities, or toxicity of *Heliotropium* species. The remaining 120 articles were subjected to full-text evaluation. Of these, 55 studies were excluded due to insufficient experimental data, limited relevance, or the unavailability of full texts. Ultimately, 65 studies met the inclusion criteria and were included in the qualitative synthesis of the phytochemical composition, pharmacological activities, and toxicological risks associated with *Heliotropium* species.

Inclusion and exclusion criteria

Studies were included in this review if they:

- Reported phytochemical constituents of *Heliotropium* species;
- Investigated pharmacological activities, including antimicrobial, antioxidant, anti-inflammatory, cytotoxic, or wound-healing properties;
- Discussed toxicological aspects, particularly the occurrence and effects of pyrrolizidine alkaloids;
- Were peer-reviewed research articles, review papers, or authoritative scientific books.

Studies were excluded if they:

- Were not written in English;
- Lacked sufficient scientific or experimental data;
- Were duplicate records across databases;
- Consisted solely of conference abstracts without accessible full texts.

Data extraction

Relevant information was systematically extracted from the selected studies using a standardized approach. The extracted data included:

- Botanical classification and geographical distribution of *Heliotropium* species;
- Ethnomedicinal uses and traditional applications;
- Identified phytochemical constituents and major chemical classes;
- Experimentally validated pharmacological activities;
- Reported toxicological effects and safety concerns.

The extracted information was organized into thematic categories to facilitate comparison and synthesis across studies.

Data synthesis and analysis

The collected data were critically analyzed and synthesized to provide a comprehensive overview of the current scientific knowledge on *Heliotropium* species. Particular emphasis was placed on identifying:

- Major phytochemical groups reported within the genus;
- Experimentally validated biological and

pharmacological activities;
- Toxicological risks associated with pyrrolizidine alkaloids;
- Existing research gaps and future prospects for drug discovery.

Findings were summarized descriptively and supported with tables highlighting key phytochemicals, pharmacological activities, and toxicity profiles associated with different *Heliotropium* species.

THE GENUS *HELIOTROPIUM*

The genus *Heliotropium* was historically classified within the family Boraginaceae; however, modern taxonomic revisions now place it in the family Heliotropiaceae. It is a cosmopolitan genus of flowering plants comprising approximately 325–350 recognized species (POWO, 2024). Morphologically, the genus encompasses diverse life forms, ranging from herbs (e.g., *H. indicum*) to shrubs (e.g., *H. curassavicum*) and small trees. Characteristic diagnostic features include alternate, simple leaves, small actinomorphic flowers, and nutlet-type fruits.

Ethnomedicinally, *Heliotropium* species have long been valued across Africa, Asia, and the Americas for the management of inflammatory disorders, wounds, skin diseases, fevers, respiratory ailments, and gastrointestinal disturbances (Rajitha, 2021; Sarkar et al., 2021). Modern phytochemical and pharmacological investigations have corroborated many of these traditional applications, confirming the presence of diverse bioactive metabolites (Sarkar et al., 2021).

In vitro and in vivo studies of *Heliotropium* species

Extensive research has been conducted to evaluate the pharmacological potential of *Heliotropium* species using both in vitro and in vivo models. Tables 1 and 2 summarize the reported pharmacological and toxicological studies of *Heliotropium* species occurring in Sub-Saharan Africa.

Table 1. Summary of in vitro pharmacological activities of *Heliotropium* species.

Species	Extract / solvent	In vitro model / assay	Observed effect	Reference
H. indicum	Ethanol / Aqueous leaves	DPPH and hydroxyl radical scavenging	Dose-dependent antioxidant activity correlated with phenolic and flavonoid content	Jayachitra and Bharathi, 2021
H. bacciferum	Ethanol leaves	DPPH assay	High antioxidant activity (88.3% at 225 µg/mL); phenolic and aromatic groups confirmed by FTIR	Ahmad et al., 2016
H. indicum	Methanol extracts	HeLa cervical cancer cell line	Inhibited cell growth (IC_{50} ≈ 200 µg/mL); stem extracts more active than leaves	Sivajothi et al., 2015
H. bacciferum	Ethanolic extracts	MCF-7 breast cancer cell line	~55% proliferation inhibition; modulation of GSK3β, Wnt2, β-catenin pathways	Gauranga et al., 2024
H. curassavicum	Hexane extracts	Cancer cell lines (various)	Seasonal variation affected phytochemical profile and anticancer efficacy	Shaimaa et al., 2023

Table 2. Summary of in vivo pharmacological and toxicological studies of *Heliotropium* species.

Species	Extract / solvent	Animal model	Observed effect	Reference
H. indicum	Ethanolic / Aqueous leaves	Rodents (rats/mice)	Dose-dependent antioxidant activity; reduced oxidative stress biomarkers	Jayachitra and Bharathi, 2021
H. bacciferum	Ethanolic extracts	Rats	Anti-inflammatory effects; reduction in paw edema and inflammatory mediators	Ahmad et al., 2016
H. indicum	Methanolic extracts	Rodent ulcer model	Gastroprotective effect against experimentally induced ulcers	Sivajothi et al., 2015
H. bacciferum	Ethanolic extracts	Rodent breast cancer model	Reduced tumor growth; modulation of anti-metastatic signaling pathways	Gauranga et al., 2024
H. curassavicum	Hexane extracts	Rodent cancer / inflammatory models	Anti-inflammatory and cytotoxic effects; seasonal variation influenced efficacy	Shaimaa et al., 2023

In vitro studies of Heliotropium species

In vitro investigations demonstrate that *Heliotropium* species possess a broad spectrum of pharmacological activities, largely attributable to their rich secondary metabolite profiles, including flavonoids, phenolic acids,

and terpenoids. These bioactivities include antioxidant, antimicrobial, anti-inflammatory, and cytotoxic effects, providing experimental support for their widespread ethnomedicinal use.

The antioxidant potential of *Heliotropium* species is well documented. Several species exhibit strong free radical scavenging activity, primarily linked to their phenolic and flavonoid constituents. Ethanol and aqueous leaf extracts of *H. indicum* demonstrate dose-dependent scavenging of DPPH and hydroxyl radicals, with activity strongly correlated with total phenolic and flavonoid content (Jayachitra and Bharathi, 2021). Similarly, *H. bacciferum* shows high antioxidant capacity, achieving up to 88.3% scavenging activity at 225 µg/mL. FTIR analysis confirms the presence of phenolic and aromatic functional groups associated with this activity (Ahmad et al., 2016).

Antimicrobial efficacy is consistently reported across the genus. Extracts of *Heliotropium* species exhibit inhibitory effects against a range of bacterial and fungal pathogens, supporting their traditional use in managing infectious diseases. These antimicrobial properties are commonly attributed to phenolic compounds, flavonoids, and alkaloids. Methanolic extracts of *H. indicum* show inhibitory activity against pathogenic microorganisms, including *Bacillus subtilis*, *Streptococcus mutans*, *Escherichia coli*, and *Bacillus cereus*, as demonstrated by agar diffusion assays (Aswini et al., 2017). Similarly, crude and solvent-partitioned extracts of *H. bacciferum* produce measurable inhibition zones against multiple bacterial strains, including antibiotic-resistant pathogens (Ahmad et al., 2016).

In contrast, dichloromethane extracts of *H. strigosum* exhibit pronounced cytotoxicity in brine shrimp lethality assays but only weak antimicrobial and antioxidant effects (Khurm et al., 2016). These findings highlight the influence of solvent polarity and extraction methodology on observed biological activities.

In vitro studies also confirm significant anti-inflammatory effects, primarily mediated through modulation of inflammatory mediators and inhibition of key enzymes involved in inflammatory pathways. Flavonoids, phenolic acids, and terpenoids are considered the major contributors to these effects.

The cytotoxic and anticancer activities of *Heliotropium* species have been extensively explored in vitro. Methanolic extracts of *H. indicum* inhibit HeLa cervical cancer cell growth, with IC_{50} values near 200 µg/mL; stem extracts exhibit greater activity (~64.5% inhibition) compared with leaf extracts (~49.7%) (Sivajothi et al., 2015). Ethanolic extracts of *H. bacciferum* suppress proliferation of MCF-7 breast cancer cells by approximately 55% at 100 µg/mL. Mechanistic investigations reveal modulation of anti-metastatic signaling pathways, including GSK3β, Wnt2, and β-catenin, indicating pathway-specific effects beyond nonspecific cytotoxicity (Gauranga et al., 2024).

In *H. curassavicum*, seasonal variation significantly influences phytochemical composition and anticancer efficacy. Hexane extracts collected at different times display distinct phytochemical profiles and differential cytotoxic effects (El-Beltagi et al., 2023). These findings highlight that *Heliotropium* species possess both direct cytotoxic and pathway-specific anticancer activities, with efficacy influenced by plant part, extraction method, and environmental factors.

In vivo studies of Heliotropium species

Compared with in vitro research, in vivo studies on *Heliotropium* species remain relatively limited but provide essential insights into pharmacological efficacy and toxicological risks. Such studies are critical for validating ethnomedicinal claims, understanding systemic effects, and identifying therapeutic windows.

Animal studies have demonstrated anti-inflammatory and analgesic activities. Extracts of *H. bacciferum* reduce inflammation and pain, supporting traditional ethnomedicinal claims (Ahmad et al., 2016). Similarly, *H. indicum* extracts exhibit significant anti-inflammatory effects in carrageenan-induced rat paw edema models, reducing swelling in a dose-dependent manner comparable to indomethacin (Akinmoladun et al., 2020). Ethanolic leaf extracts also show analgesic activity in hot-plate and tail-flick models, supporting their use in pain and inflammation management (Kumar et al., 2007).

Gastroprotective effects have also been reported. Extracts of *Heliotropium* species demonstrate protective effects against experimentally induced ulcers in rodents (Jayachitra and Bharathi, 2021). In particular, *H. crispum* exhibits strong gastroprotective properties in ethanol-induced gastric ulcer models, attributed to modulation of gastric acidity, antioxidant defenses, and prostaglandin-mediated mechanisms (Fatima et al., 2022).

Hepatoprotective effects have been reported for methanolic extracts of *H. indicum*, which reduce serum liver enzyme levels (ALT and AST) in CCl_4-induced hepatotoxic rats (Baheti et al., 2006). However, given the known presence of hepatotoxic pyrrolizidine alkaloids, these findings present a paradox and warrant further dose-dependent toxicological evaluation.

Wound-healing activity has also been demonstrated. Topical application of *H. indicum* extracts accelerates wound contraction, collagen deposition, and epithelialization in excision wound models in rats (Dash and Murthy, 2011). These effects are likely due to synergistic antimicrobial, antioxidant, and anti-inflammatory properties.

Toxicological assessments highlight significant safety concerns. Subacute toxicity studies in rodents indicate dose-dependent hepatotoxic changes consistent with pyrrolizidine alkaloid exposure (Owolabi et al., 2015). Chronic exposure studies further report genotoxicity and DNA damage, emphasizing the need for controlled

dosing and careful evaluation prior to clinical application. Collectively, these findings underscore the dual nature of *Heliotropium* species, therapeutically beneficial at lower doses but potentially harmful with prolonged or high-dose use.

Pharmacological efficacy of *Heliotropium* species

The pharmacological efficacy of *Heliotropium* species has been demonstrated in various gastrointestinal and metabolic disease models, as outlined below (Figure 2):

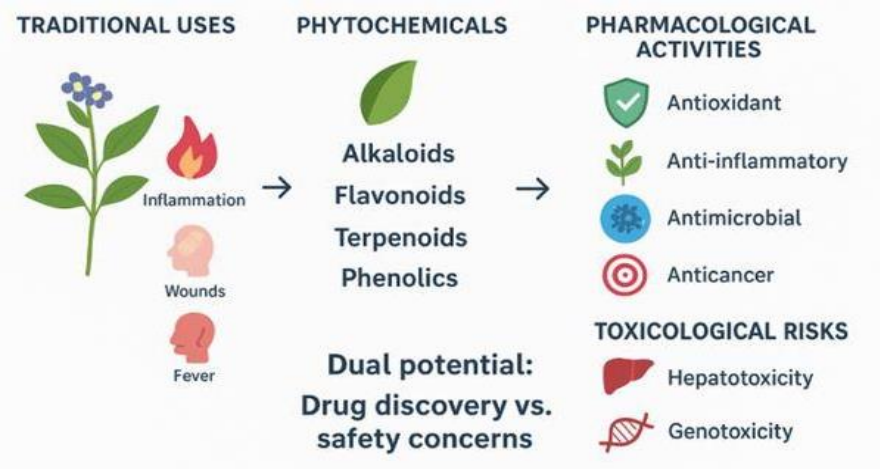

Figure 2. *Heliotropium*: Traditional uses, phytochemicals, pharmacological activities and toxic risks. (Jayachitra and Bharathi, 2021; Gaurangaet al., 2024).

Anti-ulcer activity

Ethanolic leaf and root extracts of *H. indicum* significantly reduce gastric volume, free acidity, total acidity, and ulcer index in rat pylorus-ligation models, confirming their in vivo gastroprotective effects (Nethaji et al., 2013).

Antidiabetic effects

In streptozotocin-induced diabetic rats, *H. indicum* leaf extract, administered alone or in combination with *Anthocleista djalonensis*, reduces blood glucose and phospholipid levels. However, toxic effects are observed at high combined doses, underscoring the need for careful dose optimization and synergy studies (Lawal et al., 2022).

Antimicrobial activity

Several *Heliotropium* species exhibit antimicrobial activity against a range of pathogenic microorganisms. Extracts of *H. indicum* show inhibitory effects against Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, as well as fungal species. These effects are attributed to bioactive phytochemicals such as alkaloids, flavonoids, and terpenoids (Dash and Murthy, 2011).

Anti-inflammatory activity

Extracts of *H. indicum* demonstrate significant anti-inflammatory activity in experimental models. In vivo studies show a marked reduction in carrageenan-induced paw edema in rats, suggesting inhibition of inflammatory mediators such as prostaglandins and cytokines. These effects are attributed to bioactive constituents, including flavonoids, tannins, and alkaloids (Dash and Murthy, 2011).

Wound-healing activity

Topical application of *H. indicum* extracts enhances wound healing, as evidenced by faster wound contraction, increased collagen formation, and improved epithelialization. These effects are likely due to the plant's combined antimicrobial, antioxidant, and anti-inflammatory properties (Dash and Murthy, 2011).

Antioxidant activity

Various extracts of *Heliotropium* species exhibit notable antioxidant activity in vitro. This activity is largely attributed to phenolic compounds and flavonoids that scavenge free radicals and mitigate oxidative stress, thereby contributing to therapeutic potential in oxidative stress-related diseases (Meher et al., 2011).

Analgesic activity

Analgesic properties of *H. indicum* have been demonstrated in experimental models. Extracts significantly reduce pain responses in acetic acid-induced writhing and hot-plate tests in rodents, indicating both peripheral and central analgesic effects (Dash and Murthy, 2011).

Anticancer/cytotoxic activity

Several studies report the cytotoxic and anticancer potential of *Heliotropium* species. Extracts of *H. indicum* exhibit cytotoxic activity against various cancer cell lines in vitro, largely attributed to bioactive secondary metabolites such as alkaloids, flavonoids, and phenolic compounds. Notably, certain pyrrolizidine alkaloids isolated from *Heliotropium* species demonstrate strong biological activity, including cytotoxic and antitumor effects; however, these compounds are also associated with hepatotoxicity (Fu et al., 2004; Wiedenfeld and Edgar, 2011).

TOXICOLOGICAL STUDIES

Experimental toxicity studies

Despite the therapeutic potential of *Heliotropium* species, toxicological investigations highlight significant safety concerns due to the presence of pyrrolizidine alkaloids (PAs).

Animal toxicity

Ingestion of *H. europaeum* through contaminated hay has been reported to cause severe hepatotoxicity in cattle, characterized by bile duct proliferation, fibrosis, and megalocytosis. Notably, PA-derived DNA adducts persist in liver tissue for up to 2.5 months post-exposure, confirming the long-term genotoxic potential of these compounds (Fu et al., 2017).

Rodent studies

A 28-day oral toxicity study using structurally diverse PAs, including heliotrine derived from *Heliotropium*, revealed transcriptional alterations consistent with hepatocellular injury, even at non-acutely toxic doses (0.1–3.3 mg/kg body weight). These findings suggest that subclinical exposure may still pose significant genotoxic and hepatotoxic risks (Ebmeyer et al., 2020).

Collectively, these results reinforce the therapeutic–toxic paradox of *Heliotropium* species: potent pharmacological effects at lower doses, but severe and persistent toxicity risks with chronic or unregulated use. While *Heliotropium* species demonstrate antioxidant, cytotoxic, and antimicrobial activities in vitro, and pharmacological efficacy in vivo—particularly in gastrointestinal and metabolic disease models—these benefits are counterbalanced by serious hepatotoxic and genotoxic risks associated with pyrrolizidine alkaloids.

This dual nature underscores the importance of rigorous toxicological evaluation. Although *Heliotropium* species represent a rich source of bioactive compounds for drug discovery, stringent safety assessments are essential for their safe clinical application. Pharmacological activities and toxicological risks of selected *Heliotropium* species are summarized in Table 3.

Toxicological aspects of *Heliotropium* species

Mechanisms of hepatotoxicity

The hepatotoxic effects associated with many *Heliotropium* species are largely attributed to pyrrolizidine alkaloids (PAs), a class of naturally occurring hepatotoxic secondary metabolites commonly found in members of the order Boraginales. These compounds are considered protoxins that require metabolic activation to exert their toxic effects.

Following ingestion, PAs are absorbed from the gastrointestinal tract and transported to the liver, where they undergo biotransformation by hepatic cytochrome P450 enzymes (Fu et al., 2004; Edgar et al., 2011). This metabolic activation generates highly reactive dehydropyrrolizidine metabolites that form covalent adducts with cellular macromolecules such as proteins and DNA. These interactions disrupt normal cellular processes, resulting in hepatocellular injury, sinusoidal endothelial damage, and obstruction of hepatic veins (Wiedenfeld and Edgar, 2011).

Prolonged exposure to these toxic metabolites may lead to severe liver conditions, including hepatic veno-occlusive disease, liver fibrosis, and cirrhosis, and has also been associated with genotoxic and carcinogenic effects (EFSA, 2017).

Metabolic activation pathways of pyrrolizidine alkaloids

The toxicity of pyrrolizidine alkaloids is closely linked to their metabolic activation in the liver. Once ingested, PAs undergo oxidation mediated by cytochrome P450 enzymes, particularly CYP3A and CYP2B isoforms, resulting in the formation of unstable dehydropyrrolizidine alkaloids (pyrrolic esters) (Fu et al., 2004).

These electrophilic intermediates readily react with

Table 3. Pharmacological activities and toxicological risks of selected *Heliotropium* species.

Species	Phytochemicals identified	Key pharmacological activities (in vitro / in vivo)	Toxicological findings	References
H. indicum	Alkaloids, flavonoids, sterols, triterpenes, amines, volatile oils	Antioxidant (radical scavenging) Anticancer (HeLa inhibition, IC_{50} ~200 µg/mL) Antimicrobial (B. subtilis, E. coli, S. mutans) Anti-ulcer (reduced gastric acidity, ulcer index in rats) Antidiabetic (reduced glucose and phospholipids in diabetic rats)	Toxicity at high combined doses with *A. djalonensis*	Jayachitra and Bharathi, 2021; Sivajothi et al., 2015; Nethaji et al., 2013; Lawal et al., 2022
H. bacciferum	Phenolics, flavonoids, alkaloids, fatty acids	Antioxidant (88.3% scavenging at 225 µg/mL) Anticancer (MCF-7 inhibition ~55% at 100 µg/mL; modulation of Wnt/β-catenin pathway) Antibacterial activity, including resistant strains	Not well studied in vivo	Ahmad et al., 2016; Gauranga et al., 2024
H. curassavicum	Seasonal-dependent phytoconstituents (hexane extracts)	Anticancer activity varies with season and extraction	Data not available	Shaimaa et al., 2023
H. crispum	Metabolites from profiling studies	Anti-ulcer activity confirmed in vivo (animal models)	Data not available	Fatima et al., 2022
H. verdcourtii	Root bioactive phytochemicals	Potential therapeutic activities (preliminary evidence)	Data not available	Tesfaye et al., 2024
H. strigosum	Dichloromethane extracts	Weak antimicrobial and antioxidant activity Cytotoxic in brine shrimp lethality assay	Not well studied	Khurm et al., 2016
H. europaeum	Pyrrolizidine alkaloids (heliotrine, others)	Limited pharmacological studies reported	Hepatotoxicity in livestock (fibrosis, bileduct proliferation, megalocytosis) Genotoxic PA-DNA adducts persisting for months	Fu et al., 2017
Mixed species (PAs study)	Pyrrolizidine alkaloids (heliotrine, lasiocarpinesenecionine, etc.)	Not directly tested for efficacy	Rodent studies show hepatotoxic gene expression changes even at low doses (0.1–3.3 mg/kg)	Ebmeyer et al., 2020

nucleophilic sites in proteins, nucleic acids, and cellular membranes, forming pyrrole–protein and pyrrole–DNA adducts that compromise cellular integrity and induce oxidative stress (Moreira et al., 2018).

In addition to this toxic activation pathway, alternative detoxification mechanisms exist, including N-oxidation and conjugation with glutathione, which facilitate elimination of these compounds from the body. However, when exposure exceeds the detoxification capacity of the liver, toxic metabolites accumulate, leading to hepatocellular damage and progressive liver injury (Edgar et al., 2011).

Regulatory perspectives

The presence of pyrrolizidine alkaloids in medicinal plants and food products has raised significant public health concerns due to their hepatotoxic, genotoxic, and potentially carcinogenic properties. Consequently, several international regulatory bodies have conducted risk assessments to evaluate human exposure to these compounds.

The European Food Safety Authority (EFSA) has played a leading role in assessing the occurrence and toxicity of pyrrolizidine alkaloids in food and herbal

products. In its scientific opinion, EFSA identified these compounds as genotoxic carcinogens and highlighted the potential health risks associated with chronic dietary exposure (EFSA, 2011). The report emphasized that even low levels of long-term exposure may pose significant risks to human health.

Subsequent EFSA assessments have examined the occurrence of pyrrolizidine alkaloids in food commodities such as honey, herbal teas, and dietary supplements (EFSA, 2015). These studies demonstrated that contamination may occur through the inclusion of PA-producing plants, including *Heliotropium* species, during harvesting or processing. As a result, EFSA recommended continuous monitoring and improved quality control measures to minimize contamination in food and herbal products.

These regulatory evaluations have informed safety guidelines and risk management strategies aimed at reducing human exposure to pyrrolizidine alkaloids and ensuring the safety of plant-derived medicinal preparations.

Risk assessment related to herbal use

Despite their traditional medicinal applications, several *Heliotropium* species pose potential health risks due to their pyrrolizidine alkaloid content. Risk assessment studies indicate that chronic exposure to PA-containing herbal products may lead to cumulative toxicity, particularly affecting the liver (Moreira et al., 2018).

Vulnerable populations, including children, pregnant women, and individuals with pre-existing liver disorders, may be particularly susceptible to the adverse effects of these compounds. Consequently, the therapeutic use of *Heliotropium* species in herbal medicine requires careful evaluation of safety, dosage, and duration of exposure.

Improved regulatory oversight, rigorous toxicological studies, and increased public awareness are essential to ensure the safe use of medicinal plants containing potentially toxic constituents (Wiedenfeld and Edgar, 2011).

ESSENTIAL OILS OF *HELIOTROPIUM* SPECIES

Studies on the essential oils (EOs) and volatile constituents of *Heliotropium* species reveal remarkable chemical diversity and ecological relevance (Figure 3). *Heliotropium arborescens*, notable for its fragrant flowers, emits a pleasant vanilla-like aroma with caramel undertones (Fayed, 2021). Its floral scent profile is dominated by benzenoids and terpenoids, particularly benzaldehyde, linalool, (E)-β-ocimene, and limonene, which collectively contribute to its characteristic ornamental fragrance (Kays and Paull, 2005).

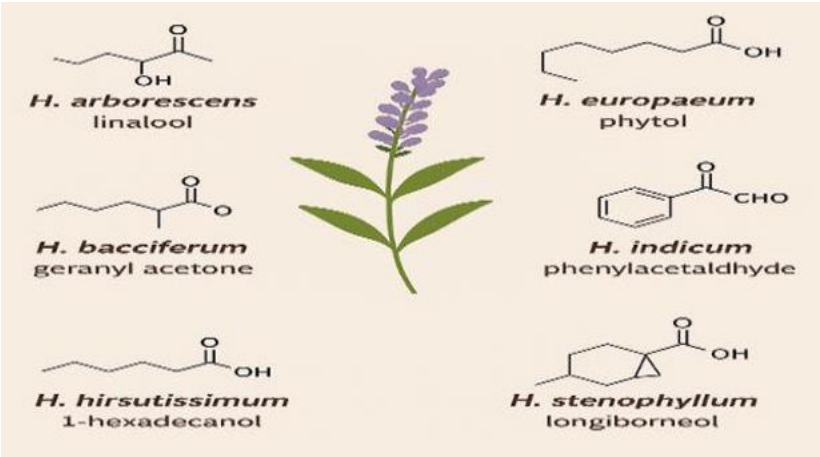

Figure 3. Essential oils of *Heliotropium* species (Fayed, 2021; Hasni et al., 2023).

The essential oil of *H. europaeum*, obtained from aerial parts, exhibits a complex composition, including phytol (28.7%), cis-linoleic acid methyl ester (7.3%), geranyl acetone (6.3%), (E)-β-ionone (4.8%), and phytol acetate (4.3%). These constituents collectively demonstrate antimicrobial activity against selected bacterial and fungal strains (Saeedi and Morteza-Semnani, 2009). Similarly, *H. bacciferum* yields a hydrodistilled oil rich in oxygenated sesquiterpenes such as agarospirol, rosifoliol, elemol, and τ-cadinol, compounds associated with anti-inflammatory and antibacterial effects (Hasni et al., 2023).

In *H. indicum*, aldehydes constitute approximately 52.8% of the essential oil, with phenylacetaldehyde (22.2%), (E)-2-nonenal (8.3%), and (E,Z)-2-nonadienal (6.1%) identified as major components, alongside hexahydrofarnesylacetone (8.4%) (Ogunbinu et al., 2009). GC–MS analysis of bioactive fractions has further

revealed volatile and semi-volatile constituents associated with antioxidant and anti-inflammatory properties, supported by in silico molecular docking studies (Shoily et al., 2025).

The essential oil of *H. hirsutissimum* is characterized by long-chain alcohols and fatty acid esters, including 1-hexadecanol, tetracosanoic acid, butyl 2-methylpropyl ester, and 2-monostearin (Demiray et al., 2013). In contrast, *H. stenophyllum* is dominated by sesquiterpenes and their oxygenated derivatives, notably junenol (19.08%), longiborneol (9.34%), (E,Z)-geranyl linalool (6.81%), selina-3,11-dien-6α-ol (6.70%), α-cedrene epoxide (6.60%), heliofolen-12-al D (6.23%), and β-epi-bisabolol (4.83%) (Urzúa et al., 2013).

Environmental factors also play a significant role in shaping EO profiles. In *H. curassavicum*, samples collected from coastal and inland habitats exhibit marked differences in terpene and oxygenated sesquiterpene content, influencing their allelopathic and antioxidant activities (Abd-ElGawad et al., 2019).

Collectively, these findings demonstrate that essential oil composition in *Heliotropium* species is both species-specific and habitat-dependent. This variability has important implications for chemotaxonomy, ecological adaptation, and the pharmacological potential of these plants.

SOME SPECIES OF *HELIOTROPIUM*

The genus *Heliotropium* comprises species with contrasting pharmacological profiles, ranging from promising medicinal resources to plants of significant toxicological concern. While several species are widely used in traditional medicine and are supported by experimental evidence of bioactivity, others are dominated by hepatotoxic and genotoxic pyrrolizidine alkaloids, which limit their therapeutic applicability.

To clearly distinguish these divergent profiles, Table 4 summarizes *Heliotropium* species with documented medicinal potential, while Table 5 highlights species primarily associated with toxicity and safety risks. Together, these tables provide a comparative framework for evaluating the benefit–risk balance of *Heliotropium* species in ethnopharmacology and drug discovery. In addition, Table 6 summarizes selected species commonly distributed across Sub-Saharan Africa.

Table 4. Medicinally promising *Heliotropium* species with reported pharmacological potential.

Species	Common name(s)	Distribution	Traditional / ethnomedicinal uses	Key phytochemicals	Experimentally reported activities
H. verdcourtii	Chiggery grapes	West and East Africa	Malaria, fever, wounds, GI disorders, epilepsy, ulcers, laxative, aphrodisiac	Phenolics, flavonoids, lignans, triterpenoids, steroids, Pas	Antidiabetic, antibacterial, antihyperglycemic, antioxidant Tesfaye et al., 2024
H. bacciferum	Velvet heliotrope	North Africa	Skin infections, burns, abscesses, tonsillitis	PAs, phenolics, flavonoids	Antimicrobial, antioxidant, anti-inflammatory Hammiche and Maiza, 2006; Hanane et al., 2018
H. angiospermum	Scorpion's tail	Caribbean, Mexico	Wounds, diarrhea, colic, conjunctivitis	Polyamines, alkaloids	DNA-binding activity; potential cytotoxic effects Erosa-Rejón et al., 2009
H. indicum	Indian heliotrope	Tropics worldwide	Wounds, fever, eye infections, fractures, inflammation	Tannins, saponins, essential oils, PAs	Anti-inflammatory, wound healing, anticancer, anticataract Chandan et al., 2021
H. strigosum	Bhangra, Kharsan	South Asia	GI disorders, bites, ulcers, hormonal disorders	Strigosine (PA), enzymes	Antimicrobial, antioxidant, anticonvulsant, antidiabetic Huma et al., 2017
H. ramosissimum	Desert heliotrope	Arid regions (Africa, Middle East)	Wounds, burns, restorative uses	Phenolics, flavonoids, alkaloids	Antioxidant; anticancer (Colo-205, IC_{50} ≈ 18.6 µg/mL) Fayed et al., 2022
H. arborescens	Garden heliotrope	Cultivated globally	Historical respiratory and febrile uses	Phenolics, flavonoids, aromatics	Antioxidant, antibacterial (external use) Alvarado et al., 2024

Table 5. Toxic or high-risk *Heliotropium* species with limited therapeutic applicability.

Species	Common name(s)	Distribution	Major toxic constituents	Documented toxic effects	Exposure risk
H. europaeum	European heliotrope	Mediterranean, Middle East	Europine, heliotrine, lasiocarpine (PAs)	Severe hepatotoxicity, genotoxicity, livestock poisoning	Contaminated hay, feed, herbal misuse Shimshoni et al., 2015, Shimshoni et al., 2017
H. amplexicaule	Blue heliotrope	Global (invasive weed)	Heliotrine and related PAs	Veno-occlusive disease, liver fibrosis, carcinogenicity	Grazing livestock, contaminated grains Carpinelli de Jesus et al., 2019; Roberts et al., 2024
H. indicum (oral use)	Indian heliotrope	Tropics worldwide	Indicine N-oxide, heliotrine	Hepatotoxicity upon chronic exposure	Herbal remedies, teas Schoental, 1968; Hartmann and Ober, 2000
H. arborescens	Garden heliotrope	Cultivated globally	Pyrrolizidine alkaloids	Livestock poisoning, liver damage	Accidental ingestion Moreira et al., 2018
H. polyphyllum	Pineland heliotrope	Americas	Unknown (genus PA-rich)	Not evaluated	Data deficient Feuillet, 2016
H. gnaphalodes	Sea lavender	Coastal Americas	Unknown	Not studied	Data deficient Brown et al., 2018

Table 6. Selected *Heliotropium* species in Sub-Saharan Africa.

Heliotropium species	Common name	Distribution in Sub-Saharan Africa	Ethnomedicinal uses	Major bioactive compounds	References
Heliotropium indicum L.	Indian heliotrope	Widely distributed in West and East Africa including Nigeria, Ghana and Kenya	Wound healing, skin infections, fever, inflammation, eye diseases	Pyrrolizidine alkaloids, flavonoids, phenolics	Fu et al., 2004; Burkill, 2000
Heliotropium ovalifolium Forssk.	Oval-leaf heliotrope	Found in dry regions of Ethiopia, Somalia and Sudan	Treatment of inflammation, wounds and skin disorders	Alkaloids, flavonoids, terpenoids	El-Shazly and Wink, 2014
Heliotropium bacciferum Forssk.	Desert heliotrope	Arid regions of East Africa including Kenya and Ethiopia	Used for infections and inflammatory conditions	Pyrrolizidine alkaloids, phenolic compounds	El-Shazly and Wink, 2014
Heliotropium zeylanicum (Burm. f.) Lam.	Wild heliotrope	Tropical Africa including Nigeria, Cameroon and Democratic Republic of the Congo	Used for wounds, fever, and gastrointestinal disorders	Flavonoids, alkaloids, terpenoids	Burkill, 2000; El-Shazly and Wink, 2014
Heliotropium steudneri Vatke	—	Distributed in East Africa including Uganda, Kenya and Tanzania	Used traditionally for infections and inflammatory diseases	Alkaloids, phenolic compounds	El-Shazly and Wink, 2014
Heliotropium ramosissimum	Branched heliotrope	Occurs in dry regions extending into East Africa	Wound healing and treatment of skin infections	Alkaloids, flavonoids	El-Shazly and Wink, 2014

Heliotropium verdcourtii

Phytochemical analyses of *Heliotropium* species, including *H. verdcourtii* (Figure 4), have identified diverse classes of secondary metabolites such as phenolic acids, lignans, flavonoids, nitrile glycosides, quinonoids, steroids, triterpenoids, and pyrrolizidine alkaloids (Jeruto et al., 2011; Li et al., 2010). Bioassay-guided studies of *H. verdcourtii* extracts have demonstrated antidiabetic, antibacterial, antihyperglycemic, and antioxidant activities (Maroyi, 2021).

The species' widespread distribution, extensive traditional use, and rich phytochemical profile underscore its value as a promising medicinal resource in West and East Africa. However, comprehensive studies on its toxicity, pharmacodynamics, and clinical potential remain

Figure 4. Floral picture of *H. verdcourtii.*

limited, warranting further investigation.

Heliotropium europaeum

Phytochemically, *H. europaeum* (Figure 5) is characterized by the presence of pyrrolizidine alkaloids (PAs), notably europine, heliotrine, and lasiocarpine, which are potent hepatotoxins. Numerous reports document livestock poisoning, particularly in cattle consuming contaminated hay. Affected animals exhibit severe hepatic injury marked by bile duct proliferation, megalocytosis, and fibrosis, with PA–DNA adducts detected in liver tissue, confirming genotoxic damage (Shimshoni et al., 2015; Fu et al., 2017).

Figure 5. Floral picture of *H. europaeum.*

Beyond its alkaloid content, *H. europaeum* also contains beneficial phenolic compounds such as kaempferol, syringic acid, genistein, and apigenin, which are associated with antioxidant and enzyme inhibitory activities (Jasim and Hamad, 2021). Advanced UHPLC–MS/MS metabolomic profiling reveals significant chemodiversity, supporting in vitro antioxidant and enzyme inhibitory activities targeting α-amylase and cholinesterase pathways (Mustafa et al., 2025).

Despite these pharmacologically relevant constituents, the co-occurrence of free-base PAs and their N-oxides significantly increases toxicity risks, particularly through contaminated feed or improperly processed herbal preparations. Thus, *H. europaeum* exemplifies a dual nature: a toxic invasive species and a potential reservoir of bioactive compounds requiring careful evaluation.

Heliotropium bacciferum (Forssk.)

H. bacciferum (Figure 6) is widely distributed across arid and semi-arid regions of North Africa, particularly in Algeria, where it thrives under harsh climatic conditions. The species has attracted scientific interest due to its broad spectrum of biological activities.

Figure 6. Floral picture of *H. bacciferum.*

Phytochemical investigations indicate that *H. bacciferum* contains diverse bioactive compounds, including pyrrolizidine alkaloids, which contribute to its antimicrobial and antioxidant activities (Aïssaoui et al., 2018). Although these alkaloids may pose toxicity risks at high concentrations, they are also integral to the plant's ecological adaptability and pharmacological relevance.

Ethnobotanical evidence supports its long-standing use in traditional North African medicine (Hammiche and Maiza, 2006). The convergence of traditional knowledge and scientific validation highlights its potential as a source of novel therapeutic agents.

Heliotropium angiospermum Murray

H. angiospermum (Figure 7) is widely used in traditional medicine in the Caribbean. In the Bahamas, decoctions and poultices are used to treat skin irritations, infant colic, and wounds (LLNPP, 2023).

Phytochemical investigations have identified polyamines such as putrescine, spermidine, and spermine, which are involved in cellular growth regulation and stress responses (Erosa-Rejón et al., 2009). Bio-

Figure 7. Floral picture of *H. angiospermum.*

prospecting studies further demonstrate DNA-binding activity of leaf extracts, suggesting potential cytotoxic or genoprotective properties.

These findings highlight the species' biotechnological potential and support further pharmacological and toxicological evaluation.

Heliotropium indicum L.

H. indicum (Figure 8) is widely used in traditional medicine across tropical and subtropical regions. It is employed in the treatment of wounds, fever, ocular infections, menstrual irregularities, neurological disorders, and renal conditions. It is also used as a detoxifying agent, antidote, and topical antiseptic (Sarkar et al., 2021).

Figure 8. Floral picture of *H. indicum.*

Phytochemical analyses reveal a rich composition of tannins, saponins, steroids, essential oils, and glycosides. Notably, pyrrolizidine alkaloids such as indicine N-oxide and heliotrine contribute to both its pharmacological activity and toxicity profile (Schoental, 1968; Hartmann and Ober, 2000).

Experimental studies demonstrate anti-inflammatory, wound-healing, anticancer, and anticataract activities, supporting its ethnomedicinal applications. However, its PA content necessitates careful safety evaluation.

Heliotropium strigosum Willd.

H. strigosum (Figure 9) is widely used in traditional medicine for treating gastrointestinal disorders, insect bites, skin infections, eye diseases, and hormonal imbalances (Qureshi and Bhatti, 2008).

Figure 9. Floral picture of *H. strigosum.*

Scientific studies validate its pharmacological potential, demonstrating antimicrobial, antioxidant, anti-inflammatory, analgesic, anticonvulsant, cytotoxic, bronchodilatory, and vasorelaxant activities (Ullah et al., 2010; Khan et al., 2013; Aslam et al., 2017).

Phytochemical analyses identify strigosine (a pyrrolizidine alkaloid), a trypsin inhibitor, and phthalic acid esters as key constituents. Additionally, methanolic extracts show significant antidiabetic activity in animal models, indicating potential for metabolic disease management.

Heliotropium polyphyllum Lehmann

H. polyphyllum (Figure 10) is adapted to open, sunlit environments in tropical and subtropical coastal ecosystems. However, ethnobotanical and phytochemical data on this species remain limited.

Figure 10. Floral picture of *H. polyphyllum.*

Given that the genus *Heliotropium* is known to produce diverse bioactive compounds, including pyrrolizidine alkaloids, flavonoids, and phenolic acids, *H. polyphyllum* represents an underexplored species with potential for future phytochemical and pharmacological investigation.

Heliotropium ramosissimum

Phytochemical studies indicate that *H. ramosissimum* (Figure 11) contains phenolic acids, flavonoids,

Figure 11. Floral picture of *H. ramosissimum.*

coumarins, and alkaloids, contributing to its antioxidant and cytoprotective properties (Fayed et al., 2022).

Methanolic extracts demonstrate strong antioxidant activity, while cytotoxic studies reveal significant anticancer activity against colorectal carcinoma (Colo-205) cells, with an IC_{50} of approximately 18.6 µg/mL. Mechanistic studies suggest apoptosis induction as the underlying pathway (Chaluma et al., 2018).

Heliotropium amplexicaule

H. amplexicaule (Figure 12) contains pyrrolizidine alkaloids such as heliotrine, which are associated with hepatotoxic and carcinogenic effects (Smith and Culvenor, 1981). These compounds undergo hepatic activation to form reactive intermediates that cause liver damage, including veno-occlusive disease (Fu et al., 2004).

Figure 12. Floral picture of *H. amplexicaule.*

The species is primarily associated with toxicity, with documented cases of poisoning in livestock and humans. It also poses ecological challenges due to its invasive nature and impact on pasture productivity.

Despite its toxicity, *H. amplexicaule* has contributed significantly to understanding PA metabolism and hepatotoxicity mechanisms.

Heliotropium gnaphalodes (L.)

Phytochemical data on *H. gnaphalodes* (Figure 13) remain limited. However, its tolerance to environmental stress suggests the potential presence of protective secondary metabolites such as flavonoids and phenolic compounds.

Figure 13. Floral picture of *H. gnaphalodes.*

The species is valued ecologically for dune stabilization, habitat restoration, and coastal ecosystem management (Brown et al., 2018).

Heliotropium arborescens L.

Volatile compound analysis of *H. arborescens* (Figure 14) identifies benzaldehyde, benzyl acetate, and *p*-anisaldehyde as key contributors to its fragrance (Kays and Paull, 2005). Ethanolic extracts contain phenolic acids and flavonoids associated with antioxidant and antibacterial activity (Alvarado et al., 2024).

Figure 14. Floral picture of *H.arborescens.*

However, the presence of hepatotoxic pyrrolizidine alkaloids limits its internal medicinal use. Reports of livestock poisoning further underscore its toxicological risk (Moreira et al., 2018; Friedman and Rot, 2006).

COMPARATIVE EVALUATION OF MEDICINAL POTENTIAL AND TOXICOLOGICAL RISKS

The comparative analysis of *Heliotropium* species reveals a clear dichotomy between medicinal potential and toxicological liability (Tables 3 and 4). Several species, including *H. verdcourtii*, *H. indicum*, *H. bacciferum*, *H. strigosum*, and *H. ramosissimum*, demonstrate substantial ethnomedicinal relevance supported by experimental evidence of antioxidant, antimicrobial, anti-inflammatory, antidiabetic, and anticancer activities. These bioactivities are largely attributed to phenolic acids, flavonoids, terpenoids, and other secondary metabolites that underpin their traditional therapeutic applications across Africa, Asia, and the Caribbean.

Notably, species such as *H. ramosissimum* and *H. indicum* exhibit promising cytotoxic and wound-healing properties, positioning them as valuable candidates for natural product–based drug discovery. In contrast, several members of the genus—particularly *H. europaeum* and *H. amplexicaule*—are associated with significant toxicological concerns due to high concentrations of hepatotoxic and genotoxic pyrrolizidine alkaloids. These species have been repeatedly implicated in livestock poisoning and human exposure incidents, with molecular evidence confirming the formation of PA–DNA adducts and progressive liver damage.

Even medicinally valuable species such as *H. indicum* and *H. arborescens* exhibit a dual profile, in which therapeutic benefits coexist with notable safety risks, particularly following oral administration or prolonged use. Meanwhile, species such as *H. polyphyllum* and *H. gnaphalodes* remain largely underexplored, representing important knowledge gaps that warrant targeted phytochemical and pharmacological investigation.

Overall, these findings underscore the necessity for rigorous toxicological evaluation, standardized extraction protocols, and effective risk mitigation strategies for pyrrolizidine alkaloids when considering *Heliotropium* species for therapeutic development. Harnessing their medicinal potential while minimizing toxicity will require a balanced, evidence-based approach that integrates ethnopharmacology, advanced analytical techniques, and safety-oriented drug discovery frameworks.

CONCLUSION

Heliotropium species represent valuable medicinal resources enriched with diverse bioactive constituents that underpin a wide range of pharmacological activities, including antioxidant, antimicrobial, anti-inflammatory, and anticancer effects. Ethnomedicinal applications documented across different cultures are increasingly supported by scientific evidence, highlighting the therapeutic relevance of the genus.

However, the widespread occurrence of hepatotoxic pyrrolizidine alkaloids (PAs) poses a significant safety concern, necessitating rigorous toxicological evaluation prior to any clinical or pharmacological application. While some species have been extensively studied, many remain insufficiently characterized, indicating substantial gaps in phytochemical profiling, mechanistic understanding, and safety assessment.

In conclusion, the genus *Heliotropium* holds considerable promise for novel drug discovery and development. Realizing this potential will depend on carefully balancing therapeutic benefits with toxicological risks through targeted research, standardized methodologies, and the development of safe utilization strategies.

REFERENCES

Abd-ElGawad AM, Elshamy AI, Al-Rowaily SL, El-Amier YA, **2019**. Habitat affects the chemical profile, allelopathy, and antioxidant properties of essential oils and phenolic enriched extracts of the invasive plant *Heliotropium curassavicum*. Plants, 8(11): 482. https://doi.org/10.3390/plants8110482

Ahmad S, AbdEl-Salam NM, Ullah R, **2016**. *In vitro* antimicrobial bioassays, DPPH radical scavenging activity, and FTIR spectroscopy analysis of *Heliotropium bacciferum.* BioMed Res Int, Article ID 3818945. https://doi.org/10.1155/2016/3818945

Akinmoladun AC, Ibukun EO, Afor E, Obuotor EM, Farombi EO, **2020**. Phytochemical constituents and anti-inflammatory activity of *Heliotropium indicum* L. leaf extract in carrageenan-induced rat paw edema model**.** J Ethnopharmacol*,* 249, 112385.

Alvarado AT, Chávez H, García JA, Bendezú MR, Surco-Laos F, Molina-Cabrera A, Bolarte-Arteaga M, **2024**. Biophenolic compounds and metal ions associated with the antioxidant and antibacterial activity of the ethanolic extract of *Heliotropium arborescens* L. leaves from the Andean region of Ayacucho-Peru. Pharmacia, 71: 1–12. https://doi.org/10.3897/pharmacia.71.e120315

Aswini R, Murugesan S, Murugesh S, **2017**. Preliminary phytochemical, antibacterial and in vitro anticancer activity of methanolic extracts of (leaf and stem) *Heliotropium indicum Linn*. World J Pharm Res, 6(1): 524-535.

Baheti JR, Goyal RK, Shah GB, **2006**. Hepatoprotective activity of *Hemidesmus indicus* R. Br. in rats*.* Indian J Exp Biol, 44(5): 399–402.

Brown SH, Frank MS, Koeser AK, **2018**, August. Sea lavender (*Heliotropium gnaphalodes* L.): identification and uses *(ENH1299/EP563)*. University of Florida IFAS Extension. https://doi.org/10.32473/edis-ep563-2018

Burkill HM, **2000**. The Useful Plants of West Tropical Africa (2nd ed.). Royal Botanic Gardens, Kew.

Carpinelli de Jesus M, Hungerford NL, Carter SJ, Anuj SR, Blanchfield JT, De Voss JJ, Fletcher MT, **2019**. Pyrrolizidine alkaloids of blue heliotrope *(Heliotropium amplexicaule*) and their presence in Australian honey. J Agric Food Chem, 67(28): 7995–8006. https://doi.org/10.1021/acs.jafc.9b02136

Chaluma S, Ruth S, Gemechu G, Hailemichael T, Aman D, Teshome A, Yadessa M, **2018**. Antibacterial triterpenoid from the leaves extract of *Ehretia cymosa*. Ethiop J Sci Sustain Dev, 5: 42-53.

Aïssaoui H, Mencherini T, Esposito T, De Tommasi N, Gazzerro P, Benayache S, Benayache F, Mekkiou R, **2018**. *Heliotropium*

bacciferum Forssk. (Boraginaceae) extracts: chemical constituents, antioxidant activity and cytotoxic effect in human cancer cell lines. https://doi.org/10.1080/14786419.2018.1437433

Aslam H, Arif-ullah K, Ur-Rehman N, Ali F, Nadeem H, Shah SM, **2017**. Anti-hyperglycemic activity of *Heliotropium strigosum* (Boraginaecae) whole plant extract in alloxan-induced diabetic mice. 16(10): 2425-2430

Dash GK, **Abdullah** MS, **2013**. Ethnomedicinal, phytochemical and pharmacological review of *Heliotropium indicum* Linn. Res J Pharm Biol Chem Sci, 4(1): 1155–1168.

Dash GK, **Murthy** PN, **2011**. Studies on wound healing activity of *Heliotropium indicum* Linn. leaves in rats. ISRN Pharmacology, 847980.

Demiray H, Gemici M, Yazici I, Karabey F, **2013**. Chemical constituents of *Heliotropium hirsitutissimum* Grauer (Heliotrope) (Sigil otu, Bambil) (Sonnenwende) and ecotype. Asian J Chem, *25*(7): 3725–3730.

Ebmeyer J, Rasinger JD, Hengstler JG, Schaudien D, Creutzenberg O, Lampen A, Braeuning A, Hessel-Pras S, **2020**. Hepatotoxic pyrrolizidine alkaloids induce DNA damage response in rat liver in a 28-day feeding study. Arch Toxicol, 94(9): 3019–3031.

Edgar JA, Colegate SM, Boppré M, Molyneux RJ, **2011**. Pyrrolizidine alkaloids in food: a spectrum of potential health consequences. Food Addit Contam: Part A, 28(3): 308–324. https://doi.org/10.1080/19440049.2010.547520

EFSA Panel on Contaminants in the Food Chain (CONTAM), **2011**. Scientific opinion on pyrrolizidine alkaloids in food and feed. EFSA Journal, 9(11): 2406.

El-Shazly A, **Wink** M, **2014**. Diversity of pyrrolizidine alkaloids in the *Boraginaceae:* Structures, distribution, and biological properties. Diversity, 6(2): 188–282. https://doi.org/10.3390/d6020188

Erosa-Rejón G, Peña-Rodríguez LM, Sterner O, **2009**. Secondary metabolites from *Heliotropium angiospermum*. J Mex Chem Soc, 53(2): 44–47.

European Food Safety Authority (**EFSA**), **2015**. Occurrence of pyrrolizidine alkaloids in food. EFSA Supporting Publications.

Faleye BC, Bamisaye FA, Fatoki TH, **2023**. GC-MS characterization and computational assessment of phytochemicals in *Heliotropium indicum* ethanolic leaves extract. J Complem Altern Med Res, 22(3): 10–22.

Fatima SF, Ishtiaq S, Lashkar MO, Youssef FS, Ashour ML, Elhady SS, **2022**. Metabolic profiling of *Heliotropium crispum* aerial parts using HPLC and FTIR and in vivo evaluation of its anti-ulcer activity using an ethanol-induced acute gastric ulcer model. Metabolites, 12(8): 750. https://doi.org/10.3390/metabo12080750

Fayed MAA, **2021**. *Heliotropium:* A genus rich in pyrrolizidine alkaloids: A systematic review following its phytochemistry and pharmacology. Phytomed Plus, 1(2): 100036.

Fayed MAA, Abouelela ME, Refaey MS, **2022**. *Heliotropium ramosissimum* metabolic profiling, in silico and in vitro evaluation with potent selective cytotoxicity against colorectal carcinoma. Sci Rep, 12: 12539. doi.org/10.1038/s41598-022-16552-1

Feuillet C, **2016**. Two new combinations in *Euploca* Nutt. (Heliotropiaceae). Phytotaxa, 260(1): 81–84. https://doi.org/10.11646/phytotaxa.260.1.7

Friedman H, **Rot** I, **2006**. Characterization of chilling injury in *Heliotropium arborescens* and *Lantana camara* cuttings. Postharvest Biol Technol, 40(3): 244–249. https://doi.org/10.1016/j.postharvbio.2005.12.020.

Fu PP, Xia Q, He X, Barel S, Edery N, Beland FA, Shimshoni JA, **2017**. Detection of pyrrolizidine alkaloid DNA adducts in livers of cattle poisoned with *Heliotropium europaeum*. Chem Res Toxicol, 30(3): 851–858. https://doi.org/10.1021/acs.chemrestox.6b00456

Fu PP, Xia Q, Lin G, Chou MW, **2004**. Pyrrolizidine alkaloids - Genotoxicity, metabolism enzymes, metabolic activation, and mechanisms. Drug Metab Rev, 36(1): 1–55. https://doi.org/10.1081/DMR-120028426

Gauranga R, Vasugi S, Muthamizh S, Selvaraj J, Mohammed AH, **2024**. Anti-metastatic effect of *Heliotropium bacciferum* on MCF-7 human breast cancer cell line. Cureus, 16(4): e58939. https://doi.org/10.7759/cureus.58939

Hammiche V, **Maiza** K, **2006**. Traditional medicine in Central Sahara: pharmacopoeia of Tassili N'ajjer. J Ethnopharmacol, 105: 358–367.

Hasni M, Belboukhari N, Sekkoum K, Stefan-van Staden R-I, Alothman ZA, Demir E, Ali I, **2023**. *Heliotropium bacciferum* essential extraction: Compositions determination by GC-MS and anti-inflammatory and antibacterial activities evaluation. Anall Biochem, 115366. https://doi.org/10.1016/j.ab.2023.115366

Idowu OT, **Tolulope** O,**2023**. Phytochemical screening, antibacterial activity and fatty acids from *Heliotropium indicum*. Pharm J, 15(6): 1187–1194.

Jasim WH, **Hamad** MN, **2021**. Extraction and identification of phenolic compounds from the Iraqi *Heliotropium europaeum* L. plant. Iraqi J Pharm Sci, 30(2): 158–166. https://doi.org/10.31351/vol30iss2pp158-166

Jayachitra J, **Bharathi** T, **2021**. Antioxidant activity of *Heliotropium indicum*. Int J Res Pharm Pharmacol.

Jeruto P, Mutai C, Lukhoba C, Ouma G, **2011**. Phytochemical constituents of some medicinal plants used by the Nandis of South Nandi district, Kenya. J Anim Plant Sci, 9(3): 1201-1210.

Kays SJ, **Paull** RE, **2005**. Volatile floral chemistry of *Heliotropium arborescens* L. 'Marine'. HortScience, 40(5): 1237–1239. https://doi.org/10.21273/HORTSCI.40.5.1237

Khan H, Khan MA, Gul F, Hussain S, Ashraf N, **2013**. Anti-inflammatory activity of *Heliotropium strigosum* in animal models. Toxicol Ind Health, 31: 1281-1287.

Khurm M, Chaudhry BA, Uzair M, Janbaz KH, **2016**. Antimicrobial, cytotoxic, phytotoxic and antioxidant potential of *Heliotropium strigosum* Willd. Medicines (Basel), 3(3): 20. https://doi.org/10.3390/medicines3030020

Krishnaveni A, Bairavi M, Prithivirajan S, Umamageshwari K, Kumar TVR, **2024**. Pharmacognostical, preliminary phytochemical probe and phenetics of *Heliotropium indicum* Linn leaves. Int J Pharm Anal Res, 13(4): 592–604.

Kumar S, Malhotra R, Kumar D, **2007**. *Heliotropium indicum* Linn: Ethnobotany, phytochemistry and pharmacology. J Ethnopharmacol, 111(3): 321-330.

Lawal BA, Ayanniyi RO, Ojuade FI, Usman SO, Olumoh-Abdul HA, Salawu KM, Njinga NS, Agunu A, **2022**. Phytochemical screening and in vivo antidiabetic evaluation of 1:1 combination of *Heliotropium indicum* and *Anthocleista djalonensis*. West Afr J Pharm, 33(1): 52–60.

León Levy Native Plant Preserve (**LLNPP**), **2023**. *Heliotropium angiospermum*. Retrieved from https://levypreserve.org/plant-listings/heliotropium-angiospermum

Li L, Li MH, Xu LJ, Guo N, Wu-Lan T, Shi R, **2010**. Distribution of seven polyphenols in several medicinal plants of Boraginaceae in China. J Med Plants Res, 4: 1216-1221.

Maroyi A, **2021**. Evaluation of medicinal uses, phytochemistry and biological activities of *Ehretia cymosa* Thonn. (Ehretiaceae). Int J Pharm Sci, 12(2): 1521–1528.

Montinari MR, Minelli S, De Caterina R, **2019**. The first 3500 years of aspirin history from its roots - A concise summary. Vasc Pharmacol, 113: 1–8. https://doi.org/10.1016/j.vph.2018.10.008

Moreira R, Pereira DM, Valentão P, Andrade PB, **2018**. Pyrrolizidine alkaloids: Chemistry, pharmacology, toxicology and food safety. Int J Mol Sci, 19(6): 1668. https://doi.org/10.3390/ijms19061668

Mustafa S, Tousif MI, Raiz N, Saleem M, Tauseef S, Zengin G, Hassan L, Hassan A, Nazir M, Muhammad S, **2025**. Mapping the chemodiversity, antioxidant and enzyme inhibitory potential and in silico studies of *Heliotropium europaeum*. Food Sci Nutr, 13(4): e70119. https://doi.org/10.1002/fsn3.70119

Nethaji S, Ushadevi T, Manoharan C, **2013**. Phytochemical screening and in vivo anti-ulcer activity of ethanolic extract of *Heliotropium indicum* L. Int J Drug Dev Res, 5(4): 140–144.

Ogunbinu AO, Flamini G, Cioni PL, Adebayo MA, Ogunwande IA, **2009**. Constituents of *Cajanus cajan* (L.) Millsp., *Moringa oleifera* Lam., *Heliotropium indicum* L. and *Bidens pilosa* L. from Nigeria. Nat Prod Commun, 4(4): 573–578.

Owolabi MA, Oribayo OO, Ukpo GE, Mbaka GO, Akindehin OE, **2015**. A 5-month toxicity study of the ethanol extract of the leaves of *Heliotropium indicum* in Sprague Dawley rats after oral administration. Nig Q J Hosp Med, 25(3): 184–192. PMID: 27295812

Plants of the World Online (**POWO**), **2024**.*Heliotropium* L. Kew Science, Royal Botanic Gardens, Kew. Retrieved September 18, 2025, from

https://powo.science.kew.org
Qureshi R, **Bhatti** GR, **2008**. Ethnobotany of plants used by the Thari people of Nara Desert, Pakistan. Fitoterapia, 79: 468-473.
Schoental R, **1968**. Toxicology and carcinogenic action of pyrrolizidine alkaloids. Can Res, 28(11): 2237–2246.
Rajitha BSR, **2021**. A systematic review on traditional ethnomedicinal uses of *Heliotropium indicum* L. (Boraginaceae). Int J Food Nutr Sci, 10(4): 1404-1415.
Refaz AD, Mohd S, Parvaiz HQ, **2017**. General overview of medicinal plants: A review. J Phytopharmacol, 6(6): 349-351.
Roberts J, Peerzada AM, Bajwa AA, **2024**. Biology, Ecology, Impacts and Management of the Invasive Weed, Blue Heliotrope (*Heliotropium amplexicaule Vahl*) - A Review. Sustainability, 16(14): 5923. https://doi.org/10.3390/su16145923
Saeedi M, **Morteza-Semnani** K, **2009**. Chemical composition and antimicrobial activity of the essential oil of *Heliotropium europaeum*. Chem Nat Comp, 45(1): 98–99. https://doi.org/10.1007/s10600-009-9239-8
Sarkar C, Mondal M, Khanom B, Hossain MM, Hossain MS, Sureda A, Islam MT, Martorell M, Kumar M, Sharifi-Rad J, Al-Harrasi A, Al-Rawahi A, **2021**. *Heliotropium indicum* L.: From Farm to a Source of Bioactive Compounds with Therapeutic Activity. Evid Based Complement Alternat Med, 9965481, 21 pages https://doi.org/10.1155/2021/9965481
El-Beltagi SA, El-Ghorab NI, El-Bakry HSM, El-Nady AI, Abd-ElGawad AM, **2023**. Seasonal variation in phytochemicals and anticancer activity of Heliotropium curassavicum. Egypt J Bot, 63(2): 421–432.
Shimshoni JA, Mulder PP, Bouznach A, Edery N, Pasval I, Barel S, Abd-El Khaliq M, Perl S, **2015**. *Heliotropium europaeum* poisoning in cattle and analysis of its pyrrolizidine alkaloid profile. J Agric Food Chem, 63(5): 1664-1672. https://doi.org/10.1021/jf5052199
Shoily MSA, Islam ME, Rasel NM, Parvin S, Barmon J, Aqib AH, Roy DN, Parvin S, **2025**. Unveiling the biological activities of *Heliotropium indicum* L. plant extracts: Anti-inflammatory activities, GC–MS analysis, and in-silico molecular docking. Sci Rep, 15: 3285. https://doi.org/10.1038/s41598-024-79559-w
Sivajothi V, Shruthi DS, Sajini JR, **2015**. Cytotoxic effect of *Heliotropium indicum* extracts on HeLa cell line. Int J Pharm Pharm Sci, 7(6): 412–414.
Smith LW, **Culvenor** CCJ, **1981**. Plant sources of hepatotoxic pyrrolizidine alkaloids. J Nat Prod, 44(2): 129-152. https://doi.org/10.1021/np50014a001
Hartmann T, **Ober** D, **2000**. Biosynthesis and Metabolism of Pyrrolizidine Alkaloids in Plants and Specialized Insect Herbivores, Springer, Berlin, Heidelberg, Germany.
Tesfaye TT, Feso HH, Adane L, **2024**. Phytochemical constituents of the roots of *Heliotropium verdcourtii* (Boraginaceae). Int J Second Metabolite, 11(2): 211–219. https://doi.org/10.21448/ijsm.1301392
Ullah F, Hussain S, Jamil M, Khan A, Ullah F, Arfan M, **2010**. Antimicrobial and antioxidant activities of the plant Heliotropium strigosum. African J Biotechnol, 9: 7738-7743.
Urzúa A, Modak B, Santander R, Heit C, Echeverria J, **2013**. Insecticidal properties of *Heliotropium stenophyllum* essential oil on the house fly, *Musca domestica* L. Bol Latinoam Caribe Plantas Med Aromat, 12(2): 196–200.
Wiedenfeld H, **Edgar** J, **2011**. Toxicity of pyrrolizidine alkaloids to humans and ruminants. Phytochem Rev, 10(1): 137–151. https://doi.org/10.1007/s11101-010-9174-0

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