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Preventive Potential and Safety Considerations of *Plantago lanceolata*: A Narrative Review of Ethnopharmacological and Preclinical Evidence

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Abstract

Background: *Plantago lanceolata* L. (ribwort plantain) is traditionally used for respiratory and wound care. Its main bioactive constituents include iridoids such as aucubin and catalpol, phenylethanoid glycosides such as acteoside and plantamajoside, flavonoids, tannins, and polysaccharides, which have been associated with antioxidant, anti-inflammatory, antimicrobial, and barrier-supporting effects. **Aim:** This review aims to synthesise ethnopharmacological, phytochemical, preclinical, environmental, and allergological evidence on the preventive potential and safety considerations of *P. lanceolata*, with particular attention to the distinction between pollen-related allergenic risk and leaf-based medicinal preparations. **Methods:** A narrative review was conducted using studies indexed in PubMed/NCBI, Web of Science, Scopus, and MDPI journals. Relevant literature on ethnobotany, phytochemistry, antimicrobial and antifungal activity, cytotoxicity, allergenicity, environmental biomonitoring, safety, and standardisation was considered. **Results:** Leaf extracts of *P. lanceolata* contain steroids, flavonoids, tannins, saponins, glycosides, and phenolics. Experimental studies report antibacterial and antifungal activity, including effects against *Candida albicans* and *Malassezia* spp. Methanolic extracts have shown preliminary *in vitro* cytotoxic effects against A549 lung cancer cells and enhanced activity of methotrexate or cytarabine, while relatively preserving macrophage viability. Immunoproteomic studies identify multiple IgE-reactive pollen allergens, indicating a clinically relevant respiratory allergy risk mainly related to airborne pollen. The plant may also accumulate environmental pollutants, emphasising the need for controlled sourcing. **Conclusion:** *P. lanceolata* shows promising but not yet clinically established preventive potential, particularly for barrier integrity, infection control, and inflammation modulation. Current evidence remains largely ethnopharmacological and preclinical, while direct clinical trials are limited. Translation to practice requires standardised, contaminant-tested, pollen-reduced preparations, dose–response studies, safety evaluation in at-risk groups, clear allergy labelling, and pharmacovigilance.

Major Findings: The review highlights the dual relevance of *P. lanceolata* as a source of bioactive leaf constituents and as a pollen-related allergen. Its preventive use remains promising but preliminary and requires stronger clinical validation and quality control.

Keywords: Antimicrobial Activity, Iridoids, Immunoproteomics, Phenylethanoid Glycosides, Wound Healing

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1. Introduction

Medicinal plants remain an important pillar of primary health care worldwide, with an estimated billion people regularly relying on herbal preparations for prevention and treatment of common conditions[1]. Their popularity is driven by cultural continuity, perceived safety, and growing interest in integrative approaches to chronic disease prevention[2]. Within this context, species of the genus *Plantago* (*Plantaginaceae*) occupy a prominent position in both traditional and modern phytotherapy[3].

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Plantago lanceolata L. (ribwort or narrowleaf plantain) is a perennial rosette herb native to Eurasia but now naturalised across temperate and subtropical regions[4]. It is easily recognised by its lanceolate, strongly veined leaves and erect flowering stalks bearing inconspicuous spike-like inflorescences, and thrives in disturbed habitats such as roadsides, grasslands, and pastures[5]. Beyond its ecological ubiquity, *P. lanceolata* has a long history of use in European, Middle Eastern, and African folk medicine, particularly for respiratory complaints (cough, bronchitis, sore throat), skin and mucosal lesions (wounds, burns, ulcers), and mild digestive disorders[6]. These uses have been translated into contemporary preparations—teas, syrups, lozenges, and topical formulations—that are marketed as "protective" or "soothing" remedies for upper respiratory tract infections and superficial skin irritation[7].

Phytochemical analyses have revealed that *P. lanceolata* is rich in iridoid glycosides (aucubin, catalpol), phenylethanoid glycosides (acteoside/verbascoside, plantamajoside), flavonoids, phenolic acids, tannins, polysaccharides, and terpenoids, as well as minor volatile and mineral components[6-8]. These constituents are associated with a broad spectrum of biological activities highly relevant to preventive medicine, including antioxidant, anti-inflammatory, wound-healing, antimicrobial, antitussive, antiulcerogenic, and cytotoxic properties[9]. Recent experimental work has extended this profile to selective antiproliferative and chemosensitising effects against lung cancer cells, with relative sparing of immune effector cells, suggesting potential chemopreventive and immunomodulatory roles.

The preventive dimension of *P. lanceolata* is especially evident in the respiratory and dermatologic domains[6]. Traditional and contemporary data converge on the use of *Plantago* leaves as soothing agents in acute cough and bronchitis, where mucilaginous polysaccharides, phenolic antioxidants, and iridoids contribute to barrier protection, modulation of local inflammation, and possible antiviral and antibacterial effects[10,11]. Although most clinical trials have been conducted with *Plantago major* or multi-herb syrups, these studies demonstrate clinically meaningful reductions in cough severity and improved tolerability in both adults and children, supporting the rationale for *Plantago*-based preparations as supportive therapy in self-limited respiratory infections[12-16].

In the area of skin and mucosal health, *P. lanceolata* extracts have shown acceleration of wound closure, improved histological organisation, and reduced inflammatory cell infiltration in animal models, effects that are attributed to combined antimicrobial and anti-inflammatory actions[17]. Complementary *in vitro* studies report notable antibacterial and antifungal activity against clinically relevant pathogens, including dermatomycotic fungi, at concentrations compatible with topical use, reinforcing the plant's potential as an adjunct in the prevention of superficial infections[18-20].

Beyond direct host-targeted mechanisms, *P. lanceolata* occupies a distinctive position at the interface of environmental and human health[21]. The species is widely used as a passive biomonitor of atmospheric pollutants—particularly heavy metals and polycyclic aromatic hydrocarbons (PAHs)—owing to its wide distribution, ease of identification, and high accumulation capacity[22,23]. Biomonitoring studies show that *P. lanceolata* leaves effectively capture PAHs and other combustion-derived contaminants in urban and roadside environments, and that morphological and biochemical stress markers in the plant correlate with air quality gradients[24]. These properties underscore a paradox: the same leaves that are harvested for medicinal use can also act as sinks for carcinogenic pollutants, so the preventive value of *P. lanceolata*-based remedies is tightly linked to sourcing and quality control[6,7,25].

Complicating the benefit profile further, *P. lanceolata* is a clinically important aeroallergen in many temperate regions[5]. Airborne *Plantago* pollen contributes a modest but consistent fraction of the annual pollen spectrum, yet sensitisation rates to *P. lanceolata* pollen extracts can reach approximately 30% among patients with seasonal respiratory allergy in some Mediterranean settings[26]. Immunoproteomic analyses have identified the major allergen Pla l 1—a glycoprotein of the Ole e 1-like family that accounts for a large proportion of the pollen's IgE-binding capacity—as well as several additional IgE-reactive proteins involved in carbohydrate metabolism and pollen development[27,28]. Structural and molecular aerobiology studies indicate that Pla l 1–mediated plantain allergy represents, at least in part, an independent sensitisation rather than

a simple cross-reaction to grass or ash pollen, and that atmospheric Pla l 1 levels do not always correlate with bulk pollen counts[29,30].

From a preventive medicine perspective, this dual identity of *P. lanceolata*—as a source of potentially beneficial phytochemicals and as a significant pollen allergen and environmental accumulator of toxicants—poses a complex risk–benefit question[31,32]. On one hand, preclinical and early clinical data support its adjunctive use for respiratory and mucosal protection, wound care, infection control, and possibly cancer chemoprevention[5,33-35]. On the other hand, uncontrolled exposure to pollen or contaminated plant material can undermine these benefits by provoking allergic disease or co-exposure to harmful pollutants[29,36]. This tension is rarely addressed explicitly in the herbal or nutraceutical literature, despite its direct relevance for clinicians, pharmacists, and regulatory agencies[5].

The present review aims to synthesise current knowledge on the preventive potential and safety considerations of *P. lanceolata* within a unified translational framework. Specifically, we summarise ethnomedicinal, phytochemical, and pharmacological evidence for its supportive roles in respiratory, dermatologic, mucosal, antimicrobial, anti-inflammatory, and antioxidant applications; examine environmental studies relevant to raw-material safety; and review the allergenic profile of *P. lanceolata* pollen and its clinical implications. Because much of the available evidence derives from *in vitro, in vivo*, ethnobotanical, and observational research, the review emphasises the preclinical nature of many claims and identifies the clinical, toxicological, and standardisation gaps that must be addressed before broader preventive recommendations can be made.

Although several previous reviews have summarised the traditional uses, phytochemical composition, and pharmacological properties of *Plantago* species, including *P. lanceolata*, important gaps remain in the way this evidence is integrated for preventive health applications. Most existing reviews focus primarily on ethnobotany, phytochemistry, or selected biological activities, whereas allergenic risk, environmental contaminant accumulation, raw-material quality, and translational limitations are often discussed only briefly or separately.

The novelty of the present review is therefore not the description of *P. lanceolata* as a medicinal plant per se, but the integration of its preventive potential with safety-relevant dimensions, including pollen allergenicity, pollution-related contamination, extract standardisation, and the predominantly preclinical nature of the available evidence. This approach allows a more balanced assessment of how *P. lanceolata* may be developed and used safely in modern preventive and supportive healthcare. Importantly, because direct clinical trials evaluating *P. lanceolata* as a preventive intervention remain scarce, the preventive claims discussed in this review should be interpreted as hypothesis-generating and translational rather than as established clinical recommendations.

2. Materials and Methods

2.1 Design of the Review

This manuscript was conceived as a narrative, literature-based review with a focus on two complementary dimensions of *P. lanceolata* in human health: (i) preventive and supportive pharmacological effects and (ii) allergenic and other safety-related risks. The review integrates data from ethnobotanical surveys, phytochemical and pharmacological studies (*in vitro* and *in vivo*), clinical and epidemiological investigations, environmental biomonitoring research, and immuno-proteomic analyses of pollen allergens. No new experiments on humans or animals were conducted. Therefore, institutional ethics approval was not required.

2.2 Data Sources and Search Strategy

A comprehensive literature search was conducted in the following electronic databases: PubMed/MEDLINE, Scopus, Web of Science Core Collection, and Google Scholar, complemented by targeted searches in ScienceDirect and the Cochrane Library for clinical and systematic reviews. Searches covered all available years up to November 2025 and were restricted to articles in English (or with an English abstract and sufficient methodological details).

The core search strings combined the botanical name with terms related to chemistry, pharmacology, prevention, and allergy. Representative examples include:

- "*Plantago lanceolata*" and (phytochemistry or phytochemical or iridoid or acteoside or plantamajoside);
- "*Plantago lanceolata*" and (antioxidant or anti-inflammatory or antimicrobial or wound or cough or bronchitis or ulcer or chemoprevent);
- "*Plantago lanceolata*" and (pollen or allergen or IgE or sensitisation or immunoproteomic);
- "*Plantago*" and (biomonitor or "polycyclic aromatic hydrocarbon" or PAH or "heavy.

In addition, relevant reviews on *Plantago* spp. (especially *P. major*) and reference lists of key papers were screened manually to identify further primary studies not captured by database queries. Regulatory monographs and pharmacopoeial texts were consulted where available to contextualise traditional and current medical uses, but only peer-reviewed articles were included in the formal synthesis.

2.3 Eligibility Criteria

Studies were considered eligible if they met the following criteria.

2.3.1 Plant Material

- Explicitly identified *P. lanceolata* (leaves, aerial parts, seeds, roots, pollen, or whole plant) as the primary species investigated, or
- Included *P. lanceolata* as a distinct component in multi-plant preparations with analyzable data for this species, or
- For comparative and background purposes, studies on *P. major* or other *Plantago* spp. were included when they addressed mechanisms or constituents directly relevant to *P. lanceolata* (*e.g.*, shared phytochemical classes, similar traditional indications).

2.3.2 Type of Data

Ethnobotanical surveys, documenting traditional or contemporary preventive/therapeutic uses in humans. Phytochemical and analytical studies describing the qualitative or quantitative composition of *P. lanceolata* extracts or plant parts. *In vitro* and *in vivo* experimental studies assessing antioxidant, anti-inflammatory, antimicrobial, wound-healing, cytotoxic/anticancer, or related pharmacological activities.

Clinical studies, observational or interventional, in which *P. lanceolata*-containing products were used for the prevention or treatment of human health conditions. Environmental and ecotoxicological studies using *P. lanceolata* as a biomonitor for pollutants (*e.g.* metals, polycyclic aromatic hydrocarbons) with implications for herbal quality and safety. Immunological and allergological studies evaluating *P. lanceolata* pollen identified allergens, IgE reactivity, sensitisation rates, or clinical manifestations of allergy.

2.3.3 Outcome Relevance

- Outcomes related to preventive or supportive effects (*e.g.*, protection of mucosal and skin barriers, reduction of oxidative or inflammatory markers, infection control, chemopreventive signals), or
- Outcomes related to risk and safety, including allergenicity, cytotoxicity toward non-target cells, and accumulation of environmental contaminants.

2.3.4 Exclusion Criteria

Publications where *P. lanceolata* was not clearly distinguished from other species; Purely agronomic or veterinary studies without any plausible translational relevance to human health; Conference abstracts without sufficient methodological detail; Non-peer-reviewed sources (unless used only for contextual background).

2.4 Study Selection

Two stages of screening were performed. First, titles and abstracts returned by the search strategy were screened to remove clearly irrelevant records (*e.g.*, agronomy without pharmacological or health-related outcomes). Second, full texts of potentially relevant articles were examined to verify species identification, plant part and extract type, experimental design, and outcome measures.

Studies meeting the eligibility criteria were included in the qualitative synthesis and were subsequently grouped into thematic domains: Ethnomedicinal and traditional uses; Phytochemical composition and extract characterisation; Pharmacological activities related to prevention (respiratory, dermatologic, gastrointestinal, systemic antioxidant/anti-inflammatory, cytotoxic/anticancer); Environmental

biomonitoring and pollution-related safety issues; Allergenic potential and molecular characterisation of pollen allergens.

2.5 Data Extraction and Synthesis

For each included study, the following information was extracted where applicable: botanical identity and plant part used; geographical origin and cultivation conditions (if reported); extraction solvent and method; chemical markers or quantitative phytochemical data; experimental model (cell line, animal species, human population); dose or concentration; comparator/control; main outcomes and direction of effect (beneficial, neutral, harmful); and any reported adverse effects or safety signals.

Given the heterogeneity of study designs, plant preparations, outcome measures, and reporting standards, a quantitative meta-analysis was not attempted. Instead, results were synthesised narratively and organised according to organ system (*e.g.* respiratory, dermatologic), mechanistic pathway (*e.g.* antioxidant, antimicrobial, immunomodulatory), and type of evidence (*in vitro, in vivo*, clinical, environmental, allergological). Where several studies addressed similar questions with comparable methodologies, patterns of consistency or discrepancy were highlighted.

2.6 Assessment of Quality and Risk of Bias

Because many of the included publications are experimental (phytochemical, *in vitro, in vivo*) or observational in nature, no single standardised risk-of-bias tool was applicable across all studies. Formal scoring systems (*e.g.* for randomised controlled trials) were therefore not systematically applied. Instead, potential sources of bias were evaluated qualitatively, including:

- Adequacy of plant identification and description of plant material;
- Clarity of extraction procedures and extract characterisation;
- Use and description of appropriate controls, randomisation, and blinding in experimental studies;
- Sample size, selection methods, and confounding control in clinical or epidemiological studies;
- Completeness of outcome reporting and discussion of limitations.

3. Results and Discussion

3.1 Botanical, Ethnomedicinal and Phytochemical Overview

Plantago lanceolata is a perennial rosette herb widely distributed in temperate regions and naturalised worldwide[37]. Its ecological plasticity allows it to colonise disturbed habitats, grasslands and roadside environments, which is relevant both for its accessibility as a medicinal resource and for its potential exposure to environmental contaminants[21].

Ethnobotanical data confirm long-standing use of *P. lanceolata* for disorders of the respiratory tract (cough, bronchitis, pharyngitis, asthma), skin and mucosal lesions (wounds, burns, insect bites), gastrointestinal complaints (diarrhoea, gastritis, peptic ulcer), and a variety of inflammatory and infectious conditions[5]. Preparations typically employ the fresh or dried leaves in decoctions, syrups, poultices and ointments[6]. Such indications already point to a primarily preventive and supportive role—enhancing barrier function, modulating inflammation and limiting microbial colonisation of exposed epithelia[33,38].

Phytochemical profiling shows that *P. lanceolata* contains multiple classes of secondary metabolites with complementary bioactivities, including iridoid glycosides (aucubin, catalpol), phenylethanoid glycosides (acteoside, plantamajoside), flavonoids, phenolic acids, tannins, triterpenoids (*e.g.* ursolic-type structures), polysaccharides and minerals[32,29]. Qualitative analyses of different solvent extracts from leaves demonstrate steroids, alkaloids, flavonoids, saponins, glycosides, phenols, tannins and terpenoids, with polar fractions particularly enriched in polyphenols and saponins[39]. These compound classes are consistent with the reported antioxidant, anti-inflammatory, antimicrobial, wound-healing and cytotoxic activities that provide the mechanistic basis for preventive health effects[7].

Taken together, ethnomedicinal and phytochemical evidence support the concept of *P. lanceolata* as a multi-target "barrier-support" plant: a species whose traditional indications and dominant constituents

converge on protecting skin and mucosal surfaces, dampening low-grade inflammation and modulating microbial ecosystems[5,37]. These same properties underpin much of its preventive potential in human health[7].

3.2 Preventive Benefits in Human Health

3.2.1 Antimicrobial and Antifungal Activity

Several *in vitro* studies confirm broad antimicrobial effects of *P. lanceolata*, aligning with its traditional use for infected wounds and respiratory illnesses[18,19]. Crude leaf extracts and partially purified fractions inhibit the growth of both Gram-positive and Gram-negative bacteria, as well as pathogenic fungi[16,20]. In a detailed phytochemical and antimicrobial study, petroleum ether, chloroform/methanol and methanol extracts all showed inhibitory effects against test bacteria and fungi, with zones of inhibition in some cases approaching those of positive controls[40].

More specifically for human superficial infections, a recent study evaluated ethyl acetate and methanol extracts of *P. lanceolata* leaves—alone and in combination with *Sidaovata*—against the dermatomycotic fungi *C. albicans*, *Malassezia furfur* and *M. globosa*. Both solvents yielded extracts with relevant antifungal activity; ethyl acetate fractions were generally more potent, producing mean inhibition zones up to ~29 mm and MIC values as low as 0.19 mg/mL. Synergistic combinations of *P. lanceolata* and *S. ovata* extracts further increased activity, achieving inhibition zones up to 32 mm against *M. globosa*[20].

From a preventive perspective, such antifungal and antibacterial effects support the rational use of *P. lanceolata* in topical formulations aimed at:

- Reducing colonisation of skin and mucosa with opportunistic pathogens,
- Limiting recurrence of superficial dermatomycoses, and
- Protecting compromised barrier surfaces (*e.g.* irritant dermatoses, minor wounds) from secondary infection[5,7].

However, most available data derive from *in vitro* assays using relatively high extract concentrations and simplified models[41]. Clinical trials confirming prophylactic or adjuvant benefits in human populations are still lacking[6,42,43].

3.2.2 Antioxidant, Anti-inflammatory and Wound-healing Properties

The polyphenol-rich profile of *P. lanceolata* underlies its antioxidant capacity[44]. Multiple extracts display free radical scavenging and reduction of reactive oxygen species in cell-free systems and experimental models[44-47]. These antioxidant effects are complemented by anti-inflammatory activity, including inhibition of nitric oxide production and modulation of pro-inflammatory mediators, often linked to iridoid glycosides and phenylethanoid glycosides[48].

Wound-healing activity, reported in both traditional practice and experimental studies, is thought to result from a combination of:

- Astringent tannins that promote local vasoconstriction and protein precipitation;
- Mucilaginous polysaccharides that form a protective film over damaged epithelium;
- Antimicrobial phenolics that reduce microbial load;
- Anti-inflammatory compounds that limit excessive exudation and tissue damage[43,47].

In preventive terms, these properties suggest that regular or early application of *P. lanceolata*-based preparations may help:

- Sustain epithelial integrity (skin and respiratory mucosa);
- Buffer oxidative stress at barrier surfaces exposed to pollutants or UV radiation;
- Shorten the transition from acute injury to chronic, non-healing lesions[17,33,34].

Again, the translational evidence is still dominated by preclinical and ethnopharmacological data. Rigorous human trials with preventive endpoints (*e.g.* reduced incidence of infected wounds or recurrent respiratory infections) remain an important research gap.

Although the traditional use and preclinical pharmacological profile of *P. lanceolata* support its preventive and supportive potential, the clinical

evidence remains limited. Available human data are mostly derived from traditional-use monographs, observational experience, or studies involving *Plantago* species, mixed herbal preparations, or related species such as *P. major*. These studies provide supportive signals for respiratory symptoms, cough relief, mucosal protection, and wound-related applications, but they do not establish strong, species-specific clinical efficacy for *P. lanceolata* as a preventive intervention.

This limitation is particularly important when interpreting claims related to recurrent respiratory infections, wound healing, antimicrobial protection, and chemoprevention. In most cases, evidence is based on mechanistic plausibility, phytochemical composition, *in vitro* antimicrobial or anti-inflammatory activity, and animal models rather than randomised controlled trials in human populations. Therefore, the current evidence should be considered preliminary and translational. Future clinical studies should use chemically standardised *P. lanceolata* preparations, clearly defined doses, well-characterised patient groups, appropriate comparators, and clinically meaningful preventive endpoints, such as reduced frequency of respiratory episodes, lower recurrence of superficial infections, faster wound resolution, or improved safety and tolerability during repeated use.

3.2.3 Cytotoxic and Potential Chemopreventive Effects

Recent work has focused on the cytotoxic and potential chemopreventive properties of *P. lanceolata*[49]. Phenylethanoid glycosides such as acteoside and plantamajoside, isolated from *Plantago* species, have demonstrated dose-dependent antiproliferative effects across several cancer cell lines with relatively low toxicity to normal cells[50].

A 2025 study evaluated a methanolic extract of *P. lanceolata*—alone and combined with chemotherapeutic agents methotrexate and cytarabine (Alexan)—on human lung adenocarcinoma A549 cells and murine J774 macrophages. Treatment with 80 µg/mL extract reduced A549 viability to about 63%, while preserving ~90% viability in macrophages. When combined with 100 µg/mL methotrexate or cytarabine, the same extract concentration further decreased A549 viability to ~44–50%, with only modest additional impact on macrophages[35].

These data suggest:

- A degree of selective toxicity towards malignant epithelial cells;
- A potentially favourable therapeutic index, with relative sparing of immune effector cells;
- Synergistic interactions with existing chemotherapeutics.

The above mentioned facts should be interpreted strictly as preclinical evidence. Although they suggest possible cytotoxic and chemosensitising properties of *P. lanceolata* extracts or constituents, they do not justify clinical chemopreventive or anticancer recommendations at this stage. Future studies should include chemically standardised extracts, *in vivo* validation, pharmacokinetic assessment, drug–herb interaction studies and controlled clinical investigations before any translational claim can be made.

While such results are far from clinical application, they raise the possibility that *P. lanceolata*-derived compounds could contribute to secondary prevention (*e.g.* reducing tumour progression or recurrence) as adjuncts to standard oncological care[19,51]. At present, evidence is limited to *in vitro* models and one species of cancer. *In vivo* studies and mechanistic work are needed before chemopreventive claims can be substantiated.

3.2.4 Nutritional and Ecological Contributions to Preventive Health

Beyond direct pharmacological effects, *P. lanceolata* has implications for preventive health via its role in agro-ecosystems and animal nutrition[52]. As a forage species, plantain has been shown to lower the environmental footprint of livestock production[53]. In farmed red deer, diets containing *P. lanceolata* reduced urinary nitrogen excretion by approximately one-third, despite higher dry matter intake, thereby decreasing nitrogen losses and potential nitrate leaching[54]. Similar benefits have been reported in dairy grassland systems[54,55].

Such changes in nutrient cycling may indirectly support human health through:

- Improved water quality (lower nitrate and ammonium contamination);
- Reduced greenhouse gas emissions from agriculture;
- Decreased need for synthetic inputs or antibiotics in animal production.

Although these ecosystem-level effects sit upstream of individual clinical outcomes, they are part of the broader preventive landscape in which *P. lanceolata* may play a beneficial role[52,56,57].

3.3 Environmental Toxicology and Quality/ Safety of Raw Material

The same traits that make *P. lanceolata* a useful environmental indicator—wide distribution, durable leaves, high leaf surface area and waxy, hairy cuticles—also mean that medicinal material can accumulate environmental pollutants. Several studies illustrate this dual role[21,24,58,59].

3.3.1 Polycyclic Aromatic Hydrocarbons (PAHs)

A dedicated investigation of PAH accumulation used *P. lanceolata* as a passive biomonitor under both field and experimental conditions. The plant effectively accumulated polycyclic aromatic hydrocarbons, particularly higher molecular weight congeners, in its foliar tissues. Leaves exposed to diesel aerosol or collected in polluted urban/industrial areas showed elevated PAH loads, largely associated with epicuticular waxes and trichomes[20].

From a preventive health standpoint, this has two critical implications:

- Risk of contaminant co-exposure. When leaves from contaminated sites are used in herbal teas, syrups or topical preparations, patients may be inadvertently exposed to carcinogenic PAHs, counteracting any preventive benefit[60].
- Opportunity for environmental surveillance. Conversely, the ability of *P. lanceolata* to integrate airborne PAH exposure over time can be exploited to map pollution hotspots and guide safer sourcing of medicinal material[24].

These findings support strict requirements for cultivation or collection of *P. lanceolata* in low-pollution areas and for routine contaminant testing, particularly when preparations are intended for long-term preventive use[59].

3.3.2 Trace Metals and Urban Pollution

Similar concerns arise for trace metals. In an urban study from southern Poland, both *P. major* and *P. lanceolata* were sampled near metallurgical and urban emission sources. Leaf tissues contained elevated levels of metals such as Cd, Pb and Zn, especially in unwashed samples, reflecting atmospheric deposition. While some measured concentrations remained below regulatory limits for edible herbs, the data clearly show that *Plantago* species efficiently intercept and accumulate particulate-bound metals[59].

At the same time, low Air Pollution Tolerance Index values indicate that *P. lanceolata* is relatively sensitive to high pollution, reinforcing its utility as a biomonitor[61]. An ethnobotanical review further notes applications of *P. lanceolata* in metal removal and phytoremediation of contaminated soils[7].

Thus, for medicinal use:

- Cultivation or collection should avoid industrial and high-traffic areas;
- Quality standards should include PAH and heavy metal testing, especially for products marketed for daily, long-term preventive use (*e.g.* respiratory syrups, teas, nutraceuticals)[62].

Without such safeguards, the preventive benefits of *P. lanceolata* could paradoxically be offset by chronic low-dose exposure to environmental toxicants[63].

3.3.3 Ecophysiological Plasticity and Resilience of Supply

Ecophysiological studies show that *P. lanceolata* exhibits substantial plasticity under extreme environmental conditions, adjusting its root system, vascular traits and photosynthetic apparatus to withstand drought, high radiation and nutrient stress[64]. This plasticity contributes to its cosmopolitan distribution and suggests resilience of medicinal supply under climate change[21].

However, stress-induced shifts in secondary metabolism are also possible, potentially altering the concentrations of key iridoids and phenylethanoids[48]. While such variation is not yet well characterised, it underscores the need for standardisation of herbal material by chemical profiling rather than relying solely on botanical identity[65].

3.3.4 Seed Microbiome and Microbiological Safety

The seeds of *P. lanceolata* harbour a relatively stable core microbiome across a gradient of plant species richness, including taxa such as *P. rhizosphaerae* and *S. faeni*. Many of these endophytes have putative

plant-growth-promoting or protective functions[66]. From a human safety perspective, the presence of a consistent seed microbiome is not inherently problematic but emphasises the importance of good manufacturing practices, appropriate drying and storage, and microbiological quality control of any products containing whole seeds or minimally processed material[67].

3.4 Allergenic Risks

In contrast to the relatively benign toxicological profile of leaf preparations, *P. lanceolata* pollen is a clinically significant aeroallergen[26]. An immunoproteomic study from Portugal identified *P. lanceolata* pollen as a relevant contributor to the regional pollen load, accounting for about 3% of total annual pollen counts. Among 372 patients with seasonal allergic rhinitis or rhinoconjunctivitis, approximately one-third (31%) had specific IgE to *P. lanceolata* pollen[31].

It is important to distinguish between two different exposure scenarios: environmental inhalation of *P. lanceolata* pollen and therapeutic exposure to leaf-based preparations. The clinically relevant allergenic risk is primarily associated with airborne pollen, which may contribute to seasonal allergic rhinitis, conjunctivitis, and asthma in sensitised individuals. By contrast, most medicinal products are prepared from leaves rather than pollen-bearing inflorescences. Nevertheless, incomplete separation of plant material, contamination during harvesting, or insufficient processing could theoretically introduce residual pollen proteins into herbal preparations. Therefore, products intended for oral or topical use should ideally be produced from pollen-reduced or pollen-free raw material, especially when marketed to patients with respiratory allergy or atopic disease.

Proteomic analysis revealed at least eight major IgE-reactive protein groups, including enzymes such as polygalacturonase, UDP-glucose dehydrogenase, inositol-3-phosphate synthase and adenosylhomocysteinase, some of which are homologous to allergens in other plant species[27]. Several proteins were novel or not yet fully characterised, suggesting that the allergen profile of *P. lanceolata* is more complex than previously recognised[29]. Cross-reactivity with structurally related allergens in other pollens is likely but not yet systematically mapped[28,31].

For pollen-based exposure (inhalation):

- *Plantago lanceolata* should be considered a relevant sensitising allergen in regions where the plant is abundant, contributing to seasonal rhinitis, conjunctivitis and, occasionally, asthma[68].
- Skin-prick testing and component-resolved diagnostics, including *P. lanceolata* allergens, could improve individualised risk assessment in polysensitised patients[69].

For herbal preparations:

- Most oral or topical products are derived from leaves rather than inflorescences, and careful processing can minimise residual pollen content[70].
- Nonetheless, in highly sensitised individuals, even trace pollen contamination could, in theory, provoke allergic symptoms[29].

Compared with other well-known pollen allergens (*e.g.* grasses, birch), clinical reports of systemic reactions to ingested *P. lanceolata* products remain rare, but robust pharmacovigilance data are lacking[5]. On current evidence, the principal allergenic risk relates to environmental exposure to airborne pollen rather than therapeutic leaf preparations. However, safety-minded product design should still aim for pollen-free extracts and transparent labelling, especially in regions with high prevalence of seasonal allergy[71].

From a clinical and regulatory perspective, allergy-related precautions should include clear identification of the plant part used, control of pollen contamination, appropriate labelling for individuals with known plantain pollen sensitisation, and post-marketing pharmacovigilance for allergic reactions. These measures are particularly relevant because sensitised individuals may not associate respiratory symptoms with herbal products derived from the same botanical species. Thus, allergenic risk should not be overstated as a general contraindication to leaf-based *P. lanceolata* preparations, but it should be explicitly addressed as a safety consideration in product development and patient counselling.

3.5 Integrated Benefit–risk Assessment

Taken together, current data portray *P. lanceolata* as a medicinal plant with a generally favourable, but nuanced, benefit–risk profile in preventive health[6]. Table 1 summarises the main preventive benefits and risk factors identified for *P. lanceolata* across different domains.

Its main strengths lie in barrier support and infection control: antimicrobial and antifungal activities against skin and mucosal pathogens, together with wound-healing, anti-inflammatory and antioxidant effects, provide a coherent basis for use in minor wounds, superficial dermatomycoses and recurrent respiratory complaints[16]. Polyphenol-rich extracts also show systemic antioxidant and anti-inflammatory activity, and early *in vitro* evidence of selective cytotoxicity toward cancer cells suggests a cautious potential for adjunct chemopreventive applications, particularly in combination with conventional therapy[72-74]. At the ecosystem level, the use of *P. lanceolata* in forage systems can reduce nitrogen losses and the environmental footprint of livestock production, indirectly supporting human health[75].

Set against these benefits, several risks and uncertainties must be acknowledged. The most immediate is the aeroallergenicity of *P. lanceolata* pollen: in regions where the plant is abundant, a notable proportion of patients with seasonal respiratory allergy show specific IgE and develop rhinitis, conjunctivitis or asthma[60,68,76]. Although medicinal products usually rely on leaves, and careful processing can minimise pollen contamination, sensitised individuals may remain vulnerable if formulations are not rigorously controlled[77]. In addition, the plant's efficiency in capturing airborne contaminants—especially polycyclic aromatic hydrocarbons and trace metals—means that leaves harvested from polluted environments may carry carcinogenic or toxic burdens that directly counteract any preventive intent[22,59]. These concerns are compounded by the limited depth of clinical evidence: many preventive claims rest on traditional use and preclinical work rather than robust, well-controlled human trials, leaving key questions on dosing, long-term safety, comparative effectiveness and drug interactions insufficiently answered[5,7].

In practical terms, the benefit–risk balance can be tipped decisively towards benefit through three strategies: strict control of sourcing and standardisation (cultivation in low-pollution areas, contaminant testing, chemical standardisation to marker compounds); allergy-aware formulation and labelling (leaf-based, pollen-reduced extracts, clear warnings for atopic patients and active pharmacovigilance); and targeted clinical research that addresses true preventive endpoints while documenting safety and interactions[78]. Under such conditions, *P. lanceolata* can be viewed as a plant with meaningful preventive potential and relatively low intrinsic toxicological burden, whose main hazards stem from its ecological context and pollen rather than its core phytochemistry[6]. Recognising and managing this complexity allows clinicians, pharmacists, regulators and producers to use *P. lanceolata* not as a harmless folk remedy, but as a pharmacologically active resource capable of contributing constructively to modern preventive medicine[79].

A major limitation of the current evidence base is the scarcity of robust clinical trials directly assessing *P. lanceolata* preparations in preventive contexts. Consequently, the benefit–risk assessment proposed here should be understood as a translational framework based on converging ethnopharmacological, phytochemical, preclinical, environmental, and allergological evidence, rather than as proof of established clinical preventive efficacy. This distinction is essential for avoiding overinterpretation of preclinical findings and for guiding future trial design.

3.6 Evidence Gaps, Limitations, and Future Research Priorities

Despite the broad ethnopharmacological relevance and promising preclinical profile of *P. lanceolata*, the current evidence base has several important limitations that restrict direct translation into preventive clinical practice (Table 2). First, many reported biological effects are derived from *in vitro* assays, animal models, or studies using chemically heterogeneous extracts. These models are valuable for identifying possible mechanisms, but they cannot fully predict clinical efficacy, optimal dosage, bioavailability, safety during repeated use, or interactions with conventional medicines. This limitation is particularly relevant for antimicrobial, wound-healing, anti-inflammatory, and cytotoxic outcomes, where active concentrations in experimental systems may not correspond to achievable concentrations in human tissues.

Second, direct clinical evidence for *P. lanceolata* remains limited. Some human data are available for *Plantago* species, traditional preparations, or multi-herbal products, but species-specific randomised controlled trials using standardised *P. lanceolata* extracts are scarce. Consequently, current claims regarding

Table 1. Summary of preventive benefits, environmental issues and allergenic risks of *P. lanceolata* in human health

Domain/Aspect	Main Findings (Benefit or Risk)	Mechanisms/Key Constituents	Evidence Base	Key Limitations/Safety Issues
Respiratory tract (cough, bronchitis, mucosal irritation)	Supportive relief of acute cough and mild bronchitis; soothing effect on irritated mucosa	Mucilaginous polysaccharides, iridoid and phenylethanoid glycosides, flavonoids; anti-inflammatory and antitussive actions	Ethnomedicinal data; *in vitro* and in *vivo* models; clinical data mainly from *Plantago* spp. mixtures	Few modern monotherapy trials; optimal dose and duration unclear; not a substitute for antibiotics or asthma control
Skin and wound healing	Faster wound closure, improved tissue organisation, and reduced superficial infection risk.	Tannins, polyphenols, iridoids; antioxidant, anti-inflammatory, astringent and antimicrobial effects	Animal models; *in vitro* antimicrobial/antifungal studies; long-term traditional use	Clinical evidence is limited; mostly topical, short-term use; formulation and concentration vary widely.
Antimicrobial and antifungal activity (skin and mucosa)	Inhibition of Gram-positive/Gram-negative bacteria and dermatomycotic fungi; potential to limit recurrence of superficial infections	Polyphenols, iridoids, saponins and other secondary metabolites; membrane damage and enzyme inhibition	Multiple *in vitro* studies; some synergistic combinations with other plants	Active concentrations may be higher than achievable *in vivo*; lack of controlled human prophylaxis studies
Systemic antioxidant, anti-inflammatory and chemopreventive signals	Reduction of oxidative stress and inflammatory mediators; selective cytotoxicity towards cancer cells with relative sparing of immune cells	Iridoid and phenylethanoid glycosides (aucubin, acteoside, plantamajoside), flavonoids and other polyphenols	*In vitro* and animal models; one *in vitro* study with chemotherapy combinations	No clinical chemoprevention trials; relevance of *in vitro* doses uncertain; potential drug–herb interactions not defined
Environmental biomonitoring and contaminant accumulation	Effective biomonitor of PAHs and heavy metals; reflects urban/industrial pollution gradients.	High leaf surface area, epicuticular waxes and trichomes that trap airborne particles	Field and experimental biomonitoring studies	Leaves from polluted sites may carry carcinogenic PAHs and toxic metals, undermine preventive benefits if used medicinally.
Ecophysiology, forage and ecosystem effects	Forage plant that reduces N losses and the environmental footprint of livestock; resilient under climate stress	Deep rooting, flexible physiology; influence on nitrogen cycling and pasture composition	Agronomic and ecological studies in grassland and deer/dairy systems	Indirect human benefits; not directly translatable to clinical endpoints; stress may alter phytochemical profile
Allergenic risks (pollen)	Clinically relevant aeroallergen; ~30% sensitisation in some allergic populations; causes seasonal rhinitis, conjunctivitis, and sometimes asthma.	Major allergen Pla l 1 and multiple other IgE-reactive proteins (Ole e 1–like and enzymatic proteins)	Aerobiological surveys; immunoproteomics; clinical allergy cohorts	Risk mainly via inhaled pollen; residual pollen in herbal products may affect highly sensitised patients; pharmacovigilance data are scarce
Overall benefit–risk balance	Favourable preventive potential when properly sourced, standardised and targeted	Multi-target barrier support plus systemic antioxidant effects; main hazards from pollen and environmental contaminants	Converging experimental, ethnomedicinal and limited clinical evidence	Need for clean cultivation, contaminant testing, pollen-reduced formulations and well-designed clinical trials with preventive endpoints

Table 2. Key evidence, limitations, and future research priorities for *P. lanceolata*

Evidence Domain	Main Findings/Available Data	Main Limitations	Future Research Priorities
Respiratory and mucosal use	Traditional use for cough, bronchitis, sore throat, and mucosal irritation; effects are biologically plausible due to mucilage, iridoids, phenylethanoid glycosides, flavonoids, and anti-inflammatory activity	Few species-specific clinical trials; evidence often comes from *Plantago* spp., related species, or mixed preparations	Randomised controlled trials using standardised *P. lanceolata* preparations, defined doses, and endpoints such as cough duration, symptom severity, recurrence, and tolerability
Antimicrobial and antifungal activity	*In vitro* antibacterial activity against Gram-positive and Gram-negative bacteria; antifungal activity against *C. albicans*, *M. furfur*, and *M. globosa*; inhibition to ~29–32 mm and MIC zones reported up to values as low as 0.19 mg/mL	Mainly *in vitro* evidence; uncertain clinical relevance of tested concentrations; limited extract standardisation	Standardised antimicrobial assays, dose–response studies, formulation testing, and clinical studies for topical or mucosal applications
Wound healing and skin protection	Experimental studies suggest faster wound closure, improved tissue organisation, reduced inflammation, and possible protection against secondary infection.	Mostly animal and *in vitro* data; limited human evidence; variable extract composition and concentration	Controlled clinical studies using standardised topical preparations for minor wounds, burns, ulcers, or irritant dermatoses
Antioxidant and anti-inflammatory activity	Polyphenol-rich extracts show free-radical scavenging and anti-inflammatory effects; activity attributed to iridoids, phenylethanoid glycosides, flavonoids, tannins, and polysaccharides.	Limited translation from cell-free and animal models to humans; insufficient data on bioavailability and metabolism	Pharmacokinetic studies, biomarker-based human trials, and standardisation by marker compounds such as aucubin, catalpol, acteoside, and plantamajoside
Cytotoxic and potential chemopreventive signals	Methanolic extract reduced A549 lung cancer cell viability to ~63% at 80 µg/mL; combinations with methotrexate or cytarabine reduced viability to ~44–50%, while macrophage viability remained around ~90%	Evidence is limited to preclinical cancer-cell models; no clinical chemoprevention trials; possible drug–herb interactions are unknown.	*In vivo* validation, mechanistic studies, pharmacokinetic assessment, and careful evaluation are only adjunctive support, not as anticancer treatment.
Environmental contamination and raw-material quality	Leaves can accumulate pollutants, including polycyclic aromatic hydrocarbons and trace metals such as Cd, Pb, and Zn, especially in urban, roadside, or industrial areas.	Contaminant levels depend on the collection site; many pharmacological studies do not report pollutant screening.	Controlled cultivation, PAH and heavy-metal testing, good agricultural and collection practices, and quality specifications for commercial products
Allergenic risk	*P. lanceolata* pollen accounted for ~3% of annual pollen counts in one regional study; ~31% of 372 patients with seasonal allergic rhinitis or rhinoconjunctivitis had specific IgE to *P. lanceolata* pollen	Risk is mainly linked to inhaled pollen; residual pollen contamination in oral/topical products is poorly quantified; pharmacovigilance data are limited.	Pollen-reduced or pollen-free preparations, allergy labelling, component-resolved diagnostics, and post-marketing surveillance
Overall translational value	Promising preventive candidate for respiratory, skin, mucosal, antimicrobial, antioxidant, and anti-inflammatory applications	Preventive efficacy is not yet clinically established; evidence remains heterogeneous and largely preclinical.	Well-designed clinical trials using standardised preparations, defined doses, safety monitoring, contaminant control, and clinically meaningful preventive endpoints.

respiratory protection, prevention of superficial infections, wound healing, and chemopreventive effects should be interpreted as preliminary and hypothesis-generating rather than clinically established. Future trials should include clearly defined preparations, standardised marker compounds such as acteoside, plantamajoside, aucubin, or catalpol, appropriate placebo or active comparators, and clinically meaningful endpoints.

Third, substantial methodological heterogeneity exists across the available literature. Studies differ in plant part used, harvesting location, extraction solvent, phytochemical characterisation, concentration ranges, tested organisms or cell lines, and outcome measures. This heterogeneity limits comparability between studies and makes it difficult to identify dose–response relationships or define safe and effective formulations. In many studies, extract standardisation is incomplete, which complicates reproducibility and regulatory interpretation.

Fourth, the environmental safety of raw material remains a critical but often underestimated issue. Because *P. lanceolata* can accumulate airborne pollutants, including polycyclic aromatic hydrocarbons and trace metals, medicinal material collected from roadside, urban, or industrial areas may carry contaminants that undermine its preventive value. This is particularly important for products intended for repeated or long-term use, such as teas, syrups, nutraceuticals, and topical preparations. Therefore, future research and product development should include contaminant testing, controlled cultivation, and good agricultural and collection practices.

Fifth, allergenic risk requires a more nuanced interpretation. The principal allergenic concern relates to inhalation of airborne *P. lanceolata* pollen, which has been associated with seasonal respiratory allergy in sensitised individuals. However, most medicinal preparations are based on leaves rather than pollen. The key safety issue for herbal products is therefore not the inherent allergenicity of all *P. lanceolata* preparations, but the possibility of residual pollen contamination, insufficient labelling, and lack of pharmacovigilance in atopic populations.

Finally, evidence regarding long-term safety, vulnerable groups, and drug–herb interactions remains insufficient. Data are particularly limited for children, pregnant or breastfeeding women, patients with asthma or severe allergic disease, immunocompromised individuals, and patients receiving chemotherapy, anticoagulants, immunomodulators, or other long-term medications. These gaps should be addressed before stronger preventive or adjunctive therapeutic recommendations are made.

3.7 Novel Contribution of the Present Review

The present review differs from previous overviews of *P. lanceolata* by placing the plant within a translational preventive-health framework rather than presenting only its traditional uses or pharmacological activities. Its main contribution is the integration of three usually separated evidence domains:

Ethnopharmacological and preclinical data supporting respiratory, dermatologic, mucosal, antimicrobial, antioxidant, anti-inflammatory, and potential chemopreventive effects;

- Environmental and quality-control evidence showing that *P. lanceolata* may accumulate pollutants such as polycyclic aromatic hydrocarbons and trace metals;
- Allergological evidence demonstrating that *P. lanceolata* pollen is a clinically relevant aeroallergen in sensitised individuals.

This combined perspective is important because the preventive value of *P. lanceolata* cannot be evaluated only through its bioactive constituents. It also depends on the plant part used, harvesting conditions, contaminant burden, pollen contamination, extract standardisation, and the clinical vulnerability of the target population. By explicitly distinguishing between leaf-based medicinal preparations and airborne pollen exposure, the review provides a more precise safety interpretation than approaches that treat allergenicity as a general property of the whole plant. Moreover, by emphasising that many preventive and chemopreventive claims remain preclinical, the review identifies the research steps needed before stronger clinical recommendations can be made.

Thus, the novelty of this manuscript lies in proposing a unified benefit–risk and translational framework for *P. lanceolata*, linking phytochemistry, preventive pharmacology, environmental safety, allergen control, and clinical evidence gaps.

4. Conclusion

Current evidence suggests that *P. lanceolata* has meaningful preventive potential, particularly in respiratory, skin, mucosal, antimicrobial, antioxidant, and anti-inflammatory contexts. However, this is supported mainly by ethnopharmacological use, phytochemical plausibility, *in vitro* studies, animal models, and limited clinical evidence. Therefore, *P. lanceolata* should be presented not as an already established preventive intervention, but as a promising botanical resource that requires further clinical validation, dose standardisation, long-term safety assessment, and clearer regulatory control.

Parallel trends in functional foods and integrative nutrition will probably see *P. lanceolata* incorporated into teas, nutraceuticals and fortified products aimed at modulating low-grade inflammation and oxidative stress, with omics-guided research helping to optimise extraction methods and synergistic combinations with other botanicals. At the same time, its role as a biomonitor and pollen allergen will drive cleaner cultivation systems, routine contaminant testing and the development of pollen-reduced or pollen-free formulations, along with better allergy diagnostics that explicitly consider plantain.

Nevertheless, the current evidence base remains uneven. The strongest support comes from ethnopharmacological experience, phytochemical plausibility, *in vitro* antimicrobial and anti-inflammatory studies, animal models, environmental biomonitoring, and allergological investigations of pollen. In contrast, direct clinical trials with standardised *P. lanceolata* preparations are scarce. This limits the strength of preventive recommendations and requires a cautious interpretation of the available data. Future research should prioritise controlled clinical trials, standardised extracts, contaminant screening, pollen-control procedures, pharmacokinetic evaluation, long-term safety monitoring, and assessment of vulnerable populations.

Overall, the future of *P. lanceolata* in human health will depend less on discovering new effects and more on refining how it is grown, standardised and targeted, aligning phytochemistry, environmental quality and allergen safety so that its preventive potential can be used confidently in everyday clinical and self-care practice. By integrating preventive pharmacological evidence with environmental quality concerns and pollen-related allergenic risk, this review offers a more balanced and translationally oriented perspective than previous reviews focused mainly on traditional use, phytochemistry, or isolated biological activities.

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