

Review Article

Ethnobotanical Uses, Chemical Constituents, and Application of *Plantago lanceolata* L.

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The medicinal benefits of *P. lanceolata* L. have been acknowledged worldwide for hundreds of years. The plant is now distributed worldwide, especially in temperate zones. This review gives an overview of ethnomedicinal use, phytochemistry, pharmacological activities, and other potential application of *P. lanceolate* L. Several effective chemical constituents such as polyphenols, tannins, flavonoids, alkaloids, terpenoids, iridoid glycosides, fatty acids, and polysaccharides are found in *P. lanceolata* L., which contribute to its exerting specific therapeutic effects. Correspondingly, studies have found that *P. lanceolata* L. has different biological activities, including antioxidant, antibacterial, wound-healing, anti-inflammatory, cytotoxic, and antiulcerogenic activity. The plant also treats various diseases related to the skin, respiratory organs, digestive organs, reproduction, circulation, cancer, pain relief, and infections. The plant has many applications in cosmetics such as lotion and creams; it is also used as an excellent indicator to know the presence and absence of heavy metals and the accumulation in industrial and urban areas. The plant suppresses soil nitrogen mineralization in agriculture due to allelochemicals such as aucubin. The biological activities, medicinal properties, and industrial application of *P. lanceolata* mainly depend on the activities of the responsible, active chemical constituents. However, this field still needs more study to determine the exact mechanisms and the main bioactive compound activity accountable for these activities. Also, most of the studies have been performed in vitro, so further in vivo studies are recommended for the future.

1. Introduction

Under the plant kingdom, medicinal plants have been mainly used by local peoples found in developing countries, especially in resource-limited areas. Many peoples in this region directly or indirectly use medicinal plants to satisfy their primary health care needs [1]. Consumers' interest in using herbal products for personal and health care has grown worldwide [2]. From the World Health Organization's (WHO) perspective, medicinal plants (MP) have become popular. Approximately 4000 million people utilize herbal remedies regularly [3]. Phytomedicines, derived from seeds, roots, leaves, fruits, bark, seeds, and flowers of medicinal plants, can treat diseases [4]. Many researchers have given more attention to medicinal plants because they can generate many uses and applications in medicine and pharmacy [5]. It is estimated that half of the pharmaceutical drugs are derived from medicinal plants due to their capacity of the chemical constituents that bring therapeutic effects [6].

Plantago is a genus of medicinal plants belonging to the Plantaginaceae family [7]. It has around 275 species that grow annually and permanently [8]. Its name comes from the Latin "planta," meaning "sole," to represent the broad leaves lying touching the ground [9]. It is known for its pharmaceutical activities [10]. *Plantago* has a wide range of uses, including raw materials for salads, soups, baking, and animal feed to improve health and reduce antibiotic use [8]. Phytochemicals derived from root, leaf, and stem of genus Plantago have shown medicinal potential [11]. *P. major* L., *P. halepensis* Miller, *P. lentiscus* D., *P. trimula* L., and *P. lanceolata* L. are the most common species [12].

P. lanceolata L. is a well-known species of the genus Plantago; it is widely distributed in meadows, roadside strips, pastures, and green areas in the temperate world 800 m above sea level [13, 14]. It has been used for medicinal purposes to treat diseases such as wound healing, inflammation, cancer, respiratory system disorder, blood circulation, reproductive system, and digestive organs [13]. It has various applications as cosmetics [15], as metal removal from polluted areas [16], as an additive in foods [17], and as an insecticide [18]. The extracts of the plant also showed different properties as antioxidant [19], antibacterial [20], anti-inflammatory [21], rheological [22], and viscoelastic [22] (Figure 1). Phytochemicals in the root, leaf, and seed of P. lanceolata L. include iridoid glycosides, polyphenols, polysaccharides, and flavonoids, which have therapeutic potential [11].

The available information about *P. lanceolata* L. is scattered and not all in one site. There is much literature on ethnomedicine, phytochemistry, and pharmacological activities of *P. lanceolata* L. The current review brings together all of the disparate information on the various possible applications of extracts and bioactive compounds obtained from *P. lanceolate* L. in one location.

2. Materials and Methods

Published research papers, review papers, proceedings, short communications, and book chapters describing P. lanceolate L. or *Ribwort plantain* are the primary information for writing this article. More than 100 publications were obtained from 1993 to 2021. In the search process, keyword phytochemistry of *P. lanceolata* L, traditional medicinal use of *P.* lanceolata L., ethnomedicinal use of P. lanceolata L., and bioactive compounds isolated from the different parts of the plant, history, and distribution about the plant were used. We classified the data according to ethnomedicinal, pharmacological activities, phytochemistry, and application of P. lanceolata L. ChemDraw was used to draw the structure of bioactive compounds, while EndNote performed reference writing. We use the Natural products database for Africa (NDA) to write the botanical name and the local name of the medicinal plant.

3. History and Distribution

P. lanceolata L.is an international species distributed in European countries from Iceland found south and east of Spain and Asia's Northern and Central parts. Historically, the plants originated from the Eurasia continent; however, they slowly expanded worldwide, including the colonizers from Europe. Historically, *P. lanceolata* L. for medicinal purposes started from ancient Greeks and Roman peoples [21]. Also, in the country China, the plants were used 3000 years ago [17]. Most of the time, this plant is considered a weed and wild plant, but it is the most cultivated plant, and in

small amounts, it is also cultivated in Romania. However, it is a new crop in the UK [15]. Even though the species are common and native to Europe, the North part of Africa, the south and west part of Asia, and Europe [23], currently, they occur in every aspect of the world, such as the USA, Australia, New Zealand, Japan, and in many countries of Africa [23]. It became cultivated in temperate zones and naturalized in many continents except Antarctica [24].

4. Ethnomedicinal Use of *Plantago lanceolate* L.

Different people use P. lanceolata L. leaf as emollient, demulcent, and expectorant. It is effective for dysmenorrhea, abdominal pain, laxatives, and astringents [10]. The inflamed wounds can be treated by applying the leaf powder of P. lanceolata L. [15]. It effectively stops bleeding and encourages the treatment of damaged tissue [9]. In church ceremonies, the leaves of *P. lanceolata* L. were utilized as incense smoke. This plant's inflorescences were combined with Helichrysum stalks and burned to perfume clothes and rooms [17]. The seeds of P. lanceolata L. are essential in treating parasitic worms; the mucilage from the plant is used as a laxative and alleviates irritated membranes. Eye lotion is highly treated with distilled water obtained from the whole parts of the plant [9]. Eye illness wound repairing, antibacterial, anti-inflammatory, antiasthmatic, and diuretic properties are also treated by the aerial parts of P. lanceolata L. [25]. Mixing juice from the plant with honey or wine relieves gout, and arthritis can be treated by consuming crushed leaves with salt. It is also used as a topical application for skin diseases [8]. Ethnomedicinal uses of various parts of P. lanceolata L. in different countries have been summarized in Table 1.

5. Pharmacological Activities

Many studies have investigated the cytotoxic, antispasmodic, antibacterial, antioxidant, anti-inflammatory, and wound healing effects of different portions of the *P. lanceolata* L. (Table 2) [31–34]. Methanolic, 30% acetonitrile, 80% methanol, 80% ethanol, and hot water extract of leaves, roots, flowers, fruits, and seeds of *P. lanceolata* L. had been studied for their bioactivities. These extracts showed strong, cytotoxic, antiobesity, anti-inflammatory, wound healing, anti-oxidant, and antimicrobial effects [35].

5.1. Antioxidant Activities. Different studies were conducted to test the antioxidant activities of the *P. lanceolata* L. extracts using different antioxidant methods such as cupric reducing antioxidant capacity (CUPRAC), oxygen radical absorbance capacity (ORAC), dimethyl-4-phenylenediamine (DMPD), ferric reducing antioxidant power (FRAP), 2, 2' -azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS), oxygen radical absorbance capacity (ORAC), and DPPH (2,2-diphenyl-1-picrylhydrazyl) β -carotene bleaching method [27]. Various extraction procedures were employed to get extracts from the aerial portion of *P. lanceolata* L. including supercritical fluid extraction (SFE), ultrasound-assisted

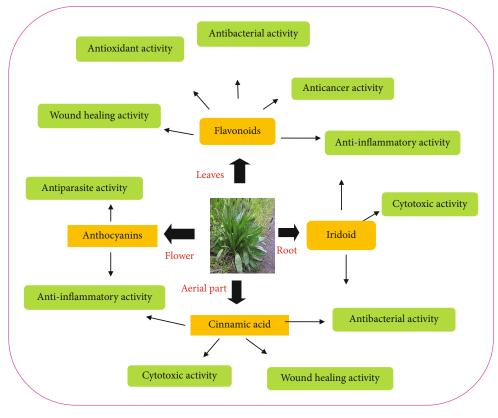


FIGURE 1: Biological activity of P. lanceolate L.

extraction (UE), and Soxhlet (SOX). The antioxidant activities of these extracts were examined for antioxidant activities according to linoleic acid/ β -carotene and DPPH assays. The results showed that the plant has a strong antioxidant potential [36]. In another study, the aerial part of the plant extract was also performed for antioxidant activities using some antioxidant assays such as reducing power (FRAP assay), lipid peroxidation, superoxide anion and NO scavenger capacity, hydroxyl radical, and DPPH radical. The findings suggest that P. lanceolata L. has antioxidant properties comparable to the synthetic antioxidant BHT [21]. Furthermore, using different solvent extractions such as aqueous, methanol, and ethanol leaf extracts of the plant also showed antioxidant activity potential based on the result obtained from antioxidant assays [36, 37]. Acidified methanol ((80%) and HCl (1%)) extracts of root, stem, flower, and fruit parts of P. lanceolata L. exhibited significantly higher antioxidant capacities compared to the value of the plant M. neglecta. Methanol (60%) extracts from the seeds of the plants also showed an antioxidant behavior using assays like DPPH, OH radical scavenging, and cellular antioxidant activity [4].

P. lanceolata L. antioxidant activity is influenced by several factors. According to research, the extracted solvent affects antioxidant activity. For example, in one study, ethanol extracts were found to have a stronger antioxidant capacity than water and methanol extracts [28]. Parts of the plant such as aerial, leaves, root, and flower also affect the antioxidant behavior. The type and concentration of phytochemicals responsible for antioxidant activities vary from one part of a plant to another [8]. Different solvents have different free radical scavenging activities on the same part of the plant. For instance, methanol, acetone, ethyl acetate, chloroform and n-hexane leaf extracts had the value of IC50 1.81, 2.02, 0.56, 0.41, and 0.41 μ g/m, respectively, based on DPPH assay [1]. The antioxidant properties of herbal products are mainly attributed to phenolic compounds such as flavonoids and polyphenolic derivates (cinnamic acid, p-coumaric acid, syringic acid, vanillic acid, and salicylic acid), compounds that are found in the leaves of *P. lanceolata* L. [21]. Antioxidant behaviors of different parts of the *P. lanceolate* L. with their assay are listed in Table 3.

5.2. Antimicrobial Activities. Medicinal herbs, shrubs, and trees and their products have shown the potential with antimicrobial agents [42]. A study was conducted to show the effects of the extracts of P. lanceolata L. on antibacterial activities against monocytogenes, Streptococcus, S. aureus, Salmonella, and E. coli species. The agar disc diffusion method showed that the leaf extracts of the plant have better antibacterial activity against selected bacterial pathogens [20]. P. lanceolata L. leaf extracts also showed antibacterial activity against S. pneumoniae, MRSA, S. aureus, S. boydii, E. coli, and K. pneumoniae using various solvents such as water, methanol, and acetone [43]. The antibacterial tests on leaf extracts of P. lanceolata L. were also done against some bacterial species like K. pneumoniae, S. boydii, E. coli, S. pneumoniae, MRSA, and S. aureus; the result showed that a higher degree of antimicrobial activity was observed with

Parts of the plant	Ethnomedicinal use	Country	Reference
Aerial parts	(i) Treatment of decoction internally, embolism, diarrhea for children, infusion cough, expectorant	Turkey	[4]
Leaves	 (i) Bath with the infusion of the plant with <i>R. canina</i> to treat infertility (ii) Fresh leaves spread on a cloth and heated and put on the skin can reduce poultice wound healing. The mixture of water plants, flour, and black pepper used for decoction internally (iii) When the flour of the plant is added in boiled water, treat colds (iv) Treat hemorrhoids, cancer, disorders like gynecological decoction if it is eaten cooked and decoction as tea (v) If the leaf is mixed in boiled milk, decrease muscle pain, stop diabetes, kyphos, coughs, and menstrual aches 	Algeria	[25]
	(vi) Small leaves are inserted in the nostrils to heal a headache	South Africa	[26]
	(vii) Used for discontinuing too much bleeding and wound repairing, anti-inflammatory, cough medication, antibacterial cause, sore throat treatment, and antidiarrheal	South Africa	[1]; [27]
	(viii) Used to treat insect and snake bites, cervicitis, rectal fissures, hemorrhoids, cuts, and abscess (ix) Used for wound repairing, intestinal and internal disorder, stomach pain, maturation of an abscess, diabetes, burn treatment, shortness of breath	Duzce	[28]
	(x) Infusion is essential for emollient, expectorant, and demulcent(xi) Burned wounds can be treated when powdered leaves are applied(xii) The heated leaves are essential for wet dressing for wounds and swellings	Pakistan	[10]; [9]
	(xiii) To alleviate the problems on external animal skin parasites, use ground leaves or juice from fresh leaves	Poland	[17]
	(xiv) Prepare an infusion of the leaves; then, use it to wash the eyes	Island of Mauritius	[3]
	(xv)The juice of the freshly squeezed leaf is pasted with butter and made into ointment	Ethiopia	[29]
	(i) Root juices are used to cure earache	South Africa	[30]
Root	(ii) The mixture of its root with the root of M . <i>vulgare</i> with equal amounts is a medicine for the bite of rattlesnakes	Not specified	[9]
	(i) Extracts used as purgative and laxative	Pakistan	[10]
Seed	(ii) Seeds were also commonly used as a natural laxative due to their high content of fibers, also having external uses for skin inflammations and wound healing, and also used as a rubefacient	Baghdad-Iraq	[24]

TABLE 1: Ethnomedicinal use of *P. lanceolata* L.

MIC and MBC values in the range of 6.25 to 25%, respectively [37]. In another research, methanol extract of leaves of *P. lanceolata* L. was found to inhibit *S. aureus* and *P. mirabilis* more than ethanol extract. However, the ethanol extract displayed better activity than the methanol extract against *E. coli* and *K. pneumoniae* [31]. The value of antibacterial activities (inhibition zone) can be affected by the type of solvent used to extract bioactive compounds, type of bacteria species, and parts of the plant (Table 4) [33].

5.3. Wound Healing Activities. Different practices have been used for centuries to treat injuries due to burning. Among those, 1/3 of medicinal plants have been used for wound healing caused by burning. Studies performed on extracts obtained from the leaves of *P. lanceolata* L. have shown a wound healing effect [45]. Aqueous and methanol extract of *P. lanceolata* L. showed wound healing potential by reducing the levels of TBARs in mice and rats. Furthermore, *P. lanceolata* L. was revealed to have the ability to enhance tissue Zn^{+2} and Cu^{+2} levels, both of which are essential indicators in the wound healing formation process [46]. The aqueous aerial parts of *P. lanceolata* L. also showed wound healing activities on 48 injured rats. The burned sur-

face area of rats decreases by 10% when the extracts are placed on the surface [47]. In another research, wound healing activities were also observed when P. *lanceolata* L. extracts were applied to the skin of donkeys and Sprague-Dawley rats [48, 49].

5.4. Anti-Inflammatory Activities. The biological answer for the immune system caused by different factors such as pathogens, cell damage, cut, and compounds that cause toxicity is termed inflammation [17]. The disorders like gastritis, tumors, arthritis, atherosclerosis, and others involve inflammation in their progress [34]. Different studies have been carried out to assess the anti-inflammatory properties of different parts of *P. lanceolate* L. The anti-inflammatory efficacy of methanol extract aerial parts of the plant was investigated using COX-1 and 12-LOX inhibition. The result confirmed that COX-1 inhibitory activity (IC50) was 2.00, and for that of 12-LOX, the inhibitory activity (IC50) was 0.75 [21]. In vivo anti-inflammatory activities of P. lanceolataL. dichloromethane extract were examined using an in vitro enzymatic assay. The result indicated antiinflammatory characteristics in mice using 160 mg/kg, 80 mg/kg, and 40 mg/kg [34].

Plant's part (s)	Solvent used	Concentration of solvent	Response to antioxidant assay	
Whole plant	Ethanol	80%	1100 μ mol Fe ²⁺ /g DW in FRAP, and for ORAC, it is 3500 μ mol TE/g DW	
	Mixture of methanol and hydrochloric acid	80%:1%	For FRAP =201.4 μ mol Fe ²⁺ /g DW and for ORAC = 930.5 μ mol TE/g DW,	[4]
Aerial	Methanol	80%	$IC_{50} = 4.20 \ \mu$ g/ml in DPPH, $IC_{50} = 236.12 \ \mu$ g/ml in hydroxyl radical scavenging, $IC_{50} = 23.85$ superoxide anion scavenging $IC_{50} = 24.83$ for lipid peroxidation.	
	Ethanol	80%	1100 μ mol Fe ²⁺ /g DW in FRAP and 3500 μ mol TE/g DW for ORAC	
	Mixture of methanol and water	40%:1%	$IC_{50} = 24.83 \text{ mg/mL}$ in lipid Peroxidation & FRAP= 109.80 mg of AAE/g of DW	[21]
Leaves	Acetonitrile	30%	DPPH radical inhibition at 25 μ g/ml is 12.77% to 15.78%	[39]
	Mixture of methanol with hydrochloric acid	80%:1%	130.4 μ mol Fe ²⁺ /g DW	[4]
	Water and dilute hydrochloric acid		29.39 = DPPH in %, 137.83 in FRAP μ M TE/5 mg	[40]
Root	Methanol and 80%:1%		190.1 µmol Fe ²⁺ /g DW	
Fruit	hydrochloric acid	80%:1%	255.2 μ mol Fe ²⁺ /g DW	[4]
Seeds	Methanol (60%)	60%	118.58 in μ mol TE/g in DPPH 499.53 μ mol TE/g in hydroxyl radical scavenging assays 27.00 μ mol QE/g in cellular antioxidant activity assay	
Flower	Methanol and hydrochloric acid	80%:1%	369.1 μmol Fe ²⁺ /g DW	

TABLE 2: Antioxidant behaviors of different parts of the plant.

5.5. Cytotoxic Activity. A study was conducted to test the cytotoxic activities of P. lanceolata L. extract using an MTT assay. The result confirmed that chloroform leaf extract of the plants showed a good cell feasibility report in the range of 100% to 75.35% on the mouse leukemic macrophage cell line (RAW 264.7). The secondary phytocompounds like terpenoids and phenols could be responsible for this cytotoxicity effect [1]. The cytotoxicity activities of aerial part of P. lanceolata L. extracts were also conducted on human cell line such as MRC-5, HT-29, MCF7, and HeLa. The result showed a stronger cytotoxic activity due to some bioactive compounds such as gallic acid, luteolin-7-O-glucoside chlorogenic, apigenin, and vanillic [21]. The cytotoxic effects of aqueous leaf extracts of P. lanceolata L. on MCF-7 cells were investigated, and the results revealed that the plant's leaf extracts decreased MCF-7 cell proliferation [50]. In another study, bioactive compounds from methanol extract of the plant showed the cytotoxic activities on MCF-7 with the value of $GI_{50} = 114.45$, TGI > 240, and $LC_{50} > 250$ [32, 51]. This showed that methanolic *P. lanceo*lata L. leaf extracts exhibit cytotoxicity against breast cancer cell lines. The result also showed that the leaf extract of P. lanceolata L. decreased the proliferation of CAL51 triplenegative breast cancer cells but had only a minor effect on MCF7, AMJ13, and MDAMB breast cancer cells.

5.6. Antispasmodic Activity. Plantago species have been found to have a wide range of biological activities, including cytotoxic, anti-inflammatory, antioxidant, and antispasmodic properties [52]. The aerial parts of *P. lanceolata* L. was examined for antispasmodic activity on isolated ileum

and trachea of the guinea-pig [21]. The result indicated that the *P. lanceolata* L. extract suppressed the contractions of the guinea-pig ileum generated by diverse compounds such as acetylcholine, histamine, potassium, and barium ions. The compounds aucubin, lavandulifolioside, isoacteoside, catalpol peracetate, plantamajoside, acteoside, and luteolin (Figure 2 and Table 2) inhibited the ACh-induced contractions of the guinea-pig ileum [31]. Flavonoids also possess antispasmodic activities for *P. lanceolata* L. [21].

6. Phytochemistry of P. lanceolata L.

A study showed that different concentrations of bioactive compounds such as flavonoids [58], coumarins [59], lipids and cinnamic acids [60], and tannins [61] are found in the whole or separated parts of *P. lanceolata* L. such as flowers, leaves, and roots. For instance, in the whole part of the plant, the average amount of the main classes of compounds: flavonoids, coumarins, lipids, cinnamic acid content, and phenolic content were 358, 9, 1120, 200, and 1368 μ g/g of DW, respectively [54]. The levels of total phenolics and various groups of phenolic compounds in *P. lanceolata* L. extracts ranged from 12.2 ± 1.7 (stem) to 35.3 ± 2.8 (leaf) mg GAE/g DW [4]. The following subsections explain some bioactive compounds found in *P. lanceolata* L.

6.1. Phenolic Compounds. Different types of phenolic compounds are recently reported in *P. lanceolata* L. Some of these compounds are 3,4-dihydroxyphenylacetic acid, (+)-catechin, pyrocatechol, vanillin, verbascoside, epicatechin, taxifolin, hesperidin, rosmarinic acid, pinoresinol,

Microorganism	Solvent used	Concentration of solvent	Inhibition zone(mm)	Reference
	Chloroform		8	[20]
	Acetone	95%	16.3	[42]
	Methanol	95%	17.3	[43]
	Ethanol		14	[20]
S. aureus	Methanol		15.8	[20]
	Water		16.3	[43]
	Methanol	70%	8	
	Petroleum ether	20 µl	23	[5]
	Chloroform /methanol	20 <i>µ</i> l	23	
	Methanol	70%	6	[20]
	Chloroform /methanol	20 µl	24	[5]
	Ethyl acetate extract		8	[33]
	Chloroform		7.6	[44]
E.coli	Petroleum ether	20 µl	24	[5]
	Acetone	95%	12.7	
	Methanol	95%	15	[43]
	Water		13.3	
	Ethanol		15	[44]
	Acetone	95%	10.7	
S. pneumoniae	Methanol	95%	10.3	[20]
	Water		13.6	
	Acetone	95%	16	
S.boydii	Methanol	95%	16.6	[43]
	Water		15.3	
	Acetone	95%	17	[43]
17	Ethyl acetate		8	[33]
K. pneumoniae	Methanol	95%	26	[42]
	Water		15.7	[43]
	Acetone		8.7	
C. albicans	Methanol		15.3	[43]
	Water		22	
S. aureus	Methanol	70%	9	[20]
L. monocytogenes	Methanol	70%	16	[20]
	Petroleum ether	20 <i>µ</i> l	17	
S. agalactiae	Chloroform /methanol	20 µl	19	[5]
	Methanol	20 µl	16	
P. mirabilis	Methanol		8	[33]
D annuminess	Chloroform	50mg	9	[5]
P. aeruginosa	Ethanol	50mg	16	

TABLE 3: Antibacterial properties of different solvent extracts of *P. lanceolata* L. on gram-positive and negative bacteria species based on inhibition zone response.

eriodictyol, and kaempferol (Figure 3) [62]. Different concentrations of phenolic bioactive compounds such as gallic acid $(18 \pm 1 \,\mu\text{g/g})$, protocatechuic acid $(92 \pm 0.2 \,\mu\text{g/g})$, 3,4-dihydroxyphenylacetic acid $(9 \pm 0.2 \,\mu\text{g/g})$, caffeic acid $(156 \pm 4 \,\mu\text{g/g})$, vanillic acid $(90 \pm 1 \,\mu\text{g/g})$, syringic acid $(31 \pm 1 \,\mu\text{g/g})$, and vanillin $26 \pm 2 \,(\mu\text{g/g})$ were found in the methanolic extract of *P. lanceolata* L. [35]. In other studies,

the concentration of bioactive compounds like gallic acid (2.73 mg/g), protocatechuic acid (24.11 mg/g), vanillin (9.18 mg/g), p-coumaric acid (61.16 mg/g), kaempferol (43.64 mg/g), luteolin (5.35 mg/g), apigenin (8.27 mg/g) [63], p-hydroxybenzoic acid (149.46 mg/g), 2,5-dihydroxybenzoic acid (16.20 mg/g), protocatechuic acid (103.48 mg/g), vanillic acid (411.52 mg/g), gallic acid (212.01 mg/g), apigenin

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Part used	Pharmacological activities	Bioactive compounds	Reference
Aerial part	Antioxidant, anti-inflammatory and cytotoxic activities	P-hydroxybenzoic, vanillic, gallic acid, chlorogenic acid, apigenin, luteolin and luteolin-7-O-glucoside	[21]
Aerial parts	Wound healing, eye infections	Not identified	[25]
Aerial parts and leaves	Wound healing activity	Iridoidglucosides	[49]
Aerial parts and leaves	Cytotoxic activity	Flavonoids	[21]
Aerial parts, leaves, seeds and whole plan	Anti-inflammatory activity	-	[21, 53]
Flowers	Antimicrobial and antioxidant activities	Flavonoids and anthocyanin	[54]
Flowers, leaves, and roots	Antimicrobial activity	Phenolics and flavonoid	[21]
Flowers, leaves, and roots	Antimicrobial activities	Flavonoids, coumarins, lipids, cinnamic acids, lignans, and phenolic compound	[54]
Leave	Cytotoxic activity	Luteolin-7-O-glucoside	[32]
Leave	Anti-inflammatory	Polyphenols	[53]
Leave	UV-protecting and fibroblast growth-stimulating activity	Phenolic and flavonoid compounds	[55]
Leave	Antimicrobial activity	Polyphenolic compounds and flavonoids	[8]
Leave	Antioxidant activity	Flavonoids, tannins and saponins	[1]
Leave	Anti-inflammatory activity	Aucubin and flavonoids	[53]
Leave	Anti-ulcer activity	Polyphenol and flavonoids	[21]
Leave	Free radical scavenging activities	Polyphenolic compounds, iridoid glucosides, phenylethanoid glycoside, aucubin and flavonoids	[17]
Leave, flower, root	Antioxidant activity	Phenolic compounds	[4]
Leaves	Anti-ulcer activity	-	[56]
Seed	Wound healing activity	Catalpol, aucubin, and acteoside	[57]
Seed	Anti-inflammatory activity	Iridoid glucosides	[53]
Seed	Parasite worms	Iridoid glucosides	[9]
Whole part	Wound healing activity	Iridoid glucosides	[49]
Whole plant, leaves	Anti-obesity	-	[4]

TABLE 4: Pharmacological activities of different parts of P. lanceolata L.

(184.38 mg/g), luteolin-7-O-glucoside (119.15 mg/g), and quercetin-3-O-glucoside (34.67 mg/g) [21] was found.

6.2. Flavonoids. Several flavonoid bioactive substances, including luteolin-7-O-glucuronide, luteolin, apigenin, luteolin-7-O-glucoside, and quercetin-3-O-D-galactopyranoside, were found in P. lanceolata L. Other flavonoids such as 3, 5, 7, 4-tetrahydroxyflavonol, apigenin-6,8-di-C-glucoside, luteolin-7-Oglucoside, and 7-O-glucuronide-3'-glucoside, as well as quercetin-3-rutinoside, 7-O-glucuronide, and apigenin-7-O-glucoside, were also identified in P. lanceolata L. (Figure 4) [11, 64]. Some flavonoids like cinnamic acids (Figure 5) are present in of P. lanceolata L. [30]. Aqueous extraction of the plant contains some flavonoids such as catechin with its derivatives, epicatechin with its derivative, and luteolin derivatives. The ethanol extracts of the plant also contain epicatechin, luteolin, epicatechin, and luteolin derivatives [21]. In the latest study, a new flavonoid compound called isorhamnetin 3-O-α-L-⁴C₁-arabinopyranosyl- $(1 \rightarrow 2)$ - β -D- $^{4}C_{1}$ -glucopyranoside) was isolated from the leaves of P. lanceolata L. [65].

6.3. Iridoid Glycosides. Several iridoid glycosides are isolated from the leaves of P. lanceolata L. Aucubin and catalpol are the main iridoid glycosides present in it; asperuloside, globularin, gardoside, geniposidic acid, mayoroside, melittoside, and desacetylasperuloside acid methyl ester are also present in the leaf of P. lanceolata L. [66]. The study that was performed to know acteoside content in Plantago species using the HPTLC method indicated that P. lanceolata L. has a significantly higher acetonide than P. reniformis Beck, P. atrata Hoppe, P. holosteum Scop, P. schwarzenbergiana Schur, and P. coronopus L. [11]. The maturity of P. lanceolata L. leaves affects the contents of iridoid glycosides; for instance, catalpol is found in the highest quantity in intermediate and immature age leaves, while aucubin is found in them the less amount [15]. Catalpol, aucubin, acteoside, and verbascoside are the most important bioactive compounds obtained from P. lanceolata L. These compounds gave the plant a potential of anti-inflammatory, antioxidant, antineoplastic, and hepatoprotective [67]. In another research, a new phenolic compound, named phenylethanoid glycoside 2-(3, 4-dihy-L1C4rhamnopyranosyl $(1 \rightarrow 3)$] [*E*-caffeoyl-1 \rightarrow 4]- β -D-

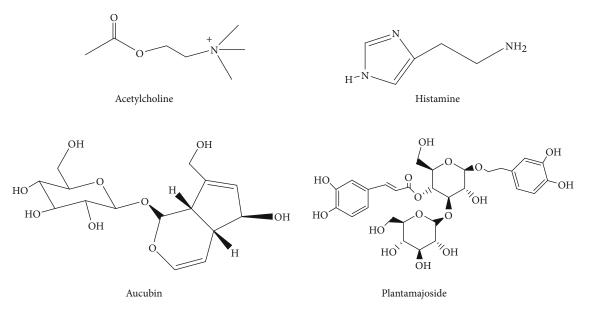


FIGURE 2: Structures of bioactive compounds used as antispasmodic activity.

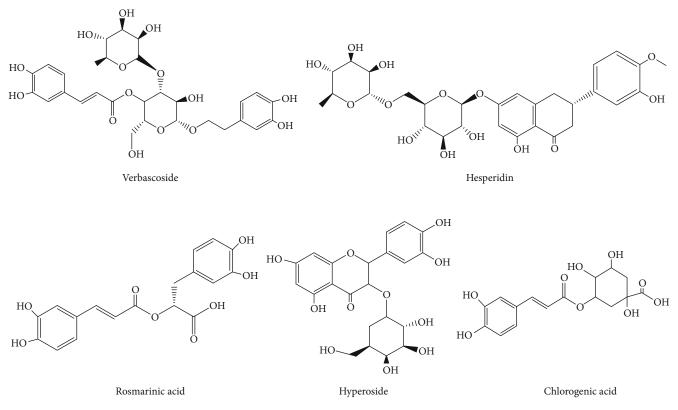


FIGURE 3: Major phenolic compounds of P. lanceolata L.

4C1 glucopyranoside (Figure 6) was isolated from *P. lanceolata* L. leaves [65].

6.4. Volatile Oil and Essential Oils. The isolation of volatile components from aqueous *P. lanceolata* L. extracts was studied using hydrodistillation [68]. The findings confirmed the presence of monoterpenes, sesquiterpenes, oxidized

monoterpenes, oxidized diterpenes, apocarotenoids, and aldehydes. The other compounds present were ketones, phenols, phenolic ethers, esters, aliphatic hydrocarbons, aromatic hydrocarbons, oxidized sesquiterpenes, alcohols, and fatty acids [15]. The volatile oils in the fruits and leaves of *P. lanceolata* L. were identified using GC-MS analytical techniques. The result confirmed the presence of 6-(3-hydroxy-

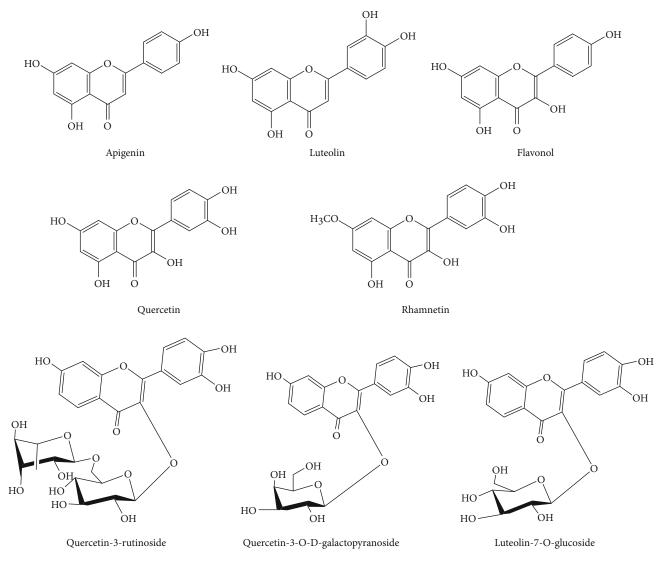


FIGURE 4: Structures of important flavonoids isolated from P. lanceolata L.

1-butenyl)-1,5,5-trimethyl-7-oxabicyclo [4,1,0] heptane-3-ol and (E),4(3-oxo-2,6,6-trimethylcyclo-hex-2-en-1-yl)-3-buten-2-ol, benzoic acid, oct-1-en-3-ol, oct-1-en-3-ol, and vanillic acid (Figure 7) [15].

Varicose fatty acid compounds present in the n-hexane extract of *P. lanceolate* L. leaves were identified using GC-MS. Some of the fatty acids observed in the GC-MS data were palmitic acid, myristic acid, and stearic acid (Figure 8) [24]. An investigation of the plant's proximate composition analysis also confirmed the presence of polyun-saturated fatty acids in *P. lanceolata* L. leaf extract [69]. In aqueous extracts on *P. lanceolata* L., some fatty acid components, including capric acid, palmitic acid, and margaric acid, were detected. Additional fatty acids such as linolenic acid, myristic acid, pentadecanoic acid, and linoleic acid were detected using GC-FID and GC-MS methods [68].

6.5. *Phenolic Carboxylic Acid.* Phenolic compounds are important bioactive compounds in *P. lanceolata* L. [28].

From the leaves of *P. lanceolata* L., phenolic compounds such as p-hydroxybenzoic acid, protocatechuic, gentisic, chlorogenic, and neochlorogenic acid were isolated [66]. Aqueous extracts of dried leaves of *P. lanceolata* L. contain benzoic acid derivatives, gallic acid, and benzoic acid, and ethanol extracts of the plant also contain some phenolic compounds like caffeic acid derivatives, ferulic acid, benzoic acid derivatives, ferulic acid, and benzoic acid (Figure 8) [65].

6.6. Terpenoids. Terpenoids are essential compounds in the genus *Plantago* [70]. Different classes of terpenoids were reported in *P. lanceolata* L. These include the (E)- β -farnesene, (E)- α -bergamotene, and sesquiterpenes (E)- β caryophyllene. Also, other terpenoids like C11 homoterpene (E)-4,8-dimethyl-1,3,7 nonatriene (DMNT) and monoterpene (E)- β -ocimene are also present in the plant [71]. Many terpenoids such as loliolide, ursolic acid, and oleanolic acid (Figure 9) are detected in petroleum ether and chloroform/ methanol extract *P. lanceolata* L. leaves [16].

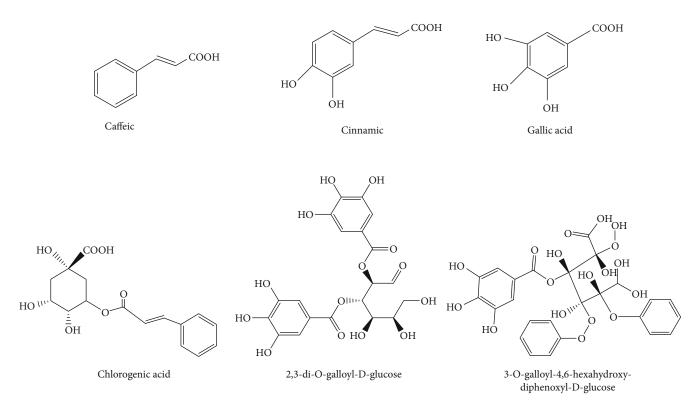


FIGURE 5: Cinnamic derivatives isolated from P. lanceolata L.

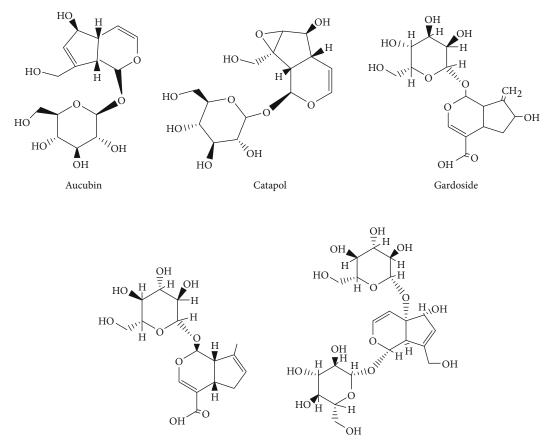
6.7. Acteoside. Acteoside (Act), a phenylethanoid glycoside, is an active compound in several plants and traditional herbal medicines [72]. Acteoside (Figure 10) is one of the main bioactive compounds in *P. lanceolate* L. [67, 73]. A study indicated that the aerial parts of *P. lanceolata* L. had much more acetonide than other Plantago species such as *P. atrata* Hoppe, *P. coronopus* L., *P. reniformis* Beck, *P. holosteum* Scop, and *P. schwarzenbergiana* Schur, according to HPTL technique quantification data [11]. Acetonide is also present in ethanolic extracts of *P. lanceolata* L. Antispasmodic action was conferred by the presence of these chemicals in the plant [31].

6.8. Polysaccharides. Some polysaccharides such as L-mannose, D-glucuronic acid, D-glucose, D-galactose, D-galacturonic acid, L-arabinose, D-mannose, and minor proportions of L-fructose and D-xylose are present in different parts of *P. lanceolata* L. [15]. Pectic, rhamnogalacturonan, arabinogalactan, and α -D-glucan polysaccharides were also isolated from the leaves [40]. The leaves of *P. lanceolata* L. contain galacturonic acid from 62.64% to 70.58%, arabinose content from 37.36% to 29.42%, galacturonic acid 35.8%, and glucuronic 21.9%. At the same time, rhamnose was found only in traces [74].

6.9. Other Bioactive Compounds. A study was conducted for isolating bioactive compounds from methanol extract of leaf of *P. lanceolata* L. using silica gel column chromatography techniques. The ¹H NMR and ¹³C-NMR spectrum afforded one important compound, 6"-O-ethyl-4"-acetyl verbascoside (Figure 10). This compound possesses the plant to have antioxidant and antibacterial activities [5], and using DEPT-

135, FT-IR, ¹H-NMR, and ¹³C-NMR spectra, a second bioactive compound named as(E)-butyl 2-(4-(2-(2-hydroxyl-2-methyl cyclohexyl)ethyl)-7-methyloctahydro-1H-inden-1-yl)-5-methylhept-4-enoate was isolated using methanol as a solvent [28]. Important phytochemicals such as hexahydro-pseudo-ionone, diheptyl phthalate, and phytol were extracted from leaves of *P. lanceolata* L. The plant leaf extract also contains bioactive chemicals such as ditridecyl phthalate, hexahydro farnesyl acetone, stigmasterol methyl ether, stearyl aldehyde, alpha-bisabolene epoxide, and allantoin (Figure 11) [24]. Bioactive anthocyanins such cyanidin glycoside, delphinidin glycoside, peonidin glycoside, and petunidin glycoside were identified in the flower of *P. lanceolata* L. [75].

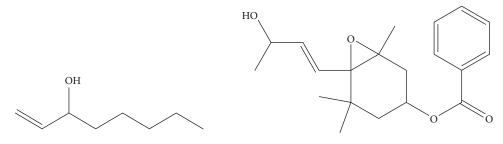
6.10. Minerals. The Plantago leaf extracts possess different metallic elements such as arsenic, cadmium, copper, and cobalt. Metals such as iron, nickel, lead, zinc, magnesium, sodium, calcium, and phosphorus are also found in the leaves of the plant [44]. On other investigations, some metallic elements like nickel and cobalt also found in the leaves of *P. lanceolata* L.; however, the plant's roots, on the other hand, have the largest quantities of Ni and Co compared to the leaves [76]. Cadmium concentrations in the leaves of *P. lanceolata* L. ranged from 0.89 to 0.44 mg/kg [76, 77]. A study also indicated that from the washed leaves of *P. lanceolata* L., some metallic elements like lead, iron, Manganese, cadmium, zinc, and lead were also analyzed [21, 69]. In a study conducted on analyzing the nutritional requirements of grazing livestock in *P. lanceolata* L. and other species, the highest



Geniposidic acid

Melittoside

FIGURE 6: Iridoid glucosides and phenylethanoid glycosides isolated from P. lanceolata L.



Oct-1en-3-ol, n(E)

6-(3-hydroxy-1-butenyl)-1,5,5,-trimethyl-7oxaicyclo[4,1,0]heptan-3-ol benzoic acid

FIGURE 7: Major volatile oils from P. lanceolata L.

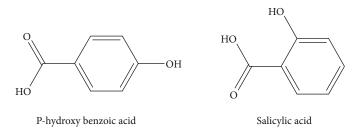


FIGURE 8: Some phenolic compounds from *P. lanceolata* L.

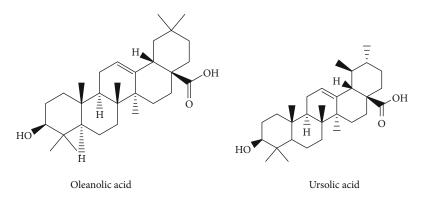


FIGURE 9: Some terpenoids in the leaves of P. lanceolata L.

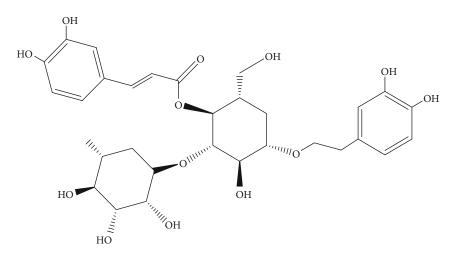


FIGURE 10: Structure of acteoside.

phosphorus and potassium were found in *P. lanceolata* L. before the flowering period [78].

7. Application of P. lanceolata L.

7.1. Cosmetics. P. lanceolata L.is included in the list of cosmetic plants. It is used in the cosmetic industry in many European industries [15]. Aqueous infusions and stabilized fresh juice from leaves of *Plantago* species are used in cosmetics [17]. The leaves of *P. lanceolata* L. can be used to manufacture lotion, creams, and face masks in the European industry. The presence of salicylic acid in the plant's leaves effectively reduces existent skin impurities and optimizes the skin appearance due to its antibacterial, keratolytic, and anti-inflammatory action [15].

7.2. Biological Activities. P. lanceolata L. leaves are used externally to treat sores and wounds and internally treat bronchitis, antibacterial, astringent, anti-inflammatory, emollient, antitussive, furuncles, bug, and snake bites [79]. Ethanolic extract of the aerial portions of P. lanceolata L. was examined for the antispasmodic activities against guinea-pig ileum and trachea. The result showed that various agonists such as acetylcholine, histamine, barium, and potassium ions inhibited the guinea-pig ileum's contractions

[31]. European manufacturers use *P*. lanceolata L. alone or in combination with other plants for different medicinal purposes: in Finland and Romania used for digestion expectorant; in Slovenia, Italy and Romania used as astringent, soothing irritations, and antimicrobial; and in Poland and Belgium used for various forms such as herbal tea, tablets, and syrup [79]. Traditionally, coughs, dysentery, and diarrhea can be treated using tea from the plant's leaves. Blisters, rashes, swelling, and insect stings are also treated with leaves of *P. lanceolata* L. Mucilage from *P. lanceolata* L. seed has been shown to lower cholesterol levels in the blood [80].

7.3. Metal Removal. P. lanceolata L. can also be used as a metal indicator and metal removal from the atmosphere during air pollution [76]. P. lanceolata L. can be used as a good bioindicator for heavy metal accumulation in urban and industrial areas. Data on accumulative capacity allow us to recommend this species to indicate the presence of metals like lead, zinc, and cadmium [81]. Studies assessing Cu resistance by a microorganism called rhizosphere of P. lanceolata L. have shown potential agents for bioremoval of Cu and bacterial stimulation of Cu bio adsorption by this plant species [82]. P. lanceolata L. is the best indicator of environmental pollution. A study on environmental pollution in an urban area of Poland using P. lanceolata L. as

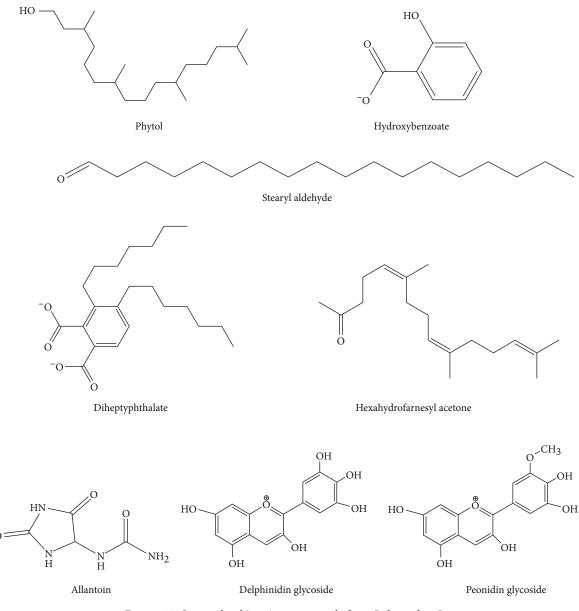


FIGURE 11: Some other bioactive compounds from P. lanceolata L.

indicators gives information about the concentration of metal in the area [16, 83]. The studies were carried out to determine the metal concentration in samples taken from the metallurgical site. The result showed that some metals such as Cd, Zn, and Pb had been detected in P. lanceolata L. which exceeded the permitted limits $(Zn > 300 \text{ mg kg}^{-1})$, $Pb > 100 \text{ mg kg}^{-1}$, and $Cd > 4 \text{ mg kg}^{-1}$). In the plant material, unwashed samples had significantly more significant Zn, Cd, Pb, Mn, and Fe than washed ones. This revealed the plant's ability to remove metals from highly contaminated environments [16]. Regardless of high concentrations of heavy metals in soil, especially Ni, Zn, and Cr, P. lanceolata L. showed remarkable tolerance to ecophysiological conditions of serpentine soils. This indicates the potential application of this species in the remediation of heavy metal-polluted soils [84].

7.4. Additive in Foods. P. lanceolata L. is an edible plant in Italy, and its leaves are used as an additive to some foods like wine, salads, tea, tincture, and macerate, or it can be eaten like lettuce. It is also used for animal nutrition like rabbits; when given to porkers, it can enhance the taste of meat and increase the number of unsaturated acids [17]. Leaves of various species of *Plantago* are taken as cooked or raw. Only young leaves are consumed in the form of salads [85]. The leaves of P. lanceolata L. are significant as cooked vegetables and soups. People used to eat the plants during the spring when vegetables were in short supply. The leaves are significant in preparing macerate, an infusion, juice, wine, tincture, and tea [17]. Dried leaves of P. lanceolate L. are used as a tea and appetizer and are good for digestion. The fresh leaves are topically applied with cream from cows' milk and bread or clay as a suppurative [86].

7.5. Insecticide. P. lanceolata L. extracts can be used as an insecticide to control insects. Secondary metabolites such as glycosylated iridoids produced from the plant contribute to these insecticide activities [18]. Specifically, plants attribute the polar molecules aucubin and catalpol (Figure 3) to this effect [87]. The concentration of catalpol in *P. lanceolata* L. showed an increase under herbivore attack. Consequently, the reduction in the oviposition of *L. coffeella* on leaves treated with the methanol polar fraction of the *P. lanceolata* L. extract may be induced by catalpol or aucubin [88].

7.6. Agriculture. P. lanceolata L. has a significant role in agricultural application. The advantages of this plant in the agriculture sector lie in its high content of valuable substances for human and grazing animals [14]. P. lanceolata L. has emerged as forage with the ability to reduce reactive nitrogen (N) losses, in particular N leaching, from grazing dairy systems [89]. It is most commonly used on farms as part of mixed pasture swards. It has a more prominent contribution when grass production decreases and gaps in the sward, especially in low-fertility dryland pastures. Where the grass or legume growth is poor, P. lanceolata L. contributes less than 20% of the sward [90]. In P. lanceolata L., chemical aucubin is responsible for nitrogen mineralization and nitrification [91]. Fertilization may affect not only plant species diversity but also insect dynamics by altering plant nitrogen supplies. P. lanceolata L. is grown on the farm to improve trophic levels and species interactions in managed grassland ecosystems, which occurred due to fertilizer [91]. P. lanceolata L. influences the distribution of soil mineral N in dairy grassland on peat soil. It has been recognized as a potential relief approach for reducing nitrogen (N) losses [92]. The iridoid glycosides and catalpol, as well as the phenylpropanoid glycoside and verbascoside, may be responsible for these effects [93].

8. Conclusion

P. lanceolata L. is one of the well-known species of the genus Plantago. It is distributed in European countries and the northern and central parts of Asia. P. lanceolata L. plays a vital role in managing certain ailments and diseases such as antimicrobial, wound-healing, anti-inflammatory, cytotoxic, and antispasmodic. It has many applications like cosmetics, pharmaceutical, antibacterial, synergetic, insecticide, metal indicators, heavy metal removal from the polluted area, and food additives. Phytochemicals such as iridoid glycoside, fatty acids, phenol, flavonoids, tannins, alkaloids, terpenoids, steroids, coumarins, saponins, glycosides, and quinines are present in different parts of P. lanceolata L. The biological activities and medicinal properties of P. lanceolata L. mainly depend on the activities of the chemical constituents. This field still needs more study to determine the exact mechanisms and the main bioactive compounds responsible for treating specific diseases. It is of great importance to investigate their chemical profile and biopotential. Most of the research has been done in vitro; further in vivo investigations of P. lanceolata L. are required.

Conflicts of Interest

The authors declare that they have no competing interests.

Authors' Contributions

LA and AB have drafted the review. MGT prepared different tables and figures required for the manuscript, provided guidance during the development of idea, and wrote and revised the manuscript. The authors read and approved the final manuscript.

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