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Phytochemistry and Pharmacological Activities of Testa Plantaginis: A Review

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Abstract: Testa plantaginis is the epidermis of *Plantago ovata* (Family Plantaginaceae), Forsk plant seeds. Testa Plantaginis is known by many names, including Indian plantago, psyllium, plantain, and spogel seed plantain. Plantago ovata is a common medicinal plant widely grown in tropical regions worldwide. This article focuses on phytochemistry, chemical constituents, medicinal uses, pharmacology, toxicology, and the dose of Testa plantaginis. Many polyphenols are found in Plantago species, primarily in the form of flavonoids (luteoline 7-rutinoside, luteoline 7-rhamnoside) and hydroxycinnamic acids (caffeic acid). n-Hexadecanoic acid, linolenic acid, palmitic acid, methyl ester, and stearic acid were detected in the Plantago ovata plant. Polyunsaturated fatty acids represent 40–80% of total fatty acids in Plantago ovata seeds. Plantago ovata is effective in treating a variety of gastrointestinal problems. The Plantago ovata plant is used to treat neurological conditions, anxiety, depression, mixed anxiety-depressive syndromes, irreversible dementia, respiratory disorders, circulatory disorders, and cardiac problems. Pharmacology activity includes experimental pharmacology and clinical pharmacology. Experimental pharmacology includes antioxidant, antiulcerogenic, antidiarrheal, antihypercholesterolemic, antihyperglycemic, gastrointestinal activities, and effects on bile acids. Clinical pharmacology includes antidiarrheal, antihypercholesterolemic, laxative, and wound healing activities. There are no precautions for the use of Testa Plantaginis in pediatrics, nursing mothers, carcinogenesis, mutagenesis, or fertility impairment. Testa Plantaginis in the form of powder, wafers, granules, and tablets occurs. Polysaccharides and flavonoids are the major chemical constituents of Testa plantaginis. Testa plantaginis pharmacological activities include antioxidant, antiulcerogenic, antidiarrheal, antihypercholesterolemic, antihyperglycemic, gastrointestinal, laxative, and wound healing activities.

Keywords: testa plantaginis; *Plantago ovata*; medicine; toxicity; contraindications; dose.

1. Introduction

The epidermis of Plantago ovata Forsk plant seeds (Family: Plantaginaceae) is referred to as "Testa plantaginis" [1, 2]. Testa Plantaginis is known by many names, including Ashwagolam, bazarqutuna, blond psyllium, esfarzeh, esopgol, esparzeh, ghoda, grappicol, Indian plantago, isabakolu, isabgol, isabgul, isapagala-vittulu, ishppukol-virai, isphagol, vithai, issufgul, jiru, kabbeche, lokmet, naaja, obako, psyllium, plantain, and spogel seed plantain [3]. Testa Plantaginis has a lengthy history of helping patients with chronic renal disease and

hyperuricemia [4]. Testa Plantaginis is a pinkish-colored or pale brown patch. Testa Plantaginis = 2 mm in length and 1 mm in width [2]. The flavor of Testa Plantaginis is mucilaginous, and its odor is mild and unique [5]. Testa Plantaginis powder has a distinct smell with a slight pinkish tinge. Testa Plantaginis is composed of epidermal cells (polygonal or spherical shape) and is composed of complete or patchy epidermal cells. Testa Plantaginis consists of 2—4 starch constituents. These constituents have a diameter of 2 to 25 μm. There are some elongated and rectangular cells present in the lower part of the epidermis in Testa Plantaginis [2]. Testa Plantaginis, also known as ispaghula husk or blond psyllium husk, is a herbal drug derived from the seeds of Plantago ovata primarily used to treat constipation and other conditions requiring increased fiber intake, due to its high mucilage and fiber content. It can also help manage mild to moderate hypercholesterolemia and may be used in conditions where softening stools is desirable, such as anal fissures or hemorrhoids [6].

This review aims to focus on the importance of Testa Plantaginis, its ingredients, medicinal uses, and pharmacological and toxicological activities. This review postulated that Testa Plantaginis can treat constipation and gastrointestinal disorders due to its high fiber content; however, fewer publications on Testa Plantaginis have been published, despite its wide range of medical and clinical applications. Therefore, the purpose of this review is to investigate the chemical constituents, medicinal uses, pharmacology, toxicology, precautions, contradictions, and dose of Testa Plantaginis.

2. *Plantago ovata* Forsk Plant Phytochemistry and Morphology

A common medicinal plant that is extensively grown in tropical regions of the world is *Plantago ovata*. Products containing *Plantago ovata* husk are an excellent source of health-beneficial fiber since the outer seed coat of the plant includes soluble and insoluble fiber in a ratio of 7:3 [7]. *Plantago ovata* is used in dairy products like yogurts because of its capacity to lower cholesterol, reduce cardiovascular disease, lower the glycaemic index, and alleviate constipation [8]. *Plantago ovata* is a genome-rich crop that has been shown to increase crop disease susceptibility, to improve the yield and quality of its fruit, and include 41,820 protein-coding genes, 411 non-coding RNAs, 108 ribosomal RNAs, and 1295 transfer RNAs [9]. Asia and the Mediterranean are seeing an increase in the *Plantago ovata* Forsk plant cultivation. It spreads in Western Europe, Pakistan, and India [10–12]. It is an herb that grows annually. The linear leaves on the *Plantago ovata* Forsk stem are lanceolate, dentate, and hairy. The plant's flowers are arranged as cylindrical spikes and are white in color. The sepals of the plant include a noticeable midrib that extends from the base to the tip. The oval-shaped plant petal lobes have a pronounced peak. The oval-shaped, 2-3 mm long, grey-pink seeds of *Plantago ovata* Forsk have a brown streak running across their convex side [10]. The *Plantago ovata* Forsk plant, which has excellent health advantages, is a natural source of dietary fiber. It can be employed as a hydrocolloid in food applications [13]. *Plantago ovata* Forsk plant decreased oxidative stress indicators and increased activities of antioxidant chemicals [14].

3. Chemical Constituents of Testa Plantaginis

Plantago ovata Forssk seed polysaccharide (POFP) is a major constituent of *Plantago ovata* seeds and represents 20–30% of the chemical constituents [5]. Two novel polysaccharides (AH-POFP1 and AH-POFP3) were isolated, and they were defined as xylose-rich polysaccharides. The backbone of these polysaccharides is 1 → 4-linked Xylp, and they

were made of xylose, which has a molecular weight of 484.3 and 618.1 kilodaltons for AH-POFP1 and AH-POFP3, respectively. These polysaccharides possess strong antioxidant activity, inhibit the secretion of pro-inflammatory cytokines, and increase the secretion of anti-inflammatory factors, thereby exerting anti-inflammatory effects [15]. Many polyphenols are found in Plantago species, primarily in the form of flavonoids (5─10%) (luteoline 7-rutinoside (Figure 1), luteoline 7-rhamnoside (Figure 2), and hydroxycinnamic acids (caffeic acid, Figure 3) [5,16], which have been shown to have antibacterial, anticancer, and antioxidant properties [17]. The active components of Plantago are plantagoamidinic acid A, geniposidic acid, and acteoside [18]. Sixteen components were identified in the phytochemical analysis of Plantago ovata seeds using hydroalcoholic maceration, mass spectrometry, nuclear magnetic resonance, and other techniques [19, 20]. Fiber content, which can be determined analytically, is a defining characteristic of Testa Plantaginis [21]. *Plantago asiatica* L. yielded efficiently detected total phenylethanosides [22]. According to Ramahamouz-Haghighi *et al*. [23], *Plantago major* includes compounds that have antibacterial activity, such as gallic acid, catalpol, and apigenin. Two novel compounds were identified: a phenylethanoid glycoside-2-(3,4-dihydroxyphenyl) and a flavonoid-isorhamnetin 3-O-α-L-4C1-arabinopyranosyl-(1→2)-β-D-4C1-glucopyranoside.[α-L-1C4-rhamnopyranosyl-(1→3)] ethyl O-α-L-arabinofuranosyl-(1→2)-[[E-caffeoyl-1→4]. *Plantago lanceolata* L. was shown to contain -β-D-4C1-glucopyranoside [24]. According to Fisher *et al*. [25], *Plantago ovata* has additional sugars along with 22.6% arabinose and 74.6% xylose. Furthermore, Aucubin (iridoid glucoside) [26], crude fibers, proteins, lipids, and carbs (their concentrations vary depending on the plant part and extraction method) are present in *Plantago ovata* leaves and seeds [27].

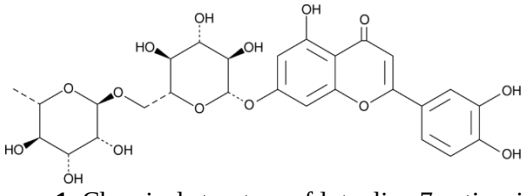

Figure 1. Chemical structure of luteoline 7-rutinoside.

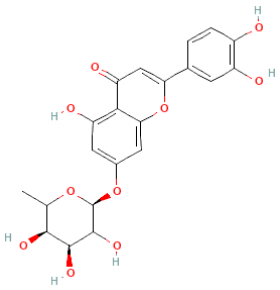

Figure 2. Chemical structure of luteoline 7-rhamnoside.

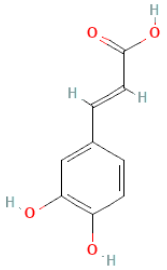

Figure 3. Chemical structure of caffeic acid.

4. Major Chemical Constituents of Testa Plantaginis

The presence of n-hexadecanoic acid, linolenic acid, palmitic acid, methyl ester, and stearic acid was revealed by a gas chromatography-mass spectrometry examination of the *Plantago ovata* plant [28]. Polyunsaturated fatty acids, which make up 40–80% of total fatty acids in *Plantago ovata* seeds, are a prominent component of the seeds and are involved in the development of atherogenicity, thrombogenicity, and the ratio of hypo-to hypercholesterolemia [29]. *Plantago Asiatica's* main component, plantamajoside, has anti-fibrosis properties that make it useful in the treatment of chronic heart failure [30]. Testa Plantaginis mostly consists of a mucilaginous hydrocolloid (20–30%), which is made up of an arabinoxylan (>85%). A xylan with 1→ 3 and 1→ 4 connections that spread irregularly serves as the primary structural component. On either C-2 or C-3 of this main chain, l-arabinose, d-xylose, and α-d-galacturonyl-1→2-l-rhamnose replace the monosaccharides. Fixed oil (5─10%) is a key component of Testa Plantaginis [31, 32].

5. Medicinal Uses of Testa Plantaginis

5.1. Uses in clinical application.

Plantago ovata is effective in treating a variety of gastrointestinal problems and demonstrates antioxidant, immunomodulatory, antiproliferative, anticancer, and antiviral properties [10]. Polysaccharides from *Plantago asiatica* L. have immune-regulatory, antiviral, anticancer, antioxidant, anti-inflammatory, and antidiabetic properties [33]. Due to its antibacterial activity, the arabinoxylan component from *Plantago ovata* seeds is ideal for delivering medication to the wound site in a sustained manner and maintaining a moist environment for rapid healing [34,35]. To preserve and restore intestinal symmetry, Testa plantaginis is used as a laxative [36-39]. It is used to treat irritable bowel syndrome, duodenal ulcer-related constipation, short-term constipation from pregnancy, and persistent constipation [39,40]. It is used to soften feces following anorectal surgery or in the event of hemorrhoids [39, 41]. As a dietary supplement, Testa plantaginis is used to lower blood glucose levels after consumption [37], to reduce coronary heart disease [40], and to regulate hypercholesterolemia [42]. According to Zhang *et al*. [18], plantain polysaccharides from the *Plantago asiatica* plant suppressed the growth and spread of breast cancers. As a result, it is used as an anticancer agent therapy in preclinical and clinical trials.

5.2. Uses in pharmacopoeia.

According to Wen *et al*. [43], *Plantago asiatica* L. possesses antibacterial, antiviral, anti-inflammatory, antioxidant, and anticancer properties. Gram-positive and Gram-negative bacteria are susceptible to the antibacterial and anticancer properties of the *Plantago ovata* plant [44]. Diarrhea resulting from several disorders is treated with Testa Plantaginis [45]. Leishmanial lesions are treated with *Plantago ovata* powder, and the process is quite easy and painless [46]. Antifungal activity has been found in *Plantago ovata* leaf extract [47].

5.3. Uses in traditional medicine.

According to Nawrot *et al*. [48], the *Plantago ovata* Forssk plant is used to treat neurological conditions, anxiety, depression, mixed anxiety-depressive syndromes, irreversible dementia, respiratory disorders, circulatory disorders, and cardiac problems. Testa Plantaginis

has antitussive, diuretic, and expectorant properties. It is used to treat glandular edema, rheumatism, gout, and bronchitis [4-9]. *Plantago ovata* Forssk plant reduces blood glucose, satiety, low-density lipoprotein cholesterol, and constipation [49].

6. Pharmacology

The mechanism of action of antioxidant, anti-inflammatory, antidiabetic, hepatoprotective, and nephroprotective effects of Testa Plantaginis depends on *Plantago ovata* Forssk polysaccharides (POFP; AH-POFP1 and AH-POFP3), which have a strong antioxidant effect. *Plantago ovata* Forssk polysaccharides inhibit the secretion of pro-inflammatory cytokines and increase the secretion of anti-inflammatory markers, thereby showing anti-inflammatory effects [16]. The polysaccharide showed the highest antioxidant and scavenging activities (347.40 ± 1.79 and 362.72 ± 2.75 μg, respectively). The polysaccharides also have anticarcinogenic activity [50]. The antioxidant enzyme levels of superoxide dismutase, catalase, and glutathione peroxidase are increased, while lipid peroxidation is decreased, after oral treatment with Plantago ovata ethanolic extract in gastric ulcer. Therefore, antioxidant and antiulcerogenic activities are observed by decreasing the ulcer index value and preserving the integrity of the gastric mucosa [51].

6.1. Experimental pharmacology.

Table 1 summarizes the experimental pharmacological activities of Testa Plantaginis as follows:

Table 1. Experimental pharmacological activities of Testa plantaginis.

Key bioactivities	Experimental models	Active compounds
Antioxidant activity	Rats	Polysaccharide, Flavonoids
Antiulcerogenic activity	Rats	Fiber, Polysaccharide
Antidiarrheal activity	Pigs Calves	Luteolin, Scutellarein
Antihypercholesterolemic activity	African green monkeys, Hamsters, Guinea-pigs, Rats	n-Hexadecanoic acid, Linolenic acid, Palmitic acid
Antihyperglycemic activity	Mice	Polysaccharide
Effects on bile acids	Rats, Dogs, Hamsters	Polysaccharide, Linolenic acid, Palmitic acid
Gastrointestinal effect	Rats, Guinea-pig ileum	Fiber, Mucilaginous hydrocolloid, Arabinoxylan

6.1.1. Antioxidant activity.

Plantago asiatica L. seeds contain polysaccharides with antioxidant properties [52]. Certain plant species have phytochemical components with strong antioxidant capabilities [53]. The ethanolic extract of *Plantago ovata* Forssk seeds significantly reduced lipid peroxidation while increasing antioxidants (glutathione peroxidase, catalase, and superoxide dismutase [51]. *Plantago ovata* seed extract increased growth performance, improved health, and strengthened resistance to oxidative stress caused by ammonia. It also improved ammonia-induced down-regulations of antioxidant-related gene expressions, such as superoxide dismutase and glutathione peroxidase, and did not affect the mRNA expression level of catalase [54].

6.1.2. Antiulcerogenic activity.

By lowering the ulcer index value and maintaining the integrity of the stomach mucosa, the ethanol extract from *Plantago ovata* Forssk seeds protects rats against ethanol-induced

gastric ulcers [55]. The *Plantago ispagula* plant prevents or treats peptic ulcers caused by a variety of substances, including alcohol, aspirin, indomethacin, and Helicobacter pylori [56].

6.1.3. Antidiarrheal activity.

Diarrhea caused by *Escherichia coli* was halted by injection with 0.4 g of Testa Plantaginis/day [57] in pigs. No reduction in the quantity or frequency of stools was seen following injection with Testa Plantaginis (18.89 g/L) in calves [58].

6.1.4. Antihypercholesterolemic activity.

Low-density lipoprotein levels decreased in African green monkeys fed Testa Plantaginis orally, and plasma cholesterol levels were consequently reduced [59]. Because of a decrease in low-density lipoprotein levels and an increase in receptor-mediated low-density lipoprotein clearance, Testa plantaginis (7.5% of the diet) decreased cholesterol levels and increased sterol loss in the liver in hamsters. The mechanism of action appears to involve a reduction in low-density lipoprotein cholesterol production and an increase in receptor-mediated low-density lipoprotein clearance [60]. Testa Plantaginis (7.5 g/100 g body weight) was given orally to guinea-pigs fed a high-cholesterol diet on a daily basis; the guinea-pigs' plasma cholesterol level decreased by 39% as compared to the control group [61]. When Testa plantaginis was given to rats fed a diet rich with fat and sugar, the number of hepatic Apolipoprotein A/E receptors increased by 45% while plasma low-density lipoproteins, triacylglycerol, Apolipoprotein B, and hepatic cholesteryl ester levels decreased [62]. The administration of 5% of Testa Plantaginis in the diet decreased the level of blood cholesterol [63]. Rats fed a high-cholesterol diet showed an increase in high-density lipoprotein and a decrease in total serum cholesterol when 10% of the food contained Testa Plantaginis [64]. A diet high in *trans*-fatty acids, such as maize oil margarine, increased serum cholesterol levels; however, the presence of Testa Plantaginis, which makes up 5% of this diet, decreased this cholesterol increase [65].

6.1.5. Antihyperglycemic activity.

When administered with 2.5% of Testa Plantaginis to the diet for eighteen weeks, Testa Plantaginis caused diabetic mice's blood glucose and insulin levels to decrease and rise, respectively [66].

6.1.6. Effects on bile acids.

When administered with 5% of Testa Plantaginis to the diet for five weeks to rats, Testa Plantaginis stimulates the production of bile acid and reduces the hydrophobicity of the bile acid pool [67]. By lowering the biliary cholesterol saturation index, the administration of Testa Plantaginis (5% of the diet) for six weeks reduced the occurrence of cholesterol gallstones in dogs fed a lithogenic diet [68]. The administration of Testa Plantaginis (4–6% of the diet) for five weeks to hamsters fed a lithogenic diet resulted in a 400% increase in the excretion of bile acids in the feces and a dose-dependent decrease in the level of taurine-conjugated bile acids. In comparison to the control, Testa Plantaginis recovers the lipid index and stops the formation of cholesterol gallstones [69]. Due to increased intestinal output, a 5-week dose of Testa Plantaginis (8% of the diet) increased daily feces neutral sterol excretion by 90%. Following

the administration of Testa Plantaginis in hamsters, there was an increase in the total fecal bile acid level and daily excretion of bile acid [70].

6.1.7. Gastrointestinal effect.

When compared to the control group, the addition of 10–20% of Testa Plantaginis to the diet for four weeks in rats increased the level of mucin in the stomach, intestines, and colon and increased the weight of the feces [71]. In an *in vitro* study, ileum contractions were increased by 6 mg/ml of Testa Plantaginis methanol extract of isolated guinea-pig ileum [72]. *Plantago ovata* is used to treat functional constipation; however, according to Coss-Adame *et al*. [73], the plant's effects were not linked to improvements in contractility or regional transit time. According to recent pharmacological studies, such as Utz *et al*. [74], *Plantago ovata* is used to treat gastrointestinal disorders, including ulcerative colitis.

6.2. Clinical pharmacology.

6.2.1. Antidiarrheal activity.

When Testa Plantaginis (10 g/day) was administered to persons suffering from acute or chronic diarrhea for seven days, the intestinal viscosity increased because Testa Plantaginis bound to the fluid, reducing the frequency of bowel movements [43]. Testa Plantaginis (3.5 g, three times/day) showed that colonic motility was slowed, small bowel transit remained unaltered, and stomach emptying was delayed by 50% in eight individuals with diarrhea, compared with a placebo-controlled crossover study. By increasing meal viscosity, Testa Plantaginis delayed stomach emptying and inhibited colonic transit by lowering gaseous fermentation yields [75]. *Plantago asiatica* L. had the lowest effective dose of antidiarrhea at 2,000 mg/kg and the highest amount of active components, 3.55 μm. Thus, it was determined that the antidiarrheal active components of *Plantago asiatica* L. are luteolin and scutellarein, which bind to sodium/potassium-ATPase to produce antidiarrheal action. Thus, it was possible to successfully manufacture and employ *Plantago asiatica* L. to treat diarrhea [76].

6.2.2. Antihypercholesterolemic activity.

In individuals with mild to severe hypercholesterolemia, Testa Plantaginis administration resulted in a decrease in serum cholesterol levels [77, 78]. This effect was linked to Testa Plantaginis's hypolipidaemic effect and safety when taken in a low-fat diet. In a clinical trial, Testa Plantaginis or cellulose placebo was administered to 384 and 272 participants, respectively. Testa Plantaginis (10.2 g) reduced cholesterol, low-density lipoprotein, and apolipoprotein A-I by 4%, 7%, and 6% when administered with a low-fat diet for at least eight weeks compared with placebo. Triacylglycerol levels or serum high-density lipoproteins were unchanged [74]. *Plantago ovata* is used in dietary regimens for blood lipid control, as it can significantly reduce low-density lipoprotein and total cholesterol levels [79]. In 404 people with mild to severe hypercholesterolemia, the cereal diet, including Testa Plantaginis, reduced levels of low-density lipoprotein and high-density lipoprotein. The levels of low-density lipoproteins and cholesterol were slightly elevated in those who ate cereals containing Testa Plantaginis, but high-density lipoproteins remained unaltered. Adults with hypercholesterolemia who consumed cereals containing Testa Plantaginis had better blood lipid profiles than those who followed a low-fat diet compared with subjects who ate a control

cereal [80]. Results of treating 340 individuals with mild-to-moderate hypercholesterolemia for 12 weeks with 7 g or 10.5 g of Testa Plantaginis/day showed that throughout the 6-month therapy period, low-density lipoprotein levels decreased by 10.6─13.2% and total cholesterol levels decreased by 7.7─8.9% [81]. Compared with the placebo group, Testa plantaginis (5.1 g) administered twice daily for 8 weeks improved glucose and lipid levels, with blood cholesterol and low-density lipoprotein decreased by 8.9% and 13.0%, respectively. Testa Plantaginis (5.1 g) reduced serum glucose levels by 11.0% and 19.2%, respectively, after lunch and throughout the day [42]. In a clinical study, adding 10 g of Testa Plantaginis (5.1 g) per day to the diets of six normal and five ileostomy participants for three weeks reduced their levels of high-density lipoproteins and total cholesterol by 9.3% and 6.4%, respectively [82]. For eight weeks, Testa Plantaginis (3.4 g, three times per day) reduced low-density lipoproteins cholesterol (-20.2%) and serum cholesterol (-14.8%) [83, 84]. The generation of new bile acids from cholesterol is increased by the increased excretion of bile acids in the feces, which is linked to the decrease in blood cholesterol [85, 86]. Administration of Testa Plantaginis resulted in a decrease in the weighted ratio of lithocholic acids to deoxycholic acid, as well as in fecal lithocholic and isolithocholic acids. This finding suggests that bile acids hydrophobicity has decreased [87].

6.2.3. Laxative activity.

Plantago ovata is useful in the treatment of intestinal disorders and hepatic encephalopathy because it can improve the synthesis of volatile fatty acids, increase levels of acetate and propionate, and increase the production of n-butyrate in the intestine [88]. When Testa Plantaginis is administered, the gastrointestinal system absorbs more fluid, which increases peristalsis and, consequently, the volume of feces [89]. Testa Plantaginis increases colon transit time, decreases intraluminal pressure, and increases frequency of defecation [40, 37, 89]. Colonic bacteria quickly break down Testa plantaginis into volatile fatty acids, which are absorbed by the colon and cause an increase in colonic mucus secretion. Treatment for Testa Plantaginis results from the mucilaginous fiber swelling when combined with water, which provides lubrication and bulk [84]. Because of the water-bound fiber residue, Testa Plantaginis increases the mass of bacteria in the feces and increases stool weight and water content [37, 40]. According to Mehmood *et al*. [90], mice treated with a 100–300 mg/kg crude extract of *Plantago ovata* experienced a laxative effect due to the activation of muscarinic and 5-HT receptors. However, at 500–1000 mg/kg, the extract demonstrated gut inhibitory (anti-secretory/anti-diarrheal) effect in mice through the activation of the nitric oxide cyclic guanosine monophosphate pathway and the blockade of the calcium ion channel. Similarly, by activating muscarinic serotonin receptors, a crude extract at 10 mg/mL showed anti-constipation activity in the ileum of Guinea pigs. Similarly, in isolated rabbit jejunum, 10 mg/mL of the crude extract activated muscarinic and serotonin receptors, resulting in gastrointestinal stimulation followed by relaxation. Plantago major treats high body temperature, colds, various body infections, bleeding, inflammation, and increased urine output, and has astringent properties in addition to being used as a laxative [91].

6.2.4. Wound healing activity.

An investigation into the potential of *Plantago ovata* seed ethanolic extract for wound healing was carried out by Singh *et al*. [92]. The extract was applied as a 10% w/w ointment

in a petroleum jelly foundation to treat the wounds as quickly as possible while causing the patients as little pain, irritation, or scarring as feasible. The findings demonstrated that wound contraction, which is typified by the organization of surrounding healthy skin to cover the exposed area, occurs in tandem with lesion healing. According to another study [93], the ethanolic extract significantly increased the percentage of wound contraction, thereby improving wound healing. Although *Plantago ovata* is not harmful, it contains biologically active compounds with anti-inflammatory, lipid-lowering, hepatoprotective, and wound-healing properties, which support its use in ethnomedicine. Moreover, *Plantago major* is used to treat wounds and inflammation [94]. *Plantago australis* has the ability to promote wound healing, improve cell migration, and reverse the oxidation effect [95].

7. Toxicology

The active medicinal ingredient in the *Plantago ovata* and *Plantago lanceolata* is accessible in pharmacies and poses no health risk to adults [96, 97]. Patients are not at risk for any health problems from *Plantago lanceolata* [98]. According to Ortiz *et al*. [99], the Plantago genus was able to significantly reduce the implications of purinergic receptor P2X7 activation (>50% at 0.1 and 1 μg/mL). By regulating the redox, inflammatory, and purinergic activity in the rat testes, a plantain-based diet was able to shield and avoid the toxicity produced by the herbicide atrazine [100].

8. Adverse Reactions of Testa Plantaginis

Swelling and gas are transient symptoms of Testa Plantaginis. A steady increase in Reducing the Testa Plantaginis dose for a few days can reduce transient gas and swelling [101]. There have been reports of allergies to plantago ingestion or inhalation [102–107]. These allergies can cause everything from uncommon anaphylaxis events to urticarial rashes [102, 108]. A single, extremely unusual instance of fatal bronchospasm in an asthmatic patient who was sensitive to Testa Plantaginis was documented [104].

9. Contraindications of Testa Plantaginis

Patients experiencing fecal impaction, unexplained stomach symptoms, abdominal discomfort, nausea, or vomiting should not be administered Testa Plantaginis. Testa Plantaginis should not be used in patients with megacolon, diabetes mellitus, rectal bleeding, with constrictions of the gastrointestinal tract, potential or existing intestinal disorders, or any sudden change in bowel habits that lasts longer than two weeks [31, 84].

10. Warnings of Testa Plantaginis

When making Testa Plantaginis powder, people should keep their airborne dust intake to a minimum. To prevent intestinal obstruction and oesophageal disorders, each 5 g Testa plantaginis powder must dissolve in 150 ml of liquid. Testa Plantaginis powder should not be prepared near those people experiencing dysphagia or other throat issues, chest pain, or vomiting. To avoid causing other medications to absorb more slowly, Testa Plantaginis should be administered at least two hours before or after other medications [108].

11. Precautions of Testa Plantaginis

11.1. General precautions.

In circumstances where Testa Plantaginis develops bowel or esophageal obstruction, a medical checkup can be required. Testa Plantaginis decreased absorption of calcium, magnesium, copper, zinc, vitamins (B_{12}), cardiac glycosides, and coumarin derivatives [3, 82, 109, 110]. According to other research [111, 112], Testa plantaginis has no effect on vitamins or minerals and does not bind to them since they do not contain phytates. Lithium absorption from the gastrointestinal tract may be inhibited, and plasma lithium levels may decrease when Testa Plantaginis is administered with lithium salts [113]. Additionally, Testa Plantaginis may decrease the amount and rate of absorption of carbamazepine. Lithium salts and carbamazepine must be taken two hours before or following the administration of Testa Plantaginis [114]. Additionally, it is advised to use Testa Plantaginis two hours prior to or following the administration of other medications [107]. Individuals administered Testa Plantaginis need to be aware of potential drug interactions, such as the possibility that those with insulin-dependent diabetes may need less insulin [31].

11.2. Other precautions.

There are no precautions for the use of Testa Plantaginis in pediatrics, nursing mothers, carcinogenesis, mutagenesis, fertility impairment, or teratogenic or non-teratogenic effects during pregnancy [115-117].

12. Dosage of Testa Plantaginis

Testa Plantaginis is available as powder, wafers, granules, and tablets. It is kept out of the heat and light in a cold, dry location in a black container that is securely closed [2, 118]. The oral dose administration of 20 g granules of *Plantago ovata* preparation for three days is used [119]. No signs of toxicity emerged from 14-day dose toxicity testing of *Plantago lanceolata* L. in rats. The animals were administered 3, 6, or 12 mL of syrup/kg by oral gavage twice daily. Body and organ weights, animal behavior, urine output, and animal testing levels at the end of the study were similar to those in the control group [120]. This beneficial effect of Testa Plantaginis is related to its fiber content, as fiber administered at 100 mg/kg for 60 min or 400 mg/kg for 20 min protects biological processes and body and organ tissues [121].

13. Conclusion

Testa plantaginis is obtained from the *Plantago ovata* plant. This plant belongs to the Family Plantaginaceae. Limited publications of Testa Plantaginis are reported, although it is used in many medicinal fields. Luteoline 7-rutinoside, luteoline 7-rhamnoside, and hydroxycinnamic acids are the main ingredients of Plantago species. Testa plantaginis is used for treating gastrointestinal, neurological, respiratory, circulatory, and cardiac diseases. It has no health risks to adults, and consequently, there are no precautions for the use of Testa Plantaginis in pediatrics, nursing mothers, or fertility. Testa Plantaginis occurs in the form of powder, wafers, granules, and tablets. The oral administration of 20 g granules of *Plantago ovata* preparation is used for clinical applications. Further studies are therefore required to determine the molecular basis of the health-promoting property of Testa plantaginis and attempt to isolate the bioactive compounds to detect their medical and clinical applications.

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