One of the prerequisites for the success of primary healthcare is the availability and use of suitable drugs. Plants have always been a common source of medicaments, which makes it reasonable for decision-makers to identify locally available plants that could usefully be added to national list of drugs or that could even replace some pharmaceutical preparations. A number of plant derived drugs which are currently used in therapy. A number of drugs have been used traditionally for treatment of different diseases such as clove obtained from Eugenia caryophyllus used in treatment of dental pain, cinchona alkaloids obtained from cinchona bark employed in treatment of malaria, castor oil extracted from Ricinus communis used as a stimulant cathartic, capsicum as an irritant and rubifacient, atropine from Atropa belladonna as an anticholinergic and cocaine as a local anesthetic. In modern era investigations are being carried out to discover novel pharmacological actions of traditionally used plants e.g., Digitalis lanata was used from many years in congestive heart failure and as a diuretic but now different glycosides are discovered in Digitalis lanata i.e., acetyl digoxin, digoxin, lanatosides A and B which are potent cardiotonic agents. Similarly, Psyllium has also been used traditionally since antiquity as laxative but at present its new pharmacological uses have been discovered (1).
used commercially for mucilage production. Plantago seed, psyllium seed or plantain seed which is cleaned, dried, ripe seed of Plantago psyllium or Plantago indica, belongs to family Plantaginaceae. The genus Plantago contains over 200 species. P. ovata and P. psyllium and P. indica are 3 important species. These are produced commercially in several European countries, the former Soviet Union, Pakistan, and India. Isabgul, the common name in India for P. ovata, comes from the Persian words “isap” and “ghol” that mean horse ear, which describes the shape of the seed. India dominates the world market in the production and export of psyllium (2).

Plantago seeds contain 10–30% of hydrocolloid in the outer seed coat which can be separated into acidic and neutral polysaccharides and upon hydrolysis L-arabinose, D-galactose, D-galacturonic acid, L-rhamnose and D-xyllose are obtained. Solution of Plantago gum is thixotropic where as its mucilage has super disintegrant property. The husk is the rosy-white membranous covering of the seed, which constitutes the drug, mainly given as a safe laxative, particularly beneficial in habitual constipation, chronic diarrhea and dysentery. It is a 100% natural product, a soluble fiber and forms gel in water. The usual dose of Plantago ovata is 7.5 g (3, 4).

The underlying study was conducted with the aim of giving a brief overview of factors affecting cultivation, growth of Plantago ovata, and its pharmaceutical and pharmacological aspects to reveal its uses in various medical fields.

**Cultivation and growth of Plantago ovata**

Isabgul (Plantago ovata Forsk), is an annual herb cultivated as a medicinal plant in recent times. Medicinal plants are rich in secondary metabolites and their biosynthesis is controlled genetically and is affected intensely by environmental factors (5). Previously, a trial was carried out to examine the impact of sowing dates (20th April, 5th and 20th May) and nitrogen-fertilizer levels (0, 50, 100 and 150 kg/ha) on growth, seed yield and seed swelling factor (mucilage content) of isabgul in Iran, under silty-clay soil conditions. The statistical design included a split-plot arrangement of randomized complete block design with three replicates. The sowing dates and nitrogen fertilizer were considered as the main and sub-main plots separately. The data obtained from results disclosed that 5th May was the best planting time for isabgul in such area and the suitable amount of nitrogen fertilizer was 100 kg/ha. Also seed yield appeared to show a substantial positive influence on seed swelling (5). Likewise, a few years back, Moosavi et al. (2012) studied the effect of planting date and plant density on yield, morphological traits and water use efficiency (WUE) of Plantago ovata in Iran (6). The planting dates were April 19, May 9 and May 30 and plant densities were 16.6, 22.2 and 33.3 plants/m². The evaluation of means showed that impeding the planting from April 19 to May 30 dwindled considerably leaf number/plant, spike length, plant height, leaf, husk and grain yield, and WUE for grain production by 18.2, 29.9, 24.5, 60.2, 65.4, 60.2 and 46.9%, correspondingly. The outcomes indicated that with an upturn of plant density from 16.6 to 33.3 plants/m²; grain yield, plant height, and WUE were amplified expressively by 82.8, 7.8 and 82.1%, respectively, nevertheless spike length, leaf number/plant, and tiller number per plant were decreased by 5.9, 24.8 and 28.9%, individually. The maximum husk and leaf yield, and WUE for biomass production were obtained at density of 33.3 plants/m² which is higher than those at the density of 16.6 plants/m² by 2.11, 2.10 and 2.06 times, respectively. Altogether, conferring to the upshots, the planting date of April 19 with density of 33.3 plants/m² was suggested to comprehend maximum produce and WUE in Plantago ovata cultivation in Birjand region, Iran.

Another experiment was steered in the course of Rabi season (2006-07) in order to study the influence of moisture stress on growth, yield and quality of Plantago ovata. Numerous treatments unveiled noteworthy extensive variability in physiological processes, physiological growth determinant, phonological characters, morphological yield ascribing parameters and in quality parameters of isabgul. The results showed that in isabgul, moisture stress enforced at development to bud formation had maximum seed yield and husk percentage (7). Similarly, Ali et al. (2010) studied the effect of different treatments on seed germination of Descurainia sophia and Plantago ovata, collected in 2009 from Tehran, and an experiment was performed with a factorial randomized complete block design in 6 treatments with 4 replications (8). Treatments employed were KNO₃ (0.1, 0.2 and 0.3%), acetylsalicylic acid (50 and 100 mg/L), 0.1 and 0.2% of pre-chilling thiourea (4°C for 10 days) and boiling water for 5 and 10 min and distilled water was used as control. Results showed that the effect of different treatments on germination percentage of two medicinal species was significantly different (p < 0.05), nevertheless, pre-chilling was the most effective treatment on seed germination of both species.
The literature review depicts that irrigation scheduling of local plants in semi-arid and arid regions provide an opportunity to optimize irrigation efficiency and water savings in water scarce areas. Formerly, Bannayan et al. (1) subjected black cumin (Nigella sativa L.) and isabgul (Plantago ovata Forsk.) to four different irrigation regimes in order to study the effect of water deficit conditions on plants over two growing seasons in northeast of Iran (9). Control was irrigated weekly and three treatments included termination of irrigation at blooming, flowering, and seed formation, respectively. The results described a lower yield of isabgul seed for all water deficit treatments compared to control but black cumin showed tolerance to water deficit except when irrigation was terminated at seed formation. The lowest seed yield was obtained when irrigation was stopped at the blooming stage, and main yield component affected was number of seeds per plant. However, no reduction in oil concentration for black cumin or mucilage percentage for isabgol across all water deficit treatments was observed.

Biofertilizers and organic manure have also been recognized as a substitute for chemical fertilizers to intensify soil fertility and crop production. Formerly, a work was carried out in Iran to evaluate the effects of organic manure, biofertilizers and chemical fertilizers on mucilage percentage, swelling factor, yield and seed chemical components of isabgul. The treatments were managed with manure (20 ton/ha) (T1); vermi-compost (10 ton/ha) (T2); phosphate bio-fertilizer (E-barvar 2) (100 g/ha) (T3); phosphate bio-fertilizer (E-barvar 3) (100 g/ha) (T4); phosphate chemical fertilizer (Triple Superphosphate) (50 kg/ha) (T5); and control (T6). Results revealed that fertilizers application had significant impact on any of the assessed traits in this experiment. The effect of vermin-composton yield (992.50 kg/ha) and mucilage (19.65%) was above other treatments. Animal manure exhibited maximum swelling factor (22.63 mmM3), N (0.33) and K (0.39%) concentration, protein (1.75%) and total carbohydrate content (4.40 mg/g DW). The effect of phosphate bio-fertilizer (E-barvar 3) on P (0.24%) uptake of seeds was beyond other treatments (10).

Biochemical properties of Plantago ovata

Various studies have been conducted in the past to study both physical and chemical properties of Plantago ovata. Study of Fisher et al. (2004) exhibited that it possesses 22.6% arabinose and 74.6% xylose with small amount of other sugars (11). Likewise, Guo et al. (2008) also investigated physicochemical properties of psyllium gum (12). Different series of psyllium gum fractions were formulated by extracting psyllium husk with hot water (80°C) and 0.5 M NaOH, 1.2 M NaOH and 2.0 M NaOH solutions, respectively. These series of psyllium gum fractions were labeled as water extractable (WE), 0.5 M alkali extractable (AES0.5), 1.2 M alkali extractable (AES1.2), and 2.0 M alkali extractable fractions. Moreover, to formulate soluble fraction (AES0.5) and a gel fraction (AEG0.5), the alkali extracted solutions were further neutralized with 0.5 M HCl and centrifuged. Mono-saccharide analysis and methylation analysis was carried out to study chemical constituents of different fractions.

The monosaccharide analysis revealed that WE, AEG and AES fractions of psyllium gum contained xylose and arabinose as major constituents whereas uronic acid was found in WE and AES0.5 fractions in comparison with AEG 0.5, which only have some neutral sugars. Methylation analysis also showed that WE and AEG 0.5 mainly contain 1 fi 4) and 1 fi 3) linked β-D-xylopyranosyl residues in the key chain while side-chains comprise of arabinose and xylose connected to the main chain by O-3 and/or O-2 linkage. The nutritional value and trace element content of Plantago ovata was studied by Buksh et al. (2007) and they revealed that both Plantago ovata leaves and seeds possess bundle of crude fibers, proteins fats and carbohydrates (13).

Furthermore, Singh et al. (2008) (14) studied swelling and drug release mechanisms from hydrogels in detail, which revealed that drug was released from the hydrogels by the non-Fickian diffusion. Additionally, Singh et al. (2007) have studied characterization and swelling behavior of pH sensitive psyllium and polyacrylamide based hydrogels for designing new controlled drug delivery system to treat colon cancer (15). The different structural features of polymeric hydrogels were studied by FTIR, SEM and TGA methods. Swelling responses were also studied in detail which showed that swelling response of polymer works as a function of temperature, time and by changing any of the above factors, swelling response of polymer and drug release from hydrogel can be modified.

Pharmaceutical properties of Plantago ovata

Mucilage

Various scientists have explored use of Plantago ovata mucilage as pharmaceutical excipients. Mucilages are most frequently used adjuvants in different pharmaceutical preparations due to their...
binding, disintegrating, emulsifying, film forming, suspending and thickening properties and they are gaining importance because of their vegetative origin and low cost (16, 17). Kulkarni et al. (2002) have studied binder properties of Plantago ovata and Trigonella foenum graecum mucilages. The mucilages were obtained by simple maceration technique and were further subjected to granule and tablet formation at different concentrations. It was clear from outcomes that Plantago ovata possesses similar binding properties as that of starch and 8% – 9% concentration showed good binding characteristics in uncoated tablets (18).

**Disintegrant**

Superdisintegrants are substances added to tablets to assist the breakup of compacted mass into particles, so as to facilitate the discharge of active ingredient and drug dissolution, when it approaches the fluid surroundings. Plantago ovata is used as a superdisintegrant owing to swelling characteristics of its mucilage. The paramount step of disintegration is appropriate media permeation. When media penetrates the tablet, disintegrant swells upon interaction with it and a swelling force develops, which brings about disintegration of tablet. Fast disintegrating tablets (FDT’s) are novel type of tablets that disintegrate/disperse or dissolve in saliva and are used by pediatrics, geriatrics, bed ridden, mentally disabled patients who have dysphagia and also by those having nausea, allergy, coughing and motion sickness. Great many studies have been performed on superdisintegrant properties of Plantago ovata in comparison with other natural and synthetic superdisintegrant for various FDT’s.

Taste masked FDTs of lisinopril were prepared by direct compression method with an objective to compare the effect of three natural superdisintegrants (isolated mucilage of Plantago ovata, Hibiscus rosasinesis, and Aloe vera) in different concentrations on lisinopril oral formulation. The lisinopril oral tablet with maximum concentration of Plantago ovata mucilage showed better disintegration time of 9 ± 0.26 s and increased dissolution rate as compared to other two disintegrants due to its swelling property (19). Similarly, in another study fexofenadine FDTs were prepared by using seed powder, husk powder and mucilage of Plantago ovata as a super disintegrant and emphasis was given to their disintegrating property. Disintegrants were used in concentration of 5% w/w Plantago ovata. The tablets formulated by using Plantago ovata mucilage presented amended drug dissolution and bioavailability as discovered by the results of disintegration time i.e. 31, 35 and 38 s for Plantago ovata mucilage, seed and husk powder, respectively (20).

A study conducted on granisetron HCl tablets compared the effects of natural (Plantago ovata) and synthetic (gum karaya, agar, croscarmellose, crospovidone and Indion 234) superdisintegrants in different concentrations (21). The experiment concluded that disintegration time of granisetron tablets came out to be 15 s when formulated by containing 5% concentration of Plantago ovata as natural superdisintegrant and drug release rate was 99.66% in 3 minutes, proving thereby natural superdisintegrant as a better disintegrant and having superior dissolution property than commonly used synthetic superdisintegrants. In addition, FDTs of carbamazepine were prepared to relate the influence of natural superdisintegrant (Plantago ovata) and synthetic superdisintegrants (croscarmellose and sodium starch glycolate) on the disintegration time of FDTs and ascertained that FDTs containing Plantago ovata mucilage had shorter disintegration time of 9 s than synthetic ones due to its swelling property (22).

The effect of natural and synthetic superdisintegrants in different concentrations (2-9%) had also been compared previously to prepare FDTs of freely soluble tramadol HCl and poorly soluble levofloxacin. The blend of all formulations was evaluated for physicochemical parameters. The results revealed that formulation of tramadol HCl prepared with mucilage of Plantago ovata and Hibiscus rosasinesis showed disintegration time of 71 and 72 s while levofloxacin tablets displayed disintegration time of 72 and 75 s, respectively. So, a conclusion was made that solubility has no effect on disintegration time and wetting efficiency with natural and synthetic superdisintegrants (23). In the same way, the effect of natural (Plantago ovata mucilage) and synthetic (sodium starch glycolate, croscarmellose sodium) superdisintegrants on disintegration time and drug release pattern of aceclofenac sodium (NSAID) FDTs was explored (24).

The study divulged better disintegration properties of Plantago ovata mucilage due to highest swelling index. The tablets formulated with Plantago ovata showed shorter disintegration time as compared to tablets prepared by sodium starch glycolate and croscarmellose sodium. Just as, FDTs of famotidine were formulated in order to check out the effects of different natural and synthetic superdisintegrants and concluded that Plantago ovata husk powder presented superior flow properties, water retention and disintegration time than maize starch. The psyllium
husk powder at 10% w/w concentration acted as a better superdisintegrant than maize starch (25).

**Gelling agent**

Different studies have been conducted with the main emphasis on the use of *Plantago ovata* as a gelling agent. According to Jain et al. (1997) isabgul could be employed as gelling agent for various tissue culture techniques and microbial culture media. They used isabgul as an alternative gelling media to observe growth of microbes like *Aspergillus flavus*, *Rhizobium mellioti* and *Penicillium chrysogenum* by culturing them on isabgul instead of agar. Isabgul jelled media favorably promoted growth of both bacterial and fungal specie, therefore showing good properties as gelling agent (26). Also, Sahay (1999) further elaborated the use of mucilage husk of *Plantago ovata* as an alternative jelling agent. According to him, 4% w/v of ground husk was used in combination with 0.5% w/v of agar media to promote microbial growth, however he had already removed undesirable properties of psyllium-gelled media by providing UV treatment, oven sterilization and autoclaving (27).

**Suspending agent**

Different studies have been conducted to evaluate use of *Plantago ovata* as a suspending agent, due to its mucilage forming property. According to Rajamaniickam et al. (2010) mucilages of different plants can be used to suspend particles in thermodynamically unstable systems, which aid in preventing sedimentation of particles and promote easy dispersion of settled particles due to their viscous and colloidal nature (28). Moreover, they evaluated ispaghula mucilage powder as suspending agent by formulating suspension with standard drug, nimisolide and compared suspending properties of mucilage powder with one of the marketed product.

Different formulations were formed and were observed for 7 days to monitor sedimentation and settling rate of particles. All formulations exhibited good shear thinning properties of suspension and particles were uniformly dispersed without formation of any deposits, therefore, confirming the property of Ispaghula mucilage powder as an effective suspending agent in different oral preparations. Similarly, Rao et al. (2007) also investigated rheological properties of psyllium seed husk as suspending agent (29). The various concentrations of mucilage of psyllium polysaccharide (PPS) were prepared and suspension was formulated by using standard drug paracetamol. Different rheological properties of suspension were studied and compared with standard suspending agent carboxymethyl cellulose. It was clear from outcomes that Psyllium polysaccharide (PPS) mucilage has appreciable potential for its use as a suspending agent in different formulations.

Recently, Bashir et al. have isolated arabinoxylan from *Plantago ovata* seed husk by alkali extraction and compared its properties as suspending agent with bentonite by formulating 1% zinc oxide suspension. Arabinoxylan produced stable, highly flocculated suspension, which fulfilled all particle size specifications and microbiological properties, therefore, it appreciated the use of arabinoxylan as effective suspending agent in ZnO suspension (30).

**Pharmacological properties of Plantago ovata**

**Wound healing activity**

Singh et al. conducted a study to investigate the wound healing activity of ethanolic extract of *Plantago ovata* seeds (31). The extract was used as an ointment (10% w/w in petroleum jelly base) to cure the wound in shortest possible time with minimal pain, discomfort and scaring to the patients in comparison to standard *Aloe vera* ointment (10% w/w). In this trial Albino rats were selected and surgical intervention was carried out to generate wound under sterile conditions. Acute dermal toxicity was performed and effective dose was selected for wound healing afterward. Healing of a lesion is accompanied by wound contraction characterized by organizing healthy skin adjacent the wound to cover the bare area. The results showed that ethanolic extract had significantly increased the percent wound contraction leading to enhanced wound healing.

**Anti-diarrheal and anti-constipation activity**

Mehmood et al. carried out an analysis to explore the antidiarrheal and anti-constipating potential of *Plantago ovata* (32). In this experiment, crude extract of *Plantago ovata* at the dose of 100-300 mg/kg exert laxative effect in mice by muscarinic, 5-HT receptor activation. While, extract showed gut inhibitory (anti-secretory/anti-diarrheal) action in mice at 500-1000 mg/kg dose by blockage of calcium ion channel and activation of NO cyclic guanosine monophosphate pathway. Similarly, in Guinea pigs ileum the crude extract at 10 mg/mL demonstrated anti-constipating effect by stimulating the muscarinic serotonin receptors. Likewise, 10 mg/mL of crude extract produced gut stimulation followed by relaxation in isolated rabbit jejunum by instigating muscarinic and serotonin receptors.

In another randomized parallel double blind study the stool softening efficacy of psyllium...
Hydrophilic muciloid (5.1 mg bid) was compared with docusate sodium (100 mg bid) and results revealed that the psyllium increased the stool water content (up to 2.3%) and stool water weight (84 g/BH). Bowel movement frequency was also considerably improved in case of psyllium than docusate. Hence, psyllium is superior to docusate for the treatment of chronic constipation (33, 34).

Hypcholestrolemic activity

Rosendaal et al. searched out that the use of Ispaghula husk (psyllium) as an adjunct to diet in patients with hypercholesterolemia is effectual (35). Likewise, a placebo controlled double blind test involving 340 patients of 18-65 years age with mild to moderate hypercholesterolemia corroborated that ispaghula (7 g/day for 6 months) when given with diet caused 8.7% reduction in LDL cholesterol level (4.10-0.42 mM/L). The total cholesterol level was reduced by 7.7-8.9%. In another appraisal it was reported that psyllium binds with the bile acids in the intestinal lumen and lowers the serum cholesterol level (36). Plantago ovata has revealed a considerable reduction in total cholesterol and LDL cholesterol in animals (16-18) and in humans as well (37-39). Furthermore, an additional scrutiny has divulged that consumption of 5.1 g of psyllium husk twice daily for the duration of eight weeks causes a 3.5% reduction in total cholesterol and a 5.1% reduction in LDL levels (40).

Anti-inflammatory activity

Psyllium has been found to decrease the inflammatory intermediaries involved in intestinal inflammatory process for example NO, leukotriene B4 and TNF when evaluated in HLA-B27 transgenic rats, supporting its use as an intestinal anti-inflammatory agent (34, 41).

Hypoglycemic activity

Siavash et al. have examined that psyllium effectively reduces the plasma glucose level by impairing the gastrointestinal carbohydrates absorption in type 2 DM (42). It has been revealed that aqueous extract of P. ovata husk suppresses the postprandial blood glucose and retards the small intestinal absorption without inducing the influx of sucrose into the large intestine thus, indicating that P. ovata may be a valuable source of active phytochemical constituents to provide new opportunities for diabetes therapy. Correspondingly, it has been scrutinized that 5.1 g bid. of psyllium (Plantago ovata Forsk.), a natural soluble fiber supplement is useful as an adjunct to dietary therapy in patients with type II diabetes to reduce glucose with excellent tolerance (43). Previous studies showed that dietary fibers from psyllium have been extensively used both as pharmacological supplements and food ingredients in processed food to assist the weight control with an intention to regulate the glucose level in diabetic patients as well as to reduce the serum lipid levels in hyperlipidemias (34).

Influence on autonomic gastrointestinal disorder

Psyllium husk can be used in Parkinson disease associated with autonomic GI dysfunction induced by anticholinergic drugs. Levodopa was extracted from collected and centrifuged plasma samples of rabbits and characterized by HPLC. 50% higher AUC values, higher Cmax values are observed after oral administration of levodopa and carbidopa (20 : 5 mg/kg), biperiden (100 µg/kg), ispaghula husk at 2 different doses 100 and 400 mg/kg in rabbits in 7-14 days treatment period. Hence, Plantago ovata husk improve the pharmacokinetics of levodopa when given in combination with levodopa/carbidopa and results in more stable plasma concentration, thus, circumventing the ‘wearing off’ phenomenon and delaying the onset of dyskinesia (44).

Treatment of metabolic disorders

In another research work diet containing 3.5% P. ovata husk was given to obese Zucker rats for 25 weeks. The results showed that this diet prevent many of metabolic abnormalities like obesity, dyslipidemia, hypertension and endothelial dysfunction and results in reduced body weight gain, decrease endothelium dependent relaxation I and response to acetylcholine and also intake of P. ovata reduces plasma concentration of adiponectin and TNF-α (45, 46). In addition, a six-month trial involving the supplementation of psyllium fiber significantly reduced the both systolic and diastolic blood pressure in hypertensive overweight subjects (47). Furthermore, one well-established way to reduce the risk of cardiovascular disease (CVD) is to lower serum LDL cholesterol levels by reducing saturated fat intake. Epidemiological studies have proposed that a diet rich in water soluble fibers like psyllium effectively lowers the serum LDL cholesterol level, without affecting HDL cholesterol or triacylglycerol concentrations consequently reducing the menace of CVD (48).

Other pharmacological actions

Water soluble polysaccharide of P. ovata seeds exhibited strong and significant effects on cell physiology of keratinocytes and fibroblast (49). In addi-
tion, *Plantago ovata* exerts cytotoxic effect pointing towards its potential use in various types of cancer (50). Moreover, *Plantago ovata* possesses antibacterial activity as well. Bokaeian et al. (2015) scrutinized the antibacterial potential of silver nanoparticles of *Plantago ovata* by seed extract against antibiotic resistant *Staphylococcus aureus* (51). The results illustrated that silver nanoparticles made up of seed extract of *Plantago ovata* had antimicrobial effect against *Staphylococcus aureus* resistant to cefixime, trimethoprim-sulfamethoxazole and penicillin.

**CONCLUSION**

It can be concluded that *Plantago ovata* has remarkable pharmaceutical properties like superdisintegrant, binder, gelling agent, suspending agent and can be widely used in the preparation of FDTs, suspensions, oral gels and it also possesses excellent pharmacological properties like wound healing, anti-diarrheal, anti-constipation, hypcholesteremic and hypoglycemic activity. Owing to aforesaid notable properties *Plantago ovata* can be used in manufacturing of novel drug delivery systems using advanced techniques and can be formulated in a safe, effective and economical drug devoid of adverse events as that associated with synthetic drugs for the treatment of number of diseases.

**Conflict of interest**

Authors declared that there is no conflict of interest.

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