Polysaccharides
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Characterization of Psyllium (*Plantago ovata*) Polysaccharide and Its Uses

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Abstract

The *Plantago* is one of the genera in family Plantaginaceae, a large genus of herbs or sub-herbs distributed mostly in the temperate region and a few in the tropics. Psyllium has been in use as a medicinal agent since ancient times throughout the world. It is used for treatment of constipation, diarrhea, hemorrhoids, and high blood pressure. In olden days it was also used topically to treat skin irritations, such as poison ivy reactions and insect bites and stings. The husk of the seeds of various species of psyllium is used for its medicinal properties. The primary ingredient of the seeds and husk is a mucilaginous polysaccharide. Psyllium has been reported for the treatment of constipation, diarrhea, and irritable bowel syndrome, inflammatory bowel disease (ulcerative colitis), colon cancer, diabetes, and hypercholesterolemia. When mixed with water, the therapeutic efficacy of the drug is due to the swelling of the mucilaginous seed coat which gives bulk and lubrication. Psyllium increases the volume of the feces by absorbing water in the gastrointestinal tract, which stimulates peristalsis. Modification of the polysaccharide by cross-linking or derivatization has been done to investigate its use as pharmaceutical excipient with multifarious roles. Various cross-linkers that have been studied include methacrylamide, *N,N*-methylenebisacrylamide, and polymethacrylamide.

Keywords

Psyllium; Ispaghula; Dietary fibers; Constipation; Irritable bowel syndrome; Cancer; Hyperlipidemia; Acrylamides; Excipients

Abbreviations

AAm	Acrylamide
APS	Ammonium persulfate
DNA	Deoxyribonucleic acid
GLUT-4	Glucose transporter protein
HEMA	Hydroxylethylmethacrylate
HLA-B2712	Human leukocyte antigen
IBS	Irritable bowel syndrome
IP	Indian Pharmacopoeia

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LDL	Low-density lipoprotein
MAAm	Methacrylamide
N,NMBAAm	*N,N*-methylenebisacrylamide
NVP	*N*-vinylpyrrolidone
PAM	Polyacrylamide
PMA	Polymethacrylic acid
PVA	Polyvinyl alcohol
RAPD	Random amplified polymorphic DNA
SCFA	Short-chain fatty acids
SHP	Seed husk of psyllium

1 Introduction

Natural carbohydrates are the world's most abundant, renewable, and biodegradable polymers. They are the most basic source of fuel for all life forms on earth. The simplest carbohydrates are the monosaccharides such as glucose, fructose, galactose, xylose, and mannose. Polysaccharides are complex carbohydrate polymers consisting of two or more monosaccharides linked together covalently by glycosidic linkages in a condensation reaction. They are usually insoluble in water because of their large molecular size. Polysaccharides can be classified as homopolysaccharides and heteropolysaccharides. A homopolysaccharide is one with repeat units of a single type of monosaccharide, whereas a heteropolysaccharide is composed of two or more types of monosaccharides. In both types of polysaccharide, the monosaccharides are linked in a linear or branched fashion. Polysaccharides are extremely important in organisms for the purposes of energy storage and structural integrity (Berg 2007).

Starch is used as a storage polysaccharide in plants in the form of both amylose and the branched amylopectin. Cellulose and chitin are examples of structural polysaccharides. Cellulose is used in the cell walls of plants and other organisms and is said to be the most abundant organic molecule on earth. Chitin has a similar structure but has nitrogen-containing side branches, increasing its strength. Polysaccharides also include callose or laminarin, chrysolaminarin, xylan, arabinoxylan, mannan, fucoidan, and galactomannan (Campbell 1996).

Complex carbohydrates are important dietary elements for humans and are commonly called as dietary fibers. Dietary fibers are classified as soluble and insoluble fibers. Soluble fibers cause an increase in intestinal transit time of food and are readily fermented in the colon into gases. Insoluble fibers may be metabolically inert and provide bulk to intestinal contents or may undergo fermentation in the large intestine. Insoluble fibers tend to hasten movement of food through the intestine (Dietary Reference Intakes for Energy et al. 2005; Eastwood and Kritchevsky 2005). Soluble fibers reportedly bind to bile acids in the small intestine, thereby reducing their absorption. This consequently leads to lower cholesterol levels in the blood (Anderson et al. 2009). Soluble fibers also interfere with the absorption of sugar, regularize blood lipid levels, and produce short-chain fatty acids as by-products of fermentation in the colon with wide-ranging physiological activities. Although insoluble fibers are associated with reduced diabetes risk, the mechanism by which this occurs is unknown (Weickert and Pfeiffer 2008).

Modern lifestyle has given rise to a plethora of diseases including diabetes, cancer, and cardiovascular diseases. The short-term and long-term side effects associated with the therapeutic regimen

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used for control of these conditions have shifted the focus to alternative methods of prevention, cure, and control which can work complementarily with the treatment. This in turn has spawned a worldwide interest in the benefits of dietary fibers, the so-called wonder food of the new millennium. Dietary fiber is regarded as important for the diet, with regulatory authorities in many developed countries recommending increase in fiber intake (Dietary Reference Intakes for Energy et al. 2005; Eastwood and Kritchevsky 2005; European Food Safety Authority 2014; Jones and Varady 2008).

1.1 Polysaccharides as Pharmaceutical Excipients

Excipients are an integral part of pharmaceutical dosage forms and comprise the greatest proportion in dosage units. Knowledge of the composition, function, and behavior of excipients is a prerequisite for the successful design, development, and manufacture of pharmaceutical dosage forms. Interest in the physical effects and properties of the excipients used in pharmaceutical formulations has increased in recent years due to the awareness of the fundamental effect that excipients can exert on the bioavailability, bioequivalence, and stability of formulations.

Globally, there is a renewed interest in investigating drugs and excipients from natural sources, especially from plant and marine sources that include starches obtained from corn, wheat, rice, and tapioca (Andreev 2004) and different types of essential and aromatic oils. A number of polysaccharides like chitosan (Park et al. 2002; Sakkinen et al. 2003; Thanou et al. 2000), tamarind seed polysaccharide (Gholardi et al. 2000; Kulkarni et al. 2005; Sumath and Ray 2002; Miyazaki et al. 1998), psyllium husk (Fischer et al. 2004a), guar gum (George and Abraham 2007), xanthum gum (Attama et al. 2006; Khourefieh et al. 2007), and rice bran wax (Dolz et al. 2007) are currently being used or investigated for varied roles as pharmaceutical excipients which include mucoadhesion, gel former, drug release retardant, plasticizer, thickener, and binder. The investigations to explore and investigate newer and newer plant sources continue unabated despite the availability of a large number of synthetic excipients.

2 Psyllium

Psyllium has been in use since ancient times throughout the world. In India the use of *P. ovata* dates back to 1500 BC in the Ayurvedic system of medicine, whereas the Chinese have used it in traditional medicine for thousands of years. The European use of the herb dates back centuries, and in North America, psyllium gained prominence in healing only near the end of the twentieth century (http://savoursomepsyllium.blogspot.in/2010/11/historytraditional-use.html 2014; Truestar Health: http://www.truestarhealth.com/Notes/2150006.html#Traditional-Use 2014). The Indian and the Chinese have used psyllium since 1500 BC for treatment of constipation, diarrhea, hemorrhoids, bladder problems, and high blood pressure. It was also used topically to treat skin irritations, such as poison ivy reactions and insect bites and stings. Europeans and North Americans began using psyllium for cholesterol and blood glucose-lowering effects (http://www.psylliums.com/psyllium.htm 2014). Typically, psyllium was administered in powder, flakes, or granular form. These would then be diluted in liquids and drank or sprinkled over meals. Only recently have they been made available in tablets, capsules, and liquid forms (http://savoursomepsyllium.blogspot.in/2010/11/historytraditional-use.html 2014; Bluementhal et al. 1998).

2.1 Biological Source

The dried, ripe seeds of *Plantago afra* (*Plantago psyllium*), *Plantago indica* (*Plantago arenaria*), and *Plantago ovata* (Plantaginaceae) are used in medicine. The *US National Formulary* includes all

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Table 1 Properties of psyllium seeds

Characters	*Plantago ovata*	*Plantago afra*	*Plantago indica*
Origin	India, Pakistan	Cuba, Spain, France	Egypt, Mediterranean, Europe
Color	Dull pinkish gray brown	Glossy deep brown	Dull blackish brown
Shape	Boat shaped; outline ovate	Boat shaped; outline elongated ovate	Boat shaped; outline elliptical
Length	1.8–3.3 mm	2.0–3.0 mm	2.0–2.5 mm
Weight of 100 seeds	0.15–0.19 g	0.09–0.10 g	0.12–0.14 g

three species under the name "Plantago Seed" (Trease and Evans 2008). Psyllium husk is the cleaned, dried seed coat (epidermis) separated by winnowing and thrashing from the seeds of *Plantago ovata* Forskal. It is commercially referred to as blond psyllium or Indian psyllium or ispaghula. The husk may also be obtained from *Plantago psyllium* Linne or from *Plantago indica* Linne (*Plantago arenaria* Waldstein et Kitaibel) commonly known as Spanish or French psyllium (Plantaginaceae), in whole or in powdered form (United States Pharmacopoeia 2006). As per British Pharmacopoeia, psyllium seed consists of the ripe, whole, dry seeds of *Plantago afra* L. (*Plantago psyllium* L.) or *Plantago indica* L. (*Plantago arenaria* L. Waldstein and Kitaibel) (British pharmacopoeia 1968). According to IP, ispaghula husk (isabgol husk, *Plantago*) consists of the epidermis and collapsed adjacent layers removed from the dried ripe seeds of *Plantago ovata* Forsk (Indian Pharmacopoeia 2010).

2.2 Geographical Source

Ispaghula is an annual herb cultivated in India in the states of Gujarat, Maharashtra, Punjab, and in parts of Rajasthan and Sindh Province of Pakistan (Rangari 2008). *Plantago psyllium* is cultivated in France and Spain for the European market. *Plantago ovate* seeds are cultivated in Southern Europe, North Africa, and West Pakistan (Gupta 2005). India exports about 90 % of the gross production of ispaghula and nearly 93 % of the export being husk. Psyllium husks and industrial powders are exported in countries such as USA, UK, France, Germany, Japan, Indonesia, Canada, Mexico, Sweden, Spain, Norway, Italy, Australia, Denmark, Korea, Pakistan, and some Gulf countries. The USA is the largest buyer of ispaghula from India and accounts for about 75 % of the total husks exports from India (http://www.psylliums.com/psyllium.htm 2014) (Table 1).

2.3 Cultivation, Collection, and Treatment

The crop requires marginal, light, well-drained sandy-loam to loamy soils having pH between 7 and 8. The plant does not have any specific nutrient requirement. It requires a cool climate and dry sunny weather during harvesting. Mild dew, cloudy, or light showers cause seed shedding (Trivedi 2004). Seeds are sown by broadcasting method in sandy, loamy soil. Addition of farmyard manure or animal manure (prepared basically using cow dung, cow urine, waste straw, and other dairy wastes) has favorable effect but generally ammonium sulfate is added as a fertilizer. Irrigation is done regularly at an interval of 8–10 days. Ispaghula is not significantly affected by pests or diseases, but the annual harvest greatly suffers due to storm and rainfall. *Plantago* wilt "*Fusarium oxyspirum*" and downy mildew are the major diseases of ispaghula. White grubs and aphids are the major insect pests. The crop is harvested when the flower spikes turn reddish brown, lower leaves dry, and upper leaves turn yellow. Harvested seeds are dried below 12 % moisture to enable cleaning, milling, and storage (Rangari 2008). Ispaghula husk is separated from the seed by crushing in flat stone grinding mills by winnowing. It is marketed as a separate commodity. It is more in demand and fetches more price than that of seeds. Raw psyllium seeds are fumigated in their storage area to avoid any

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Fig. 1 Morphology of psyllium seeds [*Plantago ovata*]

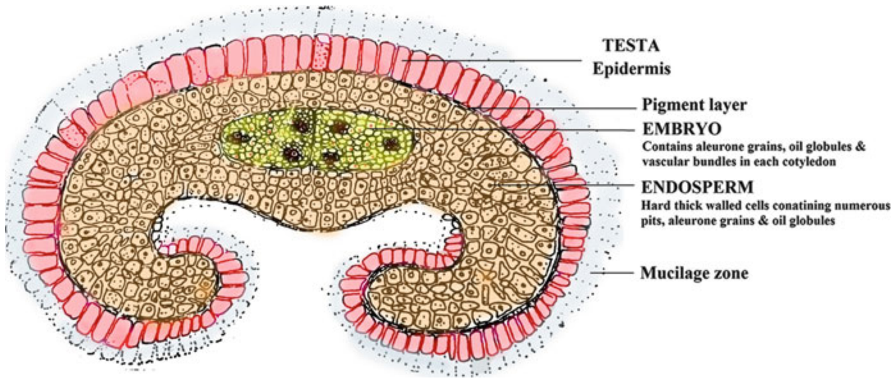

Fig. 2 Transverse section of seeds of *Psyllium ovate*

contamination. Psyllium products like husk and powder are treated in the fumigation chamber with approved chemical reagents like methyl bromide as per latest international guidelines. Psyllium products can also be sterilized by ethylene oxide or gamma radiation, if required (http://phytosanitorysolution.com/ 2014). Seeds and husks of *Plantago major* Linn, *Plantago lanceolata* Linn, *Plantago psyllium* Linn, as well as seeds of *Lepidium sativum* are used as adulterants in ispaghula (http://www.psylliums.com/psyllium.htm 2014).

2.4 Morphology

Psyllium seeds are ovoid-oblong in shape, about 2–3 mm long and 0.8–1.5 mm wide (Fig. 1). They are pinkish gray to brown in color with a convex dorsal surface and concave ventral surface with a deep groove running lengthwise along the center (http://www.psylliums.com/psyllium.htm 2014) (Figs. 2 and 3a, b).

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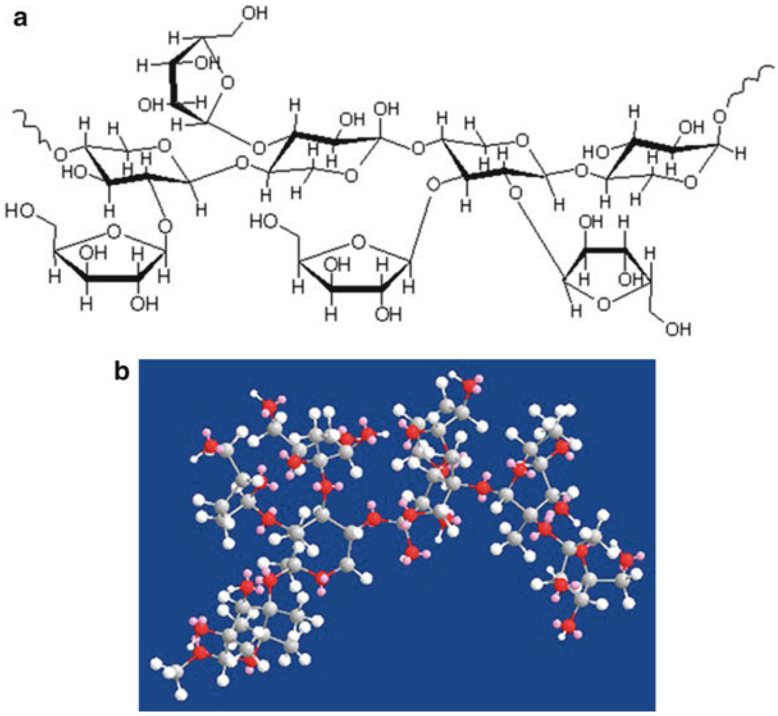

Fig. 3 (**a**) Chemical structure of arabinosyl (galactouronic acid) rhamnosylxylan. (**b**) Ball-and-stick model of arabinosyl (galactouronic acid) rhamnosylxylan

2.5 Microscopy

The transverse sections of the seed that cut through the central region possess a reniform outline and exhibit a spermoderm, endosperm, and embryo. The spermoderm shows an outer epidermis of mucilaginous epidermal cells with obliterated walls in glycerine mounts; the radial and inner walls swell and disintegrate to form a clear mucilage upon irrigation of the mount with water, and a pigment layer with brown amorphous content. The endosperm is composed of irregular-shaped, thick-walled cells with walls of reserve cellulose. The outer layer of this region consists of palisade cells 15–40 μm in height. Aleurone grains and fixed oils are found in the endosperm cells (Bruneton 1995).

2.6 Chemical Constituents

Many elements have been identified in the seed which include proteins, lipids, sterols, triterpenes, and aucubin glycoside. The mucilage level is about 30 %. The principal constituent of the mucilage is 85 % of a soluble polysaccharide fraction dominated by D-xylose. The polymer backbone is a xylan with 1→3 and 1→4 linkages with no apparent regularity in their distribution. The monosaccharides in this primary chain are substituted on C-2 or C-3 by L-arabinose, D-xylose, and α-D-galactouronyl-(1→2)-L-rhamnose (Bruneton 1999). Psyllium seed mucilage contains 22.6 % arabinose, 74.65 % xylose and traces of other sugars, and 35 % nonreducing terminal residues (Fischer et al. 2004b).

2.7 Structure

The polysaccharide structure constitutes a densely substituted main chain of (1→4)-linked D-xylopyranosyl residues, some carrying single xylopyranosyl side chains at position 2, others

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bearing, at position 3, trisaccharide branches having the sequence 1-Araf- (1→3)-1-Araf. Chemically the polysaccharide is arabinosyl (galacturonic acid) rhamnosylxylan.

3 Clinical Indications

Psyllium has been reported for the treatment of constipation, diarrhea, and irritable bowel syndrome, inflammatory bowel disease (ulcerative colitis), colon cancer, diabetes, and hypercholesterolemia (Majmudar et al. 2008; Reynolds 1993).

3.1 Constipation

Psyllium husk is widely used for treatment of constipation due to its mucilaginous components.

When mixed with water, the therapeutic efficacy of the drug is due to the swelling of the mucilaginous seed coat which gives bulk and lubrication (Tyler et al. 1988). Psyllium increases the volume of the feces by absorbing water in the gastrointestinal tract, which stimulates peristalsis (Read 1986). The intraluminal pressure is decreased, colon transit is increased, and the frequency of defecation is increased (Marteau et al. 1994; Sölter and Lorenz 1983). The effectiveness of fiber, and psyllium in particular, on constipation depends on the main cause of the constipation. In a study of 149 patients with chronic constipation, the consumption of 15–30 g daily of a psyllium seed preparation provided bowel relief in 85 % of participants who had no known pathological cause for their constipation. Only 20 % of individuals with slow transit responded to psyllium. A slightly greater percentage (37 %) of those with disorders of defecation – including rectocele, internal prolapse, anismus, and rectal hyposensitivity – found improvement (Alternative Medicine Review 2002; Voderholzer et al. 1997; Kumar et al. 1987; Qvitzau et al. 1988).

3.2 Fecal Incontinence

Psyllium has been shown to have the paradoxical property of both improving constipation by increasing stool weight and ameliorating chronic diarrhea. Because of its ability to retain water, psyllium has also been shown to benefit individuals with fecal incontinence from liquid stools or diarrhea. A placebo-controlled trial of persons with liquid stool fecal incontinence was performed in which supplementation with both gum arabic and psyllium showed approximately a 50 % decrease in the occurrence of incontinent stools. The psyllium group had the highest water-holding capacity of water-insoluble solids and total water-holding capacity of the stool (Alternative Medicine Review 2002; Bliss et al. 2001).

3.3 Hemorrhoids

With the known benefit of psyllium for both constipation and loose stools, psyllium was also reported to be beneficial for the treatment of hemorrhoids. It was found to have a significant improvement in reduction of bleeding and a dramatic reduction of congested hemorrhoidal cushions (Perez et al. 1996; Broader et al. 1974; Webster et al. 1978).

3.4 Irritable Bowel Syndrome (IBS)

Constipation is characterized by unsatisfactory defecation and infrequent stools, difficult stool passage, or both. On the other hand, the presence of clinically important abdominal discomfort or pain associated with constipation defines IBS with constipation. Intake of psyllium may be effective in alleviating chronic constipation in patients without slow colonic transit or disordered constipation. On the other hand, fiber with lactulose may improve stool consistency in patients with IBS with

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constipation. The easing of bowel dissatisfaction appears to be a major reason for the therapeutic success of psyllium in IBS (Degan and Phillips 1996; Bouchoucha et al. 2004; Koch et al. 1997).

3.5 Ulcerative Colitis (Crohn's Disease)

The two primary sites for Crohn's disease are the ileum, which is the last portion of the small bowel (ileitis, regional enteritis), and the colon (Crohn's colitis). A small number of studies have examined the ability of psyllium to maintain remission in ulcerative colitis. Dietary fiber has been proven to be beneficial in maintaining remission in human ulcerative colitis, an effect related with an increased luminal production of short-chain fatty acids (SCFA), i.e., acetate, propionate, and butyrate in the intestines. Dietary fiber supplementation ameliorated colonic damage in HLA-B2712. In an open label, randomized, multicenter trial of persons with ulcerative colitis, psyllium seed supplementation (10 g twice daily) was as effective as mesalamine in maintaining emission. It was inferred that this effect may possibly be due to increased levels of butyric acid with psyllium supplementation (Alternative Medicine Review 2002; Fernandez et al. 1999).

3.6 Appetite

Psyllium may also have an effect on appetite. A triple-blind study on 17 women looked at the effect of 20 g of psyllium seed 3 h pre-meal and again immediately post-meal during three 3-day study periods. The subjects reported significantly increased feelings of fullness 1 h after meals with the psyllium and exhibited a significantly lower fat intake with those meals (Turnbull and Thomas 1995).

3.7 Hyperlipidemia

Psyllium has been shown to reduce total cholesterol and low-density lipoprotein (LDL) cholesterol in animals and in humans (Fernandez 1995; Fernandez et al. 1995; Terpstra et al. 2000). Sprecher et al. demonstrated a 3.5 % reduction in total cholesterol and a 5.1 % reduction in LDL levels after consuming 5 g of psyllium husk twice daily for 8 weeks (Sprecher et al. 1993). Another study began with individuals on the American Heart Association Step 1 diet, followed by 8 weeks of psyllium, resulting in decreased total cholesterol (4.8 %) and LDL (8.8 %) (Bell et al. 1989). A meta-analysis was performed on eight trials of psyllium husk in conjunction with a low-fat diet in the treatment of hypercholesterolemia. After an initial 8-week, low-fat diet run-in, 10.2 g psyllium was given per day, resulting in a 4-percent reduction in serum total cholesterol and a 7-percent reduction in LDL cholesterol, compared to diet and placebo. A 6 % reduction in the ratio of apolipoprotein (apo) B to apo A-I was also noted (Anderson et al. 2000a; Levin et al. 1990; Anderson et al. 2000b; Olson et al. 1997). A meta-analysis of 12 studies of psyllium-enhanced cereal product consumption on total and LDL cholesterol in 404 adults with mild to moderate hypercholesterolemia demonstrated a reduction of 5 % of total cholesterol and 9 % of LDL cholesterol (Romero et al. 1998). Researchers studied the effect of fiber-enhanced cookies on blood lipids in hypercholesterolemic men, using wheat bran-, psyllium-, or oat bran- containing cookies (wheat bran was used as the placebo since it has no demonstrated cholesterol-lowering effect). At the end of the 8-week study, plasma LDL cholesterol had decreased to 22.6 % in the psyllium group and 26 % in the oat bran group (Burton and Manninen 1982). A 4-month study of 12 elderly patients showed psyllium husk reduced total serum cholesterol by 20 %, a figure much higher than the abovementioned studies [(Stewart et al. 1991)]. In another study, a significant reduction in total serum cholesterol was noted in 176 elderly persons who used psyllium for 1 year (Vega-Lopez et al. 2001). The authors found that for every 1 g increase in daily psyllium dose, there was a 0.022-mmol/l (0.84 mg/dl) decrease in serum total cholesterol concentration. In a study to examine age and gender differences in the effect

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of psyllium on blood lipids, men and pre- and postmenopausal women were given psyllium (15 g daily) or placebo. Psyllium lowered plasma LDL cholesterol by 7–9 % in all groups. Triglyceride levels were lowered by 17 % in men, but were increased by 16 % in postmenopausal women. Premenopausal women displayed no significant shift in triglycerides (Agrawal and Pariddhavi 2012).

The mechanism of action of psyllium's hypocholesterolemic effects has not been fully expounded. Psyllium was shown to stimulate bile acid synthesis (7 α-hydroxylase activity) in animal models (Horton et al. 1994; Matheson et al. 1995) and in humans (Everson et al. 1992). The diversion of hepatic cholesterol for bile acid production is an established mechanism for reducing serum cholesterol. Psyllium's effect on the absorption of cholesterol (Everson et al. 1992; Turley et al. 1994) and fat (Ganji and Kies 1994) is negligible but may appear to contribute to cholesterol lowering. Additional mechanisms, such as inhibition of hepatic cholesterol synthesis by propionate (Anderson 1995) and secondary effects of slowing glucose absorption (Jenkins et al. 1990), may also play a role.

3.8 Diabetes Mellitus

Dietary fibers from psyllium have been used extensively in processed food to aid weight reduction, for glucose control in diabetic patients (Anderson et al. 1999). It has been shown to improve postprandial glycemic index and insulin sensitivity. In rats it was found to suppress sucrose and glucose absorption in the gastrointestinal tract. Studies also showed enhanced blood glucose disposal by regulating skeletal muscle plasma membrane GLUT-4 protein (glucose transporter) expression without phosphatidylinositol 3-kinase activation (Yu et al. 2009). The effect of psyllium husk was studied in 34 men with type 2 diabetes and hypercholesterolemia, given either placebo or 5 g psyllium twice daily for 8 weeks. Total cholesterol was lower by 8.9 % and LDL by 1 %. In addition, the postprandial rise of glucose was significantly reduced (Duke 1985). The mechanism for hypoglycemic effect in humans may be due to suppression of diffusion of glucose to small intestinal epithelium for absorption, delayed gastric emptying time, and reduced carbohydrate digestibility by retarding their access to digestive enzymes (Liangli and Wei Liu 2012).

3.9 Cancer

Seeds of *Plantago coronopus*, *P. lanceolata*, *P. ovata*, and *P. psyllium* were used by humans against cancer (Liangli and Wei Liu 2012; Hartwell 1982). Besides, the presence of luteolin-7-*O*-*b*-glucoside, a major flavonoid present in the leaves of *P. serraria*, *P. psyllium*, *P. coronopus*, and *P. lanceolata*, was able to strongly inhibit the proliferation of human cancer cell lines (Galvez et al. 2003). Butyric acid which is reported to exhibit antineoplastic activity against colorectal cancer is the preferred oxidative substrate for colonocytes and may be helpful in the treatment of ulcerative colitis (Whitkus et al. 1994). Butyrate may also dose-dependently suppress cancer cell proliferation, promote differentiation marker expression, and lead to reversion of cells from a neoplastic to nonneoplastic phenotype (Yu et al. 2009). In a study of patients with resected colorectal cancer, those given 20 g of psyllium seeds daily for 3 months exhibited an average increase of butyric acid production of 42 %, which decreased to pretreatment levels within 2 months of cessation of supplementation (Nordgaard et al. 1996).

Psyllium might also alter colonic sphingomyelin metabolism and apoptosis which may have an impact on colon tumorigenesis and inflammation in mice (Cheng et al. 2004).

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4 Safety Data

4.1 Precautions

The recommended dose for psyllium varies as per the age and clinical indication. Nonetheless the precautions are common regarding safe use of psyllium. Psyllium should not be taken in case of suspected intestinal obstruction (ileus), diseases of the esophagus, and patients with difficulty in swallowing. It is also not recommended for patients with intestinal atresia and stenosis and for children below 6 years. It should be consumed with sufficient quantity of water, failing which may cause choking due to blockage of the throat or esophagus (New HMPC Commission 2014).

4.2 Drug Interactions

Bulking agents have been reported to reduce the absorption of some minerals (calcium, magnesium, copper, and zinc), vitamin B_{12}, cardiac glycosides, and coumarin derivatives (Gattuso and Kamm 1994; Hänsel et al. 1994a; Drews et al. 1981). The co-administration of psyllium with lithium salts has been reported to reduce the plasma concentrations of the lithium salts due to inhibition of their absorption from the gastrointestinal tract (Pearlman 1990). It has also been reported to decrease both the rate and extent of carbamazepine absorption, inducing subclinical levels of the drug. Therefore, ingestion of lithium salts or carbamazepine and psyllium should not be concomitant (Etman 1995). Insulin-dependent diabetic people may require less insulin if they are concurrently taking psyllium (Bradley 1983).

4.3 Preclinical Safety Data

The material hydrates and swells to form mucilage in vivo as it is only partially solubilized. Less than 10 % of the mucilage gets hydrolyzed in the stomach. Preclinical studies in various animal species revealed pigmentation of various organs. Albino rats showed a dark pigmentation of the suprarenal gland, kidney, marrow, and liver after 125 days on a diet of 25 % of psyllium seeds. Dogs showed gray color of kidneys after a diet containing 25 % psyllium seeds for 30 days. Similar effects were not observed in humans. The pigmentation could be attributed to the dark pigment in the pericarp of the seeds (Hänsel et al. 1994b).

5 Preserving Genetic Integrity

Proper conservation and successful breeding of commercially viable crops is facilitated by appropriate identification of the plant. Conventionally, identification and classification of plant groups are solely based on differences in morphological features, especially the floral character which was considered to be consistent. It is well established that morphological characteristics are a result of the interaction between the environment and the genotype and can also be influenced by climatic and edaphic factors. Molecular techniques using DNA markers are therefore useful not only to identify the genotypes for authentication, but also in assessing and exploiting the genetic variability (Whitkus et al. 1994b). These techniques are suitable means for estimating genetic diversity because of their abundant polymorphism and the fact that they are independent of environment (Gepts 1993). DNA fingerprinting is a remarkable tool to create the genetic blueprint of all medicinal plants. Genetic diversity in five cultivars of *P. ovate* was estimated using molecular markers by Pal (Pal and Raychoudhuri 2004) and Raychoudhuri (Raychoudhuri and Pramanik 1997). Similarly, Vahabi et al. used molecular and morphological markers for the evaluation of genetic diversity between *P. ovate* (Vahabi et al. 2008). Wolff and Morgan-Richards used random amplified polymorphic DNA

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(RAPD) markers for differentiating subspecies of *Plantago major* (Wolff et al. 2000). Samantaray et al. used RAPD markers to assess genetic relationships and variance in seven species of Plantago, i.e., *P. ovata* (Forsk.), *P. indica* (L.), *P. arenaria* (Waldst.), *P. psyllium* (Linn.), *P. lanceolata* (Linn.), *P. serraria* (Linn.), and *P. coronopus* (Linn.) (Samantaray et al. 2010). In India, facilities have been developed for long-term storage of germplasm in the National Gene Bank in New Delhi, India, to avoid frequent regeneration and to check genetic drift (Trivedi 2004).

6 Chemical Modifications

A lot of work involving derivatization/cross-linking of polysaccharide obtained from psyllium seeds and husk is underway. The objective of these studies is to modify the properties of the polysaccharide in order to exploit it as a pharmaceutical excipient. Some of the pioneering works done in this field are enlisted below:

1. Singh and Sharma have developed psyllium–PVA–acrylic acid-based novel hydrogels for use in antibiotic drug delivery through graft copolymerization. The use of a very small amount of these petroleum products has developed low energy, cost-effective, biodegradable, and biocompatible material for potential biomedical applications. In this experiment, polyvinyl alcohol and acrylic acid were used as monomers; *N,N*-methylenebisacrylamide was used as the cross-linking agent, and ammonium persulfate was used as the thermal initiator (Singh and Sharma 2010).
2. Patil et al. have developed and evaluated psyllium seed husk polysaccharide-based wound-dressing films. In this study, wound-dressing films were fabricated using seed husk of psyllium (SHP) complexed with povidone iodine and were evaluated for various physicochemical properties as well as wound healing activity in albino rats (Basavaraj et al. 2011).
3. Singh and Chauhan have prepared psyllium- and acrylamide-/methacrylamide-based hydrogels, and the effects of pH on the release dynamics of insulin from drug-loaded hydrogels were studied to evaluate the drug release mechanism. Two types of hydrogels were prepared by using acrylamide and a mixture of acrylamide/methacrylamide. The hydrogels were named as psy-cl-poly (AAm) and psy-cl-poly (AAm-*co*-MAAm) hydrogels, respectively. *N, N*-methylenebisacrylamide was used as the cross-linking agent and ammonium persulfate was used as the thermal initiator (Singh and Chauhan 2010).
4. Sen et al. conducted research on a novel microwave-initiated method for synthesis of polyacrylamide-grafted psyllium (Psy-*g*-PAM). Psyllium was modified through grafting of polyacrylamide (PAM) chains on it using microwave radiations only, in the absence of any other free radical initiator. The synthesized grades of the graft copolymer were characterized through various physicochemical techniques. The flocculation efficacy of the synthesized graft copolymers was studied in kaolin and coal fine suspension through standard “Jar test” procedure. It was found that the high flocculation efficacy of Psy-*g*-PAM makes it a good candidate to be used as a flocculant for waste water treatment and treatment of effluents discharged from coal washeries (Sen et al. 2010).
5. Singh and Kumar prepared psyllium-*N*-vinylpyrrolidone (NVP)-based hydrogels by radiation-induced cross-linking. The reaction mixture was irradiated with gamma rays of a dose rate of 2.43 kGy/h, in 60 Co gamma chamber for a specific time. The cross-linking polymers thus formed were named as psy-cl-poly (NVP) hydrogels. These hydrogels were then studied for their release dynamics of anticancer model drug (5-fluorouracil). It was found that the release of the drug from the hydrogels occurred through non-Fickian diffusion mechanism (Singh and Kumar 2008).

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6. Kumar and Sharma synthesized a new material (Psy-*g*-PMA) by grafting polymethacrylic acid onto the backbone of psyllium using a microwave-assisted method. Acetylsalicylic acid was incorporated in the various Psy-*g*-PMA samples and tablets were prepared to study the in vitro drug release. This biodegradable material is good for the fast release of medicine in acidic environments such as the human stomach. The material also demonstrated superabsorbent capacity for water and may be useful in diapers and feminine sanitary pads (Kumar and Sharma 2013).
7. Singh and Chauhan prepared psyllium 2-hydroxylethylmethacrylate (HEMA) and acrylamide (AAm)-based polymeric networks by using *N,N*-methylenebisacrylamide (*N,N*-MBAAm) as cross-linker and ammonium persulfate (APS) as initiator. It was concluded that the swelling of the modified psyllium-based hydrogels is affected by the composition of the hydrogels and pH of the swelling medium (Singh et al. 2008).

7 Conclusion

The surge in the development of newer drug molecules for the treatment of a plethora of diseases has definitely led to improved therapy, but it has also resulted in a concomitant rise in side effects and adverse reactions. This has led to a resurgence of plant-based traditional systems of medicine and nutraceuticals which either supplement or complement these therapeutic regimens. The impact of the role of dietary fibers, the "wonder food" of the new millennium, in the control and cure of many lifestyle diseases cannot be underestimated. Psyllium has been in use since ages for its various medicinal effects and continues to rule the roost for the treatment of constipation, diarrhea, irritable bowel syndrome, inflammatory bowel diseases, ulcerative colitis, colon cancer, diabetes, and hypercholesterolemia. The high mucilaginous content of psyllium seeds and husk has also spawned an interest in its use as pharmaceutical excipient. Chemical modifications have been done to improve its profile as multifunctional pharmaceutical excipient. Future studies could be aimed at exploring and discovering more uses of this remarkable but unassuming plant.

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