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FUNCTIONAL BENEFITS OF PSYLLIUM FIBER SUPPLEMENTATION

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ABSTRACT: ***Commonly called Psyllium (Ispaghula Psyllium, Plantago ispaghula and Plantago ovata), has a long history of use as a dietary fiber supplement, primarily as a gentle bulk-forming laxative to promote the regulation of large bowel function, but it has as well a potential role in the treatment and prevention of bowel diseases such as diverticulosis, irritable bowel syndrome and inflammatory bowel disease, and could even play a protective role in the prevention of colon cancer. During the last decade, dietary supplementation with Psyllium has been shown to lower blood cholesterol level (especially LDL cholesterol) and to maintain blood glucose homeostasis, which together are the most effective preventive measures against diabetes and cardiovascular diseases. Much interest is being shown by the general public, the scientific community, and federal US regulators in the medical application of foods with specific health benefits (functional foods), foods that favorably modify physiologic function. There is also considerable interest in health claims by the industry to produce functional foods and to ensure efficacy of action. The intent of this review is to summarize the functional benefits of Psyllium fiber consumption and to explore the potential application this fiber has for first-line dietary prevention of these diseases and disorders.***

KEY WORDS: Cholesterol lowering, Dietary supplementation, Intestinal regulation, Soluble fiber.

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INTRODUCTION

Commonly called Psyllium (Ispaghula Psyllium, Plantago ispaghula and Plantago ovata), has a long history of use as a dietary fiber supplement, primarily as a gentle bulk-forming laxative to promote the regulation of large bowel function. Also, during the last decade, dietary supplementation with psyllium has been shown to lower blood cholesterol levels, and especially LDL cholesterol (Williams *et al.*, 1995; Brown *et al.*, 1999; Anderson *et al.*, 2000a; Anderson *et al.*, 2000b) as well as to maintain blood glucose homeostasis, which together are the most effective preventive measures against diabetes and cardiovascular diseases (CVD). Considering that cardiovascular diseases is one of the major causes of death in most Western countries, and that dietary intervention should be the first-line approach, increasing soluble dietary fiber has been recommended as safe and practical for cardiovascular disease prevention.

Much interest has been shown internationally by the general public, the scientific community, and federal US regulators in the medical application of foods with specific health benefits (functional foods), foods that favorably modify physiologic function. There is also considerable interest in health claims by the industry to produce functional foods and to ensure efficacy of action. The intent of this review is to summarize the documented functional benefits of Psyllium fiber consumption.

WHAT IS PSYLLIUM ?

According to the European Pharmacopoeia, Psyllium seed (Psyllii semen) consists of the ripe, whole, dry seeds of Plantago afra L. (Plantago psyllium L.) or Plantago indica L. (Plantago arenaria Waldstein and Kitaibel). Husk and seeds from Plantago ovata (Plantaginis ovatae) is however commonly also referred to as Psyllium, although the correct definition of Plantago ovata Forssk. (P. ispaghula Roxb.) is Ispaghula husk and seeds. Ispaghula, or commonly psyllium husk, consists of the episperm and collapsed adjacent layers removed from the seeds of Plantago ovata Forssk and are obtained by milling the seed to remove the hulls. We are, in this review of Psyllium, referring to water-soluble fiber derived

from all above mentioned plants.

The physiologically active component of psyllium husk is shown to be a highly branched, neutral arabinoxylan consisting of a xylose backbone and arabinose- and xylose-containing side chains. In contrast to arabinoxylans in cereal grains that are extensively fermented, psyllium husk possesses a structural feature, as yet unidentified, that hinders its fermentation by typical colonic microflora (Marlett and Fischer, 2003). Psyllium is classified as a mucilaginous fiber due to its powerful ability to form a gel in water and through animal and human feeding experiments, it has been shown that a gel-forming fraction, amounting to some 55–60% of the husk, is responsible for both the laxative and cholesterol-lowering activities (Marlett and Fischer, 2002). Other viscous, non-nutrient polysaccharides, such as β-glucans and pectins, lower blood cholesterol levels by the same mechanism as psyllium, but these substances have negligible effects on bowel function. They are rapidly and completely fermented in the gut, whereas psyllium husk largely survives, increasing stool output and imparting a gel-like consistency to the excreta (Marteau *et al.*, 1994; Marlett and Fischer, 2003; Fischer *et al.*, 2004).

PSYLLIUM AND GASTROINTESTINAL REGULATION

Constipation and diarrhea

Most dietary fiber sources promote laxation by increasing colonic contents, which stimulate propulsion. Unfermented or incompletely fermented fiber and the accompanying moisture it holds contributes to increase stool mass. These fibers also provide substrate for microbial growth and induces therefore a greater bacterial mass (Stephen and Cummings, 1980; Chen et al., 1998), another factor for increased colonic content. Another benefit is that psyllium containing stools contains an unfermented gel which functions as an emollient and lubricant leading to a greater ease of passage of the stools (Marlett et al., 2000). Psyllium fiber is widely used as a fiber supplement for the treatment of constipation and has in clinical trials repeatedly reported significantly increased levels of stool moisture, as well as wet and dry stool weight in healthy subjects (Prynne and Southgate, 1979; Spiller et al., 1979; Stevens et al., 1988; Tomlin and Read, 1988; Gelissen et al., 1994; Marteau et al., 1994; Levitt et al., 1996; Marlett et al., 2000) and in patients with gastrointestinal disease (Eastwood et al., 1978; Kumar et al., 1987; Prior and Whorwell, 1987; Thorburn et al., 1992; Gelissen et al., 1994; Ashraf et al., 1995; Cheskin et al., 1995; McRorie et al., 1998). It has been proposed that each gram of Psyllium fiber increases stool weight an average of 5.9-6.1g (Marteau et al., 1994; Marlett et al., 2000) compared with 4.9 - 5.4g and 3.4 - 4.5g for consumed wheat bran fiber or oat bran fiber, respectively (Cummings, 1993; Chen et al., 1998).

On the opposite of the desired effect against constipation, and because of its great ability to retain water, Psyllium has also been shown to slow down the gastric emptying time and colon transit, this being of benefit for individuals with fecal incontinence from liquid stools or diarrhea (Washington et al., 1998; Bliss et al., 2001).

Bowel diseases

Psyllium supplementation may be helpful in the treatment of irritable bowel diseases, inflammatory bowel disease and ulcerative colitis. While the beneficial effects of Psyllium in treatment of irritable bowel syndrome is most probably associated with its anticonstipation activity, the beneficial effects on ulcerative colitis and inflammatory bowel disease seem to be due to anticonstipation activity together with increased levels of the short-chain fatty acid butyrate (Bijkerk *et al.*, 2004). Anaerobic fermentation of Psyllium fiber in the intestines results in a considerable production of the short-chain fatty acids acetate, propionate, and butyrate (Mortensen *et al.*, 1992; Marteau *et al.*, 1994; Nordgaard *et al.*, 1996; Pylkas *et al.*, 2005) which have anti-inflammatory and anti-oxidant properties (Tedelind *et al.*, 2007; Hamer *et al.*, 2008) as well as being an important source of energy-yielding substrates to the colonic mucosa (Mortensen and Clausen, 1996).

Psyllium supplementation is widely used also for hemorrhoids and diverticulitis, although evidence has been questioned (Tan and Seow-Choen, 2007). Its consumption has been shown to be beneficial for hemorrhoids with improvement in reduction of bleeding on contact and of congested hemorrhoidal cushions (Webster *et al.*, 1978; Perez-Miranda *et al.*, 1996; Alonso-Coello *et al.*, 2005). The treatment should, however, last more than a month as no amelioration was noted in another trial of 30 days . Less evidence is available for the effectiveness of fiber in the treatment of uncomplicated diverticulitis (Petruzziello *et al.*, 2006), yet widely used among patients to relieve overall symptoms.

Other conditions

Colon cancer prevention

Short chained fatty acids and specifically butyric acid nourishes the colonocytes, which is important in colon cancer prevention (Clausen *et al.*, 1991). *In vitro*, butyrate also exerts potent inhibition of inflammation and carcinogenesis, reinforcing various components of the colonic defence barrier and decreasing oxidative stress (Hamer *et al.*, 2008). As mentioned above, the colonic anaerobic fermentation of Psyllium yields a considerable production of this short-chain fatty acid (Mortensen *et al.*, 1992; Marteau *et al.*, 1994; Nordgaard *et al.*, 1996; Pylkas *et al.*, 2005) and therefore its consumption could have a preventive effect against cancer. Additionally, *in vitro* assays have proposed that an antineoplastic activity against cancer cells is provided by phytosterol beta-sitosterol that has been isolated from Psyllium (Nakamura *et al.*, 2004; Nakamura *et al.*, 2005). Together with the well known protective effect of fiber consumption for colon cancer prevention, strengthen, but doesn't explain, the possible benefits of Psyllium supplementation in colon cancer prevention.

Prebiotic effect

Prebiotics are food ingredients that stimulate selectively the growth and activity of bifidobacteria and lactobacilli in the gut and thereby benefit health (Cummings and Macfarlane, 2002). The defining property of prebiotics is their effect on the microflora of the large bowel (Kanauchi *et al.*, 2003; Rodriguez-Cabezas *et al.*, 2003). Poor microbiologic evidences are nevertheless available

concerning the ability of Psyllium derivates to promote the growth of bifidobacteria in human gut and thus act as a prebiotic. A recent study suggests that Psyllium seed husk can be metabolized by bifidobacteria only after partial hydrolysis (Elli *et al.*, 2008). This study in women demonstrates that the bifidogenic potential can only be detected in healthy subjects with low levels of fecal bifidobacteria before Psyllium supplementation.

Anti-inflammatory properties

Recent evidence suggests that inflammation may be an important mediator in the association between consumption of dietary fiber and CVD. Cross-sectional research has demonstrated an association between dietary fiber and levels of C-reactive protein (CRP), a clinical indicator of inflammation (King *et al.*, 2003; Ma *et al.*, 2006). Less consistent evidence exists for fiber supplementation. In a randomized crossover intervention trial of a naturally high-fiber diet (30-g/d) or a Psyllium-supplemented diet (30 g/d), lean normotensive participants experienced a greater relative reduction in CRP measurements (40% vs. 10%) than the obese hypertensive persons (King *et al.*, 2007). In another trial, by the same authors, again, no significant differences were observed in several inflammatory serum markers including CRP after a Psyllium supplementation for 3 months (King *et al.*, 2008).

PSYLLIUM AND CARDIOVASCULAR DISEASE PROTECTION

The role of dietary fiber in the prevention of cardiovascular disease has been the subject of considerable attention in the last decade. The functional benefits are now very well recognized and several national agencies concerned about cardiovascular health are acknowledging a role for fiber and especially soluble fiber, such as Psyllium, in cholesterol reduction. The FDA was one of the first national agencies to recognize a role for fiber in cardiovascular disease risk reduction (FDA, 1998). Products that contain 0.75 g ß-glucan or 1.78 g psyllium/serving are permitted to carry a health claim stating that the product "will reduce the risk of coronary heart disease" (FDA, 1998). The FDA further determined that 4 servings of these foods are likely to provide the effective daily dose. In the European Union, a common regulation on nutrition and health claims made on foods was introduced in 2007 (EC Regulation, 2008). This Regulation provides opportunities for the use of health claims on foods in Europe, including reduction of disease risk claims. Although the Regulation will not be fully implemented until January 2010 some European countries have applied voluntary codes of practice on health claims for foods, awaiting the Regulation (Asp and Bryngelsson, 2008). Generally most national codes already claim that soluble fiber such as ß-glucan or Psyllium reduces cholesterol, and prevents cardiovascular diseases.

Although not as documented as for cholesterol reduction, Psyllium supplementation is also widely used for weight control and to maintain glucose homeostasis that together with cholesterol reduction are the most effective preventive measures against cardiovascular diseases.

Lipid lowering

Already in 1965 it was observed that Psyllium administered as a hydrophilic mucilloid (i.e., the commercial bulk-forming laxative) reduced serum triglycerides by 9% after supplementation with 9.6 g psyllium/day for 5 wk (Garvin *et al.*, 1965). To lower serum cholesterol the first dietary fibers of interest were pectin and guar gum (Jenkins *et al.*, 1975); later attention focused on oat ß-glucan and Psyllium (Brown *et al.*, 1999).

In a large number of studies, Psyllium has generally solidly proved to lower blood lipid levels, and specially LDL cholesterol (Anderson *et al.*, 1988; Bell *et al.*, 1990; Neal and Balm, 1990; Pastors *et al.*, 1991; Everson *et al.*, 1992; Sprecher *et al.*, 1993; Gupta *et al.*, 1994; Ganji and Kies, 1996; Olson *et al.*, 1997; Anderson *et al.*, 2000a; Anderson *et al.*, 2000b; Jenkins *et al.*, 2002; Cicero *et al.*, 2007; Sola *et al.*, 2007; Uehleke *et al.*, 2008). Together with LDL cholesterol reductions, results are also observed in triglycerides and apolipoprotein B with no concluding effect on HDL-cholesterol. The postprandial exposure to triglycerides seems to be lower if the meal is supplemented with Psyllium (Khossousi *et al.*, 2008).

Also in children has the effect of Psyllium been studied for the control of hypercholesterolemia (Glassman *et al.*, 1990; Dennison and Levine, 1993; Davidson *et al.*, 1996). The effect of Psyllium to lower LDL-cholesterol serum concentrations in the management of hypercholesterolemic children, ranged from 3 to -23%; the effect in HDL-cholesterol from -4 to 3%; and the effect on triglycerides from 9 to -20% (Moreno *et al.*, 2003).

The mechanism by which Psyllium lowers LDL cholesterol concentrations is not entirely clear but several mechanisms may play a synergetic effect (Turley and Dietschy, 1995). The primary mechanism of action is likely to be related to the ability to stimulate bile acid synthesis and loss (Kritchevsky and Story, 1974; Miettinen and Tarpila, 1989). Summing up are as well an increased fecal fat loss (Ganji and Kies, 1994), and presumably a lower fat intake (Turnbull and Thomas, 1995) with Psyllium supplementation.

Diabetes Control

The aim of the management of type 2 diabetes patients is the normalisation of blood glucose values and HbA1C (American Diabetes Association, 2005). The advantages of high-fiber diets for diabetic patients include the lowering of blood glucose and cholesterol, as well as weight reduction and maintenance. It is especially soluble fiber that has beneficial effects on carbohydrate metabolism. Several studies have assessed the effect of Psyllium in the control of type 2 diabetes (Jarjis *et al.*, 1984; Pastors *et al.,* 1991; Frati Munari *et al.,* 1998; Rodriguez-Moran *et al.,* 1998; Anderson *et al.,* 1999; Sierra *et al.,* 2001; Sierra *et al.,* 2002; Moreno *et al.,* 2003; Ziai *et al.,* 2005; Cicero *et al.,* 2007; Khossousi *et al.,* 2008). The percentage change in glucose levels after Psyllium supplementation ranged from -12 to -20%.

Psyllium may slow the absorption of carbohydrates in the small intestine, thereby blunting postprandial glucose peaks (Ellis *et al.,* 1991; Wolever *et al.,* 1991; Fairchild et al., 1996).

Hypertension

Successful control of hypertension (both systolic and diastolic blood pressure) is also important in diabetes control. Psyllium, but not guar gum lowered blood pressure in a 6 months trial of hypertensive and obese subjects (Cicero *et al.,* 2007). Nevertheless, as weight reduction was observed and confounders were not controlled for, more studies need to confirm these results. Other studies have not shown any changes in blood pressure (Bell *et al.,* 1990).

Weight control

Psyllium may have a satiating effect on appetite, which may help people to reduce energy intake by earlier termination of meals (Delargy *et al.,* 1995; Turnbull and Thomas, 1995; Cicero *et al.*, 2007). Psyllium supplementation (20g pre-meal and another 20g postmeal) significantly increased feelings of fullness after meals, and significantly reduced *ad libitum* fat intake (Turnbull and Thomas, 1995).

PSYLLIUM AS A FUNCTIONAL FOOD

There are various commercial uses of Psyllium in food, pharmaceutical and other industries. Although obtaining dietary fiber from whole foods is preferable because it is accompanied by additional nutrients and phytochemicals, a fiber supplement should be recommended to close the fiber gap.

It has been a continuous effort to improve the physicochemical, functional, sensory, and biological properties of psyllium for promoting its food utilization and enhancing its safety. It is a great challenge to disperse psyllium in water or aqueous solutions even with vigorous agitation because of its extremely strong water-absorbing capacity. The readers are referred to an excellent review focused on the approaches to improve the functionality (Yu *et al.,* 2009). Psyllium is most frequently added to breakfast cereals, meal replacements, bread, biscuits and other bakery products to improve the fiber content of the food but is also added to juices, shakes, yogurt, soups and even ice creams. It can also be used as a thickener in drinks or frozen deserts. Although Psyllium fiber has positive physiologic benefits, its high viscosity could make it difficult to incorporate into food products and a task is to get it acceptable to consumers. Their clinical relevance has been questioned because of the extreme unpalatability of products tested with high content of viscose fiber (Ellis *et al.,* 1991). To incorporate lower amounts of fiber into different foods during the day is therefore important to attain the recommended amount for cholesterol lowering (FDA, 1998).

POSSIBLE ADVERSE EFFECT OF PSYLLIUM SUPPLEMENTATION

Psyllium may alter nutrient and drug absorption, decrease caloric availability by reducing food intake or suppressing appetite, increase bloating and flatulence, cause abdominal pain, and elicit anaphylactic symptoms. Many studies detected the possible adverse effects of Psyllium intake, although others demonstrated that Psyllium is generally safe for human consumption.

Psyllium is known to be the cause of occupational allergy (rhinitis, asthma) in health care and pharmaceutical workers. With the increased prevalence of consumption due to its cholesterol lowering effects has led to its recognition as an emerging food allergen (Lantner *et al.*, 1990). Clinical manifestations of allergy range from upper respiratory tract symptoms on inhalation to anaphylaxis on ingestion (Khalili *et al.*, 2003)

Fermentation of dietary fiber by anaerobic bacteria in the large intestine produces gas, which may be related to complaints of distention or flatulence as well as bloating and diarrhoea. When dietary fiber is increased, fluid intake should also be increased, and fiber intake should gradually be increased to allow the gastrointestinal tract time to adapt (Uehleke *et al.*, 2008). Normal laxation may be achieved with smaller amounts of dietary fiber, and the smallest dose that results in normal laxation should be accepted. Cholesterol reduction however, needs higher doses for optimal effects and this could compromise the adherence to treatment.

Potential negative effects of dietary fiber include reduced absorption of calcium, iron, trace metals, and certain vitamins (Heaney and Weaver, 1995; Asvarujanon *et al.*, 2004). It is unlikely that healthy adults who consume fiber in amounts within the recommended ranges will have problems with nutrient absorption; however, dietary fiber recommendations of 25 g/day may not be appropriate for children and the elderly (Slavin and Greenberg, 2003).

Because of the wide individual variability of responses to dietary fiber and the potential problems with large doses, the smallest dose of dietary fiber that produces the desired result should always be used.

CONCLUSIONS

We consider that strong scientific evidence exists that regular consumption of Psyllium provides modest reductions in blood levels of LDL cholesterol as well as total cholesterol. This reduction does however not appear to have effects on HDL cholesterol while more research is needed to clarify if Psyllium consumption reduces ApoA or triglyceride levels. There is good scientific evidence for the use of Psyllium supplementation for constipation as most studies observe an increased stool weight, an increase in bowel movements per day, and a decrease in total gut transit time. There is also good scientific evidence that Psyllium has an effective stool bulking effect, against diarrhea. Unclear scientific evidence exists to relieve or prevent the symptoms of hemorrhoids or inflammatory bowel disease or irritable bowel syndrome. Although Psyllium supplementation taken with meals could improve blood glucose homeostasis, better evidence is necessary to conclude its benefits for diabetes control. Obesity related disorders such as dyslipidemia and hyperglycemia could improve by Psyllium supplementation, but further studies are needed to elucidate mechanisms involved and how its consumption affects body weight. Finally, although promising studies attempt to show anti-carcinogenic effect of Psyllium, and specifically in colon cancer, more studies are needed to determine if Psyllium can help prevent cancer.

CONFLICT-OF-INTEREST STATEMENT

None of the authors have any conflict of interests to declare.

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