Ispaghula

Species (Family)

Plantago ovata Forsk. (Plantaginaceae)

Synonym(s)

Blond Psyllium, Indian Plantago, Ispagol, Pale Psyllium, Spogel

Part(s) Used

Seed, husk

Pharmacopoeial and Other Monographs

BHC 1992[G6]
BHP 1996[G9]
BP 2001[G15]
Complete German Commission E (Psyllium, Blonde)[G3]
ESCOP 1996[G52]
Martindale 32nd edition[G43]
PDR for Herbal Medicines 2nd edition[G36]
Ph Eur 2002[G28]
WHO volume 1 1999[G63]

Legal Category (Licensed Products)

GSL[G37]

Constituents[G2,G6,G41,G52,G59,G64]

Alkaloids Monoterpene-type. (+)-Boschniakine (indicaine), (+)-boschniakinic acid (plantagonine) and indicainine.

Mucilages 10–30%. Mucopolysaccharide consisting mainly of a highly branched arabinoxylan with a xylan backbone and branches of arabinose, xylose and 2-O-(galacturonic)-rhamnose moieties. Present mainly in the seed husk.

Other constituents Aucubin (iridoid glucoside), sugars (fructose, glucose, sucrose), planteose (trisaccharide), protein, sterols (campesterol, β-sitosterol, stigmasterol), triterpenes (α- and β-amyrin), fatty acids (e.g. linoleic, oleic, palmitic, stearic), tannins.

Food Use

In food manufacture, ispaghula may be used as a thickener or stabiliser.[G41]

Herbal Use[G2,G4,G6,G7,G8,G32,G43,G52,G64]

Ispaghula is stated to possess demulcent and laxative properties. Traditionally, ispaghula has been used in the treatment of chronic constipation, dysentery, diarrhoea and cystitis. Topically, a poultice has been used for furunculosis. The German Commission E approved use for chronic constipation and disorders in which bowel movements with loose stool are desirable, e.g. patients with anal fistulas, haemorrhoids, pregnancy, secondary medication in the treatment of various forms of diarrhoea and in the treatment of irritable bowel syndrome.[G3]

The European Medicine Evaluation Agency (EMEA) Herbal Medicinal Products Working Group (HMPWG) has proposed a core SPC (Sumristics) for ispaghula.[G23] The core SPC includes the following indications: (a) treatment of habitual constipation; conditions in which easy defecation with soft stools is desirable, e.g. in cases of painful defecation after rectal or anal surgery; (b) adjuvant symptomatic therapy in cases of diarrhoea from various causes; (c) conditions which need an increased daily fibre intake, e.g. as an adjuvant in irritable bowel syndrome.

Dosage

Seeds 5–10 g (3 g in children) three times daily;[G6,G7] 12–40 g per day, husk 4–20 g;[G3] 3–5 g.[G43] Children 6–12 years, half adult dose. Children under 6 years, treat only under medical supervision.[G52] Seeds should be soaked in warm water for several hours before taking.

Liquid extract 2–4 mL (1:1 in 25% alcohol) three times daily.[G6,G7]

Husk 3–5 g.[G46] Seeds and husk should be soaked in warm water for several hours before administration.

7–11 g in one to three doses for indication (a) and (c); 7–20 g in one to three doses for indication (b).[G23]

Pharmacological Actions

The principal pharmacological actions of ispaghula can be attributed to the mucilage component.

In vitro and animal studies

An alcoholic extract lowered the blood pressure of anaesthetised cats and dogs, inhibited isolated rabbit and frog hearts, and stimulated rabbit, rat and guinea-pig ileum.[G41] The extract exhibited cholinergic activity.[G41] A mild laxative action has also been reported in mice administered iridoid glycosides, including aucubin.[1] Four-week supplementation of a fibre-free diet with isphagula seeds (100 or 200 g/kg) was compared with that of the husks and wheat bran in rats.[2] The seeds increased faecal fresh weight by up to 100% and faecal dry weight by up to 50%. Total faecal bile acid secretion was stimulated, and β-glucuronidase activity reduced, by ispaghula. The study concluded that ispaghula acts as a partly fermentable, dietary fibre supplement increasing stool bulk, and that it probably has metabolic and mucosa-protective effects.

Ispaghula husk depressed the growth of chickens by 15% when added to their diet at 2%.[G41]

Ispaghula seed powder is stated to have strongly counteracted the deleterious effects of adding sodium cyclamate (2%), FD & C Red No. 2 (2%), and polyoxyethylene sorbitan monostearate (4%) to the diet of rats.[G41]

Clinical studies

Ispaghula is used as a bulk laxative.[G3,G43,G52] The swelling properties of the mucilage enable it to absorb water in the gastrointestinal tract, thereby increasing the volume of the faeces and promoting peristalsis. Bulk laxatives are often used for the treatment of chronic constipation and when excessive straining must be avoided following anorectal surgery or in the management of haemorrhoids. Ispaghula is also used in the management of diarrhoea and for adjusting faecal consistency in patients with colostomies and in patients with diverticular disease or irritable bowel syndrome.

Laxative effect Ispaghula increases water content of stools and total stool weight in patients,[3] thus promoting peristalsis and reducing mouth-to-rectum transit time.[4] In a short-term study, 42 adults with constipation (≤3 bowel movements per week) received either ispaghula (7.2 g/day) or ispaghula plus senna (6.5 g + 1.5 g/day).[5] Both treatments increased defecation frequency, and wet and dry stool weights, improved stool consistency, and gave subjective relief.

A randomised, double-blind, double-dummy, multicentre study involved 170 subjects with chronic idiopathic constipation.[6] The study included a two-week baseline (placebo) phase, followed by two weeks' treatment with ispaghula (Metamucil) 5.1 g, twice daily or docusate sodium 100 mg twice daily. Compared with docusate, ispaghula significantly increased stool water content (0.01% versus 2.33% for docusate and ispaghula, respectively; $p = 0.007$), and total stool output (271.9 g/week versus 359.9 g/week for docusate and ispaghula, respectively; $p = 0.005$). Furthermore, bowel movement frequency was significantly greater for ispaghula, compared with docusate. It was concluded that isphaghula has greater overall laxative efficacy than docusate in patients with chronic constipation.[6]

Antidiarrhoeal effect An open, randomised, crossover trial involving 25 patients with diarrhoea compared the effects of loperamide with those of ispaghula and calcium.[7] Nineteen patients completed both periods of treatment. The results indicated that both treatments halved stool frequency. Ispaghula and calcium were reported to be significantly better than loperamide with regard to urgency and stool consistency.[7]

Nine volunteers with phenolphthalein-induced diarrhoea were treated in random sequence with placebo, ispaghula (Konsyl), calcium polycarbophyl or wheat bran.[8] Wheat bran and calcium polycarbophyl had no effect on faecal consistency or on faecal viscosity. By contrast, ispaghula made stools firmer and increased faecal viscosity. In a dose-response study involving six subjects, 9, 18 and 30 g ispaghula per day caused a near-linear increase in faecal viscosity.[8]

The effects of ispaghula have been explored in children. In an open, uncontrolled study, 23 children with chronic non-specific diarrhoea were treated with an unrestricted diet for one week, and then treated with ispaghula (Metamucil) for two weeks (one tablespoonful twice daily). Seven patients responded to the unrestricted diet and 13 were said to respond to ispaghula treatment.[9]

Hypocholesterolaemic effects In a double-blind, placebo-controlled, parallel-group study, 26 men with mild-to-moderate hypercholesterolaemia (serum cholesterol concentration: 4.86–8.12 mmol/L) received ispaghula (Metamucil) 3.4 g, or cellulose placebo, three times daily at meal times for eight weeks.[10] At the end of the study, serum cholesterol concentrations were reduced by 14.8% in the treated group, low-density lipoprotein (LDL) cholesterol by 20.2% and ratio of LDL to high-density lipoprotein (HDL)

cholesterol by 14.8%, compared with baseline values. There were no significant changes in serum lipid concentrations with placebo treatment, compared with baseline values. Differences in serum cholesterol concentrations between the two groups were statistically significant after four weeks (p-value not reported).

A double-blind, placebo-controlled, parallel trial study compared the effects of ispaghula (Metamucil 5.1 g, daily) and placebo in 118 patients (aged 21–70 years old) with primary hypercholesterolaemia (total serum cholesterol ≥ 5.7 mmol/L).[11] Thirty-seven participants maintained a high-fat diet and 81 a low-fat diet. Treated patients in both low- and high-fat diet groups showed small significant decreases (p < 0.05) in total cholesterol and LDL cholesterol levels (5.8 and 7.2%, respectively, for high-fat diets; 4.2% and 6.4%, respectively, for low-fat diets). No significant differences were seen in LDL cholesterol response for treated patients on either diet.

In a randomised, double-blind, crossover study, 20 males (mean (SD) age 44 (4) years) with moderate hypercholesterolaemia (mean (SD) total cholesterol concentration 265 (17) mg/dL, LDL 184 (15) mg/dL) were randomised to receive a 40-day course of ispaghula (Metamucil) 15 g daily, or placebo (cellulose).[12] There was a wash-out period of more than 10 days between treatments. Ispaghula lowered LDL cholesterol (168 mg/dL) more than did cellulose placebo (179 mg/dL), decreased relative cholesterol absorption, and increased the fractional turnover of both chenodeoxycholic acid and cholic acid. Bile acid synthesis increased in subjects whose LDL cholesterol was lowered by more than 10%. It was concluded that ispaghula lowers LDL cholesterol primarily by stimulation of bile acid synthesis.[12]

A meta-analysis of eight published and four unpublished studies carried out in four countries reviewed the effect of consumption of ispaghula-enriched cereal products on blood cholesterol, and LDL and HDL cholesterol concentrations.[13] Overall, the trials included 404 adults with mild-to-moderate hypercholesterolaemia (5.17–7.8 mmol/L) who consumed low-fat diets. The meta-analysis indicated that subjects who consumed ispaghula cereal had lower total cholesterol and LDL cholesterol than subjects who ate control cereal concentrations (differences of 0.31 mmol/L (5%) and 0.35 mmol/L (9%), respectively). HDL cholesterol concentrations were not affected in subjects eating ispaghula cereal.

Another meta-analysis included eight studies involving a total of 384 patients with hypercholesterolaemia who received ispaghula and 272 subjects who received cellulose placebo.[14] Compared with placebo, consumption of 10.2 g ispaghula per day for ≥ 8 weeks lowered serum total cholesterol concentrations by 4% (p < 0.0001) and LDL cholesterol by 7% (p < 0.0001), but did not affect serum HDL cholesterol or triacyl glycerol concentrations. The ratio of apolipoprotein (apo) B to apo A-1 was lowered by 6% (p < 0.05), relative to placebo, in subjects consuming a low-fat diet.[14] It was concluded that ispaghula is a useful adjunct to a low-fat diet in individuals with mild-to-moderate hypercholesterolaemia.

A randomised, placebo-controlled, multicentre study evaluated the long-term effectiveness of ispaghula husk as an adjunct to diet in treatment of primary hypercholesterolaemia.[15] Men and women with hypercholesterolaemia followed the American Heart Association Step 1 diet for eight weeks prior to treatment. Individuals with LDL cholesterol concentrations between 3.36 and 4.91 mmol/L were randomly assigned to receive either ispaghula (Metamucil 5.1 g) or cellulose placebo twice daily for 26 weeks whilst continuing diet therapy. Overall, 163 participants completed the full protocol, 133 receiving ispaghula and 30 receiving cellulose placebo. Serum total and LDL cholesterol concentrations were 4.7% and 6.7% lower, respectively, in the ispaghula group than in the placebo group after 24–26 weeks (p < 0.001).

A randomised, double-blind, placebo-controlled crossover trial assessed the effects of ispaghula in lowering elevated LDL cholesterol concentrations in 20 children (aged 5–17 years).[16] Children with LDL cholesterol concentrations of >2.84 mmol/L after three months on a low-fat, low-cholesterol diet received five weeks' treatment with a ready-to-eat cereal containing water-soluble ispaghula husk (6 g/day) or placebo. The results indicated that there were no significant differences in total cholesterol, LDL cholesterol or HDL cholesterol concentrations between the two groups.

In a similar 12-week study, 50 children (aged 2–11 years) with LDL cholesterol concentrations ≥ 110 mg/dL received either cereal enriched with ispaghula (3.2 g soluble fibre per day) or plain cereal whilst maintaining a low-fat diet.[17] Total cholesterol decreased by 21 mg/dL for the ispaghula group in comparison with 11.5 mg/dL for the control group (p < 0.001). LDL cholesterol also decreased by 23 mg/dL for the treated group in comparison with 8.5 mg/dL for the placebo group (p < 0.01).

The effect of adding water-soluble fibre to a diet low in total fats, saturated fat and cholesterol to treat hypercholesterolaemic children and adolescents has been reviewed.[18] The review summarised that

reductions in LDL cholesterol concentrations ranged from 0 to 23%. This wide range may be related to dietary intervention and to clinical trial conditions. It was proposed that additional trials with larger numbers of well-defined subjects are needed.

Hypoglycaemic effect Several studies have shown that ispaghula husk lowered blood glucose concentrations due to delayed intestinal absorption.[G52] In one crossover study, 18 patients with non-insulin-dependent diabetes received ispaghula (Metamucil) or placebo twice (immediately before breakfast and dinner) during each 15-hour crossover phase.[19] For meals eaten immediately after ispaghula ingestion, maximum postprandial glucose elevation was reduced by 14% at breakfast and 20% at dinner, relative to placebo. Postprandial serum insulin concentrations measured after breakfast were reduced by 12%, relative to placebo. Second-meal effects after lunch showed a 31% reduction in postprandial glucose elevation, relative to placebo. No significant differences in effects were noted between patients whose diabetes was controlled by diet alone and those whose diabetes was controlled by oral hypoglycaemic drugs. It was concluded that the results indicate that ispaghula as a meal supplement reduces proximate and second-meal postprandial glucose and insulin in non-insulin dependent diabetics.[19]

Other effects Ispaghula husk has been used to treat small numbers of patients with left-sided diverticular disease.[4] Marked motility was observed for the right colon, but was not as pronounced for the left colon. The effects of ispaghula in this condition may be worth further investigation.

In an open, randomised, multicentre trial, 102 patients with ulcerative colitis (three months in remission, salicylate-treated, colitis over 20 cm) received ispaghula (10 g twice daily; *n* = 35), oral mesalazine (500 mg three times daily; *n* = 37) or ispaghula plus mesalazine (*n* = 30) for one year.[20] Assessment, including endoscopy, was carried out at 3, 6, 9 and 12 months. The results suggested that ispaghula may be equivalent to mesalazine in maintaining remission in ulcerative colitis. However, this requires further investigation in a randomised, double-blind study.

In China, the seeds of related *Plantago* species have been used to treat hypertension.[G41]

Side-effects, Toxicity

In common with all bulk laxatives, ispaghula may temporarily increase flatulence and abdominal distension, and may cause intestinal obstruction. If swallowed dry, ispaghula may cause oesophageal obstruction. In rare cases, allergic reactions may occur.[G3,G23]

Contra-indications, Warnings

In common with all bulk laxatives, ispaghula should not be gven to patients with intestinal obstruction or conditions that may lead to intestinal obstruction, such as spastic bowel conditions. Ispaghula should always be taken with plenty of fluid to avoid oesophageal obstruction or faecal impaction. Bulk laxatives lower the transit time through the gastrointestinal tract and therefore may affect the absorption of other drugs.[G45] Absorption of currently administered drugs may be delayed. There may be a need to reduce insulin dosage in diabetics who are insulin dependent.[G3]

The EMEA HMPWG proposed core SPC for ispaghula includes the following information.[G23] Ispaghula husk is not to be used by patients with faecal impaction and undiagnosed abdominal symptoms, abdominal pain, nausea and vomiting (unless advised by a doctor), a sudden change in bowel habit that persists for more than two weeks, rectal bleeding, and failure to defecate following the use of a laxative. Ispaghula husk is also not to be used by patients suffering from abnormal constrictions in the gastrointestinal tract, diseases of the oesophagus and cardia, potential or existing intestinal blockage (ileus), or megacolon, diabetes mellitus which is difficult to regulate, or by patients with known hypersensitivity to ispaghula or any other constituents of the product. The husk should be taken with at least 150 mL of water or other fluid. Taking this product without adequate fluid may cause it to swell and block the throat or oesophagus and may cause choking. Intestinal obstructions may occur if an adequate fluid intake is not maintained. Ispaghula should not be taken by anyone who has had difficulty in swallowing or any throat problems. If chest pain, vomiting or difficulty in swallowing or breathing is experienced after taking the product, immediate medical attention should be sought. The treatment of the debilitated requires medical supervision. The treatment of elderly patients should be supervised. In the case of diarrhoea, sufficient intake of water and electrolytes is important.

Interaction with other medicinal products and other forms of interaction[G23]   Enteral absorption of concomitantly administered medicines such as minerals (e.g. calcium, iron, lithium, zinc), vitamins (B_{12}), cardiac glycosides and coumarin derivatives may be delayed. For this reason the product should not be

taken 0.5–1 hour before, or after, intake of other drugs. If the product is taken together with meals in the case of insulin-dependent diabetics, it may be necessary to reduce the insulin dose.

Pregnancy and lactation Ispaghula may be used during pregnancy and lactation.

Pharmaceutical Comment

The characteristic component of ispaghula is the mucilage which provides it with its bulk laxative action. Many of the herbal uses are therefore supported although no published information was located to justify the use of ispaghula in cystitis or infective skin conditions. Adverse effects and precautions generally associated with bulk laxatives apply to ispaghula. Clinical evidence exists for hypocholesterolaemia effects but it has been recommended that reduction in dietary fat intake is preferable to food supplements.[21]

References

See also General References G2, G3, G6, G9, G12, G15, G28, G31, G36, G37, G41, G43, G52, G54, G56, G59, G63 and G64.

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