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Psyllium

DESCRIPTION

In 1998, the Food and Drug Administration (FDA) issued its final rule allowing health claims to be made on the labels of foods containing soluble fiber from whole oats (see Oat Beta-D-Glucan), noting that these foods, in conjunction with a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. Shortly afterward, the FDA amended this to include the soluble fiber psyllium in the health claim. The FDA requires that there be at least 1.7 grams of soluble fiber from psyllium seed husk per serving in any food for which this health claim is made. To achieve heart-health benefits, the consumption of 7 grams of soluble fiber from psyllium are required.

Psyllium or *Plantago ovata* Forsk is an annual plant grown primarily in India, southern Europe and the United States. Psyllium is cultivated primarily for its use as a laxative or as a dietary fiber ingredient in foods, such as ready-to-eat cereals. It is also known as blond psyllium, Indian psyllium and plantain. Although the seed alone contains the bioactive mucilage polysaccharide, the refined psyllium seed husk, known as the Ispaghula husk, is the psyllium component principally used as the soluble fiber source for laxatives, ready-to-eat cereals and nutritional supplements.

The term psyllium is used interchangeably for the seed husk, the seed and the plant. Psyllium seed husk is comprised primarily of xylans. Xylans are polysaccharides built from the five-carbon sugar D-xylose. Xylans in psyllium seed husk occur in association with cellulose. The soluble fiber derived from psyllium seed husk is also known as psyllium hydrophilic mucilloid, psyllium hydrocolloid and psyllium seed gum. It is a white to cream-colored, slightly granular powder with a slight acid taste.

ACTIONS AND PHARMACOLOGY

ACTIONS

Psyllium may have hypocholesterolemic, glucose-regulatory and bowel-regulatory actions.

MECHANISM OF ACTION

The mechanism of psyllium's possible hypocholesterolemic activity is not fully understood. The bioactive agent of psyllium is a soluble, viscous xylan fiber. It is thought that this polysaccharide stimulates the conversion of cholesterol to bile acids and that it stimulates fecal excretion of bile acids. Psyllium may also decrease the intestinal absorption of cholesterol.

Some studies indicate that psyllium may improve glycemic control in type 2 diabetics. The mechanism of the effect is unclear. Psyllium may delay the absorption of carbohydrates by increasing gastric-emptying time and/or decreasing small intestinal transit time.

The laxative effect of psyllium is thought to be due to the swelling of psyllium from absorption of water with consequent increase in stool bulk and stimulation of peristalsis.

PHARMACOKINETICS

Following ingestion of psyllium, very little is digested in the small intestine. The psyllium polysaccharides are resistant to hydrolysis by the digestive enzymes. Some fermentation of the psyllium polysaccharides takes place in the large intestine via the action of colonic bacteria. The products of fermentation include the short-chain fatty acids acetate, propionate and butyrate, as well as hydrogen and carbon dioxide. The short-chain fatty acids that escape colonic metabolism are transported via the portal circulation to the liver, where they undergo metabolism.

INDICATIONS AND USAGE

The FDA allows a health claim for psyllium to the effect that, in conjunction with a low-fat diet, it may reduce risk of heart disease if used in adequate amounts. Numerous studies have shown that psyllium is effective in lowering total

cholesterol and LDL-cholesterol levels in some with hypercholesterolemia. It is also helpful in some with constipation and may have benefit in some with diabetes. Claims that it is useful in preventing and treating anal fissures and hemorrhoids appear related to psyllium's efficacy in preventing and treating constipation. There is no credible evidence to support claims that psyllium is helpful in those with psoriasis or that it is effective in treating obesity.

RESEARCH SUMMARY

A recent meta-analysis of eight controlled trials investigating the effects of psyllium on lipids concluded that this supplement significantly lowered serum total and LDL-cholesterol concentrations in both male and female subjects who consumed a low-fat diet. Consumption of 10.2 grams of psyllium per day lowered serum total cholesterol 4% and LDL-cholesterol by 7%, compared with controls also consuming a low-fat diet but not supplementing with psyllium. No significant effects were seen in this meta-analysis on either serum HDL-cholesterol or triacylglycerol concentrations.

In one recent animal model of hypertension induced by salt ingestion, psyllium supplementation significantly attenuated salt-accelerated hypertension. The proposed possible mechanism of action was increased fecal excretion of sodium taken up by the psyllium.

In a recent study, psyllium was used adjunctively with a traditional diabetes diet to treat men with mild-to-moderate hypercholesterolemia and type 2 diabetes. Subjects were randomized to receive 5.1 grams of psyllium or cellulose placebo twice daily for eight weeks. Those receiving psyllium had significant improvement in glucose and lipid values compared with controls. Concentrations of serum total and LDL-cholesterol were 8.9% and 13% lower, respectively, in the psyllium group than in the control group.

Psyllium has been used for some time as a major ingredient in bulk laxatives. The FDA has approved this use, and the German Commission E has indicated that psyllium may be helpful in those with chronic constipation and some of the possible complications of constipation, including anal fissures and hemorrhoids. It may also be useful in some forms of diarrhea and in those who have had anal/rectal surgery. Some pregnant women are said to benefit from it as well.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Psyllium is contraindicated in those hypersensitive to psyllium or to any component of a psyllium-containing product. It is also contraindicated in those with intestinal obstruction, fecal impaction, difficulty in swallowing and esophageal narrowing.

PRECAUTIONS

Pregnant women and nursing mothers should only use psyllium supplements if recommended by their physicians.

Supplemental psyllium must be taken with adequate amounts of fluids. Inadequate fluid intake may cause psyllium to swell and block the throat, esophagus or intestines.

Supplemental psyllium should not be taken right before going to bed.

ADVERSE REACTIONS

The most common adverse reactions are flatulence and abdominal distention. Potentially severe allergic reactions, including anaphylaxis, have been reported. These are not common.

INTERACTIONS

DRUGS

Concomitant use of psyllium and lithium may reduce the absorption of lithium. Concomitant use of psyllium and carbamazepine, digoxin and warfarin may reduce the absorption of those drugs.

Psyllium may enhance the cholesterol-lowering action of cholestyramine.

NUTRITIONAL SUPPLEMENTS

Psyllium may decrease the absorption of such minerals as zinc, copper, iron, calcium and magnesium if used concomitantly.

OVERDOSAGE

No reports.

DOSAGE AND ADMINISTRATION

Psyllium supplements are typically used in powder form, along with adequate amounts of fluids.

A dose of at least 7 grams daily taken with adequate amounts of fluid (water, juice) is used by some for management of elevated cholesterol.

There are a number of psyllium products used for constipation. The usual dose is about 3.5 grams twice a day. Again, the psyllium should be taken with adequate amounts of fluid.

Psyllium is a component of several ready-to-eat cereals.

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Pycnogenol

DESCRIPTION

The term pycnogenol refers to a specific mixture of procyanidins extracted from the bark of the French maritime pine, *Pinus maritima.* The French maritime pine grows in Bay of Biscay in the Landes de Gascogne in France. Although the term pycnogenol is now confined to procyanidins from the French maritime pine, the term was originally intended to serve as scientific name for this class of flavonoids.

Procyanidins are derivatives of the flavan-3-o1 class of flavonoids. This class includes epicatechin and catechin. Procyanidins consisting of dimers of catechin and oligomers of epicatechin and catechin are found in pycnogenol. Pycnogenol has a high amount of oligomers containing 5 to 7 units. Procyanidin oligomers are also known as oligomeric procyanidins (OPC), oligomeric proanthocyanidins (also OPCs) and procyanidolic oligomers (PCOs). In addition to OPCs, pycnogenol contains catechin, epicatechin and taxifolin, and such phenolic acids as caffeic, ferulic and para-hydroxybenzoic acids as minor constituents. It also contains glycosylation products of flavonols and phenolic acids as minute constituents. Pycnogenol is abbreviated PYC.

Procyanidins, including oligomeric procyanidins, are also found in such foods as cocoa and chocolate, grape seeds, apples, peanuts, almonds, cranberries and blueberries. They are also found in such medicinal herbs as "Sangre de drago" *(Croton lechleri).*

Procyanidins are also known as leucocyanidins. Procyanidins and prodelphinidins comprise a class of polyphenolic compounds called proanthocyanidins. Whereas procyanidins are oligomers of catechin and epicatechin and their gallic acid esters, prodelphinidins are oligomers of gallocatechin and epigallocatechin and their galloylated derivatives. Proanthocyanidins are also known as condensed tannins.

ACTIONS AND PHARMACOLOGY

ACTIONS

Pycnogenol has antioxidant activity. It may also have anti-inflammatory activity and has putative cardiovascular-protective activity.

MECHANISM OF ACTION

Pycnogenol has demonstrated a number of antioxidant activities in the laboratory. These include scavenging of the superoxide radical anion, the hydroxyl radical, the lipid peroxyl radical, the peroxynitrite radical and singlet oxygen. It has also been shown to protect low-density lipoprotein (LDL) from oxidation. The oligomeric procyanidins appear to have especially potent antioxidant activity when compared with smaller molecules, such as catechin and epicatechin. The extent of the antioxidant potential of pycnogenol in *vivo* is unclear. Some studies suggest that the antioxidant potential is at least partially available *in vivo.* Pycnogenol has been shown to have anti-inflammatory activity, again in the laboratory. This activity is thought to be due, in large part, to pycnogenol's capacity as a scavenger of reactive oxygen and reactive nitrogen species.

Pycnogenol appears to inhibit the activation of the transcription factors NF-kappa B and AP-1. NF-kappa B and AP-1 upregulate the expression of several inflammatory mediators such as intercellular adhesion molecule-1 (ICAM-1). NF-kappa B is itself activated by reactive oxygen species. Pycnogenol has been found to inhibit the inducible expression of ICAM-1. Inhibition of ICAM-1 may be accounted for by inhibition, by pycnogenol, of the activation of NF-Kappa B and AP-1. Further, the inflammatory cytokine interferon-gamma (IFN-gamma) may upregulate ICAM-1 expression in keratinocytes. This has been noted in some inflammatory skin conditions, such as lupus erythematous, atopic dermatitis and psoriasis. Pycnogenol appears to inhibit IFN-gamma activation of STAT (signal transducer and activator of transcription) 1. Inhibition of ICAM-1 expression by pycnogenol could account for possible anti-inflammatory and anti-atherogenic activities of pycnogenol.

PHARMACOKINETICS

Little is known about the pharmacokinetics of pycnogenol in humans. It appears that at least some of it is absorbed. However, the extent of absorption appears to vary widely, not only among the various components of pycnogenol, but also among subjects.

Some of the components of pycnogenol (e.g., catechin) appear to undergo extensive glucuronidation and sulfation