gastrointestinal cancer who were given supplements of RNA, arginine and omega-3 fatty acids.

Nucleosides have promoted tissue repair in a number of animal studies. They have shortened recovery time in animals with liver injury and have enhanced healing of experimental intestinal ulcers. They have shortened recovery time following small and large bowel injuries.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Supplemental RNA, DNA, nucleotides and nucleosides are contraindicated in those hypersensitive to any component of products containing these substances.

PRECAUTIONS

Pregnant women and nursing mothers should avoid nucleic acid and nucleotide supplements unless recommended by their physicians.

Those with a history of hyperuricemia should be extremely cautious about use of nucleic acid and nucleotide supplements.

ADVERSE REACTIONS

No reports of adverse reactions.

DOSAGE AND ADMINISTRATION

Medical foods are available containing RNA as a delivery form of nucleotides/nucleosides, sometimes along with L-arginine and fish oils. These medical foods are used to support the immune system under conditions of metabolic stress.

RNA and DNA nutritional supplements are available, with RNA supplements being more popular. Typical doses range from 0.5 to 1.5 grams daily.

Brewer's yeast is a rich source of RNA (see Brewer's Yeast). Inosine is a nucleoside (see Inosine).

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Oat Beta-D-Glucan

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 (oat bran, oat flour and rolled oats), noting that these foods, in conjunction with a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. In order to qualify for the health claim, the whole oat-containing food must provide at least 0.75 grams of soluble fiber per serving. The soluble fiber in whole oats comprises a class of polysaccharides known as beta-D-glucans.

Beta-D-glucans, usually referred to as beta-glucans, comprise a class of non-digestible polysaccharides widely found in nature in such sources as oats, barley, yeast, bacteria, algae and mushrooms.

Beta-glucans are located primarily in the cell walls. In oats, barley and other cereal grains, they are located primarily in the endosperm cell wall.

Oat beta-glucan is a soluble fiber. It is a viscous polysaccharide made up of units of the sugar D-glucose. Oat beta-glucan is comprised of mixed-linkage polysaccharides. This means that the bonds between the D-glucose or D-glucopyranosyl units are either beta-1, 3 linkages or beta-1, 4 linkages. This type of beta-glucan is also referred to as a mixed-linkage (1→3), (1→4)-beta-D-glucan. Most of the oat bran beta-glucan molecules consist of cellotriose and cellotetraose blocks separated by (1→3)-linkages. There is, however, a smaller amount of sequences of (1→4)-linkages longer than the tetraose type. The (1→3)-linkages break up the uniform structure of the beta-D-glucan molecule and make it soluble and flexible. In comparison, the nondigestible polysaccharide cellulose is also a beta-glucan but is non-soluble. The reason that it is non-soluble is that cellulose consists only of (1→4)-beta-D-linkages. The percentages of beta-glucan in the various whole oat products are: oat bran, greater than 5.5%; rolled oats, about 4%; whole oat flour about 4%.

ACTIONS AND PHARMACOLOGY

ACTIONS

Oat beta-glucan may have hypocholesterolemic and glucose-regulating activity. It also has putative immunomodulatory activity.

MECHANISM OF ACTION

The exact mechanism of oat beta-glucan's possible hypocholesterolemic effect is not clear. Oat beta-glucan does not appear to have any effect on the biosynthesis of cholesterol. It appears to promote increased excretion of bile acids, which could explain, in large part, its possible cholesterol-lowering activity. Oat beta-glucan may also promote cholesterol clearance from the plasma via reverse cholesterol transport.

The mechanism of the possible glucose-regulatory activity of oat beta-glucan is also not well understood. Oat beta-glucan may delay gastric emptying time and consequently affect the rate of uptake of D-glucose from the small intestine. This may be one possible mechanism; the high viscosity of oat beta-glucan may delay absorption of glucose, which may be another possible mechanism. Oat beta-glucan has been found to have immunomodulatory activity in tissue culture and in mice. It appears to activate macrophages to release certain cytokines. Such activity, in mice, has been found to be protective against bacterial infection. It is unclear whether oat beta-glucan has immunomodulatory activity in humans.

PHARMACOKINETICS

Following ingestion, there is virtually no digestion of oat beta-glucan in the small intestine. Some digestion of oat beta-glucan does take place in the large intestine via bacterial beta-glucosidases. Some smaller oligosaccharides produced by the bacterial transformation of oat beta-glucan may get absorbed, but this is unclear. A large percentage of the ingested beta-glucan is excreted in the feces.

INDICATIONS AND USAGE

Oat beta-glucan has hypocholesterolemic effects and may also favorably affect some other lipids. It has demonstrated some immune-enhancing effects and may be helpful in some with diabetes.

RESEARCH SUMMARY

Evidence that oat beta-glucan can reduce cholesterol levels was sufficient to induce the FDA to allow health claims on whole oat products that provide at least 0.75 grams of soluble fiber per serving. The allowed health claim is that these products reduce the risk of heart disease by reducing levels of cholesterol.

In one study, mildly hypercholesterolemic subjects on a "typical" diet, in which 35% of calories was derived from fat, were given an oat beta-glucan extract containing 1% or 10% oat beta-glucan. There was a significant reduction in total cholesterol levels in those receiving the 10% oat beta-glucan preparation after three weeks. Cholesterol levels declined significantly in the 1% group, as well, but not as quickly. There was also a significant decline in LDL-cholesterol levels in both groups. Triglyceride and HDL-cholesterol levels were not significantly changed. Some other studies have reported similar results.

Improved glucose and insulin responses have been reported in a study of moderately hypercholesterolemic healthy subjects. Oat extracts containing 1% and 10% beta-glucan both demonstrated these beneficial effects on glucose tolerance factors.

NIDDM patients given varying concentrations of oat beta-glucan also had significantly improved glucose and insulin responses. Higher doses of the oat beta-glucan correlated with greater improvement.

There are *in vitro* and animal studies demonstrating that oat beta-glucan, like those extracted from yeast and other fungi, has favorable immunomodulatory activities. These include the ability to activate macrophages and stimulate their release of interleukin (IL)-1 and tumor necrosis factor (TNF)-alpha, among other activities

Intraperitoneal administration of oat beta-glucan has enhanced a non-specific resistance to bacterial challenge in mice. Survival times have been improved in mice pre-treated with oat beta-glucan and then challenged with *Staphylococcus aureus*. Similarly, resistance to *Eimeria vermiformis* has

been significantly increased in immunosuppressed mice given oat beta-glucan intragastrically or parenterally.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to an oat beta-D-glucan-containing product.

PRECAUTIONS

None known.

ADVERSE REACTIONS

Oat beta-glucans are generally well tolerated. Occasional flatulence is reported.

OVERDOSAGE

There are no reports of overdosage.

DOSAGE AND ADMINISTRATION

Dosage of oat beta-glucan required for a possible hypocholesterolemic effect ranges from 3 to 6 grams daily. This can be obtained from a whole oat product. There is some marketed oat beta-glucan nutritional supplements.

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Octacosanol

DESCRIPTION

Octacosanol is a 28 carbon long-chain saturated primary alcohol. It is a constituent of vegetable waxes. Octacosanol is isolated from the wax found on green blades of wheat. It is the major long-chain alcohol isolated from the waxes of sugar cane and yams. It is also found in wheat germ oil.

Octacosanol is also known as l-octacosanol, n-octacosanol and octacosyl alcohol. It has the following chemical formula:

$$CH_3(CH_2)_{26}CH_2OH$$

Octacosanol (1-Octacosanol)

Octacosanol is a solid waxy substance that is insoluble in water. Octacosanol belongs to the family of fatty alcohols.

ACTIONS AND PHARMACOLOGY

ACTIONS

The action of octacosanol is unknown. It is the major long-chain alcohol in policosanol (see Policosanol), and policosanol appears to lower cholesterol and LDL-cholesterol levels. However, the role of octacosanol in the putative cholesterol-lowering activity of policosanol is unclear.

PHARMACOKINETICS

The absorption of octacosanol is variable and low. Octacosanol absorption, following ingestion, ranges from about 11% in rats and humans to about 28% in rabbits. Less octacosanol is absorbed on an empty stomach and more with food. The higher the lipid content of food, the greater the absorption. Octacosanol is absorbed from the small intestine into the lymph and from there enters the bloodstream. Distribution is mainly to the liver, digestive tract, skeletal muscle and adipose tissue. Octacosanol may be partly oxidized to the long-chain fatty acid, octacosanoic acid, which then undergoes beta-oxidation.