**DOSAGE AND ADMINISTRATION**

Supplemental IGF-1 is available and marketed as a dietary supplement, typically in the form of an oral spray. There are no recommended doses.

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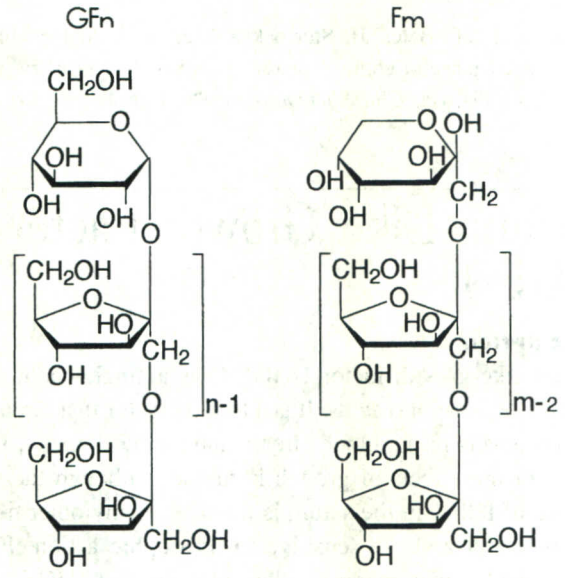
# Inulins

**DESCRIPTION**

Inulins refer to a group of naturally occurring fructose-containing oligosaccharides. They belong to a class of carbohydrates known as fructans. Fructans, in addition to inulins, include another group of naturally occurring fructose-containing oligosaccharides called levans. Inulins are usually of plant origin, while levans are found in fungi and bacteria. Inulins are mainly comprised of fructose units and typically have a terminal glucose. The bond between fructose units in inulins is a beta-(2-1) glycosidic linkage. Plant inulins contain 2 to 150 fructose units. The smallest inulin is called 1-kestose and is composed of two residues of fructose and one of glucose. Inulins are naturally synthesized from sucrose.

Chemically, inulins with a terminal glucose are known as alpha-D-glucopyranosyl-[beta-D-fructofuranosyl](n-1)-D-fructofuranosides, which is abbreviated GpyFn. Inulins without glucose are beta-D-fructopyranosyl-[D-fructofuranosyl](n-1)-D-fructofuranosides, abbreviated as FpyFn. Lower case n refers to the number of fructose residues in inulin; py is the abbreviation for pyranosyl. The basic structural formula follows:




Inulin
n or m equal the number of fructose units
G = glucose, F = fructose

Inulins are present in onions, leeks, garlic, bananas, asparagus and artichokes, among other vegetables and fruits. Because of their sweet taste and their texture, inulins are added to various foods. Inulin intake in the U.S. ranges from 1 to 4 grams daily. It is higher in the European diet.

Inulins are only slightly digested in the small intestine. They are, however, fermented by a limited number of colonic bacteria. This could lead to changes in the colonic ecosystem in favor of some bacteria, such as bifidobacteria, which may have health benefits. Inulins are considered to be bifidogenic factors. Their energy content is about half that of digestible carbohydrates or about 1 to 2 kcal/grams.

Substances such as inulins that promote the growth of beneficial bacteria in the colon are called prebiotics. Prebiotics are typically nondigestible oligosaccharides.

Inulins are marketed as nutritional supplements and functional foods. The sources of these inulins are roots of chicory (*Cichorium intybus*) and Jerusalem artichokes (*Helianthus tuberosus*). Oligofructose refers to the partial enzymatic hydrolysate of inulins. Fructooligosaccharrides usually refer

to synthetic short-chain fructans. The average chain length in inulins is 10.

## ACTIONS AND PHARMACOLOGY

### ACTIONS

Inulins may have antitumor, antimicrobial, hypolipidemic and hypoglycemic actions. They may also help to improve mineral absorption and balance and may have antiosteoporotic activity.

### MECHANISM OF ACTION

The possible antitumor activity of inulins, particularly with respect to colon cancer, might be accounted for, in part, by the possible antitumor action of butyrate. Butyrate, the anion of the short-chain fatty acid butyric acid, is produced by bacterial fermentation of inulins in the colon. Some studies suggest that butyrate may induce growth arrest and cell differentiation and upregulate apoptosis, three activities that could be significant for antitumor activity. Inulins may also aid in increasing the concentrations of calcium and magnesium in the colon. High concentrations of these cations in the colon may help control the rate of cell turnover. High concentrations of calcium may also lead to the formation of insoluble bile or salts of fatty acids. This might reduce the potential damaging effects of bile or fatty acids on colonocytes.

Inulins may promote the growth of favorable bacterial populations, such as bifidobacteria, in the colon. Bifidobacteria may inhibit the growth of pathogenic bacteria, such as *Clostridium perfringens* and diarrheogenic strains of *Escherichia coli*.

Inulins have been found to lower serum triglycerides in rats, and there is some indication that they may lower serum triglycerides in some humans, as well. The mechanism of this possible effect is unclear. It is speculated that the possible triglyceride-lowering effect is due to decreased triglyceride synthesis in the liver. Inulins may lower cholesterol levels in some type 2 diabetics. There is less evidence that inulins lower cholesterol in those with hypercholesterolemia who do not have diabetes. Propionate, a product of inulin fermentation in the colon, may inhibit hydroxymethylglutaryl-CoA (HMG-CoA) reductase, the rate-limiting step in cholesterol biosynthesis.

The possible beneficial effects of inulins on blood glucose—there is some evidence that inulins may lower fasting blood sugar in type 2 diabetics—may be explained as follows: Inulins may delay gastric emptying and/or shorten small-intestinal transit time. Propionate may inhibit gluconeogenesis. It may do this by its metabolic conversion to methylmalonyl-CoA and succinyl CoA, metabolites that may inhibit pyruvate carboxylase. Propionate may reduce plasma levels of free fatty acids. High levels of plasma free fatty acids lower glucose utilization and induce insulin resistance. Propionate may also enhance glycolysis via depletion of citrate in hepatocytes. Citrate is an allosteric inhibitor of phosphofructokinase.

Inulins, similar to dietary fiber, may bind/sequester such minerals as calcium and magnesium in the small intestine. The short-chain fatty acids (acetate, propionate, butyrate) formed from the bacterial fermentation of inulins in the intestinal tract may facilitate the colonic absorption of calcium and possibly also magnesium ions. This could be beneficial in preventing osteoporosis and osteopenia.

### PHARMACOKINETICS

Little digestion of inulins takes place in the stomach and small intestine following ingestion of inulins. Inulins are fermented in the colon by bifidobacteria and some other bacteria to produce the short-chain fatty acids acetate, propionate and butyrate; the gases hydrogen, hydrogen sulfide, carbon dioxide and methane; and lactate, pyruvate and succinate. Acetate, propionate and butyrate that are not metabolized in colonocytes are absorbed from the colon and transported via the portal circulation to the liver. These short-chain fatty acids are extensively metabolized in hepatocytes. Acetate, propionate and butyrate that are not metabolized in hepatocyes are transported by the circulation to various tissues, where they undergo further metabolism. Butyrate is an important respiratory fuel for the colonocytes and is metabolized in them to carbon dioxide and water. Energy, in the form of ATP, is produced from the catabolism of butyrate.

Those with ileostomies may have a microbial population colonizing their ileums. In those cases, inulins could be fermented by some of the bacteria in similar fashion to the way they are fermented in the colon.

## INDICATIONS AND USAGE

Inulins, like some other prebiotic substances, may help protect against colorectal cancer and some infectious bowel diseases. They may also have lipid-lowering effects. Animal research is suggestive of these benefits, but human research is in short supply.

## RESEARCH SUMMARY

There is the suggestion from animal research that inulins may help prevent colon carcinogenesis by stimulating growth of bifidobacteria. In experiments with rats, dietary administration of inulins inhibited the development of colonic aberrant crypt foci, putative preneoplastic lesions that are believed to give rise to colonic adenomas and carcinomas. Oligofructose, a partial enzymatic hydrolysate of inulins, also inhibited these crypt foci but not as effectively as inulins.

Recently, 12 healthy male volunteers ate a breakfast cereal containing 18% inulin for several weeks. At the end of the trial, plasma total cholesterol and triacylglycerol levels were significantly decreased.

**CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS**

CONTRAINDICATIONS

Inulins are contraindicated in those who are hypersensitive to these substances.

PRECAUTIONS

Those who develop gastrointestinal symptoms with the use of dietary fiber should exercise caution in the use of inulins. Those with irritable bowel syndrome should exercise caution in the use of inulins. Those receiving whole body-radiation or radiation to the gastrointestinal tract should avoid supplementation with inulins.

ADVERSE REACTIONS

Doses up to 10 grams daily are well tolerated. Higher doses may cause such gastrointestinal symptoms as flatulence, bloating and diarrhea.

Occasional allergic reactions have been reported.

**INTERACTIONS**

NUTRITIONAL SUPPLEMENTS

Inulins may enhance the colonic absorption of calcium and magnesium supplements if used concomitantly with them.

*Probiotics:* The possible beneficial effects of inulins may be enhanced if used in combination with probiotics.

FOODS

Inulins may enhance the colonic absorption of calcium and magnesium in foods.

**OVERDOSAGE**

No reports of overdosage.

**DOSAGE AND ADMINISTRATION**

Inulins are available in tablets, powder and functional foods. Dosing is variable and ranges from 4 to 10 grams daily. Those who use more than 10 grams daily should split the dosage throughout the day. Doses higher than 30 grams daily may cause significant gastrointestinal discomfort.

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# Iodine

**DESCRIPTION**

Iodine, consumed principally as its iodide salts, is an essential trace element which is vital to the function of the thyroid gland. It is an essential component of thyroid hormones, which are required for normal development and metabolism. The fact that trace element composition of foods is very much dependent on geography was first recognized with respect to iodine. Iodine is present in low amounts in the earth's crust and thus in its soil. It is plentiful in the oceans and is found in sea animals and sea plants, such as seaweeds. Iodine is a non-metallic element belonging to the halogen group. Its atomic number is 53, and its atomic mass is 126.90 daltons. Its atomic symbol is I. The terms iodine and iodide are frequently used interchangeably.

The thyroid hormones are iodine-containing substances and they do not function without iodine. Approximately 80% of the body's iodine pool, or about 15 milligrams in adults, is present in the thyroid gland. Moderate deficiency of iodine may result in a goiter. Severe iodine deficiency may result in endemic myxedema among adults and in endemic cretinism among infants. Iodine deficiency results in decreased production of the thyroid hormones thyroxine or $T_4$ and triiodothyronine or $T_3$. The fall in the level of $T_4$ leads to increased thyroid stimulating hormone (TSH) output from the pituitary gland, resulting in an increase in the size of the thyroid gland which can lead to the formation of a goiter. In addition to causing goiters, iodine deficiency may result in a wide spectrum of effects on growth and development, particularly on brain development. Iodine deficiency is the most common cause of preventable mental deficit in the world.

In the early 1900s and prior to that, iodine deficiency and endemic goiter were very common in the United States. In the early 1920s, it was demonstrated in school children in Ohio that endemic goiter could be prevented and reduced by administration of small amounts of iodine in the form of iodide. Shortly afterwards, mass prophylaxis of endemic goiter with iodized salt was introduced in the United States and Switzerland, leading to a sharp fall in the incidence of goiter, as well as cretinism. Goiter, myxedema and other