Mc Naughton L, Dalton B, Tarr J. Inosine supplementation has no effect on aerobic or anaerobic cycling performance. *Int J Sports Nutr.* 1999; 9:333-334.

Milano S, Dieli M, Millott S, et al. Effect of isoprinosine on IL-3, IFN-gamma and IL-4 production *in vivo* and *in vitro*. *Int J Immunopharmacol.* 1991; 13:1013-1018

Renoux G, Renoux M, Guillaumin J-M. Isoprinosine as an immunopotentiator. *J Immunopharmacol.* 1979; 1:337-356.

Starling RD, Trappe TA, Short KR, et al. Effect of inosine supplementation on aerobic and anaerobic cycling performance. *Med Sci Sports Exerc.* 1996; 28:1193-1198.

Williams MH, Kreider RB, Hunter DW, et al. Effect of inosine supplementation on 3-mile treadmill run performance and VO_2 peak. *Med Sci Sports Exec.* 1990; 22:517-522.

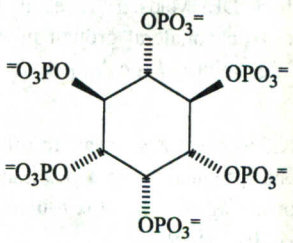
Zimmer HG. Effect of inosine on cardiac adenine nucleotide metabolism in rats. *Adv Myocardiol.* 1985; 6:173-183.

Inositol Hexaphosphate

DESCRIPTION

Inositol hexaphosphate, also known as phytate, is a component of most cereal grains and seeds, occurring in conjunction with plant fiber, and is a source of *myo*-inositol in the diet. Inositol hexaphosphate is responsible for storing more than 80 percent of the total phosphate in cereals and legumes. Phytate has strong chelating power for doubly charged metal ions, such as magnesium, calcium and zinc. Some studies suggest that phytate may slow tumor growth rates.

Inositol hexaphosphate, in addition to being known as phytate, is known as *myo*-inositol hexaphosphate, and *myo*-inositol 1,2,3,4,5,6-hexakisphosphate. Inositol hexaphosphate is abbreviated as $InsP_6$ and sometimes as IP-6. The structural formula is:



Inositol hexaphosphate

ACTIONS AND PHARMACOLOGY

ACTIONS

Inositol hexaphosphate is a putative antiproliferative agent and may have antioxidant activity.

MECHANISM OF ACTION

Some speculate that inositol hexaphosphate's possible antiproliferative activity is due to its chelating divalent cations which may be important for tumor growth. Others speculate that inositol hexaphosphate, along with inositol, are metabolized to inositol triphosphates, which are believed to be involved in cell signaling and regulating cell growth, and that this may underlie its possible effects. Chelation by inositol hexaphosphate of ferrous cations could inhibit the Fenton reaction, a reaction which generates reactive oxygen species. Enhancement of natural killer cell activity is offered as still another speculative mechanism.

PHARMACOKINETICS

It is unclear how much inositol hexaphosphate is absorbed in humans following ingestion. Inositol hexaphosphate may, in part, be hydrolyzed to *myo*-inositol. (See *myo*-inositol.)

INDICATIONS AND USAGE

There is preliminary evidence that inositol hexaphosphate may eventually find some use in the treatment of some cancers.

RESEARCH SUMMARY

A few studies performed *in vitro* and in animal models suggest that inositol hexaphosphate inhibits some cancers, specifically epithelial cancers, including breast and colon cancers. It has also significantly inhibited human rhabdomyosarcoma in an animal model. More research is needed to see whether this substance can play a role in the clinical treatment of some cancers. There is some epidemiologic data suggesting that dietary phytate may have chemopreventive activity.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to an inositol hexaphosphate-containing product.

PRECAUTIONS

Supplemental inositol hexaphosphate should be avoided by pregnant women and nursing mothers, due to lack of long-term safety studies.

ADVERSE REACTIONS

No significant adverse effects were noted in one report on the use of a daily dose of 8.8 grams of inositol hexaphosphate taken for several months.

INTERACTIONS

Inositol hexaphosphate may form chelates with divalent cations such as calcium, magnesium, manganese, zinc, copper and iron found in foods, if taken with foods or nutritional supplements containing these elements. It may also interact with food proteins.

OVERDOSAGE

No reports of overdosage.

DOSAGE AND ADMINISTRATION

None recommended.

LITERATURE

Graf E, Eaton JW. Antioxidant function of phytic acid. *Free Rad Biol Med.* 1990; 8:61-69.

Jariwalla RJ, Sabin R, Lawson S, Herman ZS. Lowering of serum cholesterol and triglycerides and modulation by dietary phytates. *J Appl Nutr.* 1990; 42:18-28.

Jariwalla RJ, Sabin R, Lawson S, et al. Effect of dietary phytic acid (phytate) on the incidence and growth rate of tumors promoted in Fisher rats by magnesium supplement. *Nutr Res.* 1988; 8:813-827.

Porres JM, Stahl CH, Cheng W-H, et al. Dietary intrinsic phytate protects colon from lipid peroxidation in pigs with a moderately high dietary iron intake. *Proc Soc Exp Biol Med.* 1999; 221:80-86.

Shamsuddin AM. Inositol phosphates have novel anticancer function. *J Nutr.* 1995; 125:725S-732S.

Shamsuddin AM. Reduction of cell proliferation and enhancement of NK-cell activity. 1992. United States Patent Number 5,082,833.

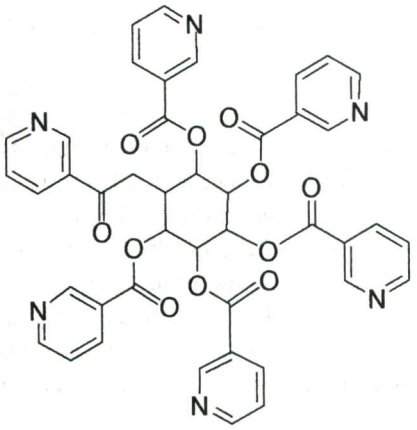
Vucenik I, Kalebic T, Tantivejkulk, Shamsuddin A. Novel anticancer function of inositol hexaphosphate. Inhibition of human rhabdomyosarcoma *in vitro* and *in vivo*. *Anticanc Res.* 1998; 18:1377-1384.

Inositol Nicotinate

DESCRIPTION

Inositol nicotinate is a delivery form of nicotinic acid that has been used in Europe and Japan for the treatment of hyperlipidemias, peripheral vascular disorders, including Raynaud's disease, intermittent claudication, Buerger's disease (thromboangiitis obliterans), and necrobiosis lipoidica, a disorder marked by shiny leg lesions due to atrophy of the skin. Inositol nicotinate is marketed in the United States as a nutritional supplement. The flushing reaction ("niacin flush") which occurs in those taking immediate-release or crystalline nicotinic acid, is usually not as severe with inositol nicotinate.

Inositol nicotinate is also known as inositol niacinate, *myo*-inositol hexa-3-pyridinecarboxylic acid, hexanicotinoyl inositol, *meso*-inositol hexanicotinate, inositol hexanicotinate, inositol hexaniacinate and hexanicotinyl *cis*-1,2,3,5-*trans*-4,6-cyclohexane. Its molecular formula is $C_{42}H_{30}N_6O_{12}$ and its molecular weight is 810.73 daltons. Each molecule of inositol nicotinate contains six molecules of nicotinic acid esterified to one molecule of *myo*-inositol. By weight, approximately 80% of inositol nicotinate is nicotinic acid and 20% is *myo*-inositol. The chemical structure of inositol nicotinate is represented as follows:



Inositol Nicotinate

ACTIONS AND PHARMACOLOGY

ACTIONS

Inositol nicotinate may have antihyperlipidemic activity. It may also have activity in the management of certain peripheral vascular diseases, such Raynaud's disease and intermittent claudication.

MECHANISM OF ACTION

The possible antihyperlipidemic activity of inositol nicotinate is accounted for by its metabolic conversion to nicotinic acid. See monograph on Niacin (Nicotinic Acid) for a discussion of the possible mechanisms of the antihyperlipidemic activity of nicotinic acid.

Inositol nicotinate has shown some activity in some with Raynaud's disease and intermittent claudication. Features of Raynaud's disease include intense vasoconstriction or vasospasm and platelet aggregation. The mechanism of inositol nicotinate's possible activity in Raynaud's disease is unknown. Nicotinic acid, the principal metabolite of inositol nicotinate, can cause vasodilation of cutaneous vessels. This results in increased blood flow principally to the face, neck and chest and is responsible for the so called niacin-flush. The vasodilatory activity of nicotinic acid is thought to be prostaglandin-mediated. However, the vasodilatory effect of nicotinic acid is transitory and unlikely to play a significant role in the possible activity of inositol nicotinate in Raynaud's disease.

Intermittent claudication results from occlusive arterial disease of the lower limbs and is characterized by pain, which develops during exercise and which disappears at rest. The pain is due to ischemia resulting from the obstruction or vasoconstriction of peripheral arteries. Inositol nicotinate may help some with this disorder. Again, the possible