

Monograph

Inositol Hexaniacinate

**Synonyms: Inositol Hexanicotinate;
Inositol Nicotinate**

Biochemistry and Pharmacokinetics

Inositol hexaniacinate (IHN) is the hexanicotinic acid ester of meso-inositol. This compound consists of six molecules of nicotinic acid (niacin) with an inositol molecule in the center (see figure). Pharmacokinetic studies indicate the molecule is, at least in part, absorbed intact, and hydrolyzed in the body with release of free niacin and inositol.¹ It appears

to be metabolized slowly, not reaching maximum serum levels until approximately 10 hours after ingestion.²

Mechanisms of Action

The mechanisms of action of inositol hexaniacinate are believed to be the same as those for niacin. These include a decrease in free fatty acid mobilization; a decrease in VLDL synthesis in the liver resulting in a decrease in LDLs, total cholesterol and triglycerides; inhibition of cholesterol synthesis in the liver; an increase in HDL levels by decreasing its catabolism,³ and fibrinolysis.^{4,5}

Clinical Indications

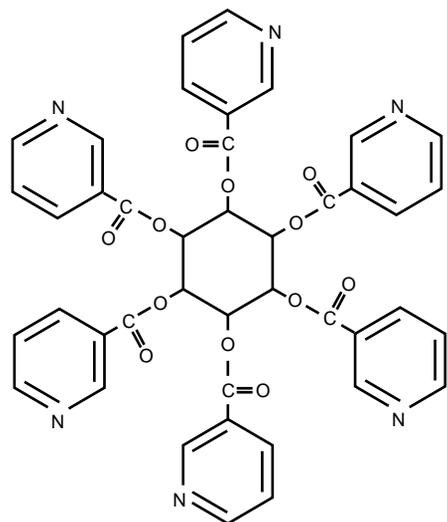
Hyperlipidemia: Studies report significant lipid-lowering effects of IHN at doses of 400 mg 3-4 times daily.⁶ Welsh and Eade found IHN more effective than niacin in its hypocholesterolemic, antihypertensive and lipotropic effects.²

Raynaud's Disease: A review of the literature reveals numerous positive studies on the use of IHN in Raynaud's Disease.^{2,4,5,7-9} The typical dosage is 1 gram qid for several months. The mechanism of action appears to be more than just a transient vasodilation, involving lipid-lowering and fibrinolysis.^{4,5} This explains the need for long-term administration.

Intermittent Claudication: The use of niacin esters for the treatment of intermittent claudication secondary to atherosclerosis has been examined extensively. Significant improvement has been reported by several investigators at dosages of 2 grams twice daily, typically for at least 3 months.¹⁰⁻¹³ While arterial dilation may be a factor, it has been postulated that reduction in fibrinogen, improvement in blood viscosity, and resultant improvement in oxygen transport are involved in the therapeutic effects.¹¹

Other Peripheral Vascular Diseases: IHN appears to have application in the treatment of other conditions resulting from peripheral vascular insufficiency, including threatened amputation from gangrene,² restless legs syndrome,² stasis dermatitis,² atherosclerosis-related migraines,² and hypertension.²

Dermatological Conditions: IHN has been used for the treatment of various dermatological conditions with mixed results. Included were lesions of scleroderma, acne, dermatitis herpetiformis, exfoliative glossitis, and psoriasis. IHN appeared to help four out of five patients with dermatitis herpetiformis.² The one patient with sclerodermal skin lesions was reported to have improved significantly on 1200 mg IHN daily.² The results with other skin conditions have been less promising. It appears the dermatological problems most benefited by IHN are those related to vascular insufficiency.²



Dosage

Recommended dosage for lipid-lowering and improving conditions related to peripheral vascular insufficiency ranges from 1500 mg to 4 grams daily, in divided dosages of two to three times daily.

Deficiency

Although the inositol hexaniacinate complex is not an essential nutrient, niacin is vital to cellular metabolism, principally through its role in the coenzymes, nicotine-adenine dinucleotide (NAD) and nicotine-adenine dinucleotide phosphate (NADP), in oxidation-reduction reactions. There are certain population fractions which may be deficient, requiring niacin supplementation to prevent pellagra. These groups include alcoholics¹⁴ and the elderly.¹⁵

Toxicity

Numerous toxic reactions, both acute and chronic, have been reported from the use of high-dose niacin. Reactions to niacin range from acute symptoms of flushing, pruritis, and GI complaints to chronic symptoms of hepatotoxicity, hyperuricemia, and impaired glucose tolerance. On the other hand, no adverse effects have been reported from the use of inositol hexaniacinate in dosages as high as four grams daily.^{4,6,8,9} Despite the lack of reported adverse reactions, use of IHN in patients with known liver disease probably should be avoided. In addition, if high doses (2 grams or greater daily) are being administered, liver enzymes should be monitored every 2-3 months for at least the first six months.

Although no adverse reactions between inositol hexaniacinate and other nutrients or drugs have been reported, due to its fibrinolytic effect it should be used with caution in conjunction with other blood thinners.

References

1. Harthon L, Brattsand R. Enzymatic hydrolysis of pentaerythritoltetranicotinate and meso-inositolhexanicotinate in blood and tissues. *Arzneim-Forsch* 1979;29:1859-1862.
2. Welsh AL, Eade M. Inositol hexanicotinate for improved nicotinic acid therapy. *Int Record Med* 1961;174:9-15.
3. El-Enein AMA, Hafez YS, Salem H, Abdel M. The role of nicotinic acid and inositol hexaniacinate as anticholesterolemic and antilipemic agents. *Nutr Reports Int* 1983;28:899-911.
4. Holti G. An experimentally controlled evaluation of the effect of inositol nicotinate upon the digital blood flow in patients with Raynaud's phenomenon. *J Int Med Res* 1979;7:473-483.
5. Aylward M. Hexopal in Raynaud's disease. *J Int Med Res* 1979;7:484-491.
6. Dorner V, Fischer FW. The influence of m-inositol hexanicotinate ester on the serum lipids and lipoproteins. *Arzneim-Forsch* 1961;11:110-113.
7. Ring EF, Bacon PA. Quantitative thermographic assessment of inositol nicotinate therapy in Raynaud's phenomena. *J Int Med Res* 1977;5:217-222.
8. Ring EFJ, Porto LO, Bacon PA. Quantitative thermal imaging to assess inositol nicotinate treatment for Raynaud's syndrome. *J Int Med Res* 1981;9:393-400.
9. Sunderland GT, Belch JF, Sturrock RD, et al. A double blind randomized placebo controlled trial of Hexopal in primary Raynaud's disease. *Clin Rheum* 1988;7:46-49.
10. O'Hara J. A double-blind placebo-controlled study of Hexopal in the treatment of intermittent claudication. *J Int Med Res* 1985;13:322-327.
11. O'Hara J, Jolly PN, Nicol CG. The therapeutic efficacy of inositol nicotinate (Hexopal) in intermittent claudication: a controlled trial. *Br J Clin Practice* 1988;42:377-383.
12. Tyson VCH. Treatment of intermittent claudication. *Practitioner* 1979;223:121-126.
13. Seckfort H. Treating circulatory problems with inositol nicotinic acid ester. *Med Klin* 1959;10:416-418.
14. Jolliffe N. Nicotinic acid deficiency encephalopathy. *JAMA* 1940;114:307-312.
15. Baker H, Frank O, Thind IS, et al. Vitamin profiles in elderly persons living at home or in nursing homes, versus profiles in healthy subjects. *J Am Geriatr Soc* 1979;27:444-450.