

Vitamin B3

(Niacin)

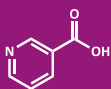


Synonyms:

Pellagra-Preventive factor (PP), nicotinic acid, nicotinamide.

Chemistry:

Nicotinic acid (pyridine-3-carboxylic acid), nicotinamide (pyridine-3-carboxamide).



Molecular formula of nicotinic acid



Food:

	mg/100g
Veal	og
Liver	15
Chicken	11
Beef	7.5
Salmon	7.5
Almonds	4.2
Peas	2.4
Potatoes	1.2
Peaches	0.9
Tomatoes	0.5
Milk (whole)	0.1

(Souci, Fachmann, Kraut)



Main functions:

- Coenzymes - Nicotinamide adenine dinucleotide (NAD) and Nicotinamide adenine dinucleotide phosphate (NADP) - in redox reactions
- NAD is a substrate for non-redox reactions

Vitamin B3 (Niacin)

Within the human body, vitamin B3 helps to release energy from the foods we eat, produce fatty acids and cholesterol, repair DNA and contribute to the stress response. Commonly known as niacin or nicotinic acid, sufficient levels of the water-soluble vitamin are typically met by eating a varied and balanced diet.



Functions

The coenzymes NAD and NADP are required for around 200 biological reduction-oxidation (redox) reactions. NAD is mainly involved in reactions that generate energy in tissues through the biochemical degradation of carbohydrates, fats and proteins. NAD is also required as a substrate for non-redox reactions. It is the source of adenosine diphosphate (ADP)-ribose, which is transferred to proteins by different enzymes. These enzymes and their products seem to be involved in DNA replication, DNA repair, cell differentiation and cellular signal transduction. NADP is important for the reductive biosynthesis of fatty acids and cholesterol.

Dietary sources

Nicotinamide and nicotinic acid occur widely in nature. Nicotinic acid is more prevalent in plants, whereas in animals, nicotinamide predominates. Most of the niacin obtained from food comes from yeast, liver, poultry, lean meats, nuts and legumes. Milk and green leafy vegetables contribute lesser amounts. Specific food processing techniques, such as the treatment of corn with lime water involved in the traditional preparation of tortillas, increase the bioavailability of nicotinic acid in these products. Tryptophan contributes as much as two thirds of the niacin activity required by adults in typical diets. Important food sources of tryptophan are meat, milk and eggs.

Absorption and body stores

Both the acid and amide forms of niacin are readily absorbed from the stomach and the small intestine. At low concentrations, the two forms are absorbed by a sodium-dependent facilitated diffusion and, at higher concentrations by passive diffusion. Niacin is present in the diet mainly as NAD and NADP, and nicotinamide is released from the coenzyme forms by enzymes in the intestine. The main storage organ, the liver, may contain a significant amount of the vitamin, which is stored as NAD. The niacin coenzymes NAD and NADP are synthesized in all tissues from nicotinic acid or nicotinamide.

Measurement

Determination of the urinary excretion of two niacin metabolites, N-methyl-nicotinamide and N-methyl-2-pyridone-5-carboxamide, has been used to assess niacin status. Excretion of 5.8 ± 3.6 mg N-methyl-nicotinamide/24hrs and 20.0 ± 12.9 mg N-methyl-2-pyridone-5-carboxamide/24hrs are considered normal. A ratio of the two metabolites is also used for status assessment. An adequate niacin status is considered when the ratio of N-methyl-2-pyridone-5-carboxamide to N-methyl-nicotinamide is between 1.3 and 4.0. Recent studies suggest that the measurement of NAD and NADP concentrations and their ratio in red blood cells may be sensitive and reliable indicators for the determination of niacin status. A ratio of erythrocyte NAD to NADP <1.0 may identify subjects at risk of developing niacin deficiency. Plasma tryptophan concentration is also used for assessment of niacin status.

Stability

Both nicotinamide and nicotinic acid are stable when exposed to heat, light, air and alkali. Little loss occurs during the cooking and storage of foods.

Physiological interactions

- Copper deficiency can inhibit the conversion of tryptophan to niacin. The drug penicillamine has been demonstrated to inhibit the tryptophan-to-niacin pathway in humans. The pathway from tryptophan to niacin is sensitive to a variety of nutritional alterations; inadequate iron, riboflavin, or vitamin B6 status reduces the synthesis.
- Long-term treatment of tuberculosis with isoniazid may cause niacin deficiency, because isoniazid is a niacin antagonist. Other drugs that interact with niacin metabolism may also lead to niacin deficiency, e.g. tranquilizers (diazepam) and anticonvulsants (phenytoin, phenobarbital).



Deficiency

Symptoms of a marginal niacin deficiency include: insomnia, loss of appetite, weight and strength loss, soreness of the tongue and mouth, indigestion, abdominal pain, burning sensations in various parts of the body, vertigo, headaches, numbness, nervousness, poor concentration, apprehension, confusion and forgetfulness.

Severe niacin deficiency leads to pellagra, a disease characterized by dermatitis, diarrhea and dementia. A pigmented rash develops symmetrically on the skin in areas exposed to sunlight. Symptoms affecting the digestive system include a bright red tongue, stomatitis, vomiting, and diarrhea. Headaches, fatigue, depression, apathy and loss of memory are neurological symptoms of pellagra. If left untreated, pellagra is fatal. Since the synthesis of NAD from tryptophan requires an adequate supply of riboflavin and vitamin B6, insufficiencies of these vitamins may also contribute to niacin deficiency.

Pellagra is rarely seen in industrialized countries, except for its occurrence in people with chronic alcoholism. In other parts of the world where maize and jowar (barley) are the major staples, pellagra persists. It also occurs in India and parts of China and Africa.

Patients with Hartnup disease, a genetic disorder, develop pellagra because their absorption of tryptophan is defective.

Carcinoid syndrome may also result in pellagra as NAD synthesis is restricted.

Groups at risk

- Patients with Hartnup disease
- Patients with carcinoid syndrome
- Alcoholics
- Those with long-term intake of certain drugs

Reducing disease risk: therapeutic use

Niacin is specific in the treatment of glossitis, dermatitis and the mental symptoms seen in pellagra. High doses of nicotinic acid (1.5 - 4 g/day) can reduce total and low-density lipoprotein cholesterol and triacylglycerols and increase high-density lipoprotein cholesterol in patients at risk of cardiovascular disease (CVD).

There is a flush reaction to high doses of nicotinic acid, which is seen primarily with a rising blood level and may wear off once a plateau level has been reached. Nicotinic acid has also been used in doses of 100 mg as a vasodilator. Type 1 diabetes mellitus results from the autoimmune destruction of insulin-secreting β -cells in the pancreas. There is evidence that nicotinamide may delay or prevent the development of diabetes. Clinical trials are in progress to investigate this effect of nicotinamide.

Recent studies suggest that human immunodeficiency virus (HIV) increases the risk of niacin deficiency. Higher intakes of niacin were associated with decreased progression rate to AIDS in an observational study of HIV-positive men.

NAD is consumed as a substrate in ADP-ribose transfer reactions to proteins which play a role in DNA repair. This has created interest in the relationship between niacin and cancer. A large case-control study found increased consumption of niacin, along with antioxidant nutrients, to be associated with decreased incidence of cancers of the mouth, throat and esophagus.



Recommended Daily Intake (RDI)

The actual daily requirement of niacin depends on the quantity of tryptophan in the diet and the efficiency of the tryptophan to niacin conversion. The conversion factor is 60 mg of tryptophan to 1 mg of niacin, which is referred to as 1 niacin equivalent (NE). This conversion factor is used for calculating both dietary contributions from tryptophan and recommended allowances of niacin. In the US, the RDI for adults is 16 mg NEs for men and 14 mg NEs for women. RDI is estimated as 6.6 mg NE per 1,000 kcal.

Recommended daily intakes (RDI) *

Group	Life stage	Dose/day**
Infants	<6 months	2 mg (AI)
Infants	7 – 12 months	4 mg (AI)
Children	1 – 3 years	6 mg
Children	4 – 8 years	8 mg
Children	9 – 13 years	12 mg
Males	>14 years	16 mg
Females	>14 years	14 mg
Pregnancy	14 – 50 years	18 mg
Breastfeeding	14 – 50 years	17 mg

* Institute of Medicine (2001).

** As NE. 1 mg niacin = 60 mg of tryptophan;
0 – 6 months = preformed niacin (not NE).

If not otherwise specified, this table presents RDIs. Allowable levels of nutrients vary depending on national regulations and the final application



Safety

There is no evidence that niacin from foods causes adverse effects. Pharmacological doses of nicotinic acid exceeding 300 mg per day have been associated with a variety of side effects including nausea, diarrhea and transient flushing of the skin. Doses exceeding 2.5 g per day have been associated with hepatotoxicity, glucose intolerance, hyperglycemia, elevated blood uric acid levels, heartburn, nausea and headaches. Severe jaundice may occur, even with doses as low as 750 mg per day, and may eventually lead to irreversible liver damage.

Doses of 1.5 to 5 g/day of nicotinic acid have been associated with blurred vision and other eye problems. Tablets with a buffer and time release capsules are available to reduce flushing and gastrointestinal irritation in individuals that are sensitive to nicotinic acid.

These should be used with caution, however, because a high intake of time-release niacin tablets has been linked to liver damage. The Food and Nutrition Board (1998) set the UL for niacin (nicotinic acid plus nicotinamide) at 35 mg/day. The EU Scientific Committee on Food (2002) developed different ULs for nicotinic acid and nicotinamide: the upper level (UL) for nicotinic acid has been set at 10 mg/day, for nicotinamide at 900 mg/day.

Supplements and food fortification

Single supplements of nicotinic acid are available in tablets, capsules and syrups. Multivitamin and B-complex vitamin infusions, tablets and capsules also contain nicotinamide. Niacin is used to fortify grain, including corn and bran breakfast cereals and wheat flour.

Production

Although other routes are known, most nicotinic acid is produced by oxidation of 5-ethyl-2-methylpyridine. Nicotinamide is produced via 3-methylpyridine. This compound is derived from two carbon sources, acetaldehyde and formaldehyde, or from acrolein plus ammonia.

3-methylpyridine is first oxidized to 3-cyanopyridine which, in a second stage, converts to nicotinamide by hydrolysis.

History

