Niacin

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Importance of niacin for health

Niacin is used as a collective term for all vitamin B3 vitamers, including nicotinamide, nicotinic acid, nicotinamide adenine dinucleotide (NAD), or nicotinamide adenine dinucleotide phosphate (NADP) (1). NAD and NADP are required in many metabolic processes in cells (2, 3):

- as a co-enzyme in electron-transfer reactions (catabolism of carbohydrates, fats, proteins, and alcohol)
- as a substrate for NAD-consuming enzymes (ADP-ribosylation, NAD-dependent deacetylation, calcium mobilization)
- as ligand (inhibitory neurotransmitter, pro-inflammatory cytokine, calcium mobilization)

Nicotinamide and nicotinic acid absorption occurs rapidly in the stomach and intestine. In liver and intestines, nicotinamide is released from NAD and transported to tissues for NAD synthesis when required (1). Additionally, nicotinic acid or nicotinamide riboside can also be utilized for NAD production as well as *de novo* synthesis from tryptophan (4). All pathways form the intermediary nicotinamide or nicotinic acid mononucleotides (3).

Various animal-source foods such as poultry, beef, and fish are a good source for dietary niacin, primarily as highly bioavailable NAD and NADP. Nuts, legumes, and grains also contain niacin, which may be bound to polysaccharides and glycopeptides resulting in reduced bioavailability (2).

Nutrient Interactions

The amino acid tryptophan can be used for niacin production via the kynurenine pathway, producing quinolinic acid, which then is converted to nicotinic acid mononucleotide, which enters the Preiss-Handler pathway for NAD synthesis (3). This multi-step metabolic pathway involves enzymes dependent on zinc, iron, riboflavin, and vitamin B6 (5). Niacin can be used to reduce levels of cholesterol, low density lipoprotein (LDL), triglycerides, and lipoprotein while it increases high density lipoprotein (HDL) (6).

Risks of deficiency:

Pellagra occurs in the late stage of severe niacin deficiency (7). Niacin deficiency can occur due to inadequate intake of NAD precursors from diet, which includes tryptophan. Other conditions that may result in niacin deficiency include Crohn's disease, megaduodenum, Hartnup's disease, or carcinoid syndrome. Skin, the digestive system, and the nervous systems are commonly affected by niacin deficiency (3).

Risks of excess:

High intakes of nicotinic acid and nicotinamide as dietary supplement or medicinal treatment may cause adverse effects, such as flushing, burning, tingling, and itching sensations. Up to 3000mg nicotinic acid per day has been shown to cause hypotension, fatigue, impaired glucose tolerance or insulin resistance, gastrointestinal effects, or hepatitis. Thus tolerable Upper Limits (UL) have been established (2).

Interactions with medications

Niacin interacts with certain types of medications, and several types of drugs might affect niacin levels (2):

- Isoniazid and pyrazinamide (Rifater®, tuberculosis treatment)
- anti-diabetes mediation

Human biomarkers for measuring niacin intake and status

Niacin can be assessed by different methods (1):

Biomarker	Analysis type	Sample	Benefits	Intricacies
Urinary excretion	indirect analysis	urine	Reliable and sensitive	Insensitive to marginal niacin intake
Niacin	Direct analysis	plasma	Rapid sample preparation	Only selected plasma metabolites are good indicators
Niacin	Direct analysis	RBC	Sensitive to niacin depletion	

RBC: red blood cells

Urinary niacin

Niacin status can be assessed by analysis of the major niacin urinary metabolites, 1-methylnicotinamide (1-MN), and 1-methyl-2-pyridone-5-carboxamide (2-PYR). 1-methyl-4-pyridone-3-carboxide, a minor urinary metabolite, is sometimes included in the analysis. 2 and 24h urine collections have been used in the past, but spot urine samples have been suggested as an alternative as they are likely to provide information of status and recent intake. For status measurements, fasting, early morning urine samples are recommended (5). However, it has also been stated that urinary niacin metabolites are not suitable to wide-scale screening and their relationship to niacin status is still not fully understood (8).

Urinary niacin, for method, see reference (5)

Plasma niacin

Several approaches have been described for niacin metabolites, including nicotinic acid, nicotinamide, nicotinuric acid (6). However, only plasma 2-PYR and to a lesser extent 1-MN have been shown to be a useful plasma niacin biomarker for status (1, 9). The usefulness of plasma niacin analysis is therefore uncertain.

Plasma niacin, for method, see references (6) and (9).

Erythrocyte niacin

While whole blood NAD and NADP measurements have been indicated to provide erroneous estimates of niacin deficiency (10), erythrocyte NAD has been proposed to be a sensitive, reliable and

convenient biomarker for niacin status assessment (11). Concentrations of erythrocyte NADP are fairly constant and therefore not affected by abnormal niacin status, which has been used to suggest a "niacin index", calculated as the NAD:NADP-ratio (1, 11).

Erythrocyte niacin, for method, see reference (12)

Other methods

General methodological approach for NAD-metabolome. For method, see reference (4)

Accreditation schemes

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https://www.labcorp.com/test-menu/36676/vitamin-bsub3-sub-niacin-and-metabolite

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E.g. Vitamin B3, plasma: http://ltd.aruplab.com/Tests/Pub/0092168

Alternatively, please see the OpeN-Global page on laboratory accreditation: https://open-global.kcl.ac.uk/accreditation/

Technical assistance

For questions on methods of niacin assessment or for technical assistance, please contact the OpeN-Global team at https://open-global.kcl.ac.uk/contact/ or write to:

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Useful links

US National Academies Press IOM Dietary reference intakes for thiamine, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline, 2000
http://nationalacademies.org/hmd/reports/2000/dietary-reference-intakes-for-thiamin-riboflavin-niacin-vitamin-b6-folate-vitamin-b12-pantothenic-acid-biotin-and-choline.aspx

Linus Pauling Institute Micronutrient Information Center (Oregon State University)
https://lpi.oregonstate.edu/mic/vitamins/niacin

NIH Health Information
https://ods.od.nih.gov/factsheets/Niacin-HealthProfessional/

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