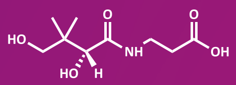
Vitamin B5
(Pantothenic acid)

Synonyms:

Pantothenate, pantothenol, D-panthenol, anti-dermatosis vitamin, chick anti-pellagra factor.

Chemistry:

Pantothenic acid is composed of β-alanine and 2,4-dihydroxy-3,3-dimethylbutyric acid (pantoic acid). Acid amide-linked pantetheine consists of pantothenic acid linked to a β-mercaptoethylamine group.



Molecular formula of pantothenic acid

Food:

	mg/100g
Veal liver	7.9
Brewer’s yeast	7.2
Peanuts	2.1

(Souci, Fachmann, Kraut)

Main functions:

- Metabolism of carbohydrates, proteins and fats
- Energy supply from nutrients – reduced tiredness and fatigue
- Biosynthesis of essential lipids, steroids, hormones, neurotransmitters and porphyrin
- Normal mental performance
- Formation of red blood cells, as well as sex and stress-related hormones

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Vitamin B5 (Pantothenic acid)

Referred to as pantothenic acid, vitamin B5 can be found throughout all living cells and in most food sources in small amounts. The water-soluble vitamin helps to produce energy by breaking down the fats and carbohydrates in food, however, it is also known to support the synthesis of fatty acids, cell membranes, neurotransmitters and hemoglobin and promote healthy skin, hair, eyes and liver. Insufficiency of the vitamin is extremely rare, however if it does occur, typical symptoms include tiredness, nausea and vomiting, numbness or 'burning feet'.

Functions

Pantothenic acid, as a metabolically active component of coenzyme-A (CoA) and acyl carrier protein (ACP, an enzyme involved in the synthesis of fatty acids), plays a key role in the metabolism of carbohydrates, proteins and fats, and is therefore essential for the maintenance and repair of all cells and tissues in the body. CoA is involved in a broad range of acetyl- and acyl-transfer steps and reactions of the oxidative metabolism and catabolism. Hence it is significant in helping to supply energy. For example, in the process of fat burning (of which the catabolic process is known as β-oxidation), pantothenic acid works with coenzyme-Q10 and L-carnitine to break down fatty acids. ACP, however, is required for biosynthetic reactions (also known as anabolic processes) such as observed during fatty acid synthesis.

CoA and ACP therefore have various functions, including the biosynthesis of essential lipids (e.g. sphingolipids, phospholipids), isoprenoids (e.g. cholesterol, bile salts) and steroids (e.g. growth, stress and sex hormones); fatty acid elongation and triglyceride synthesis (energy storage). Furthermore, CoA and ACP are involved in protein acetylation (e.g. activation of hormones) and acylation (e.g. activation of transcription factors) and in the acetylation of sugars which are required for certain cell structures.

CoA is also engaged in the synthesis of neurotransmitters (e.g. acetylcholine), porphyrin (a component of hemoglobin – the oxygen-carrying red blood cell pigment) and antibodies, as well as the metabolism of drugs (e.g. sulfonamides) and in alcohol detoxification.

Dietary sources

The active vitamin is present in virtually all plant, animal and microbial cells, with about 80% of dietary vitamin B5 in the form of CoA. Its richest sources are yeast and organ meats (liver, kidney, heart, brain), but eggs, milk, vegetables, nuts and whole-grain cereals are also common sources of pantothenic acid.

Absorption and body stores

Most of the pantothenic acid in food exists in the form of CoA or ACP, which are converted into pantetheine by a series of enzyme reactions in the small intestine. Pantetheine can be directly absorbed or is further metabolized to pantothenic acid. The absorption happens by passive diffusion and by a saturable sodium-dependent active transport system, which is also the case for biotin. Pantothenic acid is transported to the tissues via the circulation of the blood, where it is primarily incorporated into erythrocytes or bound to plasma proteins. It is then embedded into CoA and ACP once again. The cellular pantothenic acid uptake is similar to the intestinal absorption.

Intracellular concentrations are regulated by the pantothenic acid kinase. If nutritional supplement formulations such as calcium pantothenate are ingested, they must also first be converted by intestinal enzymes before being taken up by the small intestine. Approximately half of the pantothenic acid in the diet is actually absorbed.

The highest concentrations in the body are found in the liver, adrenal glands, kidneys, brain, heart and testes. Total pantothenic acid levels in whole blood range from 1.6 to 2.7 mcMol/L in healthy adults; with most existing as CoA in the red blood cells. Urinary excretion in the form of pantothenic acid generally correlates with dietary intake, but variation is large (2 – 7 mg daily). During breastfeeding, approximately 40% of a woman's daily intake reaches her milk.

Measurement

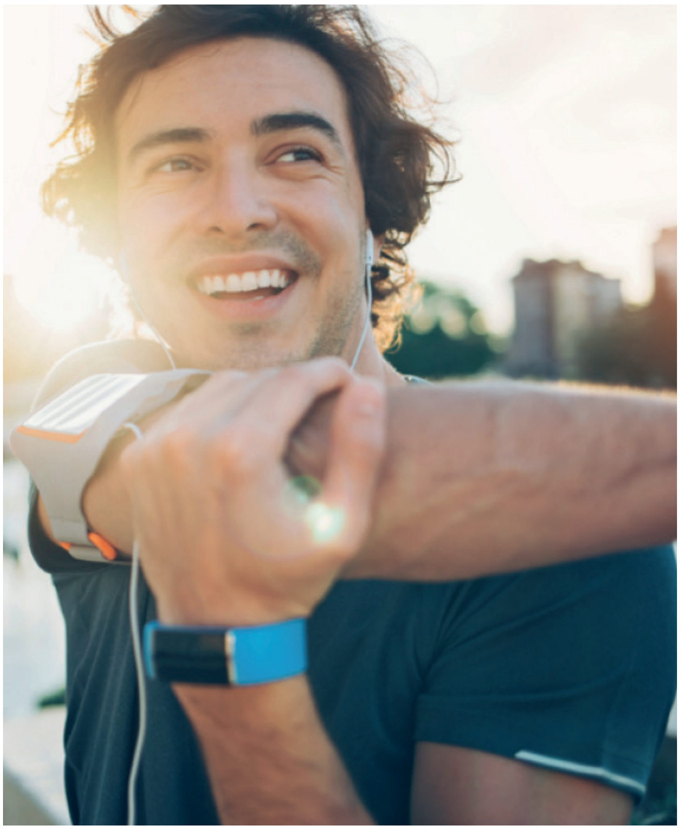
Since vitamin B5 dietary deficiency is practically unknown, little research has been conducted to assess pantothenate status in humans. Nutritional status can be deduced from amounts of pantothenate excreted in urine. Less than 1 mg daily is considered abnormally low and indicates a deficiency in the vitamin. A more thorough, sensitive approach is the determination of pantothenate in serum, or blood, by microbiological methods using Lactobacillus plantarum. New methods, such as HPLC/MS (High Performance Liquid Chromatography/Mass Spectrometry) and immunological methods (radioimmunoassay, ELISA) have also been applied. Furthermore, CoA activity in the blood may be determined to assess the levels of pantothenic acid in the body. Whole blood levels typically range from 0.9 – 1.5 µmol/L.

Stability

Pantothenic acid is stable under neutral conditions but is readily destroyed by heat or in alkaline or acid solutions. Up to 50% may be lost during cooking and up to 80% as a result of food processing and refining (including canning, freezing, milling etc.). Pasteurization of milk only causes minor losses in vitamin B5, however.

Physiological interactions

- Various studies have indicated that vitamin B12 may aid in the conversion of free pantothenic acid into CoA. In the absence of vitamin B12, CoA production is decreased and fat metabolism impaired. In animal experiments, ascorbic acid (vitamin C) was shown to lessen the severity of symptoms due to pantothenic acid deficiency; vitamin A, vitamin B6, folic acid and biotin are also necessary for proper utilization of pantothenic acid. Together with coenzyme-Q10 and L-carnitine, pantothenic acid enables the β-oxidation of fatty acids in the mitochondria.
- Ethanol causes a decrease in the amount of pantothenic acid in tissues, with a resulting increase in serum levels. It has therefore been suggested that pantothenic acid utilization is impaired in alcoholics. Birth control pills containing estrogens and progestin may increase the requirement for pantothenic acid. The most common antagonist of pantothenic acid used experimentally to accelerate the appearance of deficiency symptoms is omega-methyl pantothenic acid. L-pantothenic acid has also been shown to have an antagonistic effect in animal studies. Methyl bromide, a fumigant used to control vermin in places where food is stored, destroys the pantothenic acid in foods exposed to it.



Deficiency

Since pantothenic acid occurs to some extent in all foods, it is generally assumed that dietary deficiency of this vitamin is extremely rare. However, pantothenic acid deficiency in humans is not well documented and probably does not occur in isolation, but in conjunction with deficiencies of other B vitamins. Deficiency symptoms have been produced experimentally by administering the antagonist omega-methyl pantothenic acid in addition to a pantothenic acid-deficient diet. They include fatigue, headaches, insomnia, nausea, abdominal cramps, vomiting and flatulence. The subjects also complained of tingling sensations in the arms and legs, muscle cramps and impaired coordination. There was cardiovascular instability and impaired responses to insulin, histamine and ACTH (a stress hormone). Nearly all symptoms, however, are reversed when pantothenic acid is ingested again. The symptoms are the result of low CoA levels, impaired acetylcholine synthesis and altered carbohydrate and lipid metabolism.

Homopantothenate is a pantothenic acid antagonist that has been used in Japan to enhance mental function, especially in Alzheimer's disease patients. However, a rare side effect of this treatment is abnormal brain function resulting from the failure of the liver to eliminate toxins (hepatic encephalopathy). This condition was reversed by pantothenic acid supplementation, suggesting it was due to pantothenic acid deficiency caused by the antagonist. Interestingly, in experiments with mice it has been shown that a deficiency of pantothenic acid leads to skin irritation and greying of the fur, which were reversed by giving pantothenic acid. Panthenol has since been added to shampoo, although it has never been successful in restoring hair color in humans.

Groups at risk

- Alcoholics
- Individuals with impaired absorption

Recommended daily intakes (RDI) *

Group	Life stage	Dose/day**
Infants	0 – 6 months	1.7 mg
Infants	7 – 12 months	1.8 mg
Children	1 – 13 years	1.8 - 4 mg
Adolescents	14-18 years	5 mg
Adults	19 – 70 years	5 mg
Pregnancy	14 – 50 years	6 mg
Breastfeeding	14 – 50 years	7 mg

** EFSA (2014)*

*** Adequate intake (AI)*

Allowable levels of nutrients vary depending on national regulations and the final application.

Reducing disease risk: therapeutic use

Although isolated deficiency states are rarely observed, several investigators have noted changes in pantothenic acid levels in patients affected by various diseases, and pharmacological amounts of the vitamin are used in the treatment of numerous conditions. In most cases, however, the claimed therapeutic response has not been confirmed by controlled studies in humans.

For the treatment of deficiency due to impaired absorption, intravenous or intramuscular injections of 500 mg are recommended several times a week. Postoperative ileus (paralysis of the intestine) requires doses of up to 1,000 mg every six hours. Panthenol is applied topically to the skin and mucosa to speed up the healing of wounds, (diabetic) ulcers and inflammation, such as cuts and grazes, burns, sunburn, nappy rash, bed sores, laryngitis and bronchitis. In combination, pantothenic acid and ascorbic acid significantly enhance post-surgical therapy and wound healing. The healing process of conjunctiva and the cornea after reconstructive surgery of the epithelium has also been accelerated with vitamin B5 supplementation. Pantothenic acid has also been used, with varying levels of success, to treat multiple liver conditions, arthritis, obesity, acne and constipation in the elderly, to prevent urinary retention after surgery or childbirth, and (together with biotin) to prevent baldness. It has also been reported to have a protective effect against radiation sickness.

Recommended Daily Intake (RDI)

It is widely agreed that there is insufficient information available on which to base an RDI for pantothenic acid. Most countries that make recommendations therefore give an estimate of safe and adequate levels for daily intake. These DRIs are based on estimated dietary intakes in healthy population groups and range from 2 to 14 mg for adults.

Safety

Pantothenic acid is essentially considered to be non-toxic, and no cases of hypervitaminosis have ever been reported. A daily intake of as much as 10 g produces only minor gastrointestinal disturbance (diarrhea) in humans. Pantothenate derivatives are not mutagenic in bacterial tests, however high doses (≤ 10 – 15 g) can cause transient nausea and a lack of fatigue in humans. Due to the lack of human data detailing adverse effects, the main regulatory authorities have not defined a tolerable UL for pantothenic acid.

Supplements and food fortification

Pure pantothenic acid is a viscous hygroscopic oil that is chemically not very stable. Supplements therefore usually contain the calcium salt, or alcohol, panthenol. Both are highly water-soluble and are rapidly converted to the free acid in the body. Calcium pantothenate is often included in multivitamin preparations; panthenol is the more common form used in mono-preparations, which are available in a wide variety of pharmaceutical forms (e.g. solutions for injection and local application, aerosols, tablets, ointments and creams). Pantethine, is an active form that is used as a cholesterol and triglyceride- lowering drug in Europe and Japan and is also available in the US as a dietary supplement. Pantothenate is added to a variety of foods, the most important of which are breakfast cereals and beverages, as well as dietetic and baby foods.

Production

Pantothenic acid is primarily chemically synthesized by condensation of D-pantolactone with β-alanine. Addition of a calcium salt produces colorless crystals of calcium pantothenate, which have 100% purity.

Furthermore, pantothenic acid can be purified through a biotechnological process. Brewer's yeast is considered a low purity natural source.

Panthenol is produced as a clear, almost colorless, viscous hygroscopic liquid.

History

- **1931** Williams and Truesdail separate an acid fraction from 'bios', the growth factor for yeast.
- **1933** Williams and team show this fraction to be a single acid substance essential for the growth of yeast. It is found in a wide range of biological materials, so they suggest calling it 'pantothenic acid'.
- **1938** Williams and colleagues establish the structure of pantothenic acid.
- **1940** Kuhn and his team in Heidelberg, and Karrer and colleagues in Zurich, synthesize pure riboflavin.
- **1947** Lipmann and his group identify pantothenic acid as one of the components of the coenzyme they had discovered in liver two years earlier.
- **1953** The full structure of CoA is elucidated by Baddiley and colleagues. Lipmann receives the Nobel Prize, together with Krebs, for his work on CoA and its role in metabolism.
- **1954** Bean and Hodges report that pantothenic acid is essential in human nutrition. Subsequently, they and their colleagues conduct several further studies to produce deficiency symptoms in healthy humans using the antagonist omega-methyl pantothenic acid.
- **1965** Pugh and Wakil identify the acyl carrier protein as an additional active form of pantothenic acid.
- **1976** Fry and team measure the metabolic response of humans to deprivation.