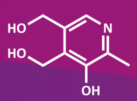
Vitamin B6
(Pyridoxin)

Synonyms:

Vitamin B6 is composed of three forms: pyridoxine or pyridoxol (the alcohol), pyridoxal (the aldehyde) and pyridoxamine (the amine).

Chemistry:

Vitamin B6 is the generic term for all 2-hydroxy 2-methylpyrimidine derivatives exhibiting the biological activity of pyridoxine. Besides the alcohol pyridoxine, these compounds include the aldehyde pyridoxal and the amine pyridoxamine and their respective 5'-phosphates (PLP, PNP, and PMP). All these compounds are nutritionally equivalent and can be metabolically converted to pyridoxalphosphate (PLP) which is the only vitamin B6 compound with known functions as an enzymatic cofactor.



Molecular formula of vitamin B6

Food:

	mg/100g
Brewer's yeast	4.4
Salmon	0.98
Walnuts	0.87
Wheat germ	0.72
Pork liver	0.59
Lentils	0.57
Avocado	0.53
Chicken	0.5
Zucchini	0.46
Bananas	0.36

(Souci, Fachmann, Kraut)

Main functions:

- Neurotransmitter synthesis
- Red blood cell formation
- Niacin formation
- Degradation of homocysteine to cysteine
- Inhibition of steroid hormone signaling
- Support of immune defense

For scientific sources, please contact **info.nutritionscience@dsm.com.**

Vitamin B6 (Pyridoxin)

One of the eight vitamins in the B vitamin group, B6 is essential in helping to convert glycogen into glucose in the body. Glucose is used to produce energy and make neurotransmitters, which carry signals from one nerve cell to the other. Vitamin B6 is also important for enzymes involved in protein metabolism and it helps to produce hormones, red blood cells and cells of the immune system. Studies show that vitamin B6 is especially important in the elderly, as this group often suffers from impaired immune function.

Functions

PLP serves as a coenzyme of more than 60 enzymes that catalyze essential chemical reactions in the human body. It plays an important role in protein, carbohydrate and lipid metabolism. It is involved in the production of serotonin from the amino acid trytophan in the brain and other neurotransmitters, and so it has a role in the regulation of mental processes and mood. Furthermore, it is involved in the conversion of tryptophan to the vitamin niacin, the formation of hemoglobin and the growth of red blood cells, the production of prostaglandins and hydrochloric acid in the gastrointestinal tract, the sodium-potassium balance, and in histamine metabolism. Vitamin B6 also plays a role in the improvement of the immune system.

Dietary sources

Vitamin B6 is widely distributed in foods and is mainly found in bound forms. Pyridoxine is found in plants, whereas pyridoxal and pyridoxamine are principally found in animal tissue, mainly in the form of PLP.

Rich sources of vitamin B6 include chicken and beef, pork and veal liver, fish (salmon, tuna, sardines, halibut, herring), nuts (walnuts, peanuts), brewer's yeast, and wheat germ.

Generally, vegetables and fruits are rather poor sources of vitamin B6, although there are members of these food classes which contain considerable amounts of pyridoxine, such as lentils, zucchinis, avocados and bananas.

Absorption and body stores

All three forms of vitamin B6 (pyridoxine, pyridoxal and pyridoxamine) are readily absorbed in the small intestine by an energy dependent process. They are all converted to pyridoxal phosphate in the liver, a process which requires zinc and riboflavin. The bioavailability of plant-based vitamin B6 varies considerably, ranging from 0% to 80%. Some plants contain pyridoxine glycosides that cannot be hydrolyzed by intestinal enzymes. Although these glycosides may be absorbed, they do not contribute to vitamin activity. The storage capacity of water-soluble vitamins is generally low compared to that of fat-soluble ones. Small quantities of pyridoxine are widely distributed in body tissue, mainly as PLP in the liver and in muscle. PLP is tightly bound to the protein's albumin and hemoglobin in plasma and red blood cells. Because the half-life of pyridoxine is about 25 days and it is not significantly bound to plasma proteins, the limited stores may be depleted within two to six weeks on a pyridoxin-free diet. Excess pyridoxine is primarily excreted in the urine as 4-pyridoxic acid (4-PA) and, to a limited extent, in feces.

Measurement

There are several direct and indirect methods that can be used for assessing an individual's vitamin B6 status. Direct methods include determination of PLP in plasma, and determination of urinary excretion of 4-pyridoxic acid (4-PA). The method of choice for quantification of both compounds is high performance liquid chromatography. Whole blood concentrations usually are 35 – 110 nmol/L PLP. Concentrations of PLP have been found to correlate well with the vitamin B6 deficiency determined by indirect methods. Indirect methods measure the stimulated activity of pyridoxine dependent enzymes in erythrocytes by addition of PLP. This mainly determines the erythrocyte alanine aminotransferase activation coefficient (EAST-AC) or the erythrocyte aspartate aminotransferase activation coefficient. The coefficient of activity with stimulation to activity without stimulation indicates the vitamin B6 status. For EAST-AC, values >1.8 are considered to show deficiency, 1.7 – 1.8 to be marginal, and <1.7 to be adequate. For large-scale population surveys, the tryptophan load test is another method of assessing vitamin B6 deficiency. Vitamin B6 participates in the conversion of tryptophan to the vitamin niacin. A vitamin B6 deficiency blocks this process, producing more xanthurenic acid. If the administration of tryptophan leads to an increased excretion of xanthurenic acid, a vitamin B6 deficiency can be diagnosed.

Stability

Pyridoxine is relatively stable to heat, but pyridoxal and pyridoxamine are not. Pasteurization therefore causes milk to lose up to 20% of its vitamin B6 content. Vitamin B6 is decomposed by oxidation, ultraviolet light and alkaline environments. Because of this light sensitivity, vitamin B6 will disappear (50% within a few hours) from milk kept in glass bottles exposed to the sun or bright daylight. Alkalis, such as baking soda, also destroy pyridoxine. The freezing of vegetables causes a reduction of up to 25%, while milling of cereals leads to wastes as high as 90%. Cooking losses of processed foods may range from a few percent to nearly half the vitamin B6 originally present. Cooking and storage losses are greater with animal products.

Physiological interactions

- Certain vitamins of the B-complex (niacin, riboflavin, biotin) may act synergistically with vitamin B6 derivatives.
- Vitamin B6 additionally requires zinc and magnesium to fulfill its physiological functions.
- There are more than 40 drugs that interfere with vitamin B6 metabolism, potentially causing low status e.g.
  - Phenytoin (an antiepileptic drug)
  - Theophylline (a drug for respiratory diseases)
  - Phenobarbitone (a barbiturate mainly used for its antiepileptic properties)
  - Desoxypyridoxine (a tuberculostatic drug)
  - Hydralazine (an antihypertensive)
  - Cycloserine (an antibiotic)
  - Vitamin B6 reduces the therapeutic effect of levodopa by accelerating its metabolism
  - Levodopa reduces vitamin B6 status as the drug forms a Schiff base complex with PLP

Recommended daily intakes (RDI) *

Group	Life stage	Dose/day**
Infants	<6 months	0.1 mg (AI)
Infants	7 – 12 months	0.3 mg (AI)
Children	1 – 3 years	0.5 mg
Children	4 – 8 years	0.6 mg
Children	9 – 13 years	1.0 mg
Males	14 – 50 years	1.3 mg
Females	14 – 18 years	1.2 mg
Females	19 – 50 years	1.3 mg
Males	>51 years	1.7 mg
Females	>51 years	1.7 mg
Pregnancy	14 – 50 years	1.9 mg
Breastfeeding	14 – 50 years	2.0 mg

** Institute of Medicine (2001)*
*** Adequate intake (AI)*
If not otherwise specified, this table presents RDIs. Allowable levels of nutrients vary depending on national regulations and the final application.

Deficiency

Vitamin B6 deficiency alone is uncommon, because it usually occurs in combination with a deficit in other B-complex vitamins, especially with riboflavin, because riboflavin is needed for the formation of the coenzyme PLP. A recent diet survey revealed that a significant part of the following population groups have B6 intakes below the RDI.

Groups at risk

- The elderly are at risk due to lower food intake, increased B6 catabolism and decreased protein binding capacity
- Pregnant and breastfeeding women (additional demands)
- Women in general, especially those taking oral contraceptives
- Patients on drugs interacting with B-vitamin metabolism
- Underweight people or people who eat poorly, (e.g. people with eating disorders)
- Chronic alcoholics (heavy drinking may severely impair the ability of the liver to synthesize PLP)

Reducing disease risk: therapeutic use

Sideroblastic anemias and pyridoxine- dependent abnormalities of metabolism

Pyridoxine is an approved treatment for sideroblastic anemias and pyridoxine- dependent abnormalities of metabolism. In such cases, therapeutic doses of approximately 40 - 200 mg vitamin B6 per day are indicated. Vitamin B6 deficiency is also associated with hypochromic microcytic anemia.

PMS (premenstrual syndrome)

Some studies suggest that vitamin B6 doses of up to 100 mg/day may be beneficial for relieving the symptoms of premenstrual syndrome.

Hyperemesis gravidarum

Pyridoxine is often administered in doses of up to 40 mg/day in the treatment of nausea and vomiting during pregnancy (hyperemesis gravidarum).

Depression

Pyridoxine is also used to assist in the relief of depression especially in women taking oral contraceptives. However, clinical trials have not yet provided evidence for its efficacy.

Carpal tunnel syndrome

Pyridoxine has been claimed to alleviate the symptoms of carpal tunnel syndrome.

Hyperhomocystinaemia/cardiovascular disease (CVD)

Elevated homocysteine levels in the blood are considered a risk factor for atherosclerotic disease. Several studies have shown that vitamin B6, vitamin B12 and folic acid can lower critical homocysteine levels.

Immune function

The elderly are a group that often suffers from impaired immune function. Adequate B6 intake is therefore important, and it has been shown that the amount of vitamin B6 required to improve the immune system is higher than the current RDI (2.4 mg/day for men; 1.9 mg/day for women).

Asthma

Asthma patients taking vitamin B6 supplements may have fewer, and less severe, attacks of wheezing, coughing and breathing difficulties.

Diabetes

Research has also suggested that certain patients with diabetes mellitus or gestational diabetes experience an improvement in glucose tolerance when given vitamin B6 supplements.

Kidney stones

Glyoxylate can be oxidized to oxalic acid that may then lead to calcium oxalate kidney stones. Pyridoxal phosphate is a cofactor for the degradation of glyoxylate to glycine. There is some evidence that high doses of vitamin B6 (>150 mg/day) may be useful for normalizing the oxalic acid metabolism to reduce the formation of kidney stones. However, the relationship between B6 and kidney stones must be studied further before any definite conclusions can be drawn.

Glutamate sensitivity

People who are sensitive to glutamate, which is often used for the preparation of Asiatic dishes, can react with headache, tachycardia (accelerated heart rate), and nausea. 50 to 100 mg of pyridoxine can then be of therapeutic value.

Autism

High dose therapy with pyridoxine improves the status of autistics in about 30% of cases.

Recommended Daily Intake (RDI)

The recommended daily intake of vitamin B6 varies according to age, sex, risk group (see 'Groups at risk') and criteria applied. Vitamin B6 requirement is increased when high-protein diets are consumed, since protein metabolism can only function properly with the assistance of vitamin B6 derivatives.

Pregnant and breastfeeding women need an additional 0.7 mg to compensate for increased demands made by the fetus or baby.

Safety

Vitamin B6 in all its forms is well tolerated, but large amounts are toxic. Daily oral doses of pyridoxine of up to 50 times the RDI (ca. 100 mg) for periods of 3 – 4 years have been administered without adverse effects. Daily doses of 500 mg and more may cause sensory neuropathy after several years of ingestion, whereas the intake of amounts in excess of 1 gram daily may lead to reversible sensory neuropathy within a few months. Sensory neuropathy has been selected as a critical end-point on which to base a tolerable upper intake level (UL) of 100 mg/day (IOM) for adults, although supplements somewhat higher than this may be safe for most individuals. Fortunately, these side-effects are largely reversible upon cessation of vitamin B6 intake. EFSA (2006) set a UL of 25 mg/day. Today, prolonged intake of doses exceeding 500 mg a day is considered to carry the risk of side-effects.

Supplements and food fortification

The most commonly available form of vitamin B6 is pyridoxine hydrochloride, which is used in food fortification, nutritional supplements and therapeutic products such as capsules, tablets and ampoules. Vitamins, mostly of the B-complex, are widely used in the enrichment of cereals. Dietetic foods such as infant formulas and slimming diets are often fortified with vitamins, including pyridoxine.

History

1926 Goldberger and colleagues feed rats a diet deficient in what is considered to be the pellagra-preventive factor; these animals develop skin lesions.

1934 György first identifies the factor as vitamin B6 or adermin, a substance capable of curing a characteristic skin disease in rats (dermatitis acrodynia). The factor is then called the rat anti-acro-dynia factor, deficiency of which causes so-called 'rat-pellagra'.

1935 Birch and György succeed in differentiating riboflavin and vitamin B6 from the specific pellagra preventive factor (P-P) of Goldberger and his team.

1938 Lepkovsky is the first to report the isolation of pure crystalline vitamin B6. Independently, but slightly later, several other groups of researchers also report the isolation of crystallized vitamin B6 from rice polishing (Keresztesy and Stevens; György; Kuhn and Wendt; Ichiba and Michi).

1939 Harris and Folkers determine the structure of pyridoxine and succeed in synthesizing the vitamin. György proposes the name pyridoxine.

1945 Snell demonstrates that two other natural forms of the vitamin exist, namely pyridoxal and pyridoxamine.

1957 Snyderman determines the levels of vitamin B6 required by humans.