B6 SAP

*Science-based B-complex with a healthy supplemental dose of vitamin B_6.**

Vitamin B_6 is involved in more bodily functions than almost any other single nutrient, with roles in homocysteine metabolism, hemoglobin formation, and neurotransmitter synthesis. It also acts as a potent antioxidant in the body.* **B6 SAP** provides a healthy supplemental dose of vitamin B_6, including 10 mg of the active form pyridoxal-5′-phosphate, in a blend of B vitamins and choline to support optimal B_6 metabolism.*

SUPPLEMENT FACTS

Serving Size: 1 Capsule

	Amount Per Serving	% Daily Value
Thiamin (thiamin hydrochloride)	50 mg	4167%
Vitamin B_2 (riboflavin)	15 mg	1154%
Vitamin B_2 (riboflavin-5′-phosphate)	5 mg	650%
Vitamin B_3 (niacinamide)	80 mg	500%
Vitamin B_6 (pyridoxine hydrochloride)	80 mg	4706%
Vitamin B_6 (pyridoxal-5′-phosphate)	20 mg	1176%
Folate (from calcium L-5-methyltetrahydrofolate)	680 mcg DFE	170%
Vitamin B_{12} (methylcobalamin)	200 mcg	8333%
Biotin	80 mcg	267%
Vitamin B_5 (pantothenic acid) (calcium D-pantothenate)	50 mg	1000%
Choline (Choline bitartrate)	40 mg	7%
Inositol	60 mg	**

**Daily Value not established

Other ingredients: Hypromellose, microcrystalline cellulose, vegetable magnesium stearate, purified water, and silicon dioxide.

This product is non-GMO and vegan friendly.

Contains no: Gluten, soy, wheat, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, or starch.

B6 SAP contains 60 capsules per bottle.

DIRECTIONS FOR USE

Adults: Take 1 capsule daily with a glass of water or juice, or as directed by your healthcare practitioner.

INDICATIONS

B6 SAP:

- Replenishes vitamin B6 stores in individuals taking pharmaceutical agents that deplete this nutrient in the body, including oral contraceptive pills, corticosteroids, theophylline, and isoniazid, and patients undergoing some forms of hemodialysis therapy.*
- Is effective for relief of symptoms associated with premenstrual syndrome as well as nausea and vomiting of pregnancy.*
- May lower blood homocysteine levels and subsequently reduce the risk of cardiovascular disease, strokes, and cancer.*
- May be effective for carpal tunnel syndrome and in the prevention and treatment of colorectal disease.*

FEATURES

B6 SAP provides enzyme forms of vitamins B_2 (riboflavin-5′-phosphate) and B_6 (pyridoxal-5′-phosphate) for direct assimilation into the bloodstream, without having to be processed by the liver.

INCREASED BIOAVAILABILITY

All of the vitamins used in this B_6 formula are USP-compliant.

B6 SAP is supplied in a vegetable capsule for easy digestion and assimilation, as opposed to conventionally compressed tablets.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **B6 SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

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Vitamin B_6 is a highly water-soluble vitamin that is required for the proper functioning of over 140 enzymes involved in amino acid, fatty acid, and homocysteine metabolism, as well as in glycogen degradation, DNA/RNA synthesis, gene expression, and hemoglobin formation.[1, 2] It is required in the synthesis of several neurotransmitters including the conversions of DOPA to dopamine, tryptophan to serotonin, and glutamic acid to γ-aminobutyric acid (GABA).[2, 3] Additionally, B_6 exhibits potent antioxidant activity greater than that of vitamins C and E.[1]

B_6 VITAMERS

B_6 exists as three related pyrimidine vitamer derivates that can be interconverted in the body: pyridoxine (PN), pyridoxamine and pyridoxal, and their phosphate esters.[1] Pyridoxal-5'-phosphate (P5P), the phosphate ester of pyridoxal, is the metabolically active form of B_6 and is considered the most relevant direct measure of B_6 status.[4] Dietary B_6 vitamers are first acted on by intestinal phosphatases and absorbed as PN, pyridoxamine, and pyridoxal, which are then taken up by the liver and phosphorylated by the enzyme pyridoxal kinase to their phosphate esters.[5] Figure 1 illustrates various pathways by which B_6 vitamers are converted into P5P.[5]

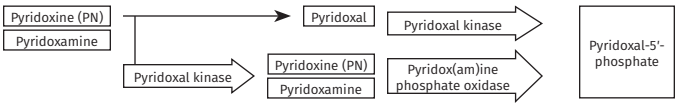

Figure 1: B_6 vitamer metabolism

Supplemental B_6 is typically available as PN hydrochloride and P5P.[4] The benefit of administering P5P is that it does not require processing by the liver for activation, which becomes an important issue in patients with liver disease[4] or a deficiency of the enzymes involved in the conversion pathway.[5]

B_6 DEFICIENCY

Deficiency symptoms of this vitamin are wide-ranging and diverse due to its role in multiple metabolic functions throughout the body, and the fact that B_6 deficiency rarely occurs in isolation from other B-complex vitamins.[2] Causes of deficiency include inadequate dietary intake, absorption disorders, genetic factors, interactions with drugs, or elevated requirements as seen with advancing age, HIV infection, alcohol abuse, celiac disease,[2, 3] and some forms of hemodialysis therapy.[2, 3, 6] Suboptimal levels or mild deficiency may be present for months or years without the appearance of clinical signs and symptoms, which most commonly include hypochromic, microcytic, iron-refractory anemia, and immunosuppression characterized by decreased interleukin (IL)-2 production and depressed lymphocyte production and activity.[2] Deficiency may also produce peripheral neuropathy, which is, ironically, one of the main symptoms associated with B_6 toxicity.[21]

In addition, four inborn errors of B_6 metabolism have been identified that cause early-onset, drug-refractory, convulsive seizures,[5] possibly due to decreased GABA synthesis.[3] Three of these conditions respond to supplementation of B_6 in any form, but patients suffering from a deficiency in the enzyme pyridox(am)ine phosphate oxidase require P5P specifically.[5]

B_6 DEPLETION BY PHARMACOLOGICAL AGENTS

Several drugs have been shown to deplete B_6 levels in the body, including oral contraceptive pills, theophylline and its derivatives (for respiratory disorders), isoniazid (for tuberculosis), penicillamine, hydralazine (a vasodilator), L-DOPA, corticosteroid medications, and some diuretics.[2, 7]

Oral Contraceptive Pills (OCPs)

Oral birth control has been in use in North America since the 1960s. Numerous studies from the 1970s and 1980s have documented impairments in B_6 status in women taking oral estro-progestational hormones,[7] and ethinylestradiol has been shown to interfere with B_6 metabolism by causing increased P5P retention in the tissues.[2] Consequent disturbances in tryptophan metabolism as a result of B_6 deficiency leads to symptoms of depression, anxiety, decreased libido, and altered glucose balance in some women.[7] Supplementation with 40 mg/d B_6 has been shown to restore normal blood levels and reverse clinical symptoms in deficient OCP users.[7] Research on more current OCP preparations is required.

To examine whether perturbances in B_6 metabolism occur shortly after initiation of OCP use, 23 young women who had never taken OCP before were given a low dose (30 mcg) ethinyl estradiol-containing Triphasil preparation and followed for 6 menstrual cycles.[8] While plasma and erythrocyte B_6 levels were not affected in the majority of patients with adequate dietary intake, P5P metabolism was found to be altered.[8]

Theophylline, Aminophylline

Theophylline and its derivatives depress plasma P5P levels; intoxification with these drugs, which may occur from acute or chronic overdose, has been known to cause drug-refractory seizures that improve with PN supplementation.[3]

Hydrazines: Hydralazine and Isoniazid

Hydralazine, a vasodilator, and isoniazid, a tuberculosis drug, are both derivatives of hydrazine, a compound that reacts with P5P and blocks its action.[2, 9] Side effects of isoniazid-induced B_6 deficiency, most commonly peripheral neuropathy, can be prevented by supplementing PN at a daily dose of 50–100 mg/d.[9, 10]

Penicillamine

Incidence of PN deficiency has dropped since the more recent use of D-penicillamine; however, it is still common practice to supplement 25 mg PN/d when using penicillamine in the treatment of Wilson's disease.[5]

THE ROLE OF B_6 IN ONE-CARBON (METHYL) METABOLISM

One-carbon metabolism, also known as the remethylation pathway, is a chain of biochemical reactions involving the transfer of one-carbon groups from one compound to another that is crucial for the synthesis of nucleic acids and methionine, and for the breakdown of homocysteine.[11]

Several B vitamins, including folate, B_6, and B_{12} are necessary coenzymes in this pathway, and methionine and choline appear as intermediary compounds.[11] Even modest dietary inadequacies of these nutrients have been implicated as contributing to diseases such as neural tube defects, cardiovascular disease, and cancer that may occur in the absence of clinical deficiency.[11]

Homocysteine

Disruptions in one-carbon metabolism may also lead to elevated levels of homocysteine (Hcy), a sulfur amino acid that has been linked with increased risk of cardiovascular disease, cognitive impairment, and cancer.[2, 11] A recent systematic review and meta-analysis quantified the relationship between Hcy and coronary heart disease (CHD), stating that for each increase of 5 µmol/L Hcy, the risk of CHD events rises by approximately 20% independently of traditional CHD risk factors.[12]

Hcy levels have also been directly associated with acute cerebrovascular disease through observational studies.[13] The Heart Outcomes Prevention Evaluation 2 (HOPE 2) study was a randomized, masked, placebo-controlled trial with 5522 subjects with a history of various Hcy-related conditions including coronary, cerebrovascular, and peripheral arterial diseases.[13] Supplementation with folic acid (2.5 mg/d), B_6 (50 mg/d), and B_{12} (1 mg/d) over a period of 5 years resulted in a 25% reduction in total stroke incidence, although stroke severity and subsequent disability were not altered.[13]

B_6 SUPPLEMENTATION IN HEALTH AND DISEASE

Premenstrual syndrome

Premenstrual syndrome (PMS) encompasses a range of physical, psychological, and emotional symptoms that occur during the luteal phase of the menstrual cycle, and are relieved at the onset of, or during, menstruation.[14] Approximately 95% of women of reproductive age experience some form of this condition, with 5% of these individuals suffering from severe, debilitating symptoms that interfere with daily life.[14]

Early research on the use of B_6 for the treatment of PMS was conflicted, mainly confounded by poor study design and low subject number;[14, 15] however, the majority of trials show benefit, and B_6 supplementation is an accepted treatment for PMS in Europe.[15] A 2007 placebo-controlled study of 60 PMS patients aged 20–45 years compared supplementation with 100 mg PN 2×/day v. 2.5 mg bromocriptine 2×/d.[16] After three months of treatment, significant improvement was seen in both intervention groups, with B_6 subjects exhibiting greater benefit and lesser incidence of side effects than those taking bromocriptine.[16]

Nausea and Vomiting of Pregnancy

Nausea in early pregnancy is so common that it is often the first sign that alerts a woman that she is pregnant.[17] Approximately 70–85% of women experience nausea, half of whom also suffer from vomiting episodes, which causes severe discomfort and may result in malnutrition.[18] Despite extensive research, the etiology of this condition remains unknown.[17, 18]

PN has been an empirical treatment for pregnancy-related nausea and vomiting for more than 40 years, which has led to its inclusion as one of only two ingredients in the pharmaceutical formula Diclectin (aka. Bendectin, Debendox).[17] Clinical trials examining the use of B_6 supplementation on its own have yielded positive results, most of which show beneficial effects to occur within a very short time period.[17, 18] In a placebo-controlled randomized double-blind study, 336 women at ≤ 17 weeks gestation suffering from nausea with or without vomiting were supplemented with PN hydrochloride at a dose of 30 mg/d for five days.[17] Although significant improvement was seen in nausea over the treatment period, significant reduction in vomiting episodes occurred only within the first three days, with effect diminishing towards the end of the supplementation period.[17] The authors speculated that this may be related to the tendency for the condition to fluctuate over time and advise intermittent treatment for 2–3 days at a time.[17]

Colorectal Disease

One-carbon metabolism is directly involved in nucleotide synthesis and DNA methylation, two processes that, if altered, may initiate carcinogenesis.[19] The roles of folate, B_6 and B_{12} in one-carbon metabolism, along with previous research demonstrating that B_6 suppresses nitric oxide, and has antiproliferative, antioxidant, and anti-angiogenic properties, has led to exploration of the potential of these B-vitamins in cancer prevention and treatment.[19]

The Nurses' Health Study, a prospective nested case-control study that began in 1976 with over 100,000 nurses, was conducted to establish the link between nutrition and colorectal disease.[19] Higher intakes of folate and vitamins B_6 and B_{12} were associated with lower Hcy levels and reduced incidence of colorectal cancer and colorectal adenoma.[19] Plasma P5P status exhibited a significant negative correlation with risk of distal colorectal adenoma independently of folate status. This effect pertained in particular to the advanced stage of the disease, suggesting that B_6 may attenuate the progression of adenoma to early cancer, possibly via its role in one-carbon metabolism.[19]

Carpal Tunnel Syndrome

Carpal tunnel syndrome (CTS) is a common condition believed to be caused by compression of the median nerve as it passes through the carpal tunnel.[20] Vitamin B_6 is a critical cofactor in the synthesis of neuronal proteins, and is involved in numerous other pathways that affect peripheral nerve function, including neurotransmitter synthesis, amino acid metabolism, and sphingolipid biosynthesis and degradation.[20] It also has the ability to act as an analgesic, possibly by up-regulating GABA and serotonin synthesis.[20] Though higher quality studies are required, the literature shows symptomatic relief for some people at doses of up to 200 mg/d, and this recommendation is reasonable, especially given the low potential for toxicity with this intervention.[20] Whether the mechanism lies in correction of B_6 deficiency-induced peripheral neuropathy, or by raising an individual's pain threshold is unclear.[20] A recent article instructing healthcare practitioners on the use of this treatment in clinical practice recommends a gradual tapering of the dose after 3 months for patients who experience an improvement in their symptoms.[21]

B_6 TOXICITY AND DOSING GUIDELINES

No negative reactions resulting from high B_6 intake from food sources have been reported,[2] but both acute toxicity and the delayed adverse effects of PN taken in supplemental form have been documented.[3] Very high single doses of 2–6 g induce peripheral neuropathy, ataxia, incoordination, seizures, and are lethal in animal models.[3] Additionally, excessive chronic administration (200–6000 mg/d) over months or years may result in the development of a peripheral sensory neuropathy associated with bilateral paraesthesia, hyperaesthesia, limb pains, ataxia, and incoordination,[5, 7] as well as seborrheic dermatitis, stomatitis, glossitis, cheilosis, depression, and irritability.[7] No motor deficit or CNS involvement is usually observed, and symptoms typically resolve within six months of PN withdrawal.[3] It should be noted that the Institute of Medicine has set the upper tolerable limit at 100 mg/d,[7] and studies using doses of up to 200 mg/d report efficacy with minimal to no cases of adverse effects.[14, 15] Furthermore, the lack of a dose-response relationship has been documented at high levels of supplementation.[14, 15]

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