

P-5-P – Pyridoxal 5 Phosphate



Active vitamin B6 for supporting neurotransmitter synthesis and healthy metabolism

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Vitamin B6 is found in three forms – pyridoxine hydrochloride, pyridoxal, and pyridoxamine – all of which must be converted into activated pyridoxal-5-phosphate (P-5-P) by the liver.^{1,2} P-5-P is the form of vitamin B6 the body ultimately uses. It is an essential cofactor for over 100 enzymes, mostly related to protein and amino acid metabolism, including the synthesis of select neurotransmitters.³ It is also critical for heme production, as well as carbohydrate metabolism and fatty acid synthesis.

P-5-P is recommended for people whose ability to convert the other forms of vitamin B6 into this active coenzyme is impaired, as seen in the elderly, children on the autism spectrum, those with impaired liver function, and those with celiac disease or other conditions that interfere with nutrient absorption. It may also be useful for people with conditions that respond to higher doses and better absorption of B6, such as:

- Carpal tunnel syndrome
- Peripheral neuropathies
- PMS (including water retention)
- Morning sickness
- High homocysteine levels
- Gestational and type 2 diabetes
- Depression/Anxiety
- Fatigue

Vitamin B6 is widely available in foods, but certain metabolic states and commonly prescribed pharmaceutical drugs may interfere with its absorption and/or induce a need for increased intake above that typically obtained through the diet. Oral contraceptives and chronic use of NSAIDs can interfere with absorption of B6.^{4,5} (Many oral contraceptives carry with them increased risk for venous thromboembolism, and the reduced B6 levels may be a contributing factor.^{4,6}) Moreover, celiac disease, increased small intestinal permeability (“leaky gut”) and other conditions that interfere with nutrient absorption may increase the need for B6.³

Neurotransmitter Synthesis

P-5-P is a required cofactor for the aromatic L-amino acid decarboxylase enzyme (AADC), which catalyzes the conversion of 5-HTP to serotonin, and L-Dopa to dopamine. Low B6 status may be why some individuals do not experience any benefit upon supplementation with L-tryptophan or 5-HTP. Serotonin is widely regarded for its role in supporting a positive mental outlook; marginal B6 status is associated with depressive symptoms in older adults.⁷

The GABA/glutamate cycle is another neurotransmitter system that requires P-5-P. The vitamin is a cofactor for glutamate decarboxylase, the enzyme that converts glutamate to GABA, as well as for GABA transaminase, which catabolizes GABA to regenerate glutamate.³ Additionally, P-5-P functions as a coenzyme of 5-aminolevulinic acid synthase, which is involved in the synthesis of heme, the iron-carrying component of hemoglobin.^{8,9} Considering the critical role of hemoglobin in transporting oxygen, combined with the function of P-5-P in neurotransmitter synthesis, it is not surprising that B6 insufficiency is associated with depression and fatigue. Low serum levels of B6 and iron are also associated with panic attacks and hyperventilation severe enough to require hospital visits.¹⁰

Carbohydrate Metabolism & Fatty Acid Synthesis

B6 is required for gluconeogenesis and glycogenolysis, two processes that are essential for maintaining steady blood glucose and energy levels. P-5-P is a coenzyme for glycogen phosphorylase, the enzyme that catalyzes the cleavage of glucose-1-phosphate molecules from stored glycogen in the liver and muscle tissue.¹¹ For this reason, much of the P-5-P in the human body is found in muscle bound to glycogen phosphorylase. P-5-P is also a coenzyme for some of the enzymes of gluconeogenesis, whereby amino acids are converted into glucose. Transaminase enzymes all require P-5-P as a cofactor; reactions catalyzed by transaminases include amino acid-interconversion and transforming amino acids into substrates for gluconeogenesis or intermediates of the ATP-producing citric acid cycle. Because of its association with muscle glycogen phosphorylase, B6 occurs mostly as the active P-5-P form in meat (including poultry and fish), while plant foods contain B6 mostly as pyridoxine.³

The role of B6 in both neurotransmitter synthesis and blood glucose regulation may be a link between depression and type 2 diabetes. Inflammation and other physiological stressors may upregulate the conversion of tryptophan into kynurenine (KYN), a substrate for biosynthesis of NAD. B6 is a cofactor for key enzymes of the KYN/NAD pathway, and insufficiency shunts KYN metabolism away from NAD production and towards synthesis of xanthurenic acid (XA) and kynurenic (KYNA) acid. These substances and their metabolites interfere with the production, release and physiological activity of insulin, leading researchers to propose that upregulation of these pathways due to vitamin B6 deficiency may underlie an association between diabetes and depression.¹² Studies in rats also support a role for B6 in healthy pancreatic function.¹³

B6 insufficiency may interfere with elongation of highly unsaturated fatty acids from their omega-6 and omega-3 precursors, as one of the enzymes involved in this process—delta-6-desaturase—requires B6. Animal studies suggest the greatest reduction is in DHA, which could have profound implications for brain health.¹⁴ B6 insufficiency may also elevate the n-6:n-3 ratio, which may be a contributing factor to cardiovascular disease risk and overall inflammation.¹⁵

Additional Roles for Vitamin B6

In addition to its roles in macronutrient metabolism and neurotransmitter synthesis, studies support a beneficial role for active B6 in a wide array of other health concerns:

- **Carpal Tunnel Syndrome (CTS):** Study results are mixed, but the preponderance of evidence suggests that supplemental B6 helps reduce CTS symptoms of pain, numbness, tingling and hand weakness, and may even obviate the need for surgery.^{16,17} Low plasma P-5-P levels are also associated with severity of rheumatoid arthritis, which may reflect an increased need for this vitamin in inflammatory states.¹⁸ (Note, however, that reduced plasma P-5-P levels may not reflect whole-body status, since muscle tissue is the main store of the vitamin.)
- **Premenstrual Syndrome (PMS):** Supplemental B6 may be helpful for alleviating the psychological and somatic symptoms of PMS.¹⁹ Symptom reduction is typically largest for depression and anxiety, likely owing to the role of B6 in neurotransmitter synthesis, but B6 may also reduce water retention and somatic symptoms, such as headache, low back pain, and breast tenderness. In a study looking at supplemental magnesium and B6 for the reduction of PMS severity, magnesium resulted in statistically significant improvement compared to placebo, but the combination of B6 with magnesium led to even greater improvements.²⁰
- **Morning Sickness:** B6 may be effective for reducing the nausea and vomiting some women experience during the early part of pregnancy. Compared to placebo, supplemental B6 reduced nausea significantly, with a more moderate reduction in episodes of vomiting.^{21,22} While much of the research on B6 and morning sickness employs pyridoxine, researchers speculate that P-5-P is likely the active antiemetic form of the vitamin.²³
- **Elevated Homocysteine:** P-5-P plays critical roles in one-carbon metabolism for methylation, activation of folate, and nucleic acid synthesis.²⁴ As P-5-P is required for the transsulfuration of homocysteine to cysteine, B6 deficiency can lead to elevated blood levels of homocysteine. Elevated homocysteine may be irritating to the blood vessel endothelium, potentially facilitating development of atherosclerosis and cardiovascular disease. Optimizing levels of B6 and other nutrients involved in these mechanisms can help reduce homocysteine levels.²⁵ Research indicates that in some patients, B vitamin insufficiency may be the primary cause of elevated homocysteine.²⁶

Supplement Facts

Serving Size 1 capsule

Amount Per Serving	% Daily Value	
Vitamin B-6 (Pyridoxal-5-Phosphate)	50 mg	2500%

Other Ingredients: Microcrystalline cellulose, cellulose (capsule), vegetable stearate.



Recommended Use:

- As a dietary supplement, take one capsule per day, or as directed by a health care practitioner.

For a list of references cited in this document, please visit:

<http://catalog.designsforhealth.com/assets/itemresources/P-5-PReferences.pdf>

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