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Non-nutritional uses of vitamin B₆

David A. Bender

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exclusive), it is likely that vitamin B₆ deficiency will result in increased end-organ responsiveness to glucocorticoids, mineralocorticoids and aldosterone; over-secretion of (and presumably also enhanced sensitivity to) any of these hormones can result in hypertension. Vitamin B₆ supplementation would be expected to reduce end-organ sensitivity to these hormones, and thus might have a hypotensive action. Fregly & Cade (1995) showed that supplements of 300 mg vitamin B₆/kg body weight per d attenuated the hypertensive response of rats treated with deoxycorticosterone acetate. At a more realistic level of supplementation (five times the usual amount provided in the diet), Lal *et al.* (1996) showed that vitamin B₆ prevented the development of hypertension in the Zucker (*fa/fa*) obese rat. Withdrawal of the vitamin supplement led to the development of hypertension. Ayback *et al.* (1995) showed that supplements of 5 mg/kg body weight per d led to reduced blood pressure in patients with essential hypertension.

Drug interactions with vitamin B₆

The antituberculosis drug isoniazid (*iso*-nicotinic acid hydrazide) reacts non-enzymatically with PLP to form a metabolically inactive hydrazone, resulting in functional vitamin B₆ deficiency (Vilter, 1964; Standal *et al.* 1974).

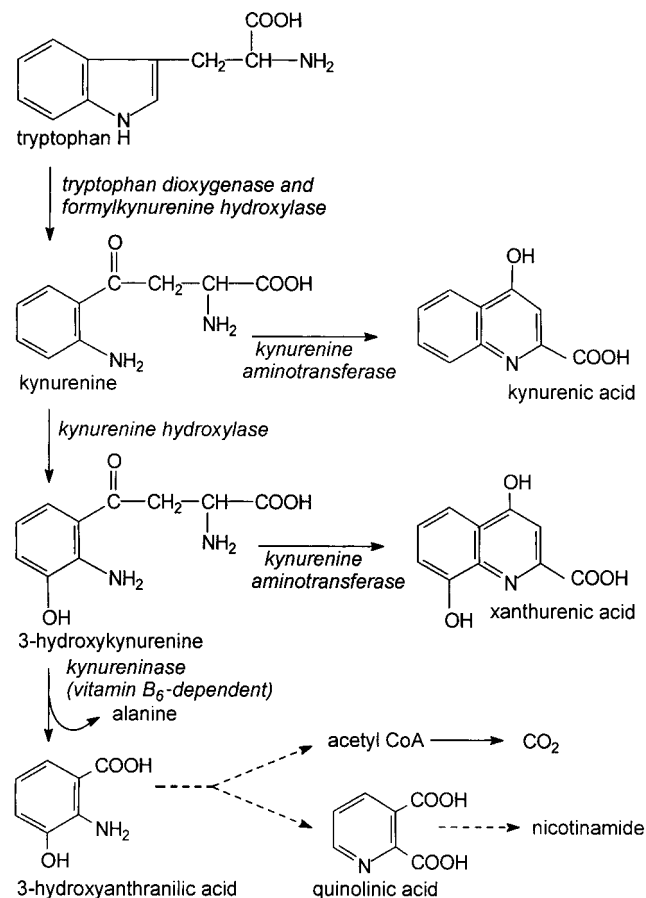


Fig. 2. Tryptophan metabolism. Tryptophan dioxygenase, EC 1.13.11.11; formylkynurenine formamidase, EC 3.5.1.9; kynurenine hydroxylase, EC 1.14.13.9; kynureninase, EC 3.7.1.3; kynurenine aminotransferase, EC 2.6.1.7 and EC 2.6.1.63.

This is most commonly seen as secondary pellagra, due to impaired activity of kynureninase (see Fig. 2), and hence impaired synthesis of nicotinamide nucleotides from tryptophan. The pellagra responds to supplements of vitamin B₆ (Biehl & Vilter, 1954). Isoniazid also leads to the development of peripheral neuropathy, which also responds to vitamin B₆ supplements (Gammon *et al.* 1953). This has led to the belief that vitamin B₆ deficiency causes peripheral neuropathy (Jones & Jones, 1963), although there is no evidence of this. The neuropathy seems to be an effect of isoniazid intoxication; the response to vitamin B₆ is the result of removing isoniazid as the pyridoxal adduct, rather than repleting vitamin B₆-deficient tissues (Snider, 1980). When relatively high doses of isoniazid were used to treat tuberculosis, it was common to give vitamin B₆ supplements; this had no effect on the therapeutic action of the drug, but did prevent the peripheral neuropathy and secondary pellagra (Biehl & Vilter, 1954). When lower doses of isoniazid were introduced, in a therapeutic cocktail with other medication, vitamin B₆ supplementation became less usual. However, cases of isoniazid-induced pellagra have been reported among people taking low doses of isoniazid; it is likely that many of those affected were genetically slow acetylators of isoniazid, so that a low dose was, for them, equivalent to a higher dose for a fast acetylator (Bender & Russell-Jones, 1979). There have been a number of reports of successful treatment of acute isoniazid intoxication with vitamin B₆ supplements (Brent *et al.* 1990; Alvarez & Guntapalli, 1995; Shah *et al.* 1995).

Other hydrazine derivatives can also cause vitamin B₆ depletion by forming hydrazones, leading to the development of secondary pellagra; these include the anti-Parkinsonian drugs Benserazide and Carbidopa (Bender *et al.* 1979; Bender, 1980a,b).

When dopa was first introduced for the treatment of Parkinsonism, one of the most frequent side-effects was persistent nausea and vomiting. Because of the (slight) evidence that vitamin B₆ has an anti-emetic and anti-nauseant action, supplements were given together with dopa. The result was a considerable reduction in the efficacy of dopa in controlling Parkinsonian signs and symptoms; the magnitude of the effect was related to the dose of pyridoxine given (Hunter *et al.* 1970). The problem was due to the formation of a stable tetrahydroisoquinoline adduct between PLP and dopa (Evered, 1971) which not only reduced the concentration of dopa available for uptake into the brain, but also acted as an inhibitor of aromatic amino acid decarboxylase (Fellman & Roth, 1971).

Theophylline therapy for asthma can cause seizures, apparently as a result of reaction with PLP, leading to low plasma concentrations, and hence reduced synthesis of γ -aminobutyric acid in the central nervous system. Glenn *et al.* (1995) showed that the administration of vitamin B₆ to mice treated with theophylline reduced the number of seizures; in rabbits, vitamin B₆ reversed the changes in electroencephalogram caused by high doses of theophylline.

High doses of vitamin B₆ may lower blood concentrations of anticonvulsant medication such as phenytoin and phenobarbitone, apparently by increasing the rate of metabolism of the drugs (Hansson & Sillanpaa, 1976).