Beyond energy boosts: a clinical review of the vitamin B complex and associated supplementation

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Abstract

The vitamin B complex is a group of water-soluble vitamins composed of eight B vitamins: thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B7), folate/folic acid (B9) and cobalamin (B12). Vitamins are crucial for optimal physiological functions, and thus adequate amounts of vitamins need to be supplied through the diet since they are not synthesised endogenously by the human body. Vitamin B deficiency may occur for a variety of reasons, and depending on the specific vitamin and its functions, symptoms may vary. Due to potential deficiencies, vitamin B supplements are considered to mitigate these effects. Available vitamin B supplementation ranges from Schedule 0 (over-the-counter) to Schedule 4 (scheduled preparations), in various formulations and routes of administration, however, specific dosages need to be considered to prevent toxicity. Vitamin B supplements are not only used for direct supplementation but also to support the function of pharmacotherapy or mitigate adverse drug reactions. This review provides a broad overview of the vitamin B complex, particularly its deficiencies, indications for supplementation, available supplements and potential drug-vitamin interactions.

Keywords: biotin, cobalamin, folate, niacin, pantothenic acid, pyridoxine, riboflavin, thiamine, vitamin B complex, vitamin B deficiency

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Introduction

Vitamins are a group of essential organic micronutrients, either water- or fat-soluble, required for normal physiological functioning but are not synthesised endogenously by the human body.[1] Instead, vitamins are synthesised by bacteria, yeasts, and plants.[2] As a result, adequate amounts of vitamins need to be supplied through the diet.[3] In total, an individual requires thirteen vitamins: four fat-soluble vitamins (A, D, E, K) and nine water-soluble vitamins, which comprise vitamin C (ascorbic acid) and eight B vitamins: thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B7), folate/folic acid (B9) and cobalamin (B12).[1,3] Together, these B vitamins are collectively referred to as the B-group or 'vitamin B complex'.[4] This review provides a broad overview of the vitamin B complex, particularly its deficiencies, indications for supplementation, formulations, over-the-counter and scheduled preparations and potential drug-vitamin interactions.

The diversity of the vitamin B complex

Common features

The vitamin B complex is a group of water-soluble vitamins, which, given their solubility, are typically absorbed via carrier-facilitated transporters from the gastrointestinal tract, and undergo renal excretion.[5,6] Given its hydrophilicity and general low storage capacity, toxicity is typically low.[5,6]

Loss of the vitamin B complex from food products generally occurs due to processing, such as milling and refinement of plant sources (where vitamins are typically lost due to separation of the bran and germ), heating (particularly for thermolabile vitamins), or loss through leaching into water (e.g., through washing grains or distribution into cooking fluids which are often discarded).[5,6] Cooking fluids, such as gravy or soup made from animal products, help retain such vitamins that are lost.[5] South African regulations mandate the fortification of certain food products (e.g., wheat flour, maize meal) with several vitamins, including thiamine (as mononitrate), riboflavin, nicotinamide or niacinamide, pyridoxine (as hydrochloride), and folic acid, due to their importance and the losses often seen during processing.

Vitamin B sources

Vitamins are crucial for optimal physiological functions, and thus, the diet needs to be maintained appropriately to facilitate sufficient vitamin B complex levels (Table I), given the intricate convergent and divergent pathways that support healthy physiological functioning.[7]

Functions

The vitamin B complex serves as an essential cofactor in various enzymatic processes[12] that support cellular and physiological functioning.[9] Depending on the vitamin, supportive functions are diverse: major functions within the brain and nervous system,[12] the metabolism of carbohydrates, amino acids, fatty acids, and lipids, the synthesis of proteins, cholesterol, neurotransmitters, S-adenosyl methionine, and nucleotide bases,[13] immunological functions,[14] and mitigating or preventing various diseases, such as cardiovascular disease, neurodegenerative disorders, and neural tube defects.[12] Broad functions for each vitamin are provided in Table II.

Table I: Vitamin B types, dietary sources and recommended dietary allowance (RDA) values of vitamin B complex for males, non-pregnant females and pregnant females[8,9]

Type of vitamin B	Dietary sources	Recommended dietary allowance* (RDA)		
		Male	Non-pregnant female	Pregnant female
Thiamine (B1)	Whole grains, nuts,[6] pork, chicken, eggs, cereal sprouts, rice, bran and beans[2]	1.2 mg	1.1 mg	1.4 mg
Riboflavin (B2)	Leafy green vegetables, liver, eggs,[2] milk and dairy products, mushrooms and legumes[1]	1.3 mg	1.1 mg	1.4 mg
Niacin (B3)	Fish, meat, beans[2,6] and whole grains[10]	16 mg	14 mg	18 mg
Pantothenic acid (B5)	Nuts, mushrooms, whole grains, legumes, potatoes, tomatoes, yeast, meat, liver, eggs and milk[6]	5 mg	5 mg	6 mg
Pyridoxine (B6)	Whole grains, bananas, nuts, pork, poultry, fish, beef and organs[5]	1-1.7 mg	1-1.7 mg	1.9 mg
Biotin (B7)	Egg yolk, milk and dairy products, nuts, legumes, meat, certain vegetables and fruits[5]	30 µg	30 µg	30 µg
Folate/folic acid (B9)	Leafy green vegetables, legumes, citrus fruits, fortified cereals, avocado and liver[10]	400 µg	400 µg	600 µg
Cobalamin (B12)	Meat, liver, fish, shellfish and dairy products[11]	2.4 µg	2.4 µg	2.6 µg

*RDA values are referred to the daily required amounts adapted from the Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes

Vitamin B deficiencies

Vitamin B deficiency may occur due to a variety of reasons, including malnutrition, malabsorption, alcoholism, genetic conditions, diseases, drug-nutrient interactions, and food processing.[5,6,21,22] For instance, diseases such as Crohn's disease, celiac disease, human immunodeficiency virus (HIV), and alcohol-use disorder may interfere with the body's ability to absorb B vitamins effectively.[23] Overall vitamin B deficiency leads to anaemia, digestive issues, skin conditions, infections, peripheral neuropathy, and psychiatric disorders,[24] however, depending on their functions and frequency of loss, unique symptoms may occur.

Given potential deficiencies, individuals may consider vitamin B supplements to mitigate these effects, either as over-the-counter or scheduled preparations (Table III). For instance, thiamine, riboflavin, pyridoxine and cobalamin are mainly involved in energy metabolism and are commonly used as dietary supplements.[21] A 2023 randomised double-blind trial found that supplementation with these B vitamins for 28 consecutive days significantly ($p < 0.05$) improved exercise endurance and reduced exercise fatigue in healthy, non-athletic adults at appropriate doses.[7] Another randomised controlled trial showed that 12 weeks of supplementation with oral thiamine, pyridoxine and cobalamin significantly decreased homocysteine levels in paediatric patients compared with baseline and placebo ($p < 0.001$)[25] as a result of homocysteine accumulation with cobalamin deficiency due to poor metabolism.[10] Furthermore, there was improved glycaemic control and renal function through lower homocysteine levels and could be a safe and effective strategy for treatment of early stage nephropathy in paediatric type 1 diabetes mellitus.[25] As such, a clear evidence-based approach can be applied in many vitamin B deficiencies.

Vitamin B-related pharmacotherapy

Examples of vitamin B supplementation is provided in Table III, with unique functions highlighted in Table II, which highlights its use not only for direct vitamin supplementation, but also to support the function of pharmacotherapy or mitigate adverse drug reactions. This includes iron and folic acid supplementation during pregnancy to improve maternal and neonatal outcomes including a reduction in low birth weight and preterm birth.[26] Additionally, the use of vitamins in tuberculosis (TB) patients are encouraged.[27] The World Health Organization (WHO) recommends pyridoxine when receiving high-dose isoniazid to patients with diabetes, uraemia, HIV infection, seizure disorders, alcohol abuse, malnutrition or peripheral neuropathy.[27]

Thiamine (B1)

Thiamine can be found in several dietary sources as its primarily phosphorylated form, including a range of plant- and animal-based foods.[2,6] Absorption is via carrier-mediated active transport, however, passive diffusion may occur at higher concentrations.[6] Anti-thiamine factors, which reduce the absorption of thiamine, are present as thermolabile and thermostable compounds in various food products, such as fermented fish, shellfish, and methylxanthine-containing teas and coffees.[6] Thermolabile factors can be deactivated by heating, but use of protective factors (such as ascorbic acid) or increasing the frequency between eating thiamine and anti-thiamine factors.[6]

Thiamine deficiency in the human diet leads to disturbances in numerous biochemical and metabolic processes, including impaired glucose metabolism, disrupted bioenergetic processes, mitochondrial dysfunction, lactic acidosis which is a consequence of pyruvate dehydrogenase (PDH) dysfunction in mitochondria.[28] Furthermore, it results in insufficient DNA synthesis due to reduced transketolase activity and ribose-5-phosphate synthesis in the pentose phosphate pathway as well as impaired neurotransmitter synthesis.[28]Although thiamine deficiency is rare in developed countries, it can occur as a result of poor dietary choices, certain medical conditions or intake of anti-thiamine elements.[10] Deficiency causes lethargy and, if left untreated, manifests in

Table II: Functions, regulatory health claims and dosage recommendations for vitamin B complex[15]

Vitamin B	Functions	Health supplement claim[a]		Recommended dose (Children)		Recommended dose (Adults)	
		Single substance products[b]	Multiple substance products[c]	Minimum	Maximum	Minimum	Maximum
Thiamine (B1) **To be calculated as thiamine*** i. Thiamine hydrochloride ii. Thiamine monochloride iii. Thiamine mononitrate iv. Thiamine monophos-phate v. Thiamine diphosphate vi. Thiamine pyrophos-phate	• Cofactor in carbohy-drate metabolism[6] • Amino and fatty acid hydrolysis[10] • Nervous system function (lipid, myelin, neurotransmitter and nucleic acid precursor synthesis)[6]	• Carbohydrate, protein and lipid metabolism • Energy production and metabolic processes • Nervous system and psychological function • Cardiac function • Growth and development • Maintenance of good health	• Carbohydrate, protein and lipid metabolism • Growth and development • Maintenance of good health • Multi-vitamin supplement/ Multi-vitamin/ mineral supplement	**1 to 13 years** 0.04 mg	≤ 100 mg	0.07 mg	≤ 100 mg
				14 to 18 years 0.07 mg	≤ 100 mg		
Riboflavin (B2) **To be calculated as riboflavin*** i. Riboflavin 5'-phosphate, sodium	• Enzymatic cofactor (flavin adenine mononucleotide [FMN], or flavin adenine dinucleotide [FAD])[6] • Carbohy-drate, protein and fat metabo-lism[10] • Niacin, folic acid, pyridoxine, and haem protein synthesis[9] • Maintenance of healthy skin, eyes, and nerve functions[10]	• Carbohydrate, protein and lipid metabolism • Energy production and metabolic processes • Nervous system functioning • Mucous membranes maintenance • Skin maintenance • Vision maintenance • Iron metabolism • Cell protection from oxidative stress • Tiredness and fatigue reduction • Tissue formation • Maintenance of good health	• Carbohydrate, protein and lipid metabolism • Tissue formation • Maintenance of good health • Multi-vitamin supplement/ Multi-vitamin/mineral supplement	**1 to 13 years** 0.04 mg	≤ 100 mg	0.08 mg	≤ 100 mg
				14 to 18 years 0.08 g	≤ 100 mg		
Nicotinic acid, Niacin and derivatives (B3) **To be calculated as niacin*,[d]** i. Nicotinic acid ii. Nicotinamide/ niacinamide iii. Nicotinamide ascorbate/ niacinamide ascorbate iv. Inositol hexanicoti-nate (inositol hexania-cinate)	• Co-factor, substrate and ligand[6] • Essential redox cofactors for cellular metabolism and antioxidant processes[6] • Supports glycolysis, Krebs cycle, fatty acid oxidation and synthesis[6] • Cholesterol and steroid production[6] • Alcohol metabolism[6] • Protection against oxidative stress and regulation of key biological processes including nutrient sensing, circadian rhythm, DNA repair, immune function, aging, and epigenetic control[6]	• Carbohydrate, protein and lipid metabolism • Mucous membranes maintenance • Skin maintenance • Psychological function • Tiredness and fatigue reduction • Growth and development • Maintenance of good health	• Carbohydrate, protein and lipid metabolism • Growth and development • Maintenance of good health • Multi-vitamin supplement/ Multi-vitamin/mineral supplement	**1 to 3 years** 0.6 mg	10 mg	1 mg	≤ 35 mg
				4 to 8 years 0.6 mg	15 mg		
				9 to 13 years 0.6 mg	20 mg		
				14 to 18 years 1 mg	30 mg		
Nicotinamide, niacinamide (B3)		• Carbohydrate, protein and lipid metabolism • Growth and development • Maintenance of good health	• Carbohydrate, protein and lipid metabolism • Growth and development • Maintenance of good health • Multi-vitamin supplement/ Multi-vitamin/mineral supplement	**1 to 3 years** 0.6 mg	10 mg	2.4 mg	≤ 500 mg
				4 to 8 years 0.6 mg	15 mg		
				9 to 13 years 0.6 mg	20 mg		
				14 to 18 years 1 mg	30 mg		

Table II: Functions, regulatory health claims and dosage recommendations for vitamin B complex[15]

Vitamin B	Functions	Health supplement claim[a]		Recommended dose (Children)		Recommended dose (Adults)	
		Single substance products[b]	Multiple substance products[c]	Minimum	Maximum	Minimum	Maximum
Pantothenic acid (B5) **To be calculated as d-pantothenic acid*,[e]** i. Calcium-d-pantothenate ii. Calcium-dl-pantothenate iii. Pantethine iv. d-Panthenol/Dexpanthenol v. dl-Panthenol vi. d-Pantothenic acid vii. dl-Pantothenic acid	• Coenzyme A and acyl-carrier protein (ACP) formation[6] • Catabolic and anabolic reactions (fatty acids, acetylcholine, and bile acid)[6] • Synthesis of fatty and amino acids[10] • Carbohydrate metabolism[10] • Fatty acid biosynthesis[10] • Biosynthesis of haemoglobin and cytochromes as a precursor of porphy-rin[16] • Gene expression[6] • Energy production and overall cellular function[10] • Maintains neurological functions, skin and mucosal health and cholesterol handling[6]	• Carbohydrate, protein and lipid metabolism • Energy production and metabolic processes • Steroid hormone, vitamin D and neurotransmitter synthesis and metabolism • Tiredness and fatigue reduction • Mental health performance • Tissue formation • Maintenance of good health	• Carbohydrate, protein and lipid metabolism • Tissue formation • Maintenance of good health • Multi-vitamin supplement/ Multi-vitamin/mineral supplement	**1 to 13 years** 0.2 mg	≤ 200 mg	0.4 mg	≤ 200 mg
				14 to 18 years 0.4 mg	≤ 200 mg		
Pyridoxine (B6) **To be calculated as pyridoxine*** i. Pyridoxal ii. Pyridoxal hydrochloride iii. Pyridoxal-5-phosphate (calcium salt) iv. Pyridoxamine v. Pyridoxamine-5-phosphate vi. Pyridoxine vii. Pyridoxine hydrochloride viii. Pyridoxine-5-phosphate	• Enzymatic cofactor[10] • Amino acid, lipid and carbohydrate metabolism[5] • Neurotransmitter synthesis[5] • Production of niacin from tryptophan[5] • Antioxidant processes[5] • Gene expression[5] • Immune and cardiovascular system health[5]	• Carbohy-drate, protein and lipid metabolism • Cysteine synthesis • Energy production and metabolic processes • Nervous system and psychological function • Homocysteine metabolism • Protein and glycogen metabolism • Red blood cell formation • Immune system function • Tissue formation • Tiredness and fatigue reduction • Hormonal activity regulation • Maintenance of good health	• Carbohydrate, protein and lipid metabolism • Tissue formation • Maintenance of good health • Multi-vitamin supplement/ Multi-vitamin/mineral supplement	**1 to 3 years** 0.05 mg	30 mg	0.1 mg	≤ 100 mg
				4 to 8 years 0.05 mg	40 mg		
				9 to 13 years 0.05 mg	60 mg		
				14 to 18 years 0.1 mg	80 mg		
Biotin (B7) **To be calculated as biotin*** i. D-biotin ii. Biocytin	• Co-enzyme in the activation of carboxylases to support fatty acid oxidation[5] • Gene expression alterations via biotinylation[5] • Promote immune function[5] • Used in beauty and wellness products for hair growth, nail strength, and improved skin[17]	• Carbohydrate, protein and lipid metabolism • Energy production and metabolic processes • Nervous system and psychological function • Normal hair maintenance • Mucous membranes maintenance • Skin maintenance • Maintenance of good health	• Carbohydrate, protein and lipid metabolism • Maintenance of good health • Multi-vitamin supplement/Multi-vitamin/mineral supplement	**1 to 13 years** 1 µg	≤ 500 µg	1.8 µg	≤ 500 µg
				14 to 18 years 1.8 µg	≤ 500 µg		

Table II: Functions, regulatory health claims and dosage recommendations for vitamin B complex[15]

Vitamin B	Functions	Health supplement claim[a]		Recommended dose (Children)		Recommended dose (Adults)	
		Single substance products[b]	Multiple substance products[c]	Minimum	Maximum	Minimum	Maximum
Folic acid/folate (B9) **To be calculated as folic acid*** i. Pteroylmonoglutamic acid ii. Calcium-L-methylfolate **Accepted source:** **5-Methyltetrahydrofolic acid**	• Synthesis of thymidine and purines for DNA construction and repair mechanisms[18] • Amino acid homeostasis[18] • Antioxidant mechanisms and epigenetic processes[18] • Promotes healthy erythrocytes and immune cells[19] • Mucosal and skin renewal, and cognitive functions[19] • Red blood cell formation[19] • Amino acid metabolism[19] • Supports embryogenesis and foetal development[18] • Prevents neural tube defects during pregnancy[20]	• Maternal tissue growth during pregnancy • Protein metabolism • Red blood cell formation • Reduces the risk of neural tube defects when taken daily prior to becoming pregnant and during early pregnancy • Maintenance of good health	• Protein metabolism • Red blood cell formation • Reduces the risk of neural tube defects when taken daily prior to becoming pregnant and during early pregnancy • Maintenance of good health • Multi-vitamin supplement/ Multi-vitamin/mineral supplement	**1 to 13 years** 15 µg	≤ 200 µg	30 µg	≤ 500 µg
				14 to 18 years 30 µg	≤ 500 µg		
Cyanocobalamin (B12) **To be calculated as cyanocobalamin*** i. Cyanocobalamin ii. Hydroxocobalamin iii. 5'-Deoxyadenosylcobalamin iv. Methylcobalamin	• Cofactor in DNA synthesis[10] • Red blood cell formation[10] • Nervous system function and maintenance [10] • Homocysteine metabolism[10] • Supports energy production [10] • Amino and fatty acid metabolism[10]	• Carbohydrate, protein and lipid metabolism • Cell division process • Red blood cell formation • Energy production and metabolic processes • Nervous system and psychological function • Homocysteine metabolism • Immune system function • Tiredness and fatigue reduction • Maintenance of good health	• Carbohydrate, protein and lipid metabolism • Red blood cell formation • Maintenance of good health • Multi-vitamin supplement/ Multi-vitamin/mineral supplement	**1 to 13 years** 0,09 µg	≤ 100 µg	0,14 µg	≤ 100 µg
				14 to 18 years 0.14 µg	≤ 100 µg		

*Various available forms of vitamin B that can be found in different sources; [a]Health supplement claim: A statement that indicates the intended beneficial effect of a product when used in accordance with its recommended conditions of use; [b]Single substance products: Fixed, pre-approved claims that apply strictly to products containing only one active ingredient, within its specified dosage range; [c]Multiple substance products: Broader, applicant-developed claims that apply to combination products where every ingredient's dosage and compatibility must collectively support the stated claim; [d]1 mg niacin equivalents = 1 mg niacin = 60 mg tryptophan; [e]1 mg d-pantothenic acid = 1.07 mg d-panthenol, 1 mg d-pantothenic acid = 0.92 mg calcium-d-pantothenate, 1 mg d-pantothenic acid = 0.5 mg dl-pantothenic acid, 1 mg d-pantothenic acid = 0.54 mg dl-panthenol, 1 mg d-pantothenic acid = 0.46 mg calcium-dl-pantothenate; f1 µg dietary folate equivalents (DFE) = 1 µg food folate, 1 µg DFE = 0.6 µg as supplement consumed with food, 1 µg DFE = 0.5 µg as supplement taken on an empty stomach

various pathologies, specifically beriberi which is cardiomyopathy with oedema and lactic acidosis, a condition that affects the peripheral nervous system and cardiovascular system,[2] and Wernicke-Korsakoff syndrome or Wernicke's encephalopathy.[28] Particularly in critically ill patients, renal excretion of thiamine may be increased, thus worsening clinical manifestations.[6] Supplementation with thiamine is generally recommended in cases of deficiency, malabsorption issues, or certain medical conditions[10] such as the management of Wernicke-Korsakoff syndrome and other disorders affecting thiamine absorption.[29]

Thiamine toxicity is low and rarely encountered unless at high doses, which in itself is often low risk considering oral supplementation above 5 mg has reduced uptake.[6] Adverse drug reactions may include heat sensitivity, allergic reactions (e.g., pruritic, urticaria, anaphylaxis), angioedema, cyanosis and excessive sweating.[6] Certain medication may induce pharmacokinetic interactions leading to reduced thiamine availability, such as diuretics (which increase urinary excretion), metformin (which reduces intestinal absorption) and 5-fluorouracil (which prevents activation).[6] Thiamine is included on the WHO's core list of essential medications for both adults and children indicating its importance as a prerequisite for a basic healthcare system.[30]

Riboflavin (B2)

Riboflavin is widely distributed in both plant- and animal-based foods.[1] Heating and washing of food products contribute to a loss of riboflavin, as well as exposure to light (350 to 560 nm), necessitating its storage in dark or shaded environments.[6] Absorption is in the small intestine via carrier-mediated transportation, while metabolism supports its conversion to active flavin mononucleotide or flavin adenine dinucleotide.[6]

Humans require dietary riboflavin for DNA repair, energy production, fatty acid and amino acid synthesis, folic acid activation, production of glutathione as free radical scavenger, and support of physiological systems, including the central nervous and renal system.[6,9] Riboflavin needs to be constantly supplied through the diet or supplementation due to it being poorly stored in the body.[31] Riboflavin deficiency rarely occurs alone, usually it is part of a generalised vitamin B deficiency because of diet or malabsorption.[31] It can occur as a result of lactation, phototherapy in infants, celiac sprue, malignancies, and alcoholism.[31] Riboflavin deficiencies may present as oedema and associated pain of the oral and mucous membranes, neurological deficiencies, hair loss, topical inflammation, cataract formation, and gastrointestinal malabsorption.[6] Additionally, riboflavin deficiency may also lead to ariboflavinosis, which presents with a sore throat, redness and swelling of the lining of the throat and corners of the lips, and inflammation and redness of the lining of the eyes.[10]

Riboflavin supplementation is recommended for treatment for deficiency, malabsorption issues, or certain medical conditions.[10] Riboflavin has shown beneficial use in deficiency-related diseases, including multiple acyl-coenzyme A dehydrogenase deficiencies, Brown-Vialetto-Von Laere syndrome and Fazio Londe disease.[6] Emerging research also explores its potential therapeutic applications in conditions such as migraine headaches[10] and potential preventable diseases management in anaemia, cancer, hyperglycaemia, hypertension, diabetes and oxidative stress.[32,33]

Toxicity induced by riboflavin is rare due to its saturable absorption from the gastrointestinal tract, and thus should it appear, it is generally confined to gastrointestinal adverse effects, such as nausea and vomiting.[6] Drug interactions are largely due to pharmacokinetic interactions with absorption or synthesis, for example, with doxorubicin (impaired flavin cofactor synthesis leading to riboflavin deficiencies) or phenothiazine-antipsychotics and tricyclic antidepressants (competitive inhibition due to structural similarities to flavin co-factors).[6]

Niacin (B3)

Niacin, generally in the form of nicotinic acid or nicotinamide, is obtained from animal-based foods which contain vitamin B3 as nicotinamide, and plant-based foods[10] which contain vitamin B3 as nicotinic acid.[2,6] However, humans can convert tryptophan to nicotinamide via the liver, although following a less preferential use pathway. Loss of niacin generally occurs via washing or milling, while heat does not significantly affect it.[6] Niacin is typically absorbed as nicotinamide intestinally via sodium-dependent facilitated diffusion, however, larger doses may occur via passive diffusion.[6] Metabolic conversion supports the formation of the active form, nicotinamide adenine dinucleotide.[6]

Common underlying reasons for niacin deficiency occurs due to poor diet, alcoholism, malabsorption or medications.[6] Severe niacin deficiency results in a condition known as pellagra,[10] which is a potential life-threating disease due to nutritional deficiencies, characterised by dermatitis, dementia, diarrhoea[6] and death if left untreated.[10] Additionally, milder forms of niacin deficiency may present as ulcerative colitis, acute cutaneous lupus erythematosus, Crohn disease, discoid lupus erythematosus, drug eruptions, drug-induced lupus erythematosus, drug-induced photosensitivity, drug-induced pemphigus and porphyria cutanea tarda.[34]

Niacin toxicity typically presents as flushing, burning and itching due to cutaneous vasodilation, which is generally the main contributor of cessation of treatment.[35] Otherwise, hypotension, headaches, gastrointestinal upsets (such as heartburn, ulceration, nausea and vomiting), and lactic acidosis may occur.[6]

Pantothenic acid (B5)

Pantothenic acid is ubiquitous and found in high levels in both plant- and animal-based products.[6] Pantothenic acid requires hydrolytic metabolism prior to intestinal absorption via sodium-dependent transporters or passive diffusion.[6] Loss of pantothenic acid generally occurs due to milling or leaching into cooking fluids, though heating does not typically contribute much to reduced levels.[6]

Deficiencies are rare given the ubiquitous nature of pantothenic acid, however, may occur due to malabsorption or malnutrition.[6]

Deficiency may appear as central nervous system (e.g., headaches, restlessness, fatigue, cramps) and digestive (diarrhoea, abdominal cramps) alterations, or insulin insensitivity.[6] Pantothenic acid supplementation is typically not required for individuals following a balanced diet, as it is easily available from various food sources.[10] However, supplementation may be considered in certain medical conditions or specific dietary restrictions, under the guidance of a healthcare professional.[10] In such cases, supplementation is administered as calcium pantothenate given its stability and solid form, as opposed to the viscous naturally occurring form of pantothenic acid.[6]

Toxicity is low and unlikely to occur within physiologically-relevant doses and use, though may precipitate diarrhoea at high levels.[6]

Pyridoxine (B6)

Pyridoxine comprises six related vitamers: pyridoxine, pyridoxal, pyridoxamine and 5′-phosphate esters (pyridoxine 5′-phosphate, pyridoxal 5′-phosphate, pyridoxamine 5′-phosphate) thereof.[5] Metabolic conversion produces the active form, pyridoxal 5′-phosphate, which serves as a co-factor.[5] Various plant and animal sources provide pyridoxine.[5] Heating of food typically causes a decrease in the available content,[5] as well as milling. Intestinal absorption of pyridoxine is facilitated by transporters.[5] Several anti-pyridoxine factors are also found in food, such as gingko, flaxseed and a variety of herbal remedies.[5] Such factors interfere with pyridoxine absorption thus precipitating potential deficiencies.[5]

Deficiencies are typically through dietary limitations and malabsorption, alcoholism, or through drug interactions or genetic variation.[5] Drug interactions which can precipitate deficiencies include caffeine and theophylline (which reduced bioactivation of pyridoxine), hydrazine, levodopa, and isoniazid (which inactivates pyridoxal 5′-phosphate),[5] or phenytoin, carbamazepine and valproate (which increase vitamer metabolism).[5] Characteristic outcomes include a variety of health disorders due to limited metabolic processing, such as poor neurotransmitter synthesis, seborrheic dermatitis, cheilosis, anaemia, neuropathy, mental health disorders, seizures (such as due to pyridoxine-dependent epilepsy), cardiovascular concerns, and immune dysfunction.[5] In cases of overdoses with anti-riboflavin factors (including certain medication, like isoniazid), pyridoxine supplementation can serve as antidote, or be given prophylactically to mitigate adverse drug reactions (such as isoniazid-induced peripheral neuropathy).[5] Pyridoxine supplementation are only necessary in certain medical conditions, such as certain types of anaemia or neurological disorders, however under the guidance of a healthcare professional.[10]

Chronic high dose supplementation may paradoxically precipitate neurodegeneration reversible peripheral neuropathy, similar to what is seen with deficiency, likely due to competition between the inactive and active form.[5]

Biotin (B7)

Biotin is present in various plant- and animal-based foods.[5,36] Biotin is commonly found either as free biotin or as protein-bound biocytin, where the latter's biotin is released by biotindase.[5] Avidin, a naturally occurring anti-biotin molecule (present in egg white), binds biotin to deactivate it and prevent its absorption, however, cooking denatures avidin to allow for the release of biotin.[5] Biotin loss during food processing is primarily due to milling and leaching (although protein-bound biotin is less likely to be lost), but heating may also cause a slight decrease.[5] Intestinal absorption of free biotin occurs via sodium-dependent transporters.[5]

Biotin deficiency is rare, due to the various available biotin-containing food sources, however may develop in certain populations who are at a higher risk.[37] This includes individuals on prolonged antibiotic treatment (disrupted intestinal microbiota), individuals receiving chronic anticonvulsant treatment (disrupted biotin metabolism), and individuals on complete parenteral nutrition with insufficient biotin supplementation.[37] Clinical presentation of biotin deficiency may include seizures, low muscle tone, uncoordinated movement, respiratory distress, rashes and decreased physical and cognitive growth.[5] Folate supplementation may be recommended to meet the increased nutritional demands in cases such as pregnancy, malabsorption issues and more severe cases.[10]

Given its extensive excretion, toxicity is low and biotin supplementation is considered safe[5] though potential neurological effects may occur.

Folate/folic acid (B9)

Vitamin B9, termed folate (naturally occurring) or folic acid (synthetic),[18] is mainly found in plant-based foods and animal-based foods.[10] Natural food sources which contain folate generally have a high bioavailability, therefore it is important to follow a well-balanced diet for maintaining adequate folate levels.[38]

Insufficient folate consumption has been associated with several health problems, including an increased risk of neural tube defects in neonates, anaemia, and possible contribution to cardiovascular diseases.[10] Folate deficiency may often be due to nutritional malabsorption or malnutrition, alcoholism or several diseases (such as atrophic gastritis).[22] Folic acid deficiency may precipitate neural tube defects during embryogenesis or megaloblastic anaemia.[18] Therefore in certain cases, such as pregnancy or individuals with malabsorption issues, folate supplementation may be recommended to meet the increased nutritional requirements.[10]

Cobalamin (B12)

Cobalamin and its analogues are collectively called cobamides (also known as corrinoid cofactors) which are found in certain food products and produced by microorganisms in the human gut.[39] However, humans are generally unable to make use of the various cobamides other than cobalamin.[39] This is due to the

Table III: Commonly used vitamin B medications in South Africa,[41] including medication where vitamin B is included for adverse drug reaction mitigation

Examples (schedule)	Active ingredient	Formulation	Dose	Administration	Indications
Vitamin supplementation-dominant indications					
A-Lennon Vitamin B Complex Injection (S3)	Nicotinamide, thiamine hydrochloride, d-panthenol, pyridoxine hydrochloride and riboflavin	Injection	Per 1 mL Nicotinamide 100 mg Thiamine hydrochloride 10 mg d-Panthenol 5 mg Pyridoxine hydrochloride 5 mg Riboflavin 2 mg	Deficiency reversible with oral thiamine doses 500 µg daily Therapeutic dose: 1-2 ml daily 2 ml injection: Intramuscular or slow intravenous injection (with caution) 10 ml injection: Slow intramuscular injection only[42]	Vitamin deficiencies
A-Lennon Vitamin B12 Injection (S3)	Cyanocobalamin	Injection	1.000 µg/mL	Intramuscular administration No neurological involvement: 250-1000 µg on alternate days (1–2 weeks), then 250 µg weekly; maintenance 1000 µg monthly Neurological involvement: 1000 µg on alternate days until clinical improvement Prophylaxis: 250-1000 µg monthly[42]	Vitamin B12 deficiencies related to megaloblastic anaemia, neurological conditions, pernicious anaemia, nutrient deficiency-linked macrocytic anaemia, intestinal malabsorption, diet-related deficiencies, and post-gastrectomy
Beespan (S1)	Combination of vitamin B1, 2, 6, and 12, and calcium pantothenate	Capsules	Vitamin B1 100 mg Vitamin B2 20 mg Vitamin.B6 200 mg Vitamin B12 200 µg Calcium pantothenate 20 mg	1 capsule daily	Vitamin B complex deficiencies, such as peripheral neuritis prophylaxis in isoniazid/ hydralazine treatment
Be-Tabs Folic Acid (S1)	Folic acid	Tablets	Folic acid 5 mg	Megaloblastic anaemia: Initial 10 to 20 mg daily for 14 days, with 2.5 to 10 mg daily maintenance thereafter Megaloblastic anaemia of pregnancy prophylaxis: 200 to 500 µg daily	Megaloblastic anaemia treatment and prophylaxis
Chocaton (S0)	Combination of vitamins A, B1, B2, B6, B12, C, D3 and E, and calcium pantothenate and nicotinamide	Syrup	Per 10 ml Vitamin A 5.000 iu Vitamin B1 2 mg Vitamin B2 2 mg Vitamin B6 2.5 mg Vitamin B12 1 µg Calcium pantothenate 1 mg Nicotinamide 5 mg Vitamin C 50 mg Vitamin D3 400 iu Vitamin E 1.65 mg	Adults: 5 to 10 mL daily Children < 6 years: 2.5 mL daily	Vitamin deficiencies
Neurobion (S1)	Combination of vitamins B1, B6 and B12	Tablets	Vitamin B1 100 mg Vitamin B6 200 mg Vitamin B12 200 µg	1 tablet daily	Vitamin deficiencies
Neurobion (S3)	Combination of vitamins B1, B6 and B12	Injection (ampoules)	Per 3 mL Vitamin B1 100 mg Vitamin B6 100 mg Vitamin B12 1000 µg	Deep intramuscular injection Severe cases: 1 ampoule daily until acute symptoms subside Mild cases and follow-up therapy: two to three ampoules per week	Vitamin deficiencies
Soluvit Novum (S3)	Combination of vitamins B1, B2, B6, B12,and C, and nicotinamide, pantothenic acid, biotin, and folic acid	Lyophilised powder for solution for infusion	Vitamin B1 3.2 mg Vitamin B2 3.6 mg Vitamin B6 4 mg Vitamin B12 5 µg Vitamin C 100 mg Nicotinamide 40 mg Pantothenic acid 15 mg Biotin 60 µg Folic acid 0.4 mg	Reconstituted mixture added to intralipid/glucose solutions for infusion Adults and children over 10 kg: 1 vial in 10 mL water for injection Children < 10 kg: 1/10 of contents of one vial per kg body mass	Adults and paediatric nutrient supplementation

Table III: Commonly used vitamin B medications in South Africa,[41] including medication where vitamin B is included for adverse drug reaction mitigation

Examples (schedule)	Active ingredient	Formulation	Dose	Administration	Indications
Vitamin supplementation included to support other active ingredients for uptake, action or adverse drug reaction mitigation					
Asic (S2)	Dicyclomine hydrochloride, doxylamine succinate and pyridoxine hydrochloride	Tablets	Dicyclomine hydrochloride 10 mg Doxylamine succinate 10 mg Pyridoxine hydrochloride 50 mg	2 tablets at bedtime Severe cases: 1 tablet before rising and 1 tablet mid-afternoon	Pregnancy-related nausea and vomiting
Autrin (S1)	Iron fumarate, ascorbic acid, intrinsic factor concentrate, folic acid and vitamin B12	Capsules	Iron fumarate 349.755 mg Ascorbic acid 150 mg Intrinsic factor concentrate 75 mg Folic acid 2 mg Vitamin B12 15 µg	1 capsule daily with or after meals	Common anaemia treatment and maintenance
Cotrizid (S4)	Isoniazid, pyridoxine hydrochloride, sulfamethoxazole and trimethoprim	Tablets	Isoniazid 300 mg Pyridoxine hydrochloride 25 mg Sulfamethoxazole 800 mg Trimethoprim 160 mg	Best taken after meals. Adults and children ≥ 25 kg: 1 tablet once daily. Children 14 to < 24.9 kg: half a tablet once daily	Pyridoxine supplementation to mitigate isoniazid-induced peripheral neuropathy
Ferrimed (S1)	Iron(III)-hydroxide polymaltose complex and folic acid	Capsules	Iron(III)-hydroxide polymaltose complex equivalent to 50 mg elemental iron Folic acid 150 µg	Take in divided doses with meals Therapeutic dose: 2 to 4 capsules/day Supplement dose: 1 to 2 capsules daily	Folic acid supplementation to support erythrocyte maturity
Yasmin Plus (S4)	Drospirenone, ethinylestradiol and levomefolate calcium	Tablets	Hormone-containing tablets Drospirenone 3 mg Ethinylestradiol 0.03 mg Levomefolate calcium 0.451 mg Hormone-free tablets Levomefolate calcium 0.451 mg	1 tablet at the same time daily for 28 days Commenced from the first day of the menstrual cycle	Levomefolate to support foetus development
Yaz Plus (S4)	Drospirenone, ethinylestradiol and levomefolate calcium	Tablets	Hormone-containing tablets Drospirenone 3 mg Ethinylestradiol 0.02 mg Levomefolate calcium 0.451 mg Hormone-free tablets Levomefolate calcium 0.451 mg	1 tablet at the same time daily for 28 days Commenced on the first day of the menstrual cycle	Levomefolate to support foetus development

selectivity of the cobalamin uptake and the trafficking system.[39] In the intestine a glycoprotein known as intrinsic factor (IF), binds to cobalamin with very high (femtomolar) affinity and facilitates its absorption into ileal cells.[39] This process includes both naturally occurring forms, such as adenosyl cobalamin, and synthetic forms, such as cyanocobalamin.[39] Cobalamin is solely obtained from the diet or supplementation, with most sources including animal-based products.[11] Cobalamin is also fortified in few plant-based foods.[10] Intestinal uptake is mediated through carrier proteins such as haptocorrin, intrinsic factor, and transcobalamin.

While cobalamin is primarily found in animal products, its absence in plant-based sources poses as a challenge for individuals following vegetarian or vegan diets[10] who remain at a higher risk of cobalamin deficiency given its lack in higher order plants.[40]

Deficiencies of cobalamin are characterised by megaloblastic anaemia, decreased cardiovascular function and neurological issues. Conditions such as pernicious anaemia, Crohn's disease, celiac disease, and gastrointestinal surgery can interfere with the absorption of cobalamin leading to deficiency.[10] Impaired intrinsic factor availability (due to parietal cell destruction immune cells) precipitates pernicious anaemia.[21,40] Neurological issues including peripheral neuropathy (tingling, numbness, and pain in the hands and feet), difficulty walking, balance problems, memory loss, confusion, and severe neurological damage in advanced cases.[10] Cobalamin deficiency may occur due to alcoholism, decreased intestinal absorption due to disease, medication use (such as proton pump inhibitors), or nutrient constraints in the diet.[21,22] As a result of the elevated levels of homocysteine due to cobalamin deficiency, there is an increase in the risk of cardiovascular disease, including heart attack and stroke.[10]

Drug-vitamin interactions

Like various other dietary supplements, vitamin B supplements may interact with clinically relevant drugs, known as a drug-vitamin interaction.[43] Dietary supplements contain active chemical constituents that can interact with drugs at physical, chemical,

Table IV: Potential drug-vitamin interactions[43]

Vitamin	Drug	Drug-Vitamin Interaction	Clinical implication
Thiamine (B1)	Furosemide	Increased thiamine urinary excretion	Thiamine deficiency
	Phenytoin (long-term use)	Decreased thiamine blood levels	
	Digoxin	Decreased thiamine absorption by cardiomyocytes (especially when combined with furosemide)	
Riboflavin (B2)	Phenobarbital (long-term use)	Increased riboflavin destruction	Riboflavin deficiency
	Hydrochlorothiazide and probenecid	Increased riboflavin urinary excretion and decreased absorption	
	Oral contraceptive pills	Decreased riboflavin nutritional status	
	Antipsychotics (phenothiazine, chlorpromazine), tricyclic antidepressants, tetracycline, antimalarials (quinacrine), anticancer (adriamycin, doxorubicin)	Inhibited incorporation of riboflavin into FAD and FMN	
	Anticholinergics, tetracycline, tricyclic antidepressants (imipramine, desipramine, amitriptyline), antiepileptics (phenytoin), antipsychotics (chlorpromazine), doxorubicin, methotrexate	Decreased riboflavin absorption	
Niacin (B3)	Statins	Additive impairment of skeletal muscle functioning	Rhabdomyolysis
	Sulfinpyrazone	Decreased uric acid excretion	Inhibited uricosuric effect
	Antihypertensives	Increased efficacy of antihypertensives	Hypotension
	Oral hypoglycaemics (metformin, glipizide, glyburide) and insulin	Decreased efficacy of oral hypoglycaemics	Hyperglycaemia
	Nicotine patches	Additive vasodilation of cutaneous blood vessels	Increased skin flushing
	Anticoagulants (warfarin)	Elevated International Normalised Ratio (INR) due to synergistic coagulopathy	Increased bleeding
	Carbamazepine, primidone	Increased niacin efficacy	Niacin toxicity
	Isoniazid, tetracycline, azathioprine, chloramphenicol, cycloserine, fluorouracil, levodopa and carbidopa, phenytoin, valproic acid, mercaptopurine, colestipol, welchol, cholestyramine	Decreased niacin efficacy	Niacin deficiency
Pantothenic acid (B5)	Oral contraceptive pills	Decreased pantothenic acid efficacy	Pantothenic acid deficiency
Pyridoxine (B6)	Antiepileptics (phenytoin, phenobarbital)	Decreased epileptic efficacy	Suboptimal control of seizures
	Levodopa	Decreased levodopa efficacy	Suboptimal control of Parkinson's disease
	Isoniazid	Decreased pyridoxine efficacy	Peripheral neuropathy
	Cycloserine	Increased pyridoxine urinary excretion	Neurotoxicity
	Amiodarone		Photosensitivity and dermatitis
	Theophylline	Decreased bioavailability of pyridoxine	Pyridoxine deficiency
	Erythropoietin therapy	Decreased pyridoxine blood levels	
	Penicillamine	Decreased pyridoxine efficacy	
	Nonsteroidal anti-inflammatory drugs, monoamine oxidase inhibitors, oral contraceptive pills, hydralazine, theophylline, tetracycline	Decreased pyridoxine metabolism	Pyridoxine toxicity
Folate/folic acid (B9)	Methotrexate	Decreased anticancer activity	Chemotherapy treatment failure
	Phenytoin, carbamazepine, valproate	Decreased serum levels of antiepileptics	Seizures
	Pyrimethamine	Decreased antimalarial efficacy	Persistent infection
	Trimethoprim, triamterene, pyrimethamine, sulfasalazine	Exhibit antifolate activity	Folate deficiency
	Histamine H2 receptor antagonists, proton pump inhibitors, nonsteroidal anti-inflammatory drugs, phenytoin, phenobarbital, primidone, cholestyramine, cholestipol	Decreased folate metabolism	Folate toxicity
Cobalamin (B12)	Metformin, histamine H2 receptor antagonists, proton pump inhibitors	Decreased cobalamin absorption	Cobalamin deficiency
	Oral contraceptive pills	Decreased serum cobalamin concentrations	
	Phenytoin, phenobarbital, primidone, methotrexate, colchicine, bile acid sequestrants (cholestyramine, colesevelam), tetracycline	Decreased cobalamin metabolism	Cobalamin toxicity

physiological, and pathophysiological levels[43] which may lead to an adverse event such as those listed in Table IV. In many cases, such interactions impact the availability of the vitamin, leading to a deficiency, or may impact the treatment success of the medication.

Conclusion

The vitamin B complex is composed of eight water-soluble B vitamins which primarily functions as an enzymatic cofactor by supporting various physiological processes such as energy production, macronutrient (carbohydrate, protein and fat) metabolism and neurological system functions. Although there is an overlap of functions, each vitamin has unique characteristics regarding food sources, absorption and transport mechanisms, required values for optimal functioning, available supplementation and clinical outcomes when interacting with other medications. As shown in this review, vitamin B deficiencies present as serious symptoms and requires supplementation when necessary. South Africa has a range of vitamin B supplements to treat deficiencies, but an individual receiving supplementation should inform their healthcare professional of currently used concomitant medication to prevent drug-vitamin interactions. It is also important to take note of the RDA values when supplementing, to prevent vitamin B toxicity.

Conflict of interest

The authors declare no conflict of interest.

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References

1. Kennedy DO. B vitamins and the brain: Mechanisms, dose and efficacy - a review. Nutrients. 2016;8(2):68. https://doi.org/10.3390/nu8020068.
2. Yoshii K, Hosomi K, Sawane K, Kunisawa J. Metabolism of dietary and microbial vitamin B family in the regulation of host immunity. Front Nutr. 2019;6:48. https://doi.org/10.3389/fnut.2019.00048.
3. Akram M, Munir N, Daniyal M, et al. Vitamins and minerals: Types, sources and their functions. Functional foods and nutraceuticals: bioactive components, formulations and innovations: Springer; 2020. p. 149-72. https://doi.org/10.1007/978-3-030-42319-3_9.
4. Schellack G, Harirari P, Schellack N. B-complex vitamin deficiency and supplementation. SA Pharm J. 2016;83(4):14-9.
5. Dias P, Siatka T, Vopršalová M, et al. Biological properties of vitamins of the B-complex, part 2: vitamins B6 and B7 (biotin, vitamin H). Nutr Res Rev. 2025;38(2):791-824. https://doi.org/10.1017/S0954422425100097.
6. Hrubša M, Siatka T, Nejmanová I, et al. Biological properties of vitamins of the B-complex, part 1: vitamins B1, B2, B3, and B5. Nutrients. 2022;14(3):484. https://doi.org/10.3390/nu14030484.
7. Lee M-C, Hsu Y-J, Shen S-Y, Ho C-S, Huang C-C. A functional evaluation of anti-fatigue and exercise performance improvement following vitamin B complex supplementation in healthy humans, a randomised double-blind trial. Int J Med Sci. 2023;20(10):1272-1281. https://doi.org/10.7150/ijms.86738.
8. Institute of Medicine (US) Standing Committee on the scientific evaluation of dietary reference intakes and its panel on folate, other B vitamins, and choline. dietary reference intakes for thiamine, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline. Washington (DC): National Academies Press (US); 1998. PMID: 23193625.
9. Hanna M, Jaqua E, Nguyen V, Clay J. Vitamins: Functions and uses in medicine. Perm. J. 2022;26(2):89-97. https://doi.org/10.7812/TPP/21.204.
10. Atasever M İM, Altun SK, Paksoy N, Harem İŞ. Article and reviews in health sciences. Güngör S AD, editor. Ankara, Turkey: Platanus Publishing; 2024.
11. O'Leary F, Samman S. Vitamin B12 in health and disease. Nutrients. 2010;2(3):299-316. https://doi.org/10.3390/nu2030299.
12. Saini S, Rathore A, Suresh N, Singh V. Vitamins A, B, C, D, E, and K as molecular modulators: Integrative roles in precision medicine, nutrigenomics, therapy, and disease prevention. Indian J Precis Med Mol Med. 2025;1(2):44-52. https://doi.org/10.4103/IJPMMM.IJPMMM_10_25.
13. Sechi G, Sechi E, Fois C, Kumar N. Advances in clinical determinants and neurological manifestations of B vitamin deficiency in adults. Nutr Rev. 2016;74(5):281-300. https://doi.org/10.1093/nutrit/nuv107.
14. Prasad S, Pandey VK, Singh K, et al. A comprehensive review on nutritional interventions and nutritive elements: Strengthening immunity for effective defense mechanism during pandemic. Food Sci Nutr. 2024;12(7):4534-45. https://doi.org/10.1002/fsn3.4138.
15. South African Health Products Regulatory Authority. Complementary medicines - Health supplements: Safety and efficacy. 2022;4(3).
16. Ball GF. Vitamins in foods: Analysis, bioavailability, and stability: CRC Press; 2005. https://doi.org/10.1201/9781420026979.
17. John JJ, Lipner SR. Consumer perception of biotin supplementation. J Cutan Med Surg. 2019;23(6):613-6. https://doi.org/10.1177/1203475419871046.
18. Premjit Y, Pandey S, Mitra J. Recent trends in folic acid (vitamin B9) encapsulation, controlled release, and mathematical modelling. Food Rev Int. 2023;39(8):5528-62. https://doi.org/10.1080/87559129.2022.2077361.
19. Subar A, Block G, James L. Folate intake and food sources in the US population. Am J Clin Nutr. 1989;50(3):508-16. https://doi.org/10.1093/ajcn/50.3.508.
20. Iyer R, Tomar S. Folate: A functional food constituent. J Food Sci. 2009;74(9):R114-22. https://doi.org/10.1111/j.1750-3841.2009.01359.x.
21. Green R, Allen LH, Bjørke-Monsen A-L, et al. Vitamin B12 deficiency. Nat Rev Dis Primers. 2017;3:17040. https://doi.org/10.1038/nrdp.2017.40. Erratum in: Nat Rev Dis Primers. 2017;3:17054. https://doi.org/10.1038/nrdp.2017.54.
22. Fenech M. The role of folic acid and Vitamin B12 in genomic stability of human cells. Mutat Res. 2001;475(1-2):57-67. https://doi.org/10.1016/S0027-5107(01)00079-3.
23. Sarwar MF, Sarwar MH. Deficiency of vitamin B-complex and its relation with body disorders [Internet]. B-complex vitamins: Sources, intakes and novel applications. IntechOpen; 2022. https://doi.org/10.5772/intechopen.99456.
24. Rathee S, Nayak V, Singh KR, Ojha A. Nanofortification of vitamin B-complex in food matrix: need, regulations, and prospects. Food Chem (Oxf). 2022;4:100100. https://doi.org/10.1016/j.fochms.2022.100100.
25. Elbarbary NS, Ismail EAR, Zaki MA, et al. Vitamin B complex supplementation as a homocysteine-lowering therapy for early stage diabetic nephropathy in pediatric patients with type 1 diabetes: A randomised controlled trial. Clin Nutr. 2020;39(1):49-56. https://doi.org/10.1016/j.clnu.2019.01.006.
26. Bekele Y, Gallagher C, Batra M, et al. Is oral iron and folate supplementation during pregnancy protective against low birth weight and preterm birth in Africa? A systematic review and meta-analysis. Nutrients. 2024;16(16):2801. https://doi.org/10.3390/nu16162801.
27. Patti G, Pellegrino C, Ricciardi A, et al. Potential role of vitamins A, B, C, D and E in TB treatment and prevention: A narrative review. Antibiotics (Basel). 2021;10(11):1354. https://doi.org/10.3390/antibiotics10111354.
28. Mrowicka M, Mrowicki J, Dragan G, Majsterek I. The importance of thiamine (vitamin B1) in humans. Biosci Rep. 2023;43(10):BSR20230374. https://doi.org/10.1042/BSR20230374.
29. Kerns JC, Arundel C, Chawla LS. Thiamin deficiency in people with obesity. Adv Nutr. 2015;6(2):147-53. https://doi.org/10.3945/an.114.007526.
30. World Health Organization [Internet]. Model List of Essential Medicines; 1977 [updated 2025 Sep; cited 2026 Apr 7]. Available from: https://list.essentialmeds.org/.
31. Buehler BA. Vitamin B2: Riboflavin. J Evid Based Complementary Altern Med. 2011;16(2):88-90. https://doi.org/10.1177/1533210110392943.
32. Pinto JT, Zempleni J. Riboflavin. Adv Nutr. 2016;7(5):973-5. https://doi.org/10.3945/an.116.012716.
33. Sina RE, Daley SF. Riboflavin Deficiency. 2026 Apr 13. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan. PMID: 29262062.
34. Redzic S, Hashmi MF, Gupta V. Niacin deficiency. [Updated 2023 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557728/.
35. Javaid A, Mudavath SL. Niacin-induced flushing: Mechanism, pathophysiology, and future perspectives. Arch Biochem Biophys. 2024;761:110163. https://doi.org/10.1016/j.abb.2024.110163.
36. EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Turck D, Bresson J-L, Burlingame B, et al. Scientific opinion on dietary reference values for riboflavin. EFSA J. 2017;15(8):4919. https://doi.org/10.2903/j.efsa.2017.4919.
37. Saleem F, Soos MP. Biotin deficiency. Cureus. 2019;9(12):e1984.
38. Chan Y-M, Bailey R, O'Connor DL. Folate. Adv Nutr. 2013;4(1):123-5. https://doi.org/10.3945/an.112.003392.
39. Sokolovskaya OM, Plessl T, Bailey H, et al. Naturally occurring cobalamin (B12) analogs can function as cofactors for human methylmalonyl-CoA mutase. Biochimie. 2021;183:35-43. https://doi.org/10.1016/j.biochi.2020.06.014.
40. Smith AD, Refsum H. Vitamin B-12 and cognition in the elderly. Am J Clin Nutr. 2009;89(2):707S-11S. https://doi.org/10.3945/ajcn.2008.26947D.
41. mobiMIMS [Internet]. mobiMIMS: Electronic. 2025 [cited 2026 Mar 21]. Available from: https://www.mobimims.co.za/.
42. SAHPRA. SAHPRA [Internet]. PI and PIL repository. [cited 2026 Apr 7]. Available from: https://pi-pil-repository.sahpra.org.za/.
43. Bachmann G, Bakris GL, Barone JA, et al. Iatrogenicity: Causes and consequences of iatrogenesis in cardiovascular medicine. Rutgers University Press; 2018.