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Vitamin B-Complex and its Relationship with the Health of Vegetarian People

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ABSTRACT: Vitamins are essential for a healthy life. Compared to other nutrients, the body needs them in very small amounts. B vitamins, often known as the vitamin B complex, are a class of water-soluble vitamins with key functions in cellular metabolism. Thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), pantothenic acid (vitamin B5), pyridoxine (vitamin B6), biotin (vitamin B7), folate (vitamin B9), often known as folic acid, and cobalamin (vitamin B12) are the eight distinct vitamins that collectively constitute the vitamin B complex. The body's energy levels, cognitive activity, and cell metabolism are all directly impacted by B vitamins. Four main factors contribute to vitamin B deficiency: an unbalanced diet, excessive alcohol intake, different drugs, and disorders that induce gut malabsorption. If these B vitamin deficiencies are left untreated, they can eventually cause symptoms such as peripheral neuropathy, heart attacks, strokes etc. B vitamins are present in natural, whole foods. Compared to their unprocessed counterparts, white flour and other processed carbohydrates like sugar often contain fewer B vitamins. Excellent sources of vitamins Bs comprise legumes (beans or pulses), potatoes, bananas, whole grains, tempeh, chilli peppers, brewer's yeast, nutritional yeast, and molasses. This paper provides an in-depth summary of the most popular types of vitamin B, emphasizing why the body needs them, the symptoms of a deficiency, and what diet or foods are rich in them.

1. INTRODUCTION

The vitamin B complex is crucial for preserving health and well-being. B vitamins are the foundation of a healthy body along with other micronutrients. They have a direct impact on your energy levels, brain function, and cell metabolism (EFSA, 2015; Hanna et al., 2022; Özilgen, 2018). Even when calories are in plentiful supply or if deficient, would result in significant sickness and maybe death. Scientists who were researching human nutrition started to categorise all of the nutrients needed for life in the 19th century. Although they were aware that the body needs nutrients like protein, lipids, and sugars to muscle buildup and drive biological processes, it soon became apparent that there were other essential elements that, even in the presence of an abundance of calories, might induce severe sickness and even death (Shaffer, 2022). Scurvy is one of them, which is caused by a lack of vitamin C, and was one of the first of these deficient disorders to be recognised. This led to the identification of vitamins Bs, a class of nutrients that work with enzymes to support a variety of physiological activities. Following that, beriberi disease was noticed, which occurs when brought on by a deficiency in vitamin B1 (thiamine). The symptoms of beriberi include swelling, breathing difficulties, heart failure, and numbness and weakness in the feet and legs (Chen et al., 2018; Ibrahim et al., 2022). There are around a billion people in the world who do not have access to healthy foods. All ages are affected by malnutrition, but the poor and those with inadequate access to nutrition, clean water, good sanitation, and health education are at a higher risk than the general population. The majority of chronic disorders including nervous problems associated with malnutrition are avoidable (Sarwar et al., 2022).

Nearly a billion people on the planet do not eat enough. The B complex is a component of eight nutrients, each of which has a specific role in maintaining bodily health. These vitamins, although frequently coexist in the same foods while having names that sound similar (B1, B2, B3, etc.), are chemically different molecules (Kennedy, 2016). For vital metabolic activities, each B vitamin either serves as a cofactor (typically a

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coenzyme) or as a precursor required for synthesising one They have a distinct role in the body and are crucial for preserving cell health and keeping them stimulated. The eight vitamins that make up the vitamin B complex are folate (B9), also referred to as folic acid, and cobalamin (B12), as well as thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6) and biotin (B7) (Figure 1) (Godswill et al., 2020; Hansen et al., 2008).

Independently, each B vitamin is essential for the body's need to start the chemical processes that regulate numerous activities of the body. As an illustration, cells use B vitamins to convert fatty acids, carbohydrates, and other nutrients into energy. So, if the body is deficient in B-complex vitamins, it may not function properly at all. Hence, it is crucial to routinely absorb B vitamins through food or supplements to prevent deficiency because the body cannot readily retain them for extended periods because B vitamins are water-soluble so these may be radially eliminated from the body through urination (Alachram et al., 2021). B vitamins are also required for the production of red blood cells that transport oxygen throughout the body, the adrenal glands' ability to produce hormones associated with sex and stress, the operation of the liver and nervous system, the health of the gastrointestinal tract, and the growth of healthy skin, hair, and eyes (Hanna et al., 2022; Sarwar et al., 2022).

Each vitamin of B complex protein is different structurally and plays a particular function in the body. The following medical issues have been linked to its supplement. A role in wound healing has been demonstrated for the B vitamins i.e. thiamine, pantothenic acid, and others. It has been suggested that taking supplements of vitamins B1, B2, and B6 will help treat canker sores. The treatments of vitamin B-complex deficiencies may lessen alcohol cravings (desires); early results also indicate an improvement in acne rosacea; and sensations of anxiety, perceived tension, and fatigue have decreased (Mikkelsen & Apostolopoulos, 2019). B-complex vitamin supplements may help women relieve the symptoms of premenstrual syndrome, significantly boost their bone density to stave off osteoporosis after menopause, and depigment vitiligo-affected skin (Dai & Koh, 2015).

Vegetarians face the risk of depleting their diets of nutrients because they avoid eating meat. Vegans, who refrain from eating any animal products, have more stringent dietary requirements. Vegans must be aware that, while diets free of eggs and dairy are thought to be healthier, they can still lead to nutrient deficiencies if they are not balanced and broadened enough to provide the daily recommended amounts of nutrients. According to research, veganism, in particular, is associated with significantly lower intakes of B vitamins, especially B12, particularly among people who do not take any vitamin supplements (Neufingerl & Eilander, 2022; Rahman et al., 2022).

Notably, regardless of which B vitamin an individual is deficient they will experience diverse symptoms of vitamin B deficiency especially vegetarian people (Table 1). These can include problems like anaemia or a weakened immune system, as well as weariness, disorientation, and skin rashes. Vitamin B deficiency is more likely to occur in older persons, pregnant women, and people with specific medical disorders (Hasbaoui et al., 2021). Therefore eating a balanced diet is essential to obtaining all the nutrients. Additionally, a dietician will likely recommend that people should take vitamin B supplements for optimal cellular and metabolic function of the body. Moreover, predicted toxicity and vegetarian sources of all vitamin Bs are mentioned below (Tables 2 and 3).

2. METHODS

2.1. Search strategy

Search methods While choosing research to compare the status of individuals eating plant-based diets, we followed a methodical process. We used a search string like PubMed, Science Direct, and Google Scholar databases that include different phrases for plant-based diets, together with terms on dietary consumption or nutritional status, i.e., Diet OR "nutritional status" OR "Vitamin B complex" OR "Vitamins" OR "Nutrients" OR "Plants" OR "Thiamine (B1)" OR "Riboflavin (B2)" OR "Niacin (B3)" OR "Pantothenic acid (B5)" OR "Pyridoxine (B6)" OR "Folate (B9)," OR "Coalmine (B12)" AND "Vegetarian" OR "Vegan" in all fields.

3. ROLE OF VITAMIN B-COMPLEX IN OVERALL HEALTH, ITS ACTION MECHANISM AND ADVERSE EFFECT

3.1. Vitamin B1 (Thiamin)

Vitamin B1, sometimes known as thiamine, is one of the water-soluble B vitamins. Thiamin is a vitamin that is present in some foods naturally, artificially, and in dietary supplements. This vitamin is necessary for energy metabolism, which has an impact on cell division, growth, and function. Vitamin B1 is necessary for the heart, muscles, and nerves to function properly and for the body to properly metabolise glucose. A person could require supplements if their diet is lacking in B vitamins, they are receiving hemodialysis, or they have another medical condition. In particular, extremely low amounts of thiamin are predominantly accumulated in the liver. Because the vitamin has a constrained half-life, humans must regularly ingest it through their foods to prevent a deficiency (Hudson, 2007).

The body needs vitamin B1 (thiamine) for the effective digestion of carbohydrates. Thiamine is used to strengthen the immune system and may lower the risk of type 2 diabetes, cardiovascular disease, age-related illnesses, eye conditions (poor vision, cataracts, and glaucoma), kidney disease, cancer, mental disorders (depression), and neurodegenerative illnesses (Alzheimer's disease) (Karuppagounder et al., 2009). Thiamine insufficiency leads to neuroinflammation and beriberi, a condition that affects the nerve and circulatory systems and produces numbing in the hands and feet as well as dementia. Improper enzymatic activity, distortion of the blood-brain barrier, astrocyte dysfunction, impaired metabolism of glucose, and prolonged proinflammatory action are additional consequences

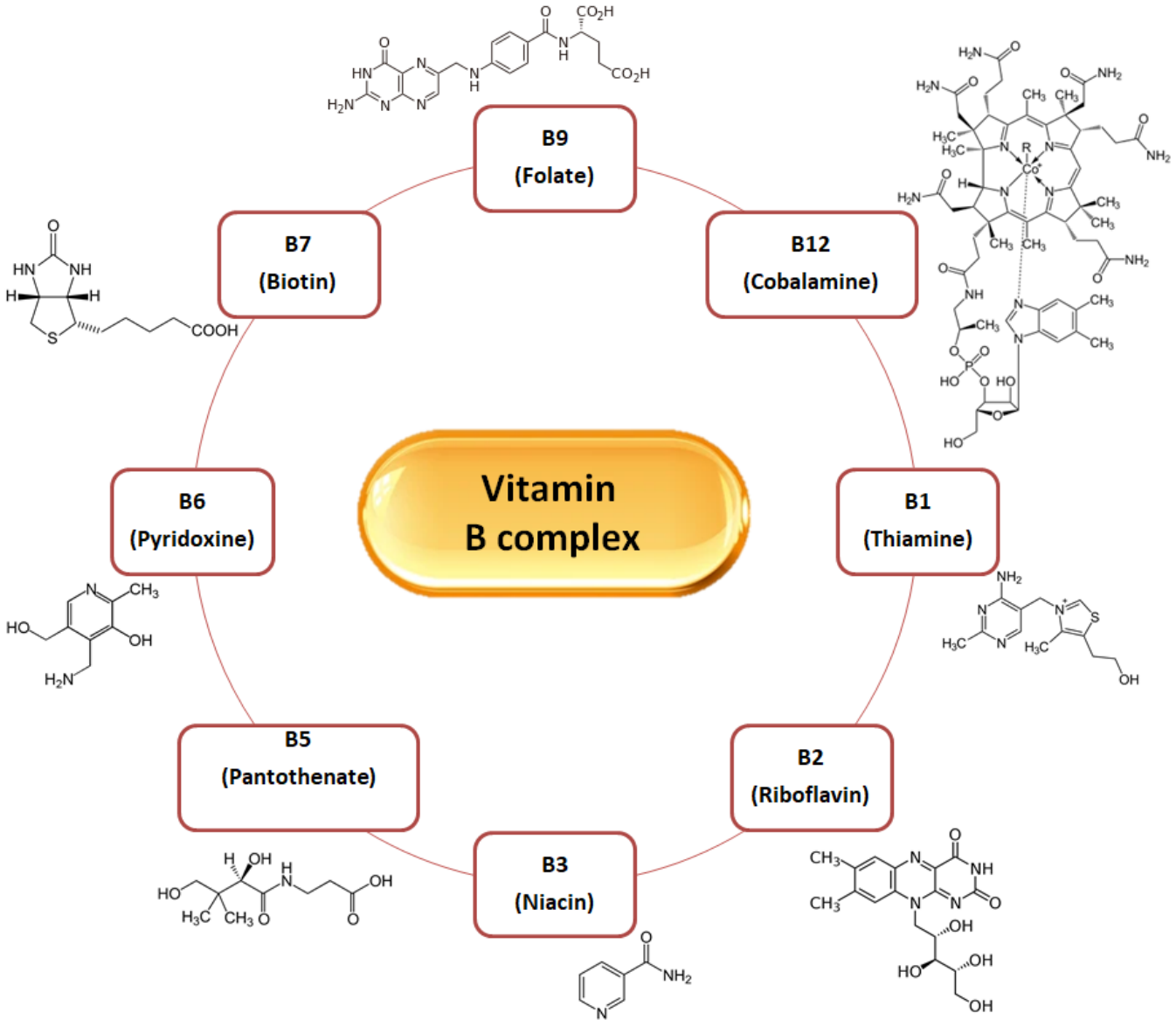

Figure 1. Types of all vitamin B complexes with chemical structure

of thiamine deficiency on oxidative metabolism (Lu'o'ng & Nguyễn, 2013). As a result, thiamine inadequate triggers pro-inflammatory reactions, abnormal tight junction proteins, antioxidant enzymes, and NF-kB. Inducible nitric oxide synthase (iNOS), which has been linked to oxidative stress and neuronal cell death in murine macrophages and microglial cells in the brain, is also upregulated in thiamine deficiency. In addition, another study using animal models found that thiamine shortage causes neurodegeneration, insufficient oxidative metabolism, inflammation, and its induced death of neurons. Furthermore, thiamine shortfall enhances the production of CD40 on microglial cells and CD40 ligands on astrocytes, both of which result in the death of neurons (De Andrade et al., 2014).

However, benfotiamine (synthetic thiamine) increases IL-10 while decreasing heat shock protein 70, iNOS, NO, COX-2, TNF-α, and NF-kB. Thiamine is, therefore, an antioxidant and anti-inflammatory vitamin that suppresses the prooxidative activity of microglial cells and may offer hope for treating neurodegenerative diseases (Bozic et al., 2015). Daily thiamine injections given to rats for three weeks days diminish paw oedema, IL-1, TNF-α and thermal hyperalgesia in complete Freund's adjuvant-induced inflammation/arthritis. These findings also support the antioxidant, anti-inflammatory, and immunomodulatory properties of thiamine and its supplementation may be helpful in the management of a variety of diseases and disorders (Yadav et al., 2010).

3.1.1 *Mechanism of Action*

Thiamin is absorbed by the small intestine through passive diffusion at pharmacologic levels and active transport at nutritional doses when it is consumed in food and dietary

Table 1
Negative impact due to vitamin B deficiency

Vitamin	Name	Deficiency effects
B1	Thiamine	Thiamine deficiency causes beriberi and symptoms of this nervous system disease comprise emotional disturbances, weight loss, weakness and pain in limbs, oedema (bodily tissues swelling) periods of irregular heartbeat and Wernicke encephalopathy (impaired sensory perception). Heart disasters and passing away could happen in progressive circumstances. Prolonged thiamine shortage may as well cause alcoholic korsakoff syndrome, an irreversible dementia regarded as compensatory confabulation and amnesia
B2	Riboflavin	Riboflavin insufficiency can cause ariboflavinosis, which might result in great sensitivity to sunlight, cheilosis (cracks in lips), glossitis (swelling of the tongue), angular cheilitis, pharyngitis (sore throat), oedema of the pharyngeal and oral mucosa, hyperemia, and pseudo-syphilis or seborrheic dermatitis (predominantly distressing the mouth, and labia majora or scrotum
B3	Niacin	Niacin shortage, together with a lack of tryptophan, results in pellagra. Signs consist of weakness, dermatitis, aggression, diarrhoea, mental confusion and insomnia (sleep disorder). In progressive circumstances, pellagra can lead to dementia and passing away.
B5	Pantothenic acid	Pantothenic acid scarcity may give rise to acne and paresthesia, even though it is rare
B6	Pyridoxine, pyridoxamine	Vitamin B6 deficiency causes seborrhoeic dermatitis-like eruptions, pink eye and neurological symptoms (epilepsy).
B7	Biotin	Biotin deficit does not normally cause indications in adults other than superficial matters like declined nail and hair development, however, can cause reduced development and nervous syndromes in children. Manifold carboxylase scarcity, an innate fault of metabolism, may cause biotin lack even at what time dietetic biotin eating is common
B9	Folic acid	Folic acid deficit leads to raised stages of homocysteine and macrocytic anaemia. Lack in expectant females may cause delivery faults, mainly neural tubes defects like anencephaly and spina bifida
B12	Cobalamins	Vitamin B12 shortage leads to loss of memory and further cognitive insufficiencies, macrocytic anaemia, peripheral neuropathy, and elevated methylmalonic acid and homocysteine. It is maximum expected to happen amongst elderly persons, as absorption through gut drops with age and autoimmune disease pernicious anaemia is one more common cause. It could likewise result in signs of psychosis and mania. In occasional risky cases, paralysis can take place.

Table 2
Predicted toxicity and recommended daily allowance of vitaminBs

Vitamin	Chemical structure	Moderate RDA value (mg)			LD50 value (mg/kg)	Predicted toxicity class
		Men	Women	Pregnancy/ Lactation		
B1	Thiamine	1.8	1.7	2.1	1000	4
B2	Riboflavin	2.5	2.4	3.0	10000	6
B3	Niacin	18	14	19	3720	5
B5	Pantothenic acid	5	5	7	10000	6
B6	Pyridoxine	2.4	1.9	2.06	3350	5
B7	Biotin	0.03	0.03	0.03-0.035	4000	5
B9	Folic acid	0.3	0.22	0.33	135	3
B12	Cobalamine	0.0022	0.0022	0.0032	NA	-

supplements. After that, it circulates through the blood until being eventually excreted through urination. The liver, heart, kidney, and brain all temporarily store trace amounts of thiamine (Wiley & Gupta, 2021).

Most of the thiamin in food is present in phosphorylated forms, whereby gastrointestinal phosphatases enzyme hydrolyze into free thiamin before it is absorbed. Thiamin is transformed by the enzyme thiamin diphosphokinase to thiamin pyrophosphate (TPP), which is the active form in the blood. TPP plays a variety of functions in the metabolic processes of glycolysis, the Krebs cycle, and the pentose phosphate pathway (Dhir et al., 2019). Additionally, it works alongside enzyme actions during the metabolism of branched-chain amino acids, carbohydrates and lipids It also serves as a cofactor during different phases of glycolysis and oxidative decarboxylation of carbohydrates. Furthermore, TPP functions as a cofactor for complexes of mitochondrial enzymes like pyruvate dehydrogenase and -ketoglutarate dehydrogenase. These enzymes are crucial for both the Krebs cycle and the tricarboxylic acid cycle in the body (Palmieri et al., 2022).

Lack of thiamin impedes these enzymes' ability to convert lactate into pyruvate, which causes an accumulation of lactic

Table 3
Vegetarian source of vitamin Bs

Name of Vitamins	Source
B1	Oats, Wheat, Rice, brown and white, Maize, Rye, Barley, Millet, Sorghum, Soybean, Lentil, Peanut, Macadamia nut, Pistachio nut, Hazelnut, Walnut, Almond, Garlic, Potato, Carrot, Cabbage, Tomato, Broccoli, Cauliflower, Spinach, Orange, Avocado, Strawberry, Apple, White bread, Brown bread, Oyster mushroom, Button mushroom
B2	Oat, Wheat, Rice, brown and white, Maize, Rye, Barley, Millet, Sorghum, Soybean, Lentil, Peanut, Macadamia nut, Pistachio nut, Hazelnut, Walnut, Almond, Garlic, Potato, Carrot, Cabbage, Tomato, Broccoli, Spinach, Cauliflower, Orange, Avocado, Strawberry, Apple, White bread, Brown bread, Oyster mushroom, Button mushroom
B3	Oat, Wheat, Rice, brown and white, Maize, Rye, Barley, Millet, Sorghum, Soybean, Lentil, Peanut, Macadamia nut, Pistachio nut, Hazelnut, Walnut, Almond, Garlic, Potato, Carrot, Cabbage, Tomato, Broccoli, Cauliflower, Spinach, Orange, Avocado, Strawberry, Apple, White bread, Brown bread, Oyster mushroom, Button mushroom
B5	Shitake and white mushrooms, Sunflower seeds, Avocados, Potatoes, Tomato, Peanuts, Broccoli, Rice brown, Oats, Carrots, Cabbage, Clementine, Tomatoes, Cherry, Apple
B6	Acorns, Apicrots, Bananas, Flax seeds, Apple, Garlic, Ginkgo, Black walnuts, Carrot, Durian, Golden seedless raisins, Jackfruit, Lemon peel, Mango, Pineapple, Pistachio nuts, Prunes, Sunflower seeds, Avocados, Casaba melon, Cherimoya, Dates, Drumstick leaves
B7	Spinach, Broccoli, Carrots, Almonds, Sunflower seeds, Avocados, Almonds, Walnuts, Sweet potatoes, Mushrooms, Peanuts, Banana
B9	Broccoli, Spinach, Romaine lettuce, Turnip greens, Asparagus, Brussels sprouts, Beans Peanuts, Sunflower seeds
B12	Spinach, Broccoli, Asparagus, Japanese butterbur, mung bean, Sprouts, Tassa jute, Water shield

acid. Lactic acidosis may result in localised damage to specific brain regions, such as the posteromedial thalamus and mamillary bodies, which can be noticed on an MRI. As a result, the TPP is required to operate throughout the pentose phosphate pathway of nucleotide synthesis as well as for the production of decreased nicotinamide adenine dinucleotide phosphate for other synthetic pathways (Lerner et al., 2016).

3.1.2 Adverse Effects

Thiamin is thought to be safe and well-tolerated. A retrospective analysis of more than 300,000 patients' adverse reactions to thiamin administration revealed no significant side effects. Lethargy, ataxia, urticaria, nausea, and reduced gastrointestinal motility are a few of the more often reported negative symptoms (Beltramo & Obeid, 2011).

3.2. Vitamin B2 (Riboflavin)

Vitamin B2 (Riboflavin), is a water-soluble and heat-stable vitamin. It is converted proteins, carbohydrates, and lipids into glucose for energy. This vitamin excellently works as an antioxidant for the enhancement of the immune system, resulting in beautiful skin and strong hair in addition to boosting energy. Additionally, it supports the maintenance of healthy blood cells and boosts energy and metabolism (Suwannasom et al., 2020). Vitamin B2 deficit makes it difficult for the body to maintain itself through metabolising macronutrients like lipids, carbohydrates, and proteins. Riboflavin is essential for physical performance, healthy growth, breastfeeding, and reproduction (Savarino et al., 2021).

Vitamin B2 deficiency may lead to desperation, exhaustion, throat swelling, and impaired vision. It can also affect the skin by causing dermatitis around the mouth, skin cracks, and itching. Hyperemia, throat oedema, degeneration of the liver, and loss of hair can also happen together with reproductive problems. Vitamin B2 also has anti-inflammatory effects and participates in oxidative metabolism (Balasubramaniam et al., 2019).

Vitamin B2 deficiency in cultured cell lines of macrophage leads to increased levels of inflammatory cytokines like TNF-α and IL-1 in addition to high-mobility group box 1 (HMGB1) protein, NO, iNOS, and monocyte chemoattractant protein-1 (MCP-1) as well as in cultured murine adipocytes show a remarkably elevated level of ROS, IL-6, TNF-α, leptin, and NF-κB and reduced expression of adiponectin. Such conditions would have an impact on insulin resistance and diseases associated with metabolic syndrome (Balasubramaniam et al., 2019; Mazur-Bialy & Pocheć, 2016). Additionally, astrocytes and macrophages suffer significant oxidative damage in actively demyelinating lesions in patients with multiple sclerosis, which can be repaired by antioxidant enzymes and riboflavin. Indeed, a clinical trial including 197 patients with multiple sclerosis revealed that riboflavin has anti-inflammatory and anti-oxidative properties. Riboflavin supplements should be taken with meals to boost absorption levels and prevent the related disease (Ghazarian et al., 2017).

Deficiencies in other nutrients frequently coexist with vitamin B2 deficiency. Vitamin B2 inadequacy is often curable, excluding structural changes like cataracts. It is becoming clearer how important riboflavin is for both health and sickness. Therefore, the primary care doctor, nurse practitioner, chemist, and nutritionist should regularly advise patients to eat either fruits and vegetables or plant-based nutritional supplements to combat the problems associated with vitamin B2 deficiency (Ibrahim et al., 2022; Mosegaard et al.,

2020).

3.2.1 Mechanism of Action

Together with the enzymes riboflavin hydrogenase, riboflavin kinase, and riboflavin synthase, it performs its function. The molecules riboflavin monophosphate (or FMN) and flavin mononucleotide (or FAD) are formed from riboflavin. The majority of riboflavin's antioxidant activity comes from its function as a precursor of FAD, a cofactor necessary for the formation of the antioxidant-reduced glutathione (Prentice & Bates, 1981). The cofactor of the glutathione peroxidases that include selenium is reduced glutathione, among others. The enzyme glutathione reductase, which contains FAD, produces reduced glutathione. In addition, riboflavin, a component of the flavoproteins that protect tissues from lipid peroxidation, is crucial for the generation of energy and also useful for the metabolism of lipids and amino acids (Lubos et al., 2011). It is essential for physical growth, facilitates the production of red blood cells and also helps proteins in releasing their kinetic energy.

3.2.2 Adverse effect

Urine may appear more yellow than usual when vitamin B2 is consumed, especially in high dosages. This is not alarming and is to be expected. However, vitamin B2 typically has no negative side effects (Buehler, 2011).

3.3. Vitamin B3 (Niacin)

Vitamin B3 is often called niacin. The word "niacin" refers to the chemical substance nicotinic acid, also known as pyridine-3-carboxylic acid or pyridine-3-carboxamide, or niacinamide, and its related derivatives, such as nicotinamide riboside (Penberthy & Kirkland, 2020). All the body tissues convert ingested niacin into the coenzyme nicotinamide adenine dinucleotide (NAD), which is the metabolically active form of niacin. With approximately 400 enzymes involved, NAD catalyses more physiological processes than any other vitamin-derived coenzyme. All tissues transform NAD into the coenzyme nicotinamide adenine dinucleotide phosphate (NADP), another active form except for skeletal muscle (Penberthy & Kirkland, 2020; Ross et al., 2012).

NAD and NADP are required for the majority of metabolic redox processes in cells that involve oxidising or reducing substrates. NAD is essential for catabolic processes that produce adenosine triphosphate (ATP), the primary energy source for cells, from the potential energy found in proteins, lipids, and carbohydrates. On the other hand, NADP encourages anabolic procedures including the production of cholesterol and fatty acids and is necessary for maintaining cellular antioxidant activity (Mackay et al., 2012).

While some meals also include minor amounts of NAD and NADP, the two main forms of niacin present in food are nicotinic acid and nicotinamide. Tryptophan, an amino acid present in proteins, is a dietary source of niacin because it is partially processed by the body into NAD. NAD and NADP are converted into nicotinamide in the gut after being consumed in food before being absorbed (Mackay et al., 2012). Niacin can be obtained as a dietary supplement, is added to some foods, and naturally occurs in a variety of foods.

3.3.1 Mechanism of Action

Niacin has long been used for the management of cardiovascular disease and lipid disorders. It has various processes, not all of which have been fully elucidated, and serves a variety of activities in the body. Niacin may alter either the liver's process for the generation of triglycerides, which breaks down apolipoprotein-B (apo-B), or the adipose tissue's lipolysis to lower lipids containing lipoproteins. Niacin also inhibits hepatocyte diacylglycerol acyltransferase-2. By stopping the last stage of triglyceride production in hepatocytes, this action restricts the amount of triglycerides that are accessible for very low-density lipoproteins (VLDL). Low-density lipoproteins, the catabolic byproduct of VLDL, are produced less frequently as a result of this activity, which also causes apo B to degrade intracellularly. Niacin also blocks a receptor that catabolizes high-density lipoprotein (HDL), increasing HDL levels and half-life (Gille et al., 2008; Montecucco et al., 2010; Zeman et al., 2015).

Furthermore, current research has expanded our understanding of how niacin works and refuted previously held beliefs. According to recent research, the essential enzyme for the synthesis of TG, hepatocyte diacylglycerol acyltransferase-2, is directly and non-competitively inhibited by niacin. Niacin's suppression of TG synthesis causes the hepatic apo B to degrade more quickly inside cells and secrete fewer VLDL and LDL particles. According to recent research, niacin enhances the redox state of vascular endothelial cells, which inhibits the production of oxidative stress and vascular inflammatory genes, two important cytokines linked to atherosclerosis (Creider et al., 2012; Zeman et al., 2015).

3.3.2 Adverse effect

Niacin toxicity from foods is uncommon, although it is possible when using high-dose supplements over an extended period. A characteristic symptom is flushed, crimson skin on the chest, arms, and face that itches or tingles. Flushing occurs more frequently while taking high amounts of nicotinic acid supplements than nicotinamide. Large dosages of niacin taken as supplements may also raise uric acid levels, which is a gout risk factor (Wierzbicki, 2011).

3.4. Vitamin B5 (P antothenic acid)

Vitamin B5 is often called pantothenic acid. Although it is rare, vitamin B5 deficiency can manifest as upper respiratory infections, fatigue, sleeplessness, sadness, irritability, vomiting, stomach pains, and burning feet (Hodges et al., 1958). The body needs glucose, which is produced whenever food (carbohydrates) are converted into fuel (B vitamins), to provide energy. These vitamins aid the body's digestion and absorption of fats and proteins. Taking these vitamins is necessary for

maintaining healthy skin, hair, eyes, and liver. They also promote normal nervous system function. Red blood cells and hormones associated with sex and stress that are produced in the small adrenal glands, which are located on top of the kidneys, depend on vitamin B5 (Özilgen, 2018; Sarwar et al., 2022). Additionally, essential for digestive health, vitamin B5 aids in the utilisation of other vitamins, particularly B2 (commonly known as riboflavin), by the body. Although it is occasionally referred to as the "anti-stress" vitamin, there is no conclusive proof that it makes the body more resilient to stress.

Pantothenic acid is required by your body to make cholesterol. Pantethine, a pantothenic acid derivative, is now being researched to determine whether it can assist in lowering blood cholesterol levels. A crucial component of numerous metabolic processes, acetyl coenzyme A, is produced only when pantothenic acid is present. The only active form is the native dextrorotatory type (Shimizu, 1999). The excellent plant food sources are wheat germ, spinach, peanuts and peas. Although there is no stated RDA, the majority of diets contain at least 10 mg daily.

3.4.1 Mechanism of Action

Vitamin B5 only affects metabolic functions because it is merely a precursor in the formation of CoA. The production of neurotransmitters, intermediate metabolism, and cell growth are only a few of the processes that are dependent on CoA in human metabolism. The CoA structure assists in these many processes by acting as a carboxyl activating group and an acyl group carrier. The citric acid cycle uses acetyl-CoA as a crucial mechanism to break down carbs, protein, and lipids so they can be used as fuel. The brain needs energy to increase memory, clarity, and focus (Calogiuri, 2021). ACP, an essential element in the synthesis of fatty acids as well as in the acylation and acetylation processes required in many enzyme functions, is also created from acetyl-CoA. Because glucose by-products can be utilised as energy, amino acids are Crucial for the growth of cells and fatty acids, which are required for the synthesis of neurotransmitters, the by-products of macronutrient breakdown are essential for appropriate brain function. B5 is essential for the body's and brain's synthesis of amino acids, which are required for healthy brain function through the regulation of cells and the production of neurotransmitters (Calogiuri, 2021).

3.4.2 Adverse Effects

Vitamin B5 toxicity is unlikely. In actuality, there is no known Tolerable Upper-Level Intake (UL) for the vitamin. Even, if someone consumed in large dosages (10 g/day), vitamin B5 does not show known negative effects, and may only cause moderate digestive irritation and, at worst, diarrhoea. However, it has been hypothesised that large dosages of vitamin B5 could exacerbate panic attacks in people who already have panic disorder by extending the time before adrenal exhaustion. It has been demonstrated that vitamin B5, at a human equivalent dose that falls within the range of typical supplementation, causes adrenal hyperresponsiveness to stress stimulation. Additionally, there are no documented negative effects from the vitamin's parenteral (injected) or topical (applied to the skin) usage (Calogiuri, 2021; Chawla & Kvarnberg, 2014).

3.5. Vitamin B6 (Pyridoxine)

Vitamin B6, known as pyridoxine (4-methanol version) is a crucial vitamin that is found in several foods. Vitamin B6 is a necessary element needed for the everyday functioning of many biological processes in the body. Excessive or insufficient consumption can be risk factors for altered B6. B6 deficiencies have specific causes, including protein-energy malnutrition, inadequate gastrointestinal absorption, hepatic dysfunction, and medication interactions or antagonists. In children, seizures might be a sign of vitamin B6 insufficiency. Adults with severe deficiencies frequently exhibit rashes and mental state abnormalities. Clinical indications of B6 deficiency include normocytic anaemia, cheilitis with scaly lip skin, a non-specific pruritic rash, cracks found in the corner of the mouth, and glossitis (tongue swelling) (Stach et al., 2021). The significance of B6 deficiency was also reported in cardiovascular disease, cancer, and cognitive decline as medical illnesses that may benefit from supplementation are being investigated in recent studies. Vitamin B6 must be taken every day because the human body cannot synthesise it endogenously as many plants and microbes can. Instead, they must receive it from dietary supplements (Field et al., 2022).

Furthermore, vitamin B6 is essential for the proper functioning of cells. It is important for the actions of transamination, decarboxylation, and the first stages of porphyrin production. Pyridoxine aids in the production of neurotransmitters, immune system function via generating interleukin-2 (IL-2) and haemoglobin, and cognitive growth. For embryonic brain development, which lasts until infancy, enough B6 is needed. The highest recommended daily amount of vitamin B6 is given to women who are pregnant or nursing, taking into account age and stage of life (Du et al., 2018).

3.5.1 Mechanism of Action

Pyridoxine, Pyridoxal, Pyridoxamine, and their phosphorylated analogues Pyridoxine 5'-phosphate, Pyridoxal 5'-phosphate, and Pyridoxamine 5'-phosphate are collectively referred to as vitamin B6, which consists of three similar compounds. Although scientifically speaking, only one of these six substances, pyridoxine, qualifies as vitamin B6, the term is frequently used to apply to all six. Vitamin B6 is a biologically active coenzyme that contributes to a variety of biochemical processes, such as the metabolism of amino acids and glycogen and the creation of nucleic acids, haemoglobin, sphingomyelin and the synthesis of several neurotransmitters like dopamine, norepinephrine, serotonin, and gamma-aminobutyric acid (Aspy et al., 2018; Brown et al., 2018).

3.5.2 Adverse Effects

Sensory neuropathy is the most well-known side effect of vitamin B6 supplementation, but this disease seldom develops at dosages below lethal levels, which for adults is 1 g/day or higher, and there is no proof that it may develop at doses of less than 100 mg/day for less than 30 weeks. It is important to remember that individuals require 1.75 mg of vitamin B6 daily. Although greater dosages of vitamin B6 below lethal levels may produce indigestion, nausea, breast soreness, photosensitivity, and vesicular dermatoses, there are no known adverse effects associated with dietary concentrations or routine supplemental doses of the vitamin (Lheureux et al., 2005). In toxicology, vitamin B6 plays a crucial role in the treatment of poisonings caused by isoniazid (INH), ethylene glycol, and gyromitrin (toxic mushrooms). To avoid polyneuropathy caused by isoniazid, it is also used as a preventative measure during tuberculosis treatment (Bhargava & Bhargava, 2019).

3.6. Vitamin B7 (Biotin)

Vitamin B7 (biotin) is an important micronutrient for human well-being because of the vital function that it plays in many metabolic pathways. Under the umbrella of the generic vitamin B6 are several active substances or vitamins. These include 2,5'-phosphate esters, pyridoxamine, pyridoxine alcohol, pyridoxal an aldehyde, and pyridoxamine, which varies from the other two by having an amine group. The two main esters, pyridoxal 5'phosphate (PLP) and pyridoxamine 5'phosphate (PMP) are the active coenzyme form. The predominant plant source of vitamin B6 is pyridoxine, which is less bioavailable, while the main form of B6 found in meats is esters (Mock, 2017; Penberthy & Kirkland, 2020). The most prevalent type of pyridoxine is found in multivitamins. Numerous carboxylases require biotin as a cofactor to catalyse important processes in gluconeogenesis, fatty acid synthesis, and amino acid catabolism. In recent years, it has been discovered that biotin also regulates gene expression, the immune system, and mitochondrial function (Godswill et al., 2020). Clinical abnormalities also spurred on by biotin deficiency include immunological dysfunction, skin changes, and neurological symptoms. Most importantly, it is noticed that biotin must be obtained from exogenous sources (dietary supplements) through intestinal absorption because humans cannot synthesise vitamin B7 endogenously (Mock, 2017; Penberthy & Kirkland, 2020).

3.6.1 Mechanism of Action

In individuals, vitamin B7 prevents the irreversible conversion of acetyl-CoA to malonyl-CoA by acting as a coenzyme for several carboxylases. These enzymes are crucial to numerous metabolic processes. Recent research has shown novel roles for vitamin B7 in cell signalling and epigenetic control and it must bind to specific lysine residues. Human colonic epithelium uptake of biotin is a carrier-mediated mechanism (Agrawal et al., 2016; Zempleni et al., 2008). Three important carboxylation events, such as the transformation of pyruvate into oxalacetate, acetyl-CoA into malonyl-CoA, and propionyl-CoA into methyl malonyl-CoA, all require vitamin B7 as a cofactor. With the help of vitamin B7, carbon is transferred during a carboxylase reaction. Food is converted through these processes, helped by biotin, into glucose, the main carbohydrate source for the body and brain (He et al., 2020; Zempleni et al., 2009).

3.6.2 Adverse Effects

Despite being an essential element, high dosages of biotin from supplements or food sources might have negative impacts on health. However, several studies recommend that individuals take 30 mcg of biotin daily. Any excess might result in skin allergies, which are characterised by rashes, flushing, and itching. Excessive thirst, frequent urination, sleeplessness, and a worrisomely low level of vitamins B6 and C are other signs of biotin overdosage (Xiang et al., 2015). Notably, people with diabetes should speak to a doctor before taking any biotin supplements because it is important for the metabolism of glucose and overdosing can be dangerous. Eosinophilic pleuropericardial effusion, which happens when blood and air enter the pleural cavity area around the lungs and produce a chronic pulmonary infection, can occasionally be brought on by excessive supplement consumption (Kadhim et al., 2022; Zempleni et al., 2009). Additionally, the need for biotin rises when using anticonvulsants like carbamazepine or phenobarbital because these drugs prevent uptake into the brush edges of membrane vesicles. Smoking also hastens the metabolism of biotin, therefore if the patient smokes, higher doses may be necessary when necessary. There is little information available regarding drug interactions with other substances. There have been documented cases of biotin shortage, but there have not been any injuries associated with taking too much biotin (Debourdeau et al., 2001).

3.7. Vitamin B9 (Folate or folic acid)

Vitamin B9 is often called folate or folic acid. It is important for the growth of the central nervous system. Megaloblastic and macrocytic anaemias caused by folate deficiency can be managed and treated with folic acid, which has FDA approval. This exercise explains the benefits of folic acid as a treatment for megaloblastic anaemia and as a way of preventing other diseases, as well as how it works and when it should not be used (Scaglione & Panzavolta, 2014). The capacity of folate to lower homocysteine levels in neural tube abnormalities appears to be one of the vitamin's positive functions. In addition, folic acid supplements should be taken by expectant mothers to lower the risk of neural tube abnormalities (NTDs), such as spina bifida, in the growing foetus. A previous study suggested that increased ubiquitination of genes related to neural tube closure, which affects their expression, is the mechanism by which NTDs develop when folate is deficient (Imbard et al., 2013). The fourth week of foetus development is the most vulnerable time when a woman could not even be aware that she is pregnant. This is why sexually active women of childbearing age should take folic acid supplements, especially when trying

to get pregnant. It can take the expectant mother 20 weeks to reach the ideal folate levels necessary to lower the risk of a neural tube abnormality if she takes 4 mg of folic acid daily. As a result, supplementing needs to start five to six months before conception. Moreover, folic acid has been attributed to a lower incidence of premature births (Ami et al., 2016; Soma-Pillay et al., 2016).

Although there are many more therapeutic uses for folic acid than those already described, these uses are less significant. Folic acid can treat vitiligo, prevent cervical dysplasia, prevent macrocytic anaemia caused by a folate shortage, boost gingival resistance to local irritants, which reduces inflammation, and restore hematopoiesis in macrocytic anaemia. Only one of these applications, including preventing NTDs, is approved by the FDA: treating megaloblastic anaemia (Liew, 2016; Mclean, 2020). Folic acid can be used as an adjuvant treatment for methanol poisoning and is an alternative to leucovorin calcium. Homocysteine levels that rise above the normal range can impair general cognition, particularly in the elderly. According to several studies, combining vitamin B12 and folate can considerably boost cognitive function and is preferable to taking only folate or B12 alone.

3.7.1 Mechanism of Action

Folic acid is biochemically inert, thus the dihydrofolate reductase enzyme, which is dependent on nicotinamide adenine dinucleotide phosphate hydrogen (NADPH), converts it into tetrahydrofolic acid (THF) and methyltetrahydrofolate (MTHF). The following transformation of THF into 5-10-methylenetetrahydrofolate (5-10-MTHF) has two potential outcomes: either it will lead to the production of methionine or DNA via dTMP (Tjong et al., 2022). The maintenance of healthy erythropoiesis, the synthesis of purine and thymidylate nucleic acids, the interconversion of amino acids, the methylation of tRNA, and the production and utilisation of formate all depend on the transfer of these folic acid congeners across cells via receptor-mediated endocytosis. By remethylating homocysteine to methionine through the enzyme methionine synthetase, which requires vitamin B12 as a cofactor, folic acid can normalise abnormally high homocysteine levels (Mai et al., 2022; Menezo et al., 2022).

3.7.2 Adverse Effects

Intakes of folic acid below the recommended dose of 1000 mcg per day for the general population have not been definitively linked to any negative health effects. The United State National Toxicology Programme (USNTP) looked at issues that had previously caused concern, such as cognition (linked to vitamin B12 deficiency), cancer, diabetes, thyroid diseases, and consequences associated with hypersensitivity. From earlier reports of individuals getting more than 400 mcg per day, researchers were able to pinpoint these regions. Overall, the NTP investigation concluded that there is not any conclusive evidence for any of the potential negative consequences of folic acid. However, there are isolated cases of GI upset (Butterworth & Tamura, 1989; Patel & Sobczyńska-Malefora, 2017).

3.8. Vitamin B12 (Cobalamin or Cynocobalamin)

Vitamin B12 is often called cobalamin or cyanocobalamin. It can be found in some foods naturally as well as in dietary supplements and prescription medications. Cobalt is a component of vitamin B12, which wherefore substances that operate like vitamin B12 are commonly referred to as "cobalamin." Methylcobalamin and 5-deoxy adenosylcobalamin are the forms of vitamin B12 that are metabolically active. However, two further forms, hydroxocobalamin and cyanocobalamin, become physiologically active after being converted into methylcobalamin or 5-deoxy adenosylcobalamin (Niklewicz et al., 2022).

For the synthesis of DNA, the growth, myelination, and proper operation of the central nervous system, and the production of healthy red blood cells, vitamin B12 is crucial. Vitamin B12 functions as a cofactor for the enzymes methionine synthase and L-methyl malonyl-CoA. The enzyme methionine synthase converts homocysteine into the essential amino acid methionine. Vitamin B12 is necessary for both DNA and red blood cells. Vitamin B12 supplementation reduces hyperhomocysteinemia, a complication of chronic kidney disease (CKD) that has harmful cardiovascular implications (Maron & Loscalzo, 2009; Theobald & Lim, 2019). Additionally, it is crucial for the growth and function of brain and nerve cells (EFSA, 2015).

It's significant to note that vitamin B12 insufficiency is uncommon but vegetarians and vegans may be more susceptible to insufficiency because general foods do not contain vitamin B12. A vitamin B12 shortage can also impact people over 65 and those with digestive issues that interfere with nutrient absorption. Thus, if left untreated, it may result in anaemia, muscle weakness, indigestion, nerve damage, and depression (Andrès et al., 2010, 2004).

3.8.1 Mechanism of Action

Vitamin B12 in nutritional supplements forms a bond with dietary proteins. In the stomach, enzymes and hydrochloric acid release vitamin B12 ligands to release it into its free form. In the stomach, enzymes and hydrochloric acid disassemble vitamin B12 covalent bonds, releasing the free vitamin. Then, vitamin B12 works with the intrinsic factor protein to ensure ongoing absorption in the small intestine (O'leary & Samman, 2010). Vitamin B12 functions as a cofactor in the synthesis of methionine from homocysteine. S-adenosylmethionine, a methyl donor for many substrates, including proteins, lipids, hormones, DNA, and RNA, can only be made from methionine. Without vitamin B12, tetrahydrofolate cannot be converted back into 5-methyltetrahydrofolate, which can result in functional folate insufficiency (Calderón-Ospina & Nava-Mesa, 2020). In this reaction, the methyl group of methyltetrahydrofolate is transferred to homocysteine to produce methionine and tetrahydrofolate, which is required on methylcobalamin (vitamin B12) as a co-factor and also

dependent on folate. Folic acid is retained in developing red blood cells because vitamin B12 assimilates the molecule. Megaloblastic anaemia is brought on by a vitamin B12 deficiency and the disruption of this process (Calderón-Ospina & Nava-Mesa, 2020; Startsev et al., 2011).

3.8.2 Adverse effect

Supplemental vitamin B12 is typically regarded as secure. Higher amounts of vitamin B12 are secure, even though people should only consume 2.4 micrograms each day. Your body only takes in what it needs, and any extra is excreted in the form of urine. High dosages of vitamin B-12, such as those prescribed to correct a deficiency, may sometimes result in headache, nausea, vomiting, diarrhoea, weakness, or exhaustion as well as tingling in the hands and feet (Carmel, 2008; Vidal-Alaball et al., 2005).

3.8.3 Use in Specific Patient Population

3.8.3.1 **Hepatic Impairment** The product labelling from the manufacturer makes no mention of the usage of cyanocobalamin in individuals with hepatic impairment. The use of vitamin B12 has not been associated with clinically obvious acute liver damage or transaminase increases.

3.8.3.2 **Renal Impairment** The product labelling from the manufacturer makes no mention of the usage of cyanocobalamin in patients with renal impairment. However, vitamin B12 supplementation may be beneficial for people with anaemia in chronic renal disease, according to kidney disease improving global outcomes (KDIGO) guidelines.

3.8.3.3 **Pregnancy Considerations** A lack of vitamin B12 raises the possibility of unfavourable pregnancy outcomes. Supplementing with vitamin B12 proactively is necessary, especially for vegetarian mothers.

3.8.3.4 **Breastfeeding Considerations** Human milk contains vitamin B12. However, breastfeeding exclusively while having vitamin B12 insufficiency due to lesser intake of animal products or malabsorption are risk factors for vitamin B12 deficiency in newborns. Babies with vitamin B12 deficiency can experience neurological issues, anaemia, and other negative health effects. As a result, it's essential to increase newborns' vitamin B12 status through maternal supplementation during nursing.

4. CONCLUSION

B vitamins are essential since they regulate each other and give the body a variety of health benefits. In order to maintain excellent health and well-being, it is crucial to have adequate amounts of all the B vitamins in your body. It has been shown that vitamin B supports and speeds up metabolism, maintains lean muscles and healthy skin, enhances immune and neurological system function, and improves red blood cell growth and division, which helps prevent anaemia. Together, these nutrients help to combat the symptoms and underlying causes of many conditions, including cardiovascular disease, stress, depression, and anxiety. In addition, vitamin B improves the body's nerves and cells as a necessary component of health and assists in the synthesis of DNA, which is a molecule from which genes are formed. A maximum amount of these nutrients are found in meat and fish, so, to maintain the level of B vitamins in the body for healthy growth and development as well as to prevent various diseases brought on by vitamin deficiencies, a vegan individual must take some dietary supplements. Conclusively, based on the reports that are available at the moment, biomedical researchers would like to recommend that vegetarians may take dietary supplements to meet their nutritional needs, such as vitamin B complex, but they should always seek the advice of dietitians, healthcare providers, and nutritionists before taking any supplements to prevent any negative side effects.

5. CONFLICTS OF INTEREST

None

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REFERENCES

Agrawal, S., Agrawal, A., Said, H.M., 2016. Biotin deficiency enhances the inflammatory response of human dendritic cells. American Journal of Physiology-Cell Physiology. 311, 386–391. https://doi.org/10.1152/ajpcell.00141.2016

Alachram, H., Chereda, H., Beißbarth, T., Wingender, E., Stegmaier, P., 2021. Text mining-based word representations for biomedical data analysis and protein-protein interaction networks in machine learning tasks. PLoS One. 16, e0258623. https://doi.org/10.1371/journal.pone.0258623

Ami, N., Bernstein, M., Boucher, F., Rieder, M., Parker, L., 2016. Folate and neural tube defects: The role of supplements and food fortification. Paediatrics & Child Health. 21, 145–149. https://doi.org/10.1093/pch/21.3.145

Andrès, E., Fothergill, H., Mecili, M., 2010. Efficacy of oral cobalamin (vitamin B12) therapy. Expert Opinion on Pharmacotherapy. 11, 249–256. https://doi.org/10.1517/14656560903456053

Andrès, E., Loukili, N.H., Noel, E., Kaltenbach, G., Abdelgheni, M.B., Perrin, A.E., 2004. Vitamin B12 (cobalamin) deficiency in elderly patients. Canadian Medical Association Journal. 171, 251–259. https://doi.org/10.1503/cmaj.1031155

Aspy, D.J., Madden, N.A., Delfabbro, P., 2018. Effects of Vitamin B6

(Pyridoxine) and a B Complex Preparation on Dreaming and Sleep. Perceptual and Motor Skills. 125, 451–462. https://doi.org/10.1177/0031512518770326

Balasubramaniam, S., Christodoulou, J., Rahman, S., 2019. Disorders of riboflavin metabolism. Journal of Inherited Metabolic Disease. 42, 608–619. https://doi.org/10.1002/jimd.12058

Beltramo, E., Obeid, R., 2011. Vitamins in the prevention of human diseases, and others, (Eds.). De Gruyter, Berlin, pp. 41–61. https://doi.org/10.1515/9783110214499

Bhargava, M., Bhargava, A., 2019. Pyridoxine for patients suffering from drug-susceptible tuberculosis in India. Public Health Action. 8, 97–97. https://doi.org/10.5588/pha.18.0017

Bozic, I., Savic, D., Laketa, D., Bjelobaba, I., Milenkovic, I., Pekovic, S., 2015. Benfotiamine attenuates inflammatory response in LPS stimulated BV-2 microglia. PLoS One. 10, e0118372. https://doi.org/10.1371/journal.pone.0118372

Brown, M.J., Ameer, M.A., Beier, K., 2018. Vitamin B6 Deficiency (Pyridoxine). StatPearls [Internet]. Treasure Island (FL):. https://www.ncbi.nlm.nih.gov/books/NBK470579/

Buehler, B.A., 2011. Vitamin B2: Riboflavin. Evidence-Based Complementary and Alternative Medicine. 16, 88–90. https://doi.org/10.2174/97816810888921121010005

Butterworth, C.E., Tamura, T., 1989. Folic acid safety and toxicity: A brief review. American Journal of Clinical Nutrition. 50, 353–358. https://doi.org/10.1093/ajcn/50.2.353

Calderón-Ospina, C.A., Nava-Mesa, M.O., 2020. B Vitamins in the nervous system: Current knowledge of the biochemical modes of action and synergies of thiamine, pyridoxine, and cobalamin. CNS Neuroscience & Therapeutics. 26, 5–13. https://doi.org/10.1111/cns.13207

Calogiuri, G., 2021. Vitamin B5 (Pantothenic Acid). Hypersensitivity to Vitamins. 8, 36–43. https://doi.org/10.2174/97816810889211210100007

Carmel, R., 2008. How I treat cobalamin (vitamin B12) deficiency. Blood. 112, 2214–2221. https://doi.org/10.1182/blood-2008-03-040253

Chawla, J., Kvarnberg, D., 2014. Hydrosoluble vitamins. Handbook of Clinical Neurology, 891–914. https://doi.org/10.1016/B978-0-7020-4087-0.00059-0

Chen, Y., Michalak, M., Agellon, B, L., 2018. Importance of nutrients and nutrient metabolism on human health. Yale Journal of Biology and Medicine. 91, 95–103. 29955217.

Creider, J.C., Hegele, R.A., Joy, T.R., 2012. Niacin: Another look at an underutilized lipid-lowering medication. Nature Reviews Endocrinology. 8, 517–528. https://doi.org/10.1038/nrendo.2012.22

Dai, Z., Koh, W.P., 2015. B-vitamins and bone health-a review of the current evidence. Nutrients. 7, 3322–3346. https://doi.org/10.3390/nu7053322

De Andrade, J.A.A., Gayer, C.R.M., Nogueira, N.P.D.A., Paes, M.C., Bastos, V.L.F.C., Neto, J.D.C.B., 2014. The effect of thiamine deficiency on inflammation, oxidative stress and cellular migration in an experimental model of sepsis. Journal of Inflammation. 11, 11. https://doi.org/10.1186/1476-9255-11-11

Debourdeau, P.M., Djezzar, S., Estival, J.L.F., Zammit, C.M., Richard, R.C., Castot, A.C., 2001. Life-threatening eosinophilic pleuropericardial effusion related to vitamins B5 and H. Annals of Pharmacotherapy. 35, 424–426. https://doi.org/10.1345/aph.10213

Dhir, S., Tarasenko, M., Napoli, E., Giulivi, C., 2019. Neurological, psychiatric, and biochemical aspects of thiamine deficiency in children and adults. Frontiers in Psychiatry. 10. https://doi.org/10.3389/fpsyt.2019.00207

Du, L., Da, Zhang, Y.W., Du, G.H., 2018. Vitamin B6. Natural Small Molecule Drugs from Plants, 647–652. https://doi.org/10.1007/978-981-10-8022-7_104

EFSA., 2015. Scientific Opinion on Dietary Reference Values for cobalamin (vitamin B12). EFSA Journal. 13, 4150. https://doi.org/10.2903/j.efsa.2015.4150

Field, D.T., Cracknell, R.O., Eastwood, J.R., Scarfe, P., Williams, C.M., Zheng, Y., 2022. High-dose Vitamin B6 supplementation reduces anxiety and strengthens visual surround suppression. Human Psychopharmacology. 37, e2852. https://doi.org/10.1002/hup.2852

Ghazarian, L., Caillat-Zucman, S., Houdouin, V., 2017. Mucosal-associated invariant T cell interactions with commensal and pathogenic bacteria: Potential role in antimicrobial immunity in the child. Frontiers in Immunology. 8. https://doi.org/10.3389/fimmu.2017.01837

Gille, A., Bodor, E.T., Ahmed, K., Offermanns, S., 2008. Nicotinic acid: Pharmacological effects and mechanisms of action. Annual Review of Pharmacology and Toxicology. 48, 79–106. https://doi.org/10.1146/annurev.pharmtox.48.113006.094746

Godswill, A.G., Somtochukwu, I.V., Ikechukwu, A.O., Kate, C, E., 2020. Health Benefits of Micronutrients (Vitamins and Minerals) and their Associated Deficiency Diseases: A Systematic Review. International Journal of Food Science. 3, 1–32. https://doi.org/10.47604/ijf.1024

Hanna, M., Jaqua, E., Nguyen, V., Clay, J., 2022. B Vitamins: Functions and Uses in Medicine. The Permanente Journal. 26, 89–97. https://doi.org/10.7812/TPP/21.204

Hansen, R.A., Gartlehner, G., Webb, A.P., Morgan, L.C., Moore, C.G., Jonas, E, D., 2008. Efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer's disease: A systematic review and meta-analysis. Clinical Interventions in Aging. 3, 211–225. 18686744.

Hasbaoui, B., El, Mebrouk, N., Saghir, S., Yajouri, A., El, Abilkassem, R., Agadr, A., 2021. Vitamin b12 deficiency: Case report and review of literature. Pan African Medical Journal. 38, 188. https://doi.org/10.11604/pamj.2021.38.188.27941

He, P., Jiang, W.D., Liu, X.A., Feng, L., Wu, P., Liu, Y., 2020. Dietary biotin deficiency decreased growth performance and impaired the immune function of the head kidney, spleen and skin in on-growing grass carp (*Ctenopharyngodon idella*). Fish & Shellfish Immunology. 97, 216–234. https://doi.org/10.1016/j.fsi.2019.12.033

Hodges, R.E., Ohlson, M.A., Bean, W.B., 1958. Pantothenic acid deficiency in man. J. Clin. Invest. 37, 1642–1657. https://doi.org/10.1172/JCI103756

Hudson, N.R., 2007. Present Knowledge in Nutrition. American Journal of Clinical Nutrition. 85, 1439–1440. https://doi.org/10.1093/ajcn/85.5.1439a

Ibrahim, M., Parveen, B., Zahiruddin, S., Gautam, G., Parveen, R., Khan, M.A., 2022. Analysis of polyphenols in *Aegle marmelos* leaf and ameliorative efficacy against diabetic mice through restoration of antioxidant and anti-inflammatory status. Journal of Food Biochemistry. 46, e13852. https://doi.org/10.1111/jfbc.13852

Imbard, A., Benoist, J.F., Blom, H.J., 2013. Neural tube defects, folic acid and methylation. International Journal of Environmental Research and Public Health. 10, 4352–4389. https://doi.org/10.3390/ijerph10094352

Kadhim, A.H., Noor, A.S., Ali, A., M., 2022. The Effectiveness of Biotin (Vitamin B7) Added to the Diet in Improving the Efficiency of Productivity, and Some Physiological Traits for Broiler Chickens (Ross-308) Exposed to Oxidative Stress. Archives of Razi Institute. 77, 1805–1811. https://doi.org/10.22092/ARI.2022.358365.2210

Karuppagounder, S.S., Xu, H., Shi, Q., Chen, L.H., Pedrini, S., Pechman, D., 2009. Thiamine deficiency induces oxidative stress and exacerbates the plaque pathology in Alzheimer's mouse model.

Neurobiology of Aging. 30, 1587–1600. https://doi.org/10.1016/j.neurobiolaging.2007.12.013
Kennedy, D.O., 2016. B vitamins and the brain: Mechanisms, dose and efficacy-A review. Nutrients. 8, 68. https://doi.org/10.3390/nu8020068
Lerner, R., Pessach, I., Rubinstein, M., Paret, G., 2016. Lactic Acidosis as Presenting Symptom of Thiamine Deficiency in Children with Hematologic Malignancy. Journal of Pediatric Intensive Care. 6, 132–135. https://doi.org/10.1055/s-0036-1587325
Lheureux, P., Penaloza, A., Gris, M., 2005. https://doi.org/10.1097/00063110-200504000-00007. European Journal of Emergency Medicine. 12, 78–85.
Liew, S.C., 2016. Folic acid and diseases - Supplement it or not? Revista da Associação Médica Brasileira. 62, 90–100. https://doi.org/10.1590/1806-9282.62.01.90
Lubos, E., Loscalzo, J., Handy, D.E., 2011. Glutathione peroxidase-1 in health and disease: From molecular mechanisms to therapeutic opportunities. Antioxidants & Redox Signaling. 15, 1957–1997. https://doi.org/10.1089/ars.2010.3586
Lu'o'ng, K.V.Q., Nguyễn, L.T.H., 2013. The role of thiamine in cancer: Possible genetic and cellular signaling mechanisms. Cancer Genomics and Proteomics. 10, 169–186. 23893925.
Mackay, D., Hathcock, J., Guarneri, E., 2012. Niacin: Chemical forms, bioavailability, and health effects. Nutrition Reviews. 70, 357–366. https://doi.org/10.1111/j.1753-4887.2012.00479.x
Mai, K., Ai, Q.H., Waagbø, R., Zhou, X.Q., Feng, L., 2022. Chapter 3 - Vitamins, In: Fourth Edition (Eds.); and others, (Eds.), Fish Nutrition . Academic Press, ondon EC2Y 5AS, United Kingdom, pp. 57–179. https://doi.org/10.1016/B978-0-12-819587-1.00014-8
Maron, B.A., Loscalzo, J., 2009. The treatment of hyperhomocysteinemia. Annual Review of Medicine. 60, 39–54. https://doi.org/10.1146/annurev.med.60.041807.123308
Mazur-Bialy, A.I., Pocheć, E., 2016. Riboflavin reduces pro-inflammatory activation of adipocyte-macrophage co-culture. Potential application of vitamin B2 enrichment for attenuation of insulin resistance and metabolic syndrome development. Molecules. 21, 1724. https://doi.org/10.3390/molecules21121724
Mclean, W., 2020. Folic acid supplementation and pregnancy - more than just neural tube defect prevention. Australian Journal of Herbal and Naturopathic Medicine. 32, 115–119. https://doi.org/10.18370/2309-4117.2017.34.57-63
Menezo, Y., Elder, K., Clement, A., Clement, P., 2022. Folic Acid, Folinic Acid, 5 Methyl TetraHydroFolate Supplementation for Mutations That Affect Epigenesis through the Folate and One-Carbon Cycles. Biomolecules. 12, 197. https://doi.org/10.3390/biom12020197
Mikkelsen, K., Apostolopoulos, V., 2019. Vitamin B1, B2, B3, B5, and B6 and the Immune System. Nutrition and Immunity, 115–125. https://doi.org/10.1007/978-3-030-16073-9_7
Mock, D.M., 2017. Biotin: From nutrition to therapeutics. Journal of Nutrition. 147, 1487–1492. https://doi.org/10.3945/jn.116.238956
Montecucco, F., Quercioli, A., Dallegri, F., Viviani, G.L., Mach, F., 2010. New evidence for nicotinic acid treatment to reduce atherosclerosis. Expert Review of Cardiovascular Therapy. 8, 1457–1467. https://doi.org/10.1586/erc.10.116
Mosegaard, S., Dipace, G., Bross, P., Carlsen, J., Gregersen, N., Olsen, R.K.J., 2020. Riboflavin deficiency-implications for general human health and inborn errors of metabolism. International Journal of Molecular Sciences. 21, 3847. https://doi.org/10.3390/ijms21113847
Neufingerl, N., Eilander, A., 2022. Nutrient intake and status in adults consuming plant-based diets compared to meat-eaters: A systematic review. Nutrients. 14, 29. https://doi.org/10.3390/nu14010029
Niklewicz, A., Smith, A.D., Smith, A., Holzer, A., Klein, A., Mccaddon, A., 2022. The importance of vitamin B12 for individuals choosing plant-based diets. European Journal of Nutrition. 62, 1551–1559. https://doi.org/10.1007/s00394-022-03025-4
O'leary, F., Samman, S., 2010. Vitamin B12 in health and disease. Nutrients. 2, 299–316. https://doi.org/10.3390/nu2030299
Özilgen, M., 2018. Nutrition and production related energies and exergies of foods. Renewable and Sustainable Energy Reviews. 96, 275–295. https://doi.org/10.1016/j.rser.2018.07.055
Palmieri, F., Monné, M., Fiermonte, G., Palmieri, L., 2022. Mitochondrial transport and metabolism of the vitamin B-derived cofactors thiamine pyrophosphate, coenzyme A, FAD and NAD+, and related diseases: A review. IUBMB Life, 592–617. https://doi.org/10.1002/iub.2612
Patel, K.R., Sobczyńska-Malefora, A., 2017. The adverse effects of an excessive folic acid intake. European Journal of Clinical Nutrition. 71, 159–163. https://doi.org/10.1038/ejcn.2016.194
Penberthy, W.T., Kirkland, J.B., 2020. Chapter 12 - Niacin, and others, (Eds.), Present Knowledge in Nutrition (Eleventh Edition) . Academic Press, ondon EC2Y 5AS, United Kingdom, pp. 209–224. https://doi.org/10.1016/B978-0-323-66162-1.00012-3
Prentice, A.M., Bates, C.J., 1981. A biochemical evaluation of the erythrocyte glutathione reductase (EC 1.6.4.2) test for riboflavin status. British Journal of Nutrition. 45, 37–52. https://doi.org/10.1079/BJN19810075
Rahman, A., Ibrahim, M., Siddiqui, J.I., Ansari, S.A., Ahmad, S., 2022. Metabolomic profiling and antidiabetic potential of *Rumex vesicarius* seed extract in high-fat diet and streptozotocin-induced diabeticrat. Brazilian Journal of Pharmaceutical Sciences. 58, e21032. https://doi.org/10.1590/s2175-97902022e21032
Ross, A.C., Caballero, B., Cousins, R.J., Tucker, K.L., Ziegler, T.R., 2012. Modern nutrition in health and disease, In: Eleventh edition (Eds.); and others, (Eds.). Wolters Kluwer Health Adis (ESP), United States, p. 2069.
Sarwar, M.F., Sarwar, M.H., Sarwar, M., 2022. Deficiency of Vitamin B-Complex and Its Relation with Body Disorders. B-Complex Vitamins - Sources, Intakes and Novel Applications. https://doi.org/10.5772/intechopen.99456
Savarino, G., Corsello, A., Corsello, G., 2021. Macronutrient balance and micronutrient amounts through growth and development. Italian Journal of Pediatrics. 47, 109. https://doi.org/10.1186/s13052-021-01061-0
Scaglione, F., Panzavolta, G., 2014. Folate, folic acid and 5-methyltetrahydrofolate are not the same thing. Xenobiotica. 44, 480–488. https://doi.org/10.3109/00498254.2013.845705
Shaffer, B.C., 2022. Vitamin B Deficiency. https://www.news-medical.net/health/Vitamin-B-Deficiency.aspx
Shimizu, S., 1999. Pantothenic acid. Nippon rinsho. Japanese Clinical Medicine. 57, 2218–2222. https://doi.org/10.1201/b14669-71
Soma-Pillay, P., Nelson-Piercy, C., Tolppanen, H., Mebazaa, A., 2016. Physiological changes in pregnancy. Cardiovascular Journal of Africa. 27, 89–94. https://doi.org/10.5830/CVJA-2016-021
Stach, K., Stach, W., Augoff, K., 2021. Vitamin B6 in health and disease. Nutrients. 13, 3229. https://doi.org/10.3390/nu13093229
Startsev, V., Smirnova, S., Kiseliov, E., 2011. New opportunities to improve erectile function in the elderly. Journal of Sexual Medicine. 8, 440–440.
Suwannasom, N., Kao, I., Pruß, A., Georgieva, R., Bäumler, H., 2020. Riboflavin: The health benefits of a forgotten natural vitamin. International Journal of Molecular Sciences. 21, 950. https://doi.org/10.3390/ijms21030950
Theobald, J., Lim, C., 2019. Folate as an Adjuvant Therapy in Methanol

Poisoning. Nutrition in Clinical Practice. 34, 521–527. https://doi.org/10.1002/ncp.10329

Tjong, E., Dimri, M., Mohiuddin, S.S., 2022. Biochemistry, Tetrahydrofolate. https://www.ncbi.nlm.nih.gov/books/NBK539712/. Date accessed: 2022-07-04

Vidal-Alaball, J., Butler, C., Cannings-John, R., Goringe, A., Hood, K., Mccaddon, A., 2005. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. Cochrane Database Systemaic Review. https://doi.org/10.1002/14651858.CD004655.pub2

Wierzbicki, A.S., 2011. Niacin: The only vitamin that reduces cardiovascular events. International Journal of Clinical Practice. 65, 379–385. https://doi.org/10.1111/j.1742-1241.2011.02630.x

Wiley, K.D., Gupta, M., 2021. Vitamin B1 Thiamine Deficiency. NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK537204/

Xiang, X., Liu, Y., Zhang, X., Zhang, W., Wang, Z., 2015. Effects of biotin on blood glucose regulation in type 2 diabetes rat model. Wei Sheng Yan Jiu. 44, 185–189.

Yadav, U.C.S., Kalariya, N.M., Srivastava, S.K., Ramana, K.V., 2010. Protective role of benfotiamine, a fat-soluble vitamin B1 analogue, in lipopolysaccharide-induced cytotoxic signals in murine macrophages. Free Radical Biology and Medicine. 48, 1423–1434. https://doi.org/10.1016/j.freeradbiomed.2010.02.031

Zeman, M., Vecka, M., Perlík, F., Hromádka, R., Staňková, B., Tvrzická, E., 2015. Niacin in the treatment of hyperlipidemias in light of new clinical trials: Has niacin lost its place? Medical Science Monitor. 21, 2156–2162. https://doi.org/10.12659/MSM.893619

Zempleni, J., Hassan, Y.I., Wijeratne, S.S.K., 2008. Biotin and biotinidase deficiency. Expert Review of Endocrinology & Metabolism. 3, 715–724. https://doi.org/10.1586/17446651.3.6.715

Zempleni, J., Wijeratne, S.S.K., Hassan, Y.I., 2009. Biotic. BioFactors. 35, 36–46. https://doi.org/10.1002/biof.8