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Vitamin B₁₂-A Vital Vitamin for Human Health: A Review

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ABSTRACT

Vitamin-B₁₂ is a vital vitamin for human health because the deficiency of this vitamin leads to the conditions like anaemia, various neurological disorders such as numbness, pins and needles sensations, a burning feeling in the feet, shaking, muscle fatigue, sleep disorders, memory loss, irrational anger, impaired mental function and Alzheimer's. Besides these effects its deficiency also exerts some psychological conditions such as dementia, depression, psychosis and obsessive-compulsive behaviour. To overcome these problems daily intake of animal based food is recommended. In case of its deficiency signs some additional or supportive drugs containing vitamin-B₁₂ either in form of pills and in emergency cases injections may be taken.

Key words: Vitamin-B₁₂, anaemia, animal foods, neurological disorders, psychological syndrome, aging, fertility

INTRODUCTION

Vitamin B₁₂ is a water-soluble vitamin that is naturally present in animal foods which is responsible for maintaining healthy central nervous system and essential for brain health. It is found naturally in animal products and can also be manufactured by bacteria. Its synthetic form is also available which can be added to some foods. It exists in several forms and contains the mineral cobalt so it is collectively known as cobalamins. There are two forms of this vitamin are active in human metabolism i.e., methylcobalamin and 5-deoxyadenosylcobalamin. It acts as a cofactor for methionine synthase and L-methylmalonyl-CoA mutase. Methionine synthase catalyzes the conversion of homocysteine to methionine (Clarke, 2008). Methionine is required for the formation of S-adenosylmethionine which is a universal methyl donor for almost 100 different substrates including DNA, RNA, hormones, proteins and lipids. L-methylmalonyl-CoA mutase converts L-methylmalonyl-CoA to succinyl-CoA in the degradation of propionate (Clarke, 2008). It is an essential biochemical reaction in fat and protein metabolism and also required for hemoglobin synthesis. It is a necessary component of haemopoietic system helps in nervous system and can be used to determine the potency of different pharmaceutical preparations and foods (Schulz, 2007).

Deficiencies of vitamin-B₁₂ can cause a person to feel tired, depressed and can cause anaemia (Khattak and Ali, 2010; Almenabbawy *et al.*, 2009). The considerable point with this vitamin is that its excess dose is not harmful to the human body as the case is with other vitamins (Ajanaku *et al.*, 2011; Qutob *et al.*, 2011; Singh and Sachan, 2010a). The reason may be that extra vitamin-B₁₂ can

be stored in liver for future use by the body or excreted out of the body (Abu-Samak *et al.*, 2008). It is thought that excess vitamin-B₁₂ that the body takes is stored and can last for up to a year if the supply runs low. The importance of this vitamin was recognised by the scientists and different societies since long back (Singh and Sachan, 2011).

The desired amount of vitamin-B₁₂ is an essential step to decide the desired dose of this vitamin by the particular person. The methods for its determination vary with its source (Kumari *et al.*, 2008). For example a convenient colorimetric assay method is more suitable for determination of vitamin-B₁₂ content in pharmaceutical preparations. This method is based on the decomposition of vitamin-B₁₂ by HNO₃ followed by subsequent formation of a stable colored complex (λ_{max} 435 nm) between the liberated cobalt ion and Nitroso-R-salt (Ahmed *et al.*, 2003). The study on vitamin-B₁₂ is utmost important not only for human well being but it can be utilized as the indicator for certain disease conditions. Thus the present manuscript was designed to cover most of the aspects of this valuable and vital vitamin.

STRUCTURE AND FUNCTIONS OF VITAMIN-B₁₂

Vitamin-B₁₂ is a largest known biomolecule and the only nutrient with a stable carbon-metal bond. One molecule of cobalt lies at the centre of each B₁₂ molecule, which has the chemical formula of C₆₁-H₈₄-N₁₄O₁₃-P₁₄Co. Isolated B₁₂ is a crystalline compound with a bright red colour, due to the presence of cobalt. Vitamin-B₁₂ works with folic acid in many body processes including synthesis of DNA, red blood cells and the insulation sheath (myelin sheath) that surrounds nerve cells and facilitates the conduction of signals in the nervous system. Severe depletion manifests as pernicious anaemia, which was invariably fatal until the discovery of B₁₂ in liver. But long before anaemia sets in, other conditions may manifest, most often neurological problems (numbness, pins and needles sensations, a burning feeling in the feet, shaking, muscle fatigue, sleep disorders, memory loss, irrational anger, impaired mental function and Alzheimer's or psychological conditions (dementia, depression, psychosis and obsessive-compulsive behaviour) (Fallon, 1987). The recommended doses of human beings at different age groups are depicted in Table 1.

SOURCES AND ITS ABSORPTION

Vitamin-B₁₂ is exclusively found in animal foods such as liver, kidney, meat, fish, shellfish, milk products and eggs (Singh *et al.*, 2010; Singh and Sachan, 2010b) as shown in Table 2 but the original source of B₁₂ in nature is bacteria. The bacteria is an only creatures able to manufacture this vitamin (Khalifa *et al.*, 2011; Maiti and Ahlawat, 2010). In humans and animals, these bacteria produce B₁₂ in the colon; however, little if any is absorbed across the colon wall so we must get our B₁₂ from animal foods. Bivalves such as clams, mussels and oysters contain high levels of B12 because they siphon large quantities of vitamin B₁₂-synthesizing micro-organisms from the sea (Herbert and Das, 1994).

Table 1: Vitamin B₁₂ recommended daily allowance (Morell and Enig, 2005)

Age	RDA
0-6 months	no RDA
7-12 months	no RDA
1-3 years	0.9 µg
4-8 years	1.2 µg
9-13 years	1.8 µg

Table 2: Sources and amount of Vitamin B₁₂ (Morell and Enig, 2005)

Sources	Amount (µg)
Mollusks (clams, oysters and mussels, etc.) 3 ounces	84.1
Liver, beef, 1 slice	47.9
Trout, wild, 3 ounces	5.4
Salmon, 3 ounces	4.9
Trout, farmraised, 3 ounces	4.2
Beef sirloin, 3 ounces	2.4

Recently, vegetarian and vegan literature claimed that certain plant foods could provide B₁₂ such as seaweeds, fermented soybeans, spirulina, even unwashed vegetables that have been fertilized with manure.

Absorption of vitamin B₁₂ is a complex process. Vitamin-B₁₂ from animal food enters the stomach as part of animal proteins. Then first of all it is be liberated by pepsin and hydrochloric acid. Free B₁₂ then attaches to R-protein, which is released from the salivary cells and parietal cells. For its rapid and efficient absorption it must be attached with protein called intrinsic factor which is secreted in the stomach. It is not possible until the R-protein complexes are broken down by pancreatic enzymes in the small intestine. B₁₂ then binds with the intrinsic factor and proceeds through the gut to the lower portion of the small intestine, where the intrinsic factor-B₁₂ complex attaches to cell receptors (a process that involves calcium). Thus, deficiencies in pepsin, hydrochloric acid, R-protein, pancreatic enzymes, intrinsic factor, calcium and cell receptors can all lead to B₁₂ deficiency through blocked absorption. Once in the bloodstream, transport proteins bind to B₁₂ and deliver it to the cells. Within the cells, enzymes liberate B₁₂ from the protein x it to its two coenzyme forms, methylcobalamin and adenosylcobalamin. Deficiency in the required enzymes can block this conversion.

Fortunately, the body absorbs about 1-5% of free B₁₂ by a process of passive diffusion. Thus supplementation with large doses of crystalline B₁₂ or with foods extremely rich in B₁₂ can successfully treat deficiencies caused by compromised protein digestion or lack of R-protein, intrinsic factor or pancreatic enzymes. Supplementation with the coenzyme forms methylcobalamin and adenosylcobalamin can overcome B₁₂ deficiency in the cells caused by lack of or malfunction of conversion enzymes.

INDICATORS OF VITAMIN B₁₂ DEFICIENCY

- The first step in determining B₁₂ deficiency is a test of B₁₂ levels in the blood. However, some of the scientist's thought that blood levels are an unreliable indicator of deficiency and that tissue levels of B₁₂ may be quite low even though blood levels are normal
- The testing of elevated levels of homocysteine and Methylmalonic Acid (MMA) is a good test to know the deficiency of this vitamin. These two precursors to the metabolic reactions controlled by B₁₂. Since, homocysteine levels can be elevated by a number of conditions like folic acid deficiency, B₆ deficiencies, renal failure, hypothyroidism and certain genetic defects. Some of the scientists consider that elevated MMA levels to be the more reliable indication of B₁₂ deficiency
- Another test is the Schilling test, in which a tiny dose of radioactive B₁₂ is given by mouth and the amount absorbed measured. If vitamin B₁₂ is absorbed only when given with intrinsic factor, the diagnosis of pernicious anaemia is confirmed

- Because testing is so complicated, the levels considered normal in dispute and disruption possible at numerous levels, many of the workers rely on the assessment of subtle B₁₂ deficiency on the blood, especially in older patients

DISEASES AND CONDITIONS ARISES DUE TO VITAMIN-B₁₂ DEFICIENCY

Vitamin-B₁₂ is a vital vitamin for human health and serves various purposes. However, its deficiency leads to the diseases and may be fatal to the live:

- **Pernicious anaemia:** Pernicious anaemia is a deadly disease occurs when a person lacks the intrinsic factor and cannot absorb vitamin-B₁₂. The most common underlying cause of pernicious anaemia is an autoimmune reaction that attacks and destroys the stomach cells that produce intrinsic factor. The disease is characterized by immature, abnormally macrocytes, which are very inefficient at carrying oxygen and by white blood cells with abnormal nuclei. Early symptoms of pernicious anaemia include paleness, weakness and fatigue while severe anaemia causes shortness of breath, dizziness and a rapid heart rate. For the correction of disease there will be the requirement of high doses of vitamin B-₁₂ which will overcome the intrinsic factor. Liver supplementation (one pond/day calf liver) can also provide about 200 µg Vitamine-B₁₂ which will be sufficient for its correction
- **Aging:** Old age ataxia showing symptoms like shaky movements and unsteady gait, muscle weakness, spasticity, incontinence, slowed reactions, memory loss, disorientation, depression and confusion can all occur when B₁₂ levels becomes low
- **Heart disease:** Dr. Kilmer McCully elucidated high blood homocysteine levels as a marker for heart disease. The homocysteine is a compound formed in the body from the amino acid methionine in a process that can be blocked by folic acid and vitamins B₆ and B₁₂. Although, high homocysteine levels can result in endothelial dysfunction which believed to be a precursor of atherosclerosis
- **Cancer:** The important function of vitamin-B₁₂ is the repair of DNA that is damaged by radiation or oxidation thus it helps in protection against cancer. Low levels of B₁₂ are associated with cancer of the cervix (Hernandez *et al.*, 2003) and the breast (Zhang *et al.*, 2005) in human beings. But the effect of vitamin-B₁₂ on cancer is contradictory
- **Nervous disorders:** Nervous disorder such as multiple sclerosis is a disease associated with the deficiency of vitamin-B₁₂. If there is a decrease in the binding capacity of vitamin-B₁₂ there will be inhibiting of the transport of B₁₂ into the cells, even in patients with normal levels in their blood (Kira *et al.*, 1994)
- **Fertility:** Vitamin-B₁₂ plays a critical role in cellular replication so its deficiency can manifest as low sperm count. As this vitamin is a frequent cause of pernicious anaemia which often leads to infertility. The supplements of vitamin-B₁₂ can helps in conception in woman
- Osteoblast activity in the bones depends on vitamin-B₁₂ and bone metabolism is affected by its deficiency (Carmel *et al.*, 1988). Bone related deformities are also associated with the deficiency vitamin-B₁₂ such as osteoporosis (Tucker *et al.*, 2000)
- The carbohydrate disruption of diabetes may indicate vitamin-B₁₂ deficiency and it has been used as a useful adjunct for the diabetic (Bhatt *et al.*, 1983)
- Its deficiency leads to the conditions like deafness (Shemish and Groenen, 1999) and various vision problems (Adams and Murray, 1979)
- The deficiency of Vitamin-B₁₂ in pregnant women has been implicated as a factor in neural tube defects such as spina bifida in offspring (Groenen and Swinkels, 2004)

- The low levels of this vitamin also leads to the impaired immunity and increased infections because it is necessary for the antibody response (Dreizen, 1979; Tamura *et al.*, 1999)

MANAGEMENT AND TREATMENT OF VITAMIN B₁₂ DEFICIENCY

- Addition of animal products like liver (Pawar *et al.*, 2011) or shellfish ensures its adequate supply (Dewi *et al.*, 2011)
- Avoid over consumption of foods such as soy foods and spirulina that can block vitamin B₁₂ intake in the body
- Avoid antacids and drugs that lower stomach acid levels: acid-suppressing drugs such as Tagamet, Zantac and Losec can lead to serious vitamin B₁₂ deficiency (Melton and Kochran, 1994)
- Avoid diabetes drugs such as Glucophage which also interfere with vitamin B₁₂ absorption
- Intake of calcium in abundant quality prevents the symptoms of deficiency. Consume plenty of Calcium is involved in the absorption of vitamin B₁₂ from the lower small intestine. Best sources are raw dairy products and bone broths (Singh and Sachan, 2000; Singh and Sachan, 2009). Dolomite powder can also be used as a calcium source
- Consumption of coconut oil and lacto-fermented foods helps in fighting against pathogens such as *Helicobacter pylori* which is associated with B₁₂ deficiency
- Always avoid fortification of folic acid in foods because in absence of vitamin B₁₂ folic acid can mask signs of vitamin B₁₂ deficiency in red blood cells but that will not protect against deficiencies in the nervous system
- Smoking of Cigarette and cigar can deplete vitamin B₁₂
- Avoid nitrous oxide anaesthesia during surgery because it may deplete vitamin B₁₂
- Avoid vaccinations containing thimerosal and other mercury-containing compounds because its mercury compound depletes Vitamin B₁₂
- Avoid moulds in the environment of the foods industry because mycotoxins produced by moulds disrupt the normal functions of vitamin-B₁₂ (Anyanwi *et al.*, 2004)
- Always avoid oral contraceptives such as pills because they may also depletes vitamin B₁₂ (Hervert, 2002; Sutterlin *et al.*, 2003; Lussana *et al.*, 2003)
- Always prefer to take vitamin-B₁₂ supplements in conditions such as celiac disease, Crohn's disease and similar intestinal disorders, especially if you are elderly or exhibit any of the symptoms of vitamin-B₁₂ deficiency
- Vitamin-B₁₂ can serve as both a therapy against increased viral load and as nutritional support for the common symptoms of AIDS. Most interesting fact is that this vitamin can inhibits the replication of the HIV virus (Palteil *et al.*, 1994)
- The standard treatment for vitamin-B₁₂ deficiency involves injections which can deliver this vitamin quickly into the bloodstream and bypass any defective components of the absorption mechanism. But the Injections are indicated in cases of extreme deficiency and in conditions when stores must be replenished very quickly. The standard protocol is 1000 micrograms daily for three days, then weekly for a month, then one injection per month indefinitely. However, a recent study showed that oral supplementation with 2000 micrograms per day three times as effective as injections in increasing vitamin-B₁₂ levels in pernicious anaemia patients

CONCLUSION

As a conclusion, we can say that supplementation of vitamin-B₁₂ in the diets or daily intake of animal foods not only provides this vitamin in desired quantity but can also helps in maintenance

of nervous and reproductive systems. In case of the deficiency of this vitamin always prefer to take supplementation or vitamin rich diets with the consultations of the qualified physician.

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