

Role of Pyridoxine in Alleviating Cardiovascular Diseases: A Brief Review

Jayachandran Halka¹, Nandakumar Vidya¹, Krishnagowdu Saravanan¹,
Muthukrishnan Arun^{2*}

¹ Ph.D Research scholars, Department of biotechnology, Bharathiar university, Coimbatore-641046, Tamil nadu, India.

² Assistant professor, Department of biotechnology, Bharathiar university, Coimbatore-641046, Tamil Nadu, India.

*Corresponding author E-Mail ID: arun@buc.edu.in

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ABSTRACT

Micronutrients are class of dietary components which are highly essential for the optimal health, growth, and development. These nutrients can overcome birth defects, maternal impairment, and increased risk of death. According to 2017 statistics, around 2 billion people in the developing countries are affected by micronutrient deficiency. There are around 13 essential vitamins which are found in nature. Vitamin B is more important as it plays a vital role in maintaining good health and well-being. Among several existing forms, the native and active form of vitamin B6 is PLP (pyridoxal 5- phosphate). PLP is a co-factor for several biochemical reactions and plays an imperative role in synthesis of amino acids, carbohydrates and fatty acids. Vitamin B6 supplementation in RDA showed to be highly health promising in controlling several clinical alignments such as cardiovascular disease, diabetes, neurological disease, premenstrual syndrome, stroke, peripheral vascular disease, coronary artery disease, pellagra skin disease, ataxia, hyperacusis, suppression of colon tumor genesis and hyper irritability. Recently, it has been reported that 43.8% people are suffering from cardiovascular disease followed by stroke (16.8%) and is also expected to reach up to 1.1 trillion by the end of 2035. It has been found that vitamin B6 lowers Homocystein in blood, which damages the inner linings of arteries causing blood clots and thereby reducing the symptoms of cardiovascular diseases. In addition to it humans have to depend on dietary sources of vitamin B6 which are produced by plants, fungi and bacteria. The present review currently focuses on the action of Vitamin B6 in the management of cardiovascular diseases.

Keywords: Vitamin B6, Homocystein, cardiovascular diseases.

1. INTRODUCTION

Vitamins are naturally occurring organic compounds that were highly essential for an organism for its vital growth and are available in little amount in selected sources. Pyridoxine (vitamin B6) is a class of water soluble vitamins which is highly vital for the conversion of nutrients into energy form and also responsible for cellular metabolism. In addition to that vitamin B6 molecule posse high Ross avenging and ROSquenching activity. They are also involved in human catabolism and anabolism processes [1, 26]. However, vitamin B6 deficiency in humans

leads to cardiovascular disease, hypertension, epilepsy, diabetes, kidney disease, neurological disorders, and pellagra [12].

Vitamin B6 is a metabolic enhancer and is also a versatile co-factor for around 200 biochemical reactions. Several form of vitamin B6 exist naturally which includes pyridoxine(PN), pyridoxal(PL),pyridoxine(PM), and pyridoxal derivatives pyridoxal 5'-phosphate (PLP), pyridoxine 5'-phosphate (PNP), and pyridoxine 5'-phosphate (PMP)[7].Out of these forms, PLP is the most active form because of its ability to synthesis amino acids, fatty acids and carbohydrates by transaminations, decarboxylations and racemisations.[23,26].According to the recommended dietary allowances (RDA) for vitB6, United States Food and Nutrition Board of the Institute of Medicine reported adults to consume about 1.3 mg, 1.7 mg (adult males) and 2 mg for lactating women. Vitamin B6 could play a vital role in protecting cells from oxidative stress because it exhibits antioxidant activity that is more powerful than vitamins C or E.It plays a crucial role in the biosynthesis of neurotransmitters, gluconeogenesis and glycogenolysis, improves immune function, aids in haemoglobin formation, and involves in development of brain. They are helpful in maintaining the levels of Homocystein in the blood [3,5,25]. Jejunum is the only region which absorbs vitamin B6 in our body. In adults it is proved that 30 nmol/L of active PLP is Phosphorylated and dephosphorylated to obtain an adequate pool of vitamins B6 in the human body [(3)]. The Food and Nutrition Board (FNB) at the Institute of Medicine of the National Academies (formerly National Academy of Sciences) uses plasma PLP level of 20 nmol/L to calculate the Recommended Dietary Allowances (RDAs) of vitamin B6 in adults [23]. Fitzpatrick et al.,8 reported that plants, bacteria, fungi are the major sources which are able to biosynthesis vitamin B 6 so subsequently animals and humans have to depend on it. Cheng et .al [6] reported that the vitamin B6 is commonly available in the form of pyridoxine hydrochloride (HCl) and PLP. Generally this Vitamin B6 is available in the form of multivitamins because this is very easy way for a common human being to intake. But due to the lack of such vitamins people are substantially depending on vitamins from other sources. As report says that multivitamins have got several advantages and disadvantages when they are taken in diet because usually body absorbs large pharmacological doses of vitamin B6, but it also quickly eliminates large amount of vitamins out.

In plants, vitamin B6 protects photosynthesis process thereby helps to alleviate both a biotic and biotic stress [11].

HOMOCYSTEIN

Homocystein is a dietary form of amino acid which is produced due to low intake of B12, B6 and B9. Other factors responsible for increase in levels of homocystein could be due to genetic level changes and environmental conditions. It has been found that high level of homocystein blood damages the inner linings of arteries causing blood clots leading to clinical conditions (<https://www.webmd.com/heart-disease/guide/homocystein-risk>). This problem can be controlled by administering vitamin B6 and intake B6 rich food crops as they reduce the symptoms of cardiovascular diseases (fig. 1) such as heart disease and rare inherited disorders[1,10].

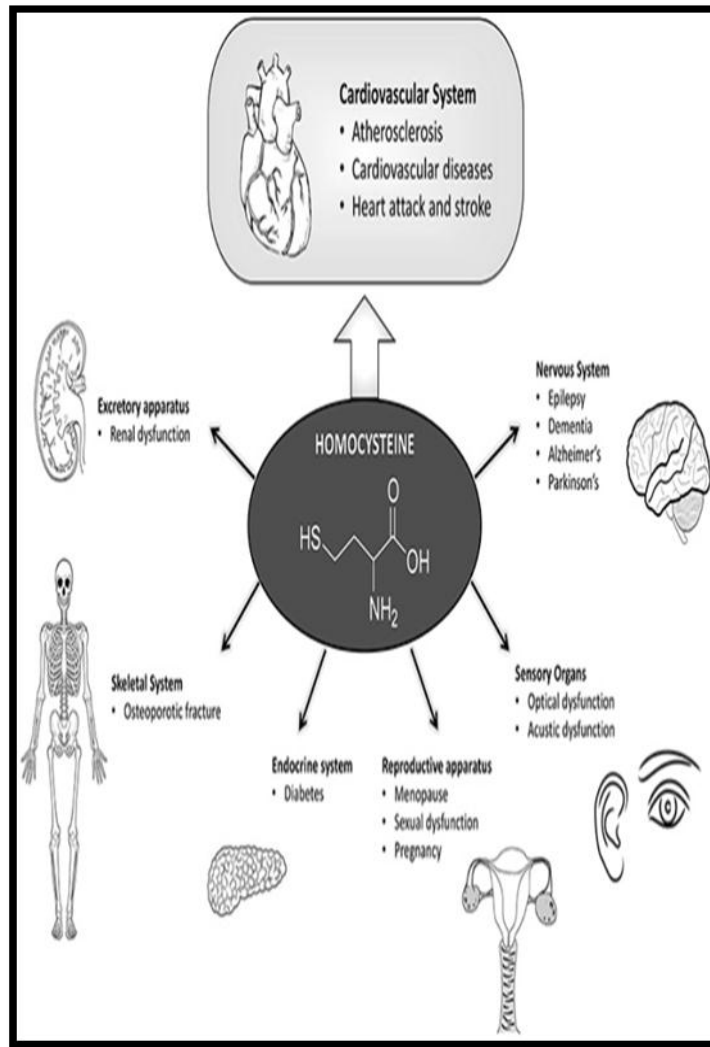


Figure 1: Homocysteine and their fundamental roles in causing diseases (source: Caterina Tinelli et al., 2019)

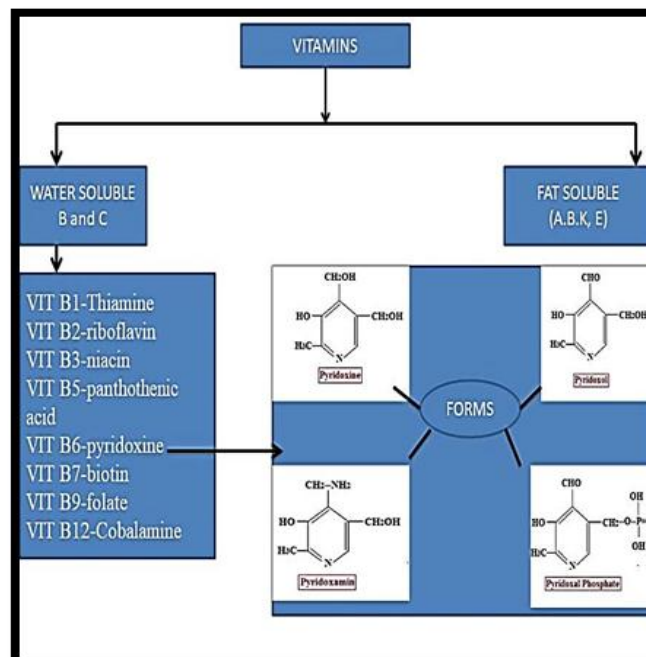


Figure.2: Vitamins and their forms

VITAMIN B6 RICH FOOD CROPS

In United States, mostly adults obtain vitamin B6 from various dietary sources such as fortified cereals, beef, poultry, starchy vegetables, and some non-citrus fruits because these are the richest source of vitamin B6. The bioavailability of vitamin B6 is around 75% [27].

Table.1 Vitamin B6 rich food sources and their daily value in (mg) [2,17].

Food	Milligrams (mg) per serving	Percent DV*
Chickpeas, canned, 1 cup	1.1	55
Beef liver, pan fried, 3 ounces	0.9	45
Tuna, yellowfin, fresh, cooked, 3 ounces	0.9	45
Salmon, sockeye, cooked, 3 ounces	0.6	30
Chicken breast, roasted, 3 ounces	0.5	25
Breakfast cereals, fortified with 25% of the DV for vitamin B6	0.5	25
Potatoes, boiled, 1 cup	0.4	20
Turkey, meat only, roasted, 3 ounces	0.4	20
Banana, 1 medium	0.4	20
Marinara (spaghetti) sauce, ready to serve, 1 cup	0.4	20
Ground beef, patty, 85% lean, broiled, 3 ounces	0.3	15
Waffles, plain, ready to heat, toasted, 1 waffle	0.3	15
Bulgur, cooked, 1 cup	0.2	10
Cottage cheese, 1% low-fat, 1 cup	0.2	10
Squash, winter, baked, ½ cup	0.2	10
Rice, white, long-grain, enriched, cooked, 1 cup	0.1	5
Nuts, mixed, dry-roasted, 1 ounce	0.1	5
Raisins, seedless, ½ cup	0.1	5
Onions, chopped, ½ cup	0.1	5
Spinach, frozen, chopped, boiled, ½ cup	0.1	5
Tofu, raw, firm, prepared with calcium sulfate, ½ cup	0.1	5
Watermelon, raw, 1 cup	0.1	5

*DV = Daily Value.

(Source: <https://ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/>)

EPIDEMIOLOGIC EVIDENCE

Vitamin B6 as a Risk Factor for Cardiovascular Disease

Many scientists have reported that vitamin B6 is one of the most important co factors which are a regulator in the Homocystein metabolism. When intake of this nutrient is very low that simultaneously causes higher accumulation of Homocystein in the blood plasma(13,14).More over for past 20 years, it is described that Homocystein amino acid and its elevated plasma concentration has got high position as it is a risk factor for causing various vascular diseases (fig.3,6) such as coronary heart diseases(15), stroke, and thrombosis (9,27). Cui Ret al [7] reported that Homocystein associated diseases could be controlled by administering vitamin B6 as a dietary intake. The authors report revealed that administration of with vitamin B6 (50mg/l) reduced Homocystein levels and 25% of stroke and cardiovascular disease was decreased [29].In another study, SaposnikG, [25]observed that supplementation of dietary vitamin B6 reduced the

levels of Homocystein for about $3\mu\text{mol/l}$. Cui Ret al [7]claimed that vitamin B6 intake reduced Homocystein level and prevented from cardiovascular disease (11%), stroke risk (19 %), and heart failure among Japanese population with a follow up for 14 years. Hyperhomocysteinemia is another condition where elevated levels of Homocystein get accumulated in the human body which results in premature atherosclerosis that leads to an increased risk of cardiovascular events [5]

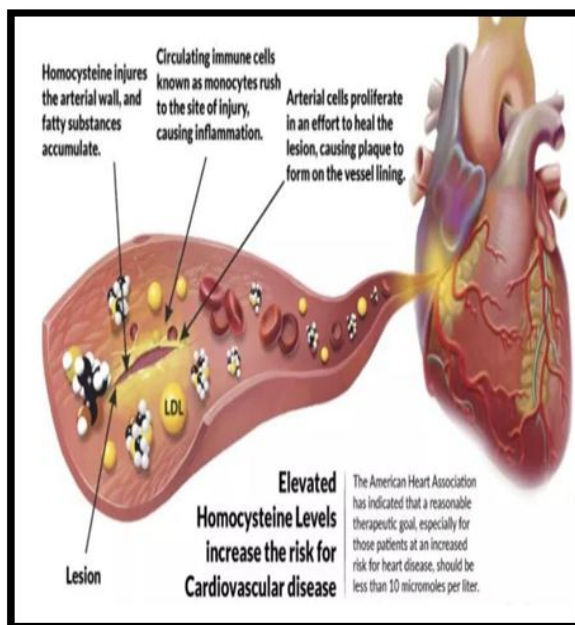


Figure.3 Homocystein molecule injuring arterial walls

(Source:<https://drjockers.com/cardiopower-testing>)

On the other hand, Huang YCet al [17] reported that there was no effect of vitamin B6 supplementation (50 mg/day) in combination with 2.5 mg folic acid and 1 mg vitamin B12 on decreasing cardiovascular disease risk.

In another clinical trial study, vitamin B6 (40mg/day) supplementation showed no benefit with or without folic acid (0.8 mg/day) plus vitamin B12 (0.4 mg/day) on major cardiovascular events in patients with ischemic heart disease [15].

HOMOCYSTEIN METABOLISM

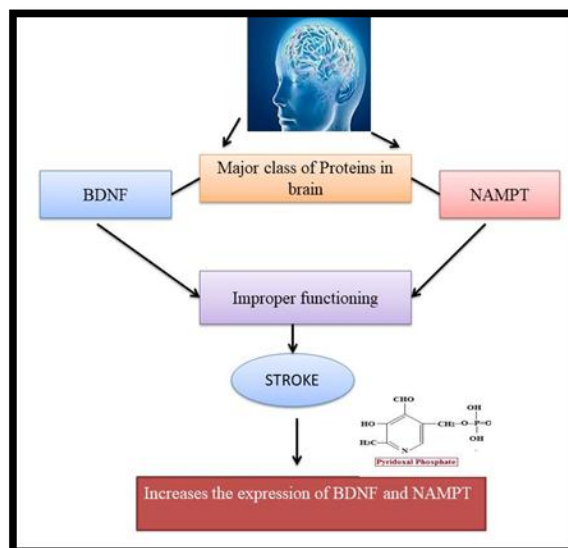


Figure.4: Homocysteinmetabolismpathway

(Source:<https://www.intechopen.com/books/the-mystery-of-glaucoma/homocysteine-in-the-pathogenesis-of-chronic-glaucoma>)

Vitamin B6 and Stroke

Sapoznik G,[25] proved that vitamin B6 is helpful in solving stroke which is a big problem currently the world is facing. Recently, it has been reported that 43.8% people are suffering from cardiovascular disease followed by stroke (16.8%) and is also expected to reach up to 1.1 trillion by the end of 2035. When Homocystein-lowering therapy (HLT) was carried out with appropriate dose of vitamin B6 reduced the incident risk of stroke. BDNF are a class of proteins found in brain which is helpful in controlling drinking, consumption, and body encumbrance.

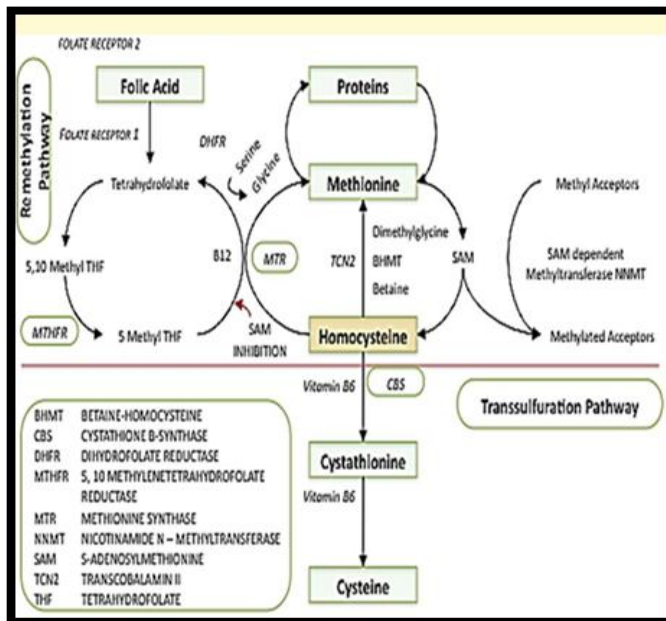


Figure.5: Role of vitamin b6 in alleviating stroke Vitamin B6 and Coronary Artery Disease (Frizo et al., [26]).

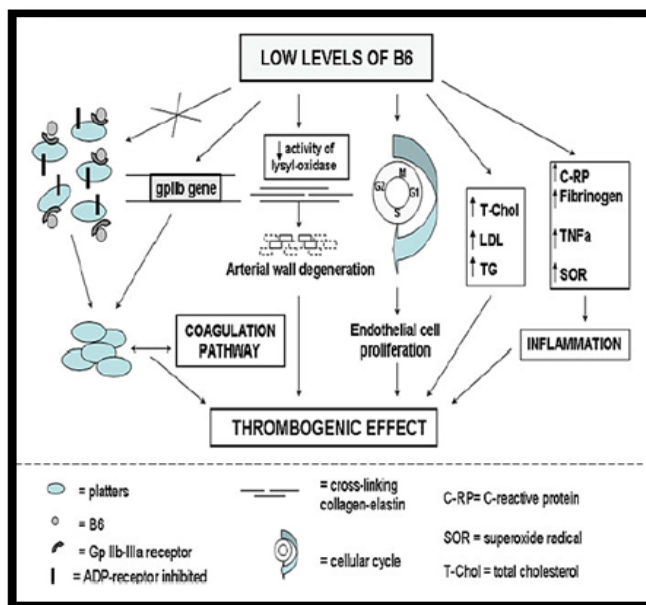


Figure.6 Mechanism for low vitamin B6 Atherogenesis(Frizo et al., [26])

On the other hand NAMPT (nicotinamidephosphoribosyltransferase) is a multifunctional protein which helps to improve post-stroke recovery, enhancing the proliferation of endothelial cells, inhibiting apoptosis, regulating vascular tone, and stimulating autophagy in disease conditions such as stroke. When vitamin B6 was administered this act as anti-stroke agent and helps in up regulating the two major genes BDNF (Brain-derived growth factor) and NAMPT(28, fig.5) Studies reported that there is an association between low plasma vitamin B6 (Fig.6) and higher risk of coronary artery disease which can leads to major thrombotic complication and myocardial infarction. Zhao et al[31]explained that homocystein-related factors including B6 vitamin are associated with the incidence of coronary artery disease.

Table.2 Mechanisms for vitamin B6 related Atherogenesis

Mechanism	Description	References
Homocysteine metabolism	Vitamin B6 deficiency induces Hyperhomocysteinemia through inhibition of cystathionine-β-synthase	Clarke and Lewington (2002), D’Angelo and Selhub (1997), Eikelboom et al. (1999), Finkelstein (1998), McCully (1970), McCully and Ragsdale (1970)
Coagulation pathway	Vitamin B6 affects platelet aggregation by inhibiting ADP receptors and prolong bleeding time, Occupancy of glycoprotein IIb/IIIa receptor or down-regulation of glycoprotein IIb gene	Brattstrom et al. (1990), Brownlee et al. (1984), Cattaneo et al. (2001), Chang et al. (1999, 2002), Packham et al. (1981)
Arterial wall degeneration	Impairment of lysyl oxidase activity by vitamin B6 deficiency induces arterial wall degeneration. Vitamin B6 also inhibits endothelial cell proliferation and induce endothelial dysfunction	Bruel et al. (1998), Ji et al. (2003), Levene and Murray (1977), Matsubara et al. (2003, 2004), Murray and Levene (1977), Rodriguez et al. (2002), Woessner (1991)
Cholesterol metabolism	Inhibition of advanced glycation and lipoxidation end-products by Vitamin B6 deficiency induces hypercholesterolemia	Brattstrom et al. (1990), de Gomez Dumm et al. (2003), Degenhardt et al. (2002), Kirsten et al. (1988), Knipscheer et al. (1997), Metz et al. (2003)
Fatty acids composition	Vitamin B6 deficiency impairs conversion of linoleic acid to arachidonic acid and the metabolism of n-3 PUFA from alpha-linoleic acid to eicosapentaenoic and docosahexaenoic acid	Bordoni et al. (1998), Cabrini et al. (2001), Cunnane et al. (1984), Harris et al. (2006), Kirschman and Coniglio (1961), Tsuge et al. (2000)
Immunological function	Vitamin B6 deficiency impairs T lymphocyte and macrophage differentiation and interleukins production	Meydani et al. (1992), Rall and Meydani (1993), Roubenoff et al. (1995)

Later it was concluded that supplementation of B6 vitamins successively reduced Coronary Artery Disease for about 50%.

CONCLUSION

The beneficial supplementation of vitamin B6 helps in solving many epidemiological actions which include Coronary Arterary Diseases, stroke and atherosclerosis which is consequentially called as cardiovascular diseases.

Owing to the progressive malnutrition, alcoholism, or pharmacological therapy, people are suffering from vitamin B6 deficiency. Due to the Vitamin B6 deficiency, levels of homocystein consequently gets boosted up and they function irregularly. Considering that pyridoxine (Vitamin B6) plays a crucial role in the development and functioning of brain, this supplementation of vitamin helps in solving the problems related to cardiovascular diseases. Thus, vitamin B6 is one of the strong candidates that can be helpful in alleviating cardiovascular diseases.

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Conflict of Interest

None of the authors have any conflicts of interest to declare.

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