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REVIEW ARTICLE

Beta-Sitosterol: A Comprehensive Review of Occurrence in Plants and its Therapeutic Potential in Treatment of Cardiovascular Disorders

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Abstract

Introduction: Phytosterols play a major role in the management of cardiovascular diseases. Beta-sitosterol sourced from various plants showed better therapeutic activity and mechanism in treating cardiovascular diseases. However, there has been no comprehensive review of the distribution of beta-sitosterol and its therapeutic activities in cardiac diseases. **Methods:** Thus, the review includes the occurrence and relevance of beta-sitosterol with its therapeutic outcomes on cardiac diseases. The literature collection process was conducted using scientific databases such as Pubmed, science direct, Google Scholar and books for the concise evaluation of the study. **Results:** The resultant review on beta-sitosterol has been concised to its biological sources and the process of isolation, therapeutic efficacy against the management of cardiovascular diseases by decreasing the cholesterol absorption which leads to a decrease in Low-density Lipoprotein (LDL) levels. **Conclusion:** Further preclinical and clinical studies can be explored to explore the efficacy of beta-sitosterol

Keywords: Beta-Sitosterol, Cardiovascular Diseases, LDL, Occurrence

1. Introduction

Beta-sitosterol, a plant sterol found in various plant-based foods such as vegetable oils, nuts, seeds and legumes, is gaining attention for its extensive health benefits due to its structural similarity to cholesterol. This phytosterol plays a vital role in managing several systemic diseases, including cardiovascular conditions, metabolic disorders, cancer and immune-related diseases. One of its most significant effects is lowering LDL cholesterol by inhibiting its absorption in the intestines, which helps prevent atherosclerosis and related cardiovascular events like heart attacks and strokes. In addition to lipid-lowering effects, beta-sitosterol acts as a potent antioxidant, neutralising free radicals and reducing oxidative stress, which is linked to chronic diseases such as cardiovascular disease, cancer and neurodegeneration[1]. Beta-sitosterol also exhibits strong anti-inflammatory properties by modulating inflammatory pathways and cytokine production, which can alleviate conditions like arthritis and inflammatory bowel disease. Moreover, it shows significant antidiabetic effects, improving insulin sensitivity, regulating blood glucose levels, and reducing complications in type 2 diabetes. Beyond metabolic health, beta-sitosterol helps modulate the immune system by enhancing immune cell function, supporting the body's defence against infections and potentially reducing autoimmune responses. It also has anticancer potential, shown to inhibit tumour cell growth and induce apoptosis in cancers like prostate, breast and colon cancer. Additionally, beta-sitosterol is beneficial for prostate health, improving symptoms of Benign Prostatic Hyperplasia (BPH) a condition

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causing prostate enlargement. With its multifaceted effects, beta-sitosterol is a promising natural therapeutic agent, offering a holistic approach to managing chronic diseases and improving overall health through its lipid-lowering, antioxidant, anti-inflammatory and immune-modulating properties. Beta-sitosterol, derived from various herbs, represents a cornerstone in natural medicine for managing a spectrum of systemic disorders. Its therapeutic efficacy stems from a different mechanism, making it a versatile agent in holistic healthcare. In this review, the comprehensive analysis of beta-sitosterol's characteristics and its diverse pharmacological activities underscores its potency in the management of various disorders[2].

2. Materials and Methods

A comprehensive literature search was conducted using electronic databases including PubMed, Google Scholar, Scopus and Web of Science. Articles published in national and international journals were included. Search terms included "Beta-sitosterol", "phytosterols", "systematic disorders", "cardiovascular disease" and related terms. Investigation studies about the role of beta-sitosterol in the treatment and management of cardiovascular disorders were considered.

2.1 Physical and Chemical Characteristics of Beta-Sitosterol

Beta-sitosterol is a plant-derived sterol with a molecular formula of $C_{29}H_{50}O$, closely resembling cholesterol in its structure, which consists of a steroid nucleus and a side chain[3]. It has a molecular weight of approximately 414.71 g/mol[3]. It typically appears as a white, waxy solid or crystalline powder that is odourless and tasteless[4]. While it is sparingly soluble in water, it is more soluble in organic solvents like ethanol, methanol, chloroform and ether[5]. Its melting point ranges from 136°C to 140°C[3] and it remains relatively stable under normal storage conditions, although it may degrade with prolonged exposure to heat or high temperatures[6]. Chemically, beta-sitosterol features a hydroxyl group at the C-3 position of the steroid nucleus and a double bond at the C-22 position in the side chain, making it functionally similar to cholesterol. This structural similarity allows beta-sitosterol to play a role in the synthesis of steroid hormones and bile acids, influencing various physiological processes in the body[7].

2.2. Biosynthesis of Beta-Sitosterol in Plants

The biosynthesis of beta-sitosterol in plants is a complex metabolic process essential for the production of phytosterols, a class of steroidal compounds crucial for plant growth and development. Beta-sitosterol, a prominent member of the phytosterol family, plays vital roles in membrane structure, hormone regulation and stress response mechanisms within plant cells [8].

Two primary pathways contribute to the biosynthesis of beta-sitosterol in plants: the Acetyl Mevalonate Pathway and the Deoxyxylulose Pathway[8,9]. In the Acetyl Mevalonate Pathway, beta-sitosterol synthesis commences with the combination of two molecules of Dimethylallyl Pyrophosphate (DMAPP) and one molecule of Isopentenyl Pyrophosphate (IPP) to form Farnesyl Pyrophosphate (FPP). Squalene, a triterpene derived from FPP, serves as the precursor for beta-sitosterol synthesis. The enzyme cycloartenol synthetase transforms squalene into cycloartenol, a structural precursor for various steroids, including beta-sitosterol[10]. The Deoxyxylulose Pathway also contributes to beta-sitosterol synthesis, although it involves different intermediate compounds and enzymes. This pathway offers an alternative route for the production of beta-sitosterol, highlighting the complexity and redundancy inherent in plant metabolic processes[8,11].

2.3. Key Enzymes and Intermediates

Several enzymes and intermediate compounds participate in the biosynthesis of beta-sitosterol, regulating the pathway's progression and ensuring the efficient conversion of precursor molecules into the final product. Enzymes such as squalene synthase and cycloartenol synthetase catalyse specific reactions, while intermediates like squalene and cycloartenol serve as critical substrates and precursors for downstream processes[8-12].

2.4. Pharmacokinetics and Bioavailability

Pharmacokinetic is the term that defines what the body does to the drug. It includes absorption, distribution metabolism and excretion.

2.4.1 Absorption

Beta-sitosterol is absorbed at a low rate of around 5% or less of the daily intake, whereas cholesterol absorption is

significantly higher, ranging from 45% to 54%[13]. Despite its low absorption rate, the 5% absorption of beta-sitosterol is sufficient to produce the desired pharmacological effects. This is because of their different mechanisms of absorption in the body[13]. Absorption of beta-sitosterol was limited by its solubility in mixed micellar solutions[14].

2.4.2 Distribution

The administered doses of beta-sitosterol ranged from 3 to 4µg. Due to the low plasma concentrations resulting from these doses, an ultrasensitive isotope ratio analytical method, accelerator mass spectrometry, was employed. The limit of quantification for beta-sitosterol was approximately 0.1 pg/ml. The oral absolute bioavailability was 0.41%, and the volume of distribution was 46L[15].

2.4.3 Metabolism

Similar to cholesterol, beta-sitosterol is a plant sterol that is mostly processed in the liver by enzymes called glucuronidation and sulfation. After metabolism, it either travels through enterohepatic circulation or is eliminated in bile. Once metabolised, it is either excreted in bile or recirculated through enterohepatic circulation. Its metabolites can exhibit various biological activities, including potential cholesterol-lowering effects. The percentage of esterified beta-sitosterol in plasma is the same as that of cholesterol. However, the rate of esterification for beta-sitosterol is slower than for cholesterol, with a metabolic turnover of 5.8 mg/ day[16].

2.4.4 Excretion

Beta-sitosterol can undergo biliary excretion, where it is secreted into the bile by the liver and then eliminated from the body through faeces. Beta-sitosterol is primarily excreted through faeces after being absorbed in the intestines. Only a small portion is excreted through urine[16].

2.5. Distribution of Beta-Sitosterol

Herbs contain ample phytosterols. A survey report is collected for the presence of beta-sitosterol and tabulated in Table Number 1.

2.6. Role of Beta-Sitosterol in Various Systemic Cardiovascular Diseases (CVD)

Cardiovascular Diseases are a wide range of disorders that affect the heart and blood vessels. The primary types of CVD include Ischemic Heart Diseases, Myocardial Infarction, Hypertension and atherosclerosis etc[41].

2.6.1 Myocardial Infarction

Heart attacks, also known as myocardial infarction, are mostly brought on by reduced oxygen or blood flow to the heart's cells. Numerous underlying coronary artery disorders could result from this. Ischemia is the term for decreased blood flow, whereas hypoxia is the term for decreased oxygen supply. This underlying cause affects the myocardial cells by various mechanisms which are mentioned in Figure 1. The major indications of Myocardial Infarctions are the permanent damage of Myocardial cells[42]. Hypoxia is a condition in which the body or a region of the body is deprived of adequate oxygen supply at the tissue level. As a result of Hypoxia Myocardial cells get damaged by various systemic mechanisms[43]. The schematic mechanism of Hypoxia-induced Myocardial damage is represented in Figure 1.

By blocking five distinct systemic pathways, beta-sitosterol functions as a powerful phytoconstituent for the treatment of hypoxia-induced cardiac injury. First off, elevated Peroxisome Proliferator-Activated Receptor Gamma (PPAR-γ) expression reduces the buildup of fat in cardiac cells. In addition to upregulating B-cell lymphoma (Bcl-2) protein, which has strong antiapoptotic properties against oxidative stress and inhibiting caspase 3 and 9[44], PPAR-γ has a protective effect against cardiomyocytes. This lowers the amount of Reactive Oxygen Species (ROS). Thirdly, pro-inflammatory mediators (cytokines) cannot be released from myocytes when Nuclear Factor-Kappa B (NF-kb) expression is inhibited. A key player in CVDs is NF-kb[45,46]. Mitochondrial Apoptotic factor release is reduced as a result of upregulating Bcl-2 protein, which is caused by enhanced PPAR-γ expression[47-49]. Ultimately, by encouraging oxidative phosphorylation, elevated mitochondrial membrane potential causes Cytochrome C oxidase to produce more Adenosine Triphosphate (ATP)[50,51]. The ultimate aim of these five mechanisms of beta-sitosterol is to inhibit Myocardial damage. All these five mechanisms were interlinked with each other.

Ischemia or ischemia is a restriction in blood supply to any tissue, muscle group, or organ of the body, causing a shortage of oxygen that is needed for cellular metabolism[52]. The pathogenesis of Ischemia is

Table 1. Distribution of beta sitosterol

S. No.	Plant name and family	Quantitative estimation of beta sitosterol	Parts of plants	Amount of beta sitosterol in each part of plants	Maximum content of beta sitosterol
1	*Albizia lebbeck (Fabaceae)*	GC/MS DNA Fingerprinting	1. Seed oil 2. Leaf 3. Pericarp 4. Stem	35.97%[17] 26.98%[18] 15.43% [18] 15.96%[18]	Maximum amount of beta sitosterol present in Tunisian cold pressed lentisk seed oil: 148.8 to 183.0 mg /100 g oil
2	*Aloe barbadensis miller (Asphodelaceae) (Liliaceae)*	GLC - MS and LC - MS	1.Fresh leaf 2. Dried leaf 3. Fresh gel 4. Fresh leaf juice	7.33 mg/g [19] 148.0 µg/100g [19] 0.05 µg/ml (GC-MS)[19] 2.3 - 4.1 ng/ml (LC - MS)[19] or 2.5-7.5 mg/g[19]	Fresh leaf juice of aloe Vera contains the highest quantity of beta sitosterol.(7.5 mg/g)
3	*Saraca asoca (Leguminosae)*	HPLC and target mass spectroscopy	1. Leaf 2. Bark 3. Root 4. Flower	124 ng/ml[20] Or 3.37×10^-3 mg/ml in methanolic extract and 4.33×10^-5 mg/ml in aqueous extract[21] 170 ng/ml[22] 0.47 ng/ ml[22] 0.25 ng/ml[22]	The methanolic extract of the leaf contains the highest amount of beta sitosterol That is 3.37×10^-3 mg/ml
4	*Cynodon dactylon (Poaceae)*	HPTLC and GC - MS Analysis	1. Whole plant 2. Rhizomes 3. Leaf	40 - 90 µg/ml[23] 0.0046 µg/ml[24] 3199.62 µg/ml which is 32.43 % of the whole content.(GC-MS)[24]	Rhizomes of cynodon dactylon contains highest amount of beta sitosterol that is 3199.62 mg /kg which is 32.43 % of whole rhizomes
5	*Clitoria ternatea (Fabaceae) (legumes)*	HPTLC	1. Root 2. Leaf 3. Stem 4. Flower	1.5-13.3 µg/mg (ethanolic extract)[24] 13.2±1.706 µg/mg (Petroleum ether)[25] 13.3 ± 0.962 µg/mg[25] 2.55 µg/mg[26] 6.77 mg/100 g[26]	Leaf has the highest amount of beta sitosterol that is 13.3+_0.92 µg/mg
6	*Psidium guajava (Myrtaceae)*	HPTLC	1. Fruit 2. Leaf 3. Flowers 4. Bark	486 g/ mole[28] or (2410 µg/ml)[27] 3210.52 µg/ml[27] 1059.47 µg/ml[27] 0.59 µg/ml[27]	Leaf contains the highest amount of beta sitosterol of 3210 µg/ml
7	*Leucas aspera (Lamiaceae)*	HPTLC	1. Flower 2. Leaf Extract 3. Whole plant	0.3-1.0 ng/ml[29] 0.1-0.5µg/ml[30] 1.58 µg/250 mg[30]	Flowers of leucas aspera contains the highest amount of beta sitosterol that is 1.0 ng/ml.
8	*Agava angustifolia (Asparagaceae)*	HPTLC and LC - MS	1. Pina 2. Leaf 3. Rhizome 4. Floral	124.76 mg/g[31] 26.67 mg/g[31] 106.19 mg/g[32] 103.96 mg/g[32]	Pina (the heart wood) contains the highest amount of beta sitosterol among all parts that is 124.76 mg /g
9	*Eclipta alba (Asteraceae)*	HPTLC	1. Leaf 2. Flower	150.76 ± 4.56 µg/ml [33] 77.09 ± 3.07 µg/ml [33] (4.72 %w/w in ethanolic extract) (4.67 % w/w in petroleum ether extract)[34]	Leaf extract contains high concentration of beta sitosterol that is 150.76 ± 4.56 µg/ml

Table 1. Continued...

S. No.	Plant name and family	Quantitative estimation of beta sitosterol	Parts of plants	Amount of beta sitosterol in each part of plants	Maximum content of beta sitosterol
10	*Spathodea campanulata Aurea (Bignoniaceae)*	HPTLC	1. Leaf 2. Bark 3. Flower	44.12 µg/ml[35] 2.04 µg/ml[35] 17.44 µg/ml[35]	Fresh leaf extract contains the maximum,amount of beta sitosterol that is 44.12 µg/ml
11	*Sesbania grandiflora (Fabaceae)*	HPTLC	1. Bark	153.09 microgram/mg [36]	Bark contains the high amount of betasitosterol 153.09 µg/mg
12	*Urginea indica (Liliaceae)*	TLC	1. Leaf 2. Rhizomes 3. Bulb	12.67 mg/g[37] 9.47 mg /g[37] 9.40 mg/g[37]	
13	*Phyllanthus emblica (Phyllanthaceae)*	HPTLC and GC-MS	1. Leaf 2. Bark 3. Fruit	0.48 - 2.75 mg/g [38] 11.50 ± 0.27 mg /100 g [38] 12.12 ± 1.90 mg/100 g [38]	Fruit contains high amount of beta sitosterol that is 12.12 ± 1.90 mg/100 g
14	*Moringa oleifera (Moringaceae)*	GC- MS	1. Leaf	90 mg/g[39]	Fresh leaf extract posses the high content of beta sitosterol (90 mg/g)
15	*Gloriosa superba (Colchicaceae)*	TLC	1. Leaf 2. Flower 3. Stem 4. Rhizomes	12.43 mg/g[40] 11.82 mg/g[40] 9.71 mg/g[40] 8.92 mg/g[40]	Leaf contains high amount of beta sitosterol that is 12.43 mg/g

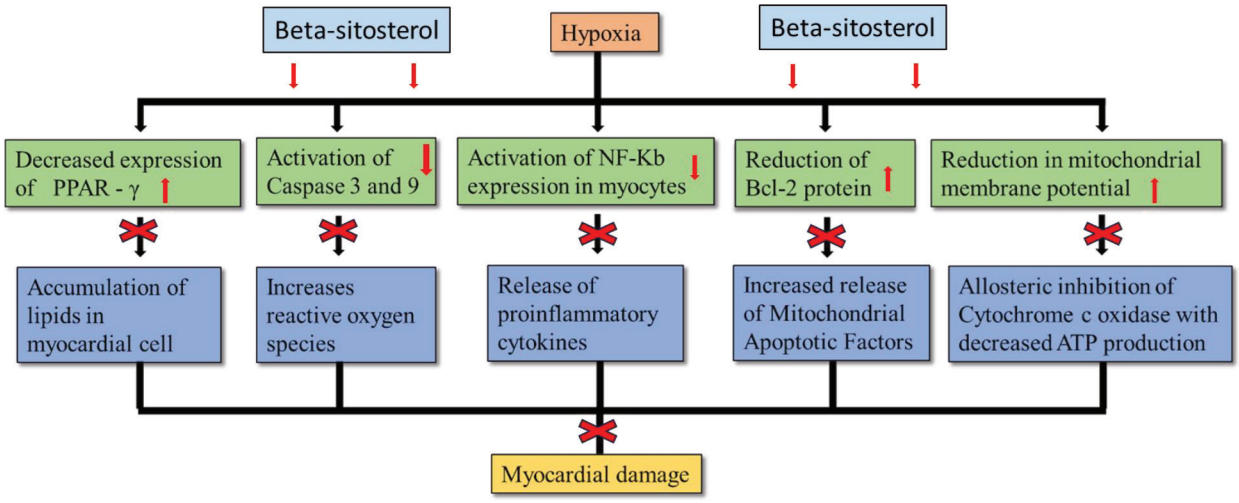


Figure 1. Mechanism of Hypoxia-induced myocardial damage.

associated with the following mechanisms mentioned in Figure 2.

Beta-sitosterol acts against ischemia-induced myocardial damage by decreased expression of direct myocardial depressant factor (IL-1)[53]. The second mechanism involves decreased accumulation of TNF-alpha, resulting in the inactivation of the Tumour Necrosis Factor (TNF) dependent NF-kb pathway which plays an important role in inhibitory expression of proinflammatory genes including cytokines, chemokines and adhesion molecules[54]. Further, the inactivation of AMP-Activated Protein Kinase (AMPK) promotor dephosphorylates the Ser1179 site on endothelial Nitric Oxide Synthase (e NOS). Endothelial

Nitric Oxide Synthases play a critical role in maintaining a healthy CVS[55]. Beta-sitosterol also regulates the glutathione antioxidant system[56]. Lastly, decreased accumulation of LDL (Hyperlipidemia)[57] decreases the accumulated peroxide in cardiomyocytes[58,59]. The inhibitory action of beta-sitosterol on these mechanisms inhibits the synthesis of Nitric oxide synthase (NOS), resulting in decreased production of Nitric oxide resulting in the prevention of Myocardial cells from damage[60].

The major result of ischemia and hypoxia in the coronary system is the permanent damage of myocardial cells. This damage will lead to impairment in systolic and diastolic function thus resulting in major and serious complications[61]. Beta-sitosterol interferes with various mechanisms. It is used in the treatment and prophylaxis of Myocardial Infarction that inhibits the damage of Myocardial Cells by ischemia and hypoxia[44].

2.6.2 Hypertension

Hypertension, commonly known as high blood pressure, is a condition where the force of blood against the artery walls is consistently too high. If left untreated, this chronic condition can lead to complications such as heart disease, stroke, and kidney problems[62,63]. There are two main types of hypertension.

2.0.0.1 Primary (Essential) Hypertension

The exact cause of primary hypertension is often unknown. It is believed to develop gradually over many years and is influenced by a combination of factors, including genetics, lifestyle choices and environmental factors[64].

2.0.0.2 Secondary Hypertension

This type of hypertension is caused by an underlying condition or medication that affects blood pressure. It typically develops suddenly and tends to be more severe than primary hypertension[65]. Causes of secondary hypertension can include kidney disease, adrenal gland tumours, thyroid problems, certain medications (such as birth control pills, cold remedies, decongestants and some prescription drugs) and illegal drugs (such as cocaine and amphetamines)[66].

Hypertension can also be categorised based on its origin into hormonal hypertension and renal hypertension. The general description of hypertension involves increased cardiac output and increased peripheral resistance[67].

2.6.2.3 Primary Hypertension

Two mechanisms, increased uptake of sodium as well as decreased uptake of potassium increase the extracellular

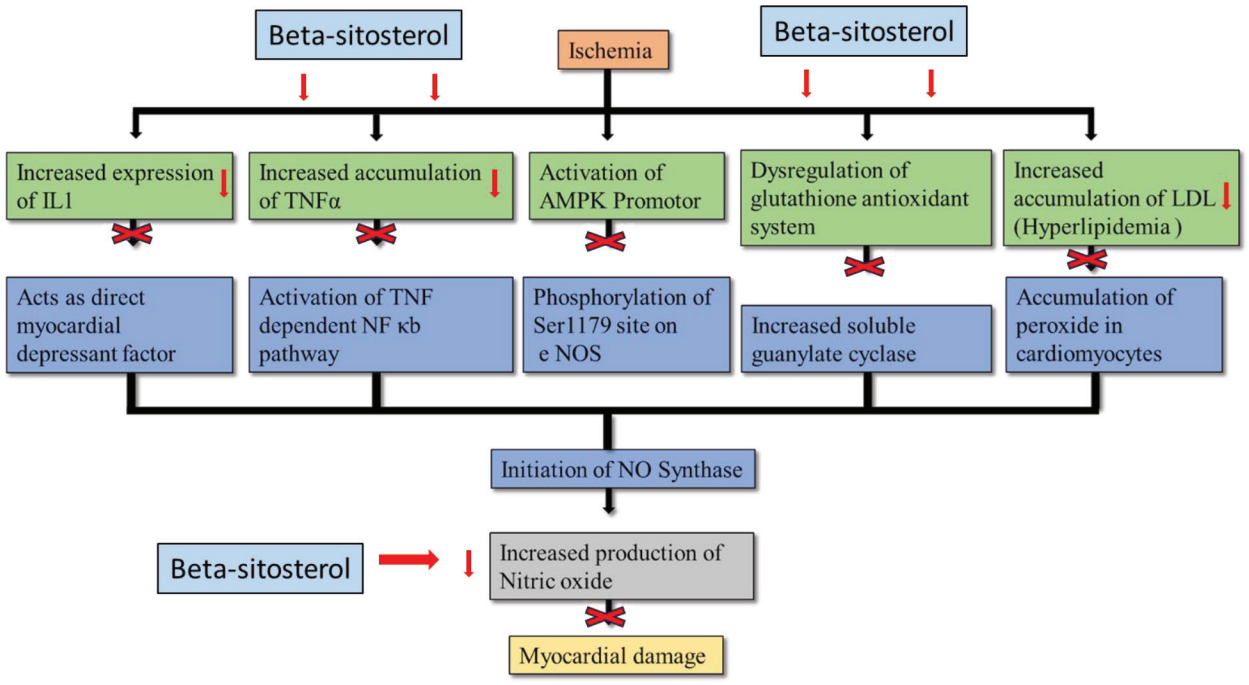


Figure 2. Mechanism of Ischemia-induced myocardial damage.

volume, which in turn increases the Calcium in the muscles of blood vessels[68]. The amplitude of action potential increases to a greater extent causing enhanced vasoconstriction which simultaneously increases cardiac stimulation as well as causing hypertrophy of vascular musculature[69]. Increased cardiac output and peripheral resistance cause primary hypertension[70], as mentioned in Figure 3.

Beta-sitosterol has a crucial role in the regulation of sodium and potassium in the blood. It mainly acts by increasing the elimination of sodium and increasing the potassium in the blood. This leads to a decrease in extracellular volume and decreases the calcium level in the blood[71]. Increased potassium ion in the blood leads to hyperpolarisation thus amplitude of action potential generation decreases[72]. Hence the vasoconstriction is also limited and promotes vasodilatation. Though calcium ion is essential for the generation of action potential, decreased calcium ion concentration reduces vasoconstriction[73]. This restriction in vasoconstriction maintains the balance between cardiac output and peripheral resistance[74].

2.6.2.4 *Renal Hypertension*

A major phenomenon, renal artery stenosis and several other renal diseases are responsible for renal ischemia[75], Renal ischemia mediates the release of Renin[76]. Renin plays a predominant role in the conversion of Angiotensinogen into Angiotensin I in the liver. The released angiotensin I circulates through the blood and reaches the lungs. In the lungs it gets converted into Angiotensin II by Angiotensin angiotensin-converting enzyme, which in turn increases Angiotensin II which is a powerful vasoconstrictor, eventually causing the release of Aldosterone[77]. Aldosterone increases sodium reuptake leading to an increase in the extracellular volume consequently increasing the cardiac output[78]. An increase in the Angiotensin I has an additional mechanism where it tends to increase the peripheral resistance causing renal hypertension. An increase in the

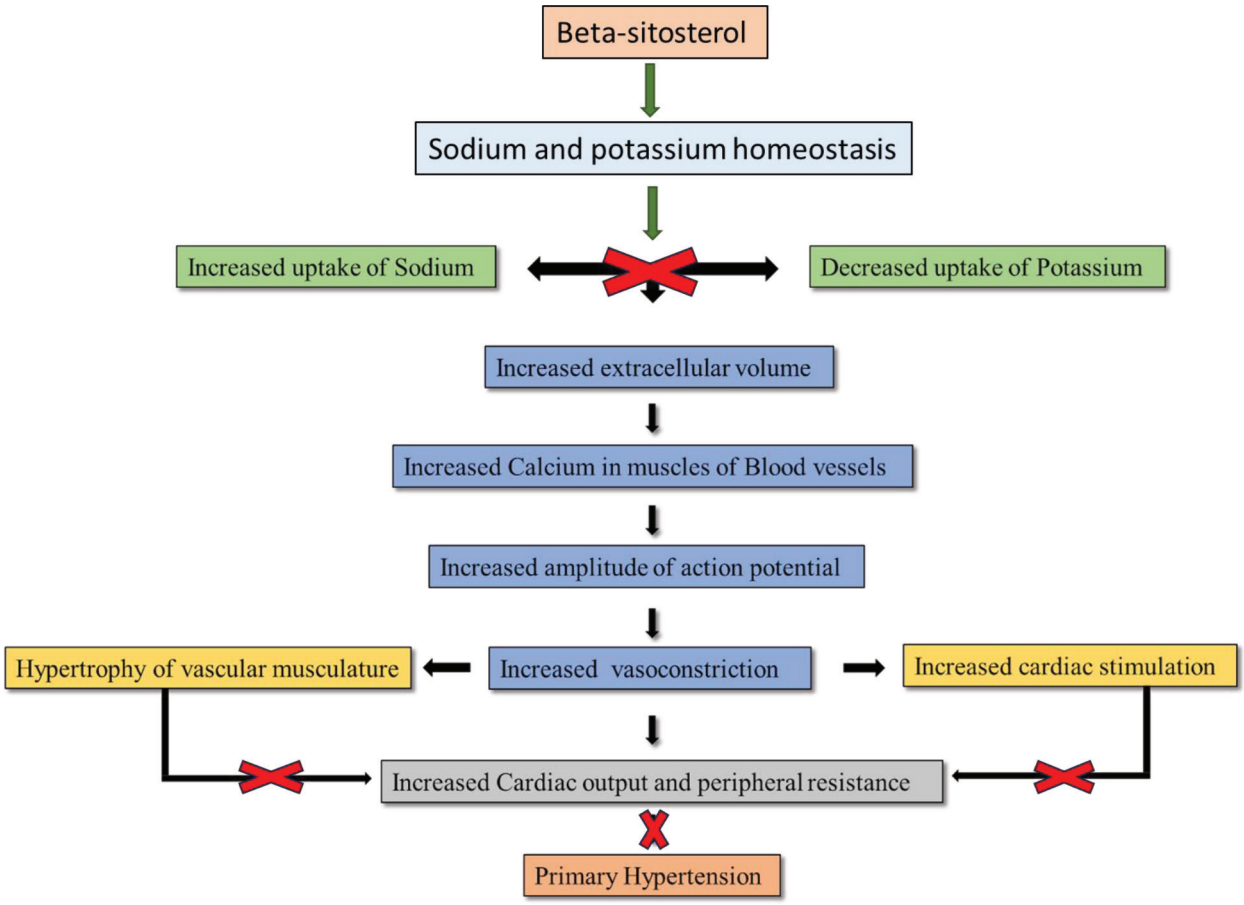


Figure 3. Mechanism of primary hypertension.

cardiac output is the ultimate output of this mechanism as well[79]. The mechanism of renal hypertension was simplified in Figure 4.

In renal hypertension, beta-sitosterol mainly targets the release of renin and Angiotensin-Converting Enzyme (ACE) in the lungs[80]. Decreased releases of renin preferentially decrease the conversion of angiotensinogen into angiotensin I. Beta-sitosterol also inhibits ACE in lungs thus decreasing the conversion of Angiotensin I into Angiotensin II. Beta-sitosterol also maintains the sodium and potassium ion balance, which decreases the sodium ion and increases the potassium ion in blood by increasing the secretion of sodium ions from blood to renal tubules[77]. Hence beta-sitosterol is widely used in renal hypertension[81].

2.6.2.5 Hormonal Hypertension

Hormonal hypertension is otherwise referred to as Endocrine hypertension. Endocrine hypertension typically refers to disorders of the adrenal gland including primary aldosteronism, glucocorticoid excess and the pheochromocytoma-paraganglioma syndromes[82]. Hormonal hypertension is a result of four major reasons, including Adrenogenital syndrome, Primary hyperaldosteronism, Cushing syndrome and Pheochromocytoma[83].Beta-sitosterolhasindirectaction on decreasing the accumulation of 11-deoxycortisol and 11-deoxycortisone, thereby decreasing cardiac output leading to blocking hormonal hypertension[84]. Secondly, primary hypertension decreases aldosterone secretion blocking mineralocorticoid effect[85] which ultimately decreases the cardiac output and peripheral resistance as well. Similarly, Beta-sitosterol decreases the release of the cortisol blocking mineralocorticoid and catecholamine effect, further hormonal hypertension is blocked by a decrease in cardiac output and peripheral resistance. Finally, decreased release of catecholamine leading to a suppressed mineralocorticoid and catecholamine effect is a characteristic of Beta-sitosterol on Pheochromocytoma causing a decrease in the cardiac output and peripheral resistance, an eventual hormonal hypertension is evident[86] as mentioned in Figure 5.

2.6.3 Atherosclerosis

Atherosclerosis is a condition characterised by the buildup of plaque (composed of fats, cholesterol, calcium and other substances) inside the arteries. This buildup gradually narrows and hardens the arteries, reducing blood flow to organs and tissues throughout the body[87]. Recent research proves that gut microbiota plays an important role in the development and progression

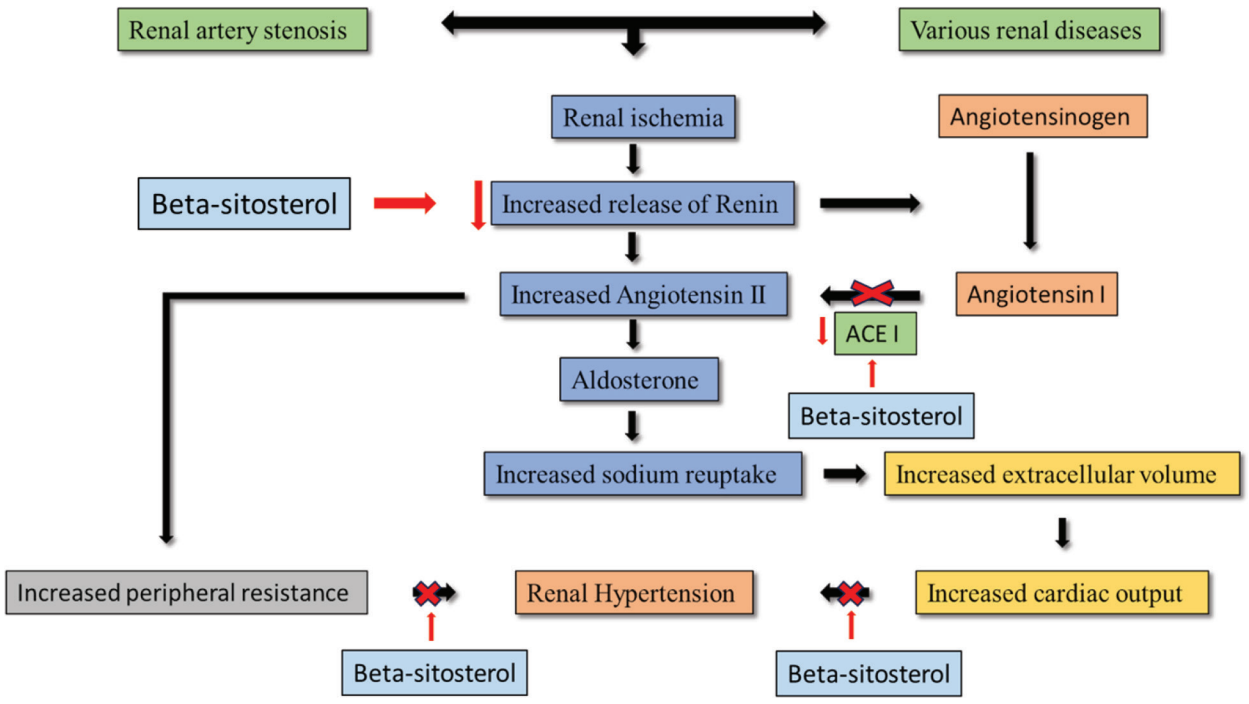


Figure 4. Mechanism of renal hypertension.

of atherosclerotic plaque[88]. Gut microbiota includes millions of microorganisms such as bacteria, viruses, fungi and archaea. Gut microbiota plays an important enzymatic role in metabolising Dietary Choline, Carnitine, Lecithin etc[89]. It results in the formation of Trimethylamine. Trimethylamine is further oxidised into Trimethylamine oxide by FMO-3 (Flavin-Containing Monooxygenase (FMO) enzymes)[90] as in Figure 6.

Activated Trimethylamine (TMA) serves as a hallmark for the formation, maturation and rupturing of Atheromatous plaque by four different mechanisms formation of foam cells, endothelial dysfunction, platelet aggregation and plaque instabilities[91]. The ultimate result of these pathways is to form plaque which decreases the blood vessel diameter and thus sufficient blood cant flow to myocardial cells and to all other organs as mentioned in Figure 7.

Beta-sitosterol mainly acts by inhibiting the cell wall formation in gut microbes[92,93], hence this interruption in the metabolism of Dietary Choline, Carnitine and Lecithin results in the depletion of Trimethylamine N-oxide (TMAO). Beta-sitosterol decreases the synthesis of TMAO also by inhibiting the action of FMO3[92]. A significant decrease in the level of TMAO is observed. A decrease in the level of trimethylamine in turn decreases the level of foam cell formation, reduced endothelial dysfunction, platelet aggregation and plaque instability. (i) Inhibiting signalling of Mitogen-activated protein kinase and NF-kb followed by the action of Beta-sitosterol on the decrease in inflammation and oxidative stress, ultimately damaging the Endothelial[94]. (ii) Reduction in platelet aggregation inhibits calcium release from intracellular calcium stores, hence calcium-dependent platelet aggregation cannot possess platelet adherence to immobilised collagen[95]. Inhibitory action of TMAO on platelet responsiveness suppresses thrombus formation[96]. (iii) Reduction in plaque instability or increased platelet stability decreases the formation of micro-vasculatures inside the plaque, which leads to balanced maintenance between the angiogenesis and pro-angiogenic factor[97]. Hence the formation and rupturing of atherosclerotic plaque ultimately decreases. (iv) Decreased foam cell formation due to decreased differentiation of monocytes into macrophages[98]. Oxidised LDL cannot be sensitised and engulfed by undifferentiated monocytes. Hence, there will be no accumulation of Ox LDL. Ultimately this results in the inhibition of the formation of foam cells. (v) The decreased endothelial dysfunction causes regulation of anti-inflammatory cytokine (IL-10), characterised by activation of circulating Endothelial Progenitor Cells (EPCs)[99].

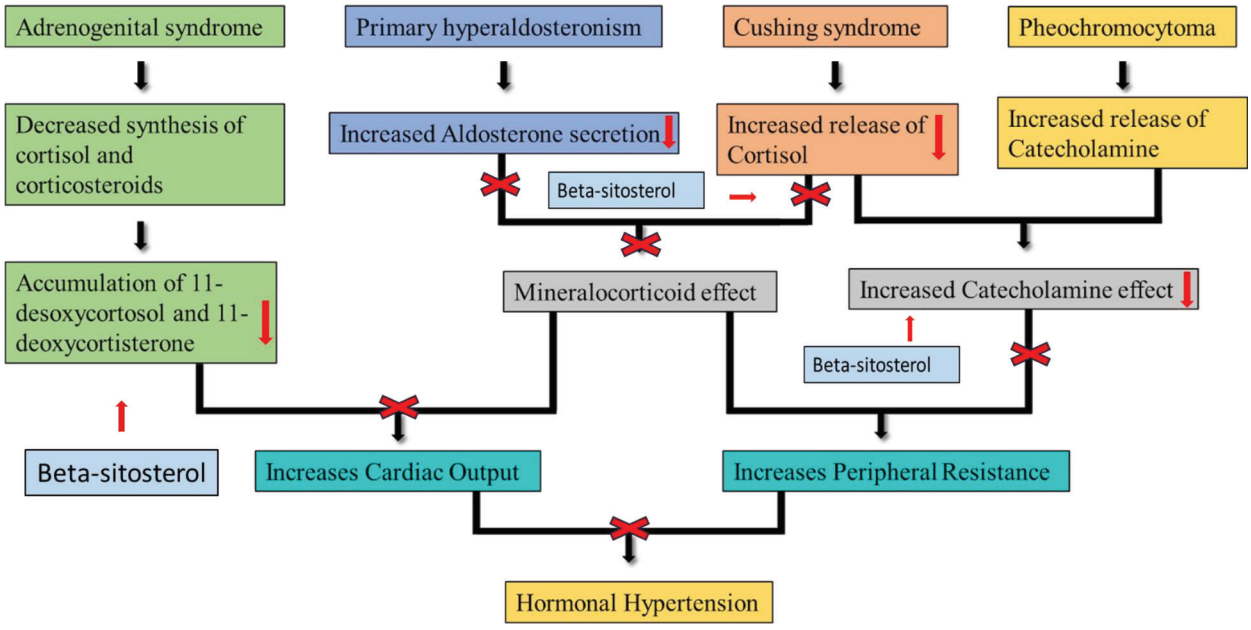


Figure 5. Mechanism of hormonal hypertension.

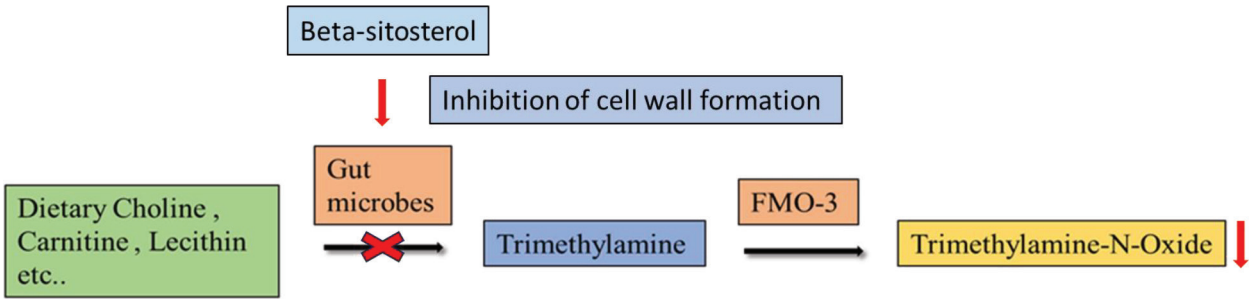


Figure 6. Mechanism of Trimethylamine N-oxide (TMNO) synthesis from the dietary supplement.

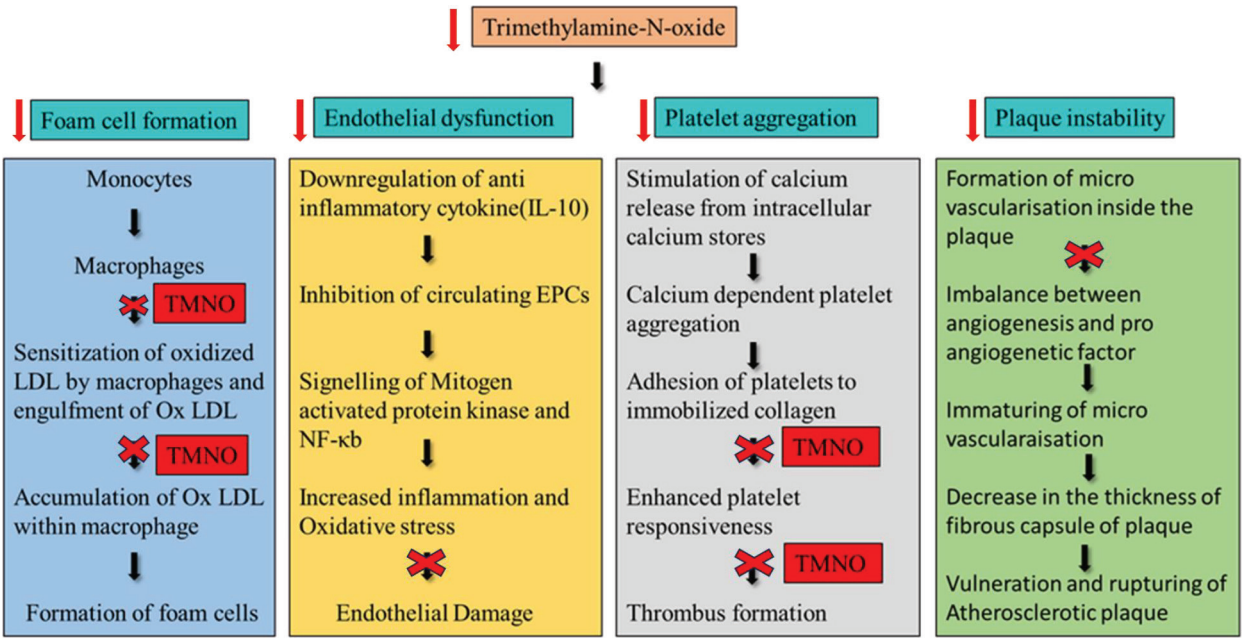


Figure 7. Mechanism of atherosclerosis by trimethylamine N-oxide TMAO.

3. Results and Discussion

Beta-sitosterol belongs to the group of phytosterols, which are plant-derived sterols structurally similar to cholesterol. It is naturally present in various plant foods such as nuts, seeds, fruits and vegetables. Common sources include soybeans, peanuts, corn oil and wheat germ. Beta-sitosterol is characterised by its ability to inhibit cholesterol absorption in the intestine. It competes with cholesterol for absorption in the gut lumen, thereby reducing the amount of cholesterol that enters the bloodstream. This mechanism is particularly significant in managing hypercholesterolemia, which is a major risk factor for cardiovascular diseases. Beta-sitosterol is well known for its cholesterol-lowering effects, anti-acrosclerotic effects, blood pressure regulation, antioxidant properties and anti-inflammatory activity. Clinical trials evaluating the efficacy of beta-sitosterol in cardiovascular health have shown positive results. A meta-analysis published in the American Journal of Cardiology concluded that phytosterol supplementation, including beta-sitosterol, significantly lowers LDL cholesterol levels, thus reducing cardiovascular risk. Beta-sitosterol shows potential in managing cardiovascular disorders, further clinical trials are necessary to establish its long-term safety profile and efficacy significance, particularly in wide-range populations and in combination with potential existing treatments.

4. Conclusion

In conclusion, beta-sitosterol holds significant promise as a natural compound with therapeutic potential in

managing cardiovascular disorders, primarily through its cholesterol-lowering, anti-inflammatory and antioxidant properties. Continued research efforts are crucial to establish its role in clinical practice, enhance therapeutic outcomes and expand our understanding of its mechanisms of action in cardiovascular health. Integrating beta-sitosterol into comprehensive cardiovascular care strategies has the potential to mitigate disease burden and improve patient outcomes in diverse populations. In conclusion, beta-sitosterol emerges as a promising natural compound with significant therapeutic potential in the management of cardiovascular disorders. Derived from various plant sources and commonly found in everyday diets, beta-sitosterol exerts its effects through multiple mechanisms that contribute to cardiovascular health. Beta-sitosterol, a natural phytosterol abundant in plant sources, holds promise in the management of cardiovascular disorders. Its ability to lower LDL cholesterol, reduce inflammation and potentially regulate blood pressure makes it a valuable candidate for adjunctive therapy in cardiovascular care. Continued research into its mechanisms and effects will provide further insights into its therapeutic potential and optimal clinical use.

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