IJMPR, 2026, 10(6), 24-30 ISSN: 2319-5878

INTERNATIONAL JOURNAL OF MODERN PHARMACEUTICAL RESEARCH

www.ijmpronline.com

Review Article

Impact Factor: 7.533

Coden USA: IJMPR3

ROLE OF NUTRACEUTICALS IN THE PREVENTION OF CARDIOVASCULAR DISEASES

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Article Received on: 01/05/2026 **Article Revised on: 22/05/2026** **Article Published on: 01/06/2026**

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https://doi.org/10.5281/zenodo.20441877

How to cite this Article: Soujanya V. K.*[1], E. R. Vishwanath[2], Abhishek Gupta N. D.[3], Varshini K. B.[4], Anusha T. S.[5]. (2026). Role of Nutraceuticals In The Prevention of Cardiovascular Diseases. International Journal of Modern Pharmaceutical Research, 10(6), 24–30.

ABSTRACT

Cardiovascular diseases (CVDs) are among the primary causes of death globally. Conditions such as hypertension, elevated cholesterol levels, diabetes, obesity and chronic inflammation significantly increases the risk of developing heart- related disorders, including atherosclerosis, coronary heart disease, and stroke. In recent years, nutraceuticals natural bioactive compounds derived from food have attracted considerable interest for their potential role in preventing cardiovascular disease risk. Various nutraceuticals, including omega-3 fatty acids, plant sterols, flavonoids, dietary fibers, probiotics, coenzyme Q10, garlic extracts, and polyphenols, demonstrate beneficial effects on heart health. Research findings indicate that incorporating specific nutraceuticals into the daily diet along with healthy lifestyle practices may contribute to the prevention and management of cardiovascular conditions. Nutraceuticals are best used as supportive therapy and should complement, rather than substitute, standard medical treatment in patients with established cardiovascular disease. Overall, nutraceuticals represent a promising adjunct approach in cardiovascular care by addressing modifiable risk factors and enhancing heart health.

KEYWORDS: Nutraceuticals, Cardiovascular disease, Omega-3 fatty acids, Dietary factors, Bioactive compounds.

INTRODUCTION

NUTRACEUTICALS

The words “nutrient” which refers to nourishing dietary components and “pharmaceutical” which denotes medicinal treatments, is combined to form the phrase nutraceutical. Nutraceuticals, which were first introduced in 1989 by Stephen De Felice, the founder and head of the Foundation for Innovation in Medicine in Cranford, New Jersey, represent the preventive philosophy of Hippocrates, the ancient Greek physician who is sometimes cited as stating, “Let food be your medicine”.[1,2]

Fig. no. 1: Nutraceuticals.

"Nutraceuticals" is a broad term used to describe any product derived from food sources that provides extra health benefits beyond the basic nutritional value of meals.

Nutraceuticals have attracted a lot of attention lately because of their possible medicinal, safety, and nutritional advantages. These compounds are involved in a variety of biological activities, including gene expression, cell division, antioxidant defence, and mitochondrial integrity preservation. Nutraceuticals can therefore be used to support the body's general functioning and integrity or to promote health, reduce chronic diseases, and slow down the aging process, all of which extend life expectancy. These products are thought to support a healthy lifestyle and are acknowledged as important sources for preventing life-threatening illnesses like diabetes, renal and gastrointestinal disorders as well as other infections.[3, 4]

Nutraceuticals beneficial benefits are mostly attributed to their anti-inflammatory and antioxidant properties, suggesting that they could be utilized as a treatment to reduce arterial stiffness in the elderly.

Numerous nutraceuticals have been shown to play a significant role in immune function and susceptibility to disease states. Nutraceuticals can also be used to treat a variety of oxidative stress-related conditions, including allergies, Alzheimer's disease, cardiovascular disorders, cancer, eye problems, Parkinson's diseases, and obesity.

The definition of nutraceuticals and associated products is typically determined by the source. These products can be classified based on their natural sources, chemical makeup, and pharmacological conditions. Nutraceuticals are classified into two primary categories: dietary supplements and functional foods.[5]

TYPES OF NUTRACEUTICALS

1. Dietary supplements
2. Functional Foods

1. Dietary supplements: Dietary supplements are products that have been processed into an appropriate dose form and contain concentrated bioactive components from food sources. These supplements may contain a wide range of chemicals, including as vitamins, minerals, vital metabolites, herbs and other botanicals, amino acids, and certain enzymes. There are many different types of dietary supplements, such as drinks, sweets, energy bars, tablets, capsules and powders.

2. Functional Foods: Functional foods are those that provide health advantages beyond simple sustenance. This category includes whole foods that can improve health when regularly consumed as part of a balanced diet. Pasta, cereal, whole grains, yogurt, snacks are examples of functional food. Functional food includes:

- Traditional Functional Foods: Lycopene in tomatoes and omega-3 fatty acids in salmon are examples of natural, nutrient-dense meals that provide health benefits beyond mere sustenance.
- Non-Traditional Functional Foods: Artificial food is supplemented with bioactive elements to enhance health and wellness. Iron-enriched cereals, wheat with additional folic acid, and fortified foods like calcium-infused drinks are few examples. Bread, yogurt, cheese, and vinegar are examples of Non-Traditional functional foods.[6]

CARDIOVASCULAR DISEASES

Cardiovascular diseases (CVDs) have become one of the leading causes of sickness and mortality in both developed and developing countries, affecting millions of individuals worldwide in recent years. Heart and blood vessel illnesses, such as stroke (cerebrovascular disease), heart attacks (coronary heart disease), high blood pressure (hypertension), rheumatic heart disease, heart failure, peripheral artery disease, and congenital heart defects, are together referred to as CVD.[7]

One of the main physiological factors causing cardiovascular and cerebrovascular events in older persons is age-related arterial dysfunction. Stiffening of the large elastic arteries, such as the aorta and carotid arteries, during midlife is particularly predictive of cardiovascular and cerebrovascular events, as well as an increased risk of Alzheimer's disease and other dementias later in life, among the various forms of arterial dysfunction. The development of high blood pressure (hypertension) and increased pulsatile stress (increased blood flow pulsatility) taking place critical organs like the heart, brain, and kidneys are two major outcomes of this arterial stiffening. Furthermore, through their interactions with other risk factors like diabetes mellitus, metabolic syndrome, and lifestyle risk factors like smoking, dietary variables have a significant impact on cardiovascular risk, either directly or indirectly. Cardiovascular disease (CVD) is extremely common; in fact, the majority of those over sixty typically have CVD. According to estimates from 2020 and 2021, CVD is projected to be responsible for 20.3 million deaths worldwide year.CVD mortality can be greatly impacted by lowering risk factors in the population, especially blood pressure and cholesterol.[8]

CARDIOVASCULAR DISEASE (CVD) AND THEIR TYPES

A variety of disorders affecting the heart or blood arteries are included under CVD. Heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, arrhythmia, congenital heart disease, vascular heart disease, carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, venous thrombosis, and coronary artery diseases (such as angina and heart attack)are all included in this category.[9]

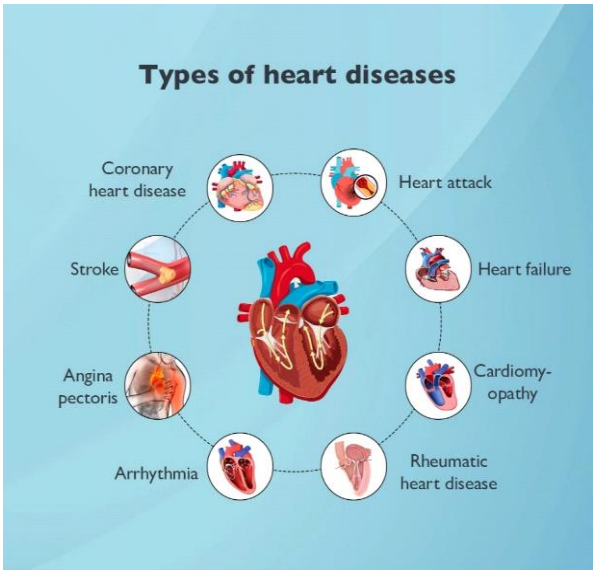

Fig no 2: Types of Cardiovascular Disease.

TYPES OF CVD

- Coronary Heart Disease
- Stroke
- Peripheral Arterial Disease
- Aortic Disease

(A) CORONARY HEART DISEASE: When fatty substances (atheroma) accumulate in the coronary arteries, the flow of blood to the heart muscle is impeded or halted, resulting in coronary heart disease (CHD). The blood flow to the heart depends on these arteries. Angina (chest pains) can occur when the coronary arteries narrow as a result of atheroma accumulation, which limits blood supply to the heart muscle. In more serious cases, a complete blockage of a coronary artery may cause a heart attack, which would require surgery.[10]

(B) STROKE: A interruption in the blood supply to the brain can result in a stroke, a serious medical illness. The bloodstream provides the brain with the oxygen and nourishment it needs to function properly, just like any other organ. Brain cells die if blood flow is restricted or stopped, which could cause brain damage or even death. A stroke is considered a medical emergency due to the severity of the condition, requiring prompt medical attention. In order to minimize potential harm, intervention timescales are quite important.

The primary symptoms of a stroke are

- Face: noticeable one-sided sagging, mouth or eye drooping
- Arms: weakness makes it difficult to elevate one arm to a higher position.
- Speech: Despite appearing alert, there is slurred speech and an inability to communicate.

(C) PERIPHERAL VASCULAR DISEASE: An obstruction in the arteries supplying blood to the limbs-usually the legs-causes peripheral vascular disease. Walking-related leg pain, usually in one or both thighs, hips, or calves, is a common sign of peripheral vascular disease. The pain may resemble cramping, a chronic soreness, or a feeling of the leg muscles being heavy. Usually intermittent, this pain gets worse when engaging in leg-intensive tasks like walking or climbing stairs.

(D) AORTIC DISEASE: Transporting blood from the heart to every region of the body is a vital function of the aorta, the body's main blood conduct. Aortic aneurysms, a common type of aortic illness, are characterized by the aorta's wall weakening and bulging outward. Pain in the chest, back, or abdomen is typically reported by those who have this illness.[11]

A) Symptoms of cardiovascular disease

- ❖ Chest Pain
- ❖ Shortness of breath
- ❖ Fatigue
- ❖ Swelling
- ❖ High Blood Pressure
- ❖ Palpitations

B) Causes of cardiovascular disease

- High Blood Pressure
- Diabetes Mellitus
- Smoking
- Stress and Mental Health
- Alcohol Consumption

C) Risk factors of cardiovascular disease

Modifiable Risk Factors:

- ➢ Unhealthy Diet
- ➢ Obesity and Overweight
- ➢ Physical Inactivity
- ➢ High Cholesterol levels
- ➢ Stress

Non-Modifiable Risk Factors

- ➢ Age
- ➢ Gender
- ➢ Family History
- ➢ Genetics

D) Complications of cardiovascular disease

- Heart Attack
- Arrhythmias
- Heart Failure
- Peripheral Artery Disease
- Pulmonary Embolism
- Endocarditis

E) Diagnosing cardiovascular disease

A combination of medical history evaluation, physical examination, diagnostic testing, and imaging procedures are usually used to diagnose cardiovascular disease (CVD). The particular diagnostic strategy may change based on the patient's risk factors and the suspected kind of CVD.

1. Medical History and Physical Examination: The medical professional will assess the patient's medical history, including any family history of cardiovascular disease, risk factors (such diabetes, smoking, or high blood pressure), and any symptoms that might point to a cardiovascular issue.
2. Blood Tests: Blood testing can provide crucial information about blood sugar, cholesterol, and indicators of heart muscle damage in cases of suspected heart attacks. Other tests, such as brain natriuretic peptide (BNP) and C-reactive protein (CRP), may be used to assess inflammation and heart function, respectively.
3. Electrocardiogram (ECG): An ECG records the electrical activity of the heart and can be used to detect irregular heart rhythms(arrhythmias),cardiac anomalies, and signs of previous myocardial infarctions.
4. Echocardiography: Echo uses ultrasonic waves to produce images of the structure and operation of the heart. It can evaluate heart valve performance, pumping efficiency, and chamber size.
5. Magnetic Resonance Imaging (MRI): Cardiac MRI creates extraordinarily accurate pictures of the structure and function of the heart using radio waves and magnetic fields. In addition to evaluating blood flow and cardiac viability, it can identify anomalies such as cardiomyopathy or congenital heart problems.
6. Coronary Calcium Scoring: This non-invasive imaging test uses computed tomography (CT) to measure the amount of calcium in the coronary arteries in order to assess the risk of coronary artery disease (CAD).[12]

Cardiovascular Disease Types and Nutraceutical Role
1. HIGH BLOOD PRESSURE: A major and quickly evolving global health concern is hypertension (HTN), which is defined as a diastolic blood pressure (DBP) of more than 90 mmHg or a systolic blood pressure (SBP) of more than 140 mmHg.

- **Nutraceuticals in Hypertension**

A. Flavonoids: Due to their antioxidant qualities and possible health advantages, flavonoids,
Which are present in a variety of plants, have drawn attention. Cruciferous vegetables, onions, black grapes, red wine, grapefruits, apples, cherries, and berries are among the foods that contain them. The treatment of cardiovascular illnesses is greatly aided by flavonoids, which include flavones, flavonones, silybin, flavonols, and rutin.

They strengthen capillaries, reduce estrogen-induced cancers, inhibit ACE, and lessen platelet stickiness.[13]

B. Quercetin: Quercetin is a potent antihypertensive substance that has anti-inflammatory and antioxidant properties in addition to scavenging blood pressure and maintaining blood pressure levels. Additionally, it has the ability to suppress the autonomic nervous system, which is the main cause of hypertension. By reducing fluid content and ENaC gene expression, quercetin can regulate blood volume by lowering sodium reabsorption in the kidney.

C. Omega-3 Polyunsaturated Fatty Acids (n-3PUFAs): According to a recent meta-analysis of 70 RCTs, consuming omega-3 polyunsaturated fatty acids (0.3–15 g/day) for 4–26 weeks can lower blood pressure by 4.5 mmHg and 3.0 mmHg in untreated individuals, EFSA states that 3 g/day of EPA and DHA are required for this effect.[14]

2. HEART FAILURE: Reduced myocardial contractility, which affects the heart's capacity to pump enough blood to meet bodily needs, is the hallmark of heart failure. Heart failure is becoming more common as the population ages; valvopathies, cardiomyopathies, hypertension, myocardial ischemia, and myocardial infarction are the most common causes.

- **Nutraceuticals in Heart Failure (HF)**

A. Hawthorn: Because of its bioactive components, which include antioxidants, inotropic agents, coronary vasodilators, and anti-inflammatory agents, hawthorn extract, which is derived from Crataegus monogyna and Oxyacantha, is a nutraceutical therapy for cardiovascular health. The cardiovascular system is protected by its flavonoids, especially the oligomeric procyanidins. It has been demonstrated that hawthorn extract enhances lipid metabolism and endothelial calcium levels. It is advised to take two or three dosages per day. [15]

B. D-Ribose: Low levels of phosphate and ATP can increase the risk of cardiac disease, including heart failure. D-ribose supplementation improves ATP levels in an animal model of ischemic damage, reducing diastolic dysfunction caused by ischemia. A clinical investigation found that D-ribose medication increased tissue doppler velocity and early diastolic filling velocity in 50% of NYHA II-IV patients after six weeks.

C. Coenzyme Q10: A chemical molecule discovered from cattle hearts in 1957, Coenzyme Q10 (CoQ10) is present in all cells but is particularly concentrated in mitochondria. It is an essential cofactor for oxidative phosphorylation, which results in ATP generation. Myocardial mitochondria have the highest concentration of CoQ10, which might cause heart failure. Bioavailability varies depending on dosage, particle size, formulation, release method, and route of administration. Oral CoQ10 supplementation improves heart failure symptoms, cardiac function, and overall quality of life.[16]

3. ATHEROSCLEROSIS: Atherosclerosis is a chronic inflammatory condition where lipid-loaded fibrous plaques accumulate in the artery wall, leading to thrombus formation. It impacts the heart, brain, lower limbs, and intestines. Atherosclerosis is a major health concern in developed nations, leading to disorders such as angina pectoris, heart attacks, and stroke. Preventive

interventions include stopping smoking, lowering stress, eating well, exercising, managing blood pressure, and controlling blood sugar levels.[17]

➢ **Nutraceuticals in Atherosclerosis**

A. Quercetin: Quercetin, present in fruits and vegetables, has anti-inflammatory characteristics that reduce CRP levels and prevent atherosclerosis. It reduces low-density lipoprotein (LDL) levels and stops macrophages from oxidizing it in obese persons. These effects entail SIRT1 activation.

B. Curcumin: Curcumin is an effective anti-atherosclerotic nutraceutical that reduces LDL and HDL levels, resulting in a 12% decline in cholesterol in healthy males. Potential pharmacodynamic pathways include downregulation of AR receptors in atherosclerosis. Curcumin can improve cholesterol and LDL levels in people with acute coronary syndrome. Clinical studies found that 500 mg of curcumin reduced triglycerides and increased HDL-c levels, but total cholesterol and LDL-c levels remained stable.

C. Brassica: Brassica, a substance with fascinating effects, has been proven to diminish LDL oxidation levels in rats and total serum cholesterol without affecting lipid profiles. Human studies have connected GST gene polymorphisms to brassica effects, with GSTT-1 carriers showing improved lipid profiles. Clinical investigations demonstrate considerable decreases in cholesterol levels.

D. Resveratrol: When taken with statins, RES reduces HMG-CoA reductase, lowers LDL cholesterol, and boosts antioxidants, successfully treating atherosclerosis. It lowers hepatocyte LDL receptor expression, smooth cell migration, and achieves a 20% reduction in ox-LDL and 4.5% in LDL cholesterol levels.[18]

4. DYSLIPIDEMIA: Dyslipidemia refers to lipid abnormalities that increase the risk of cardiovascular disease. Lowering total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) is useful for both primary and secondary prevention of cardiovascular disease (CVD). Maintaining low LDL-C levels is associated with a lower risk of major coronary events.[19]

➢ **Nutraceuticals in Dyslipidemia**

A. Sterols/stanols: Consuming plant sterols/stanols has been linked to lower levels of total cholesterol in people. The predominant effect is a reduction in LDL cholesterol (LDL-C), with minimal impact on HDL-C or triglycerides. Sterols and stanols reduce LDL-C levels by reducing cholesterol absorption in the intestines, increasing hepatic LDL receptors, and decreasing endogenous cholesterol synthesis.[20]

B. Polyphenols: According to severalof studies, grape polyphenols may have an impact on plasma lipid levels. HDL-C levels have been linked to grape juice drinking. An investigation into the impact of a 700 mg polyphenol-rich grape extract supplement on cardiovascular risk in healthy persons revealed a drop in plasma TC and LDL-C concentrations. Nevertheless, a more thorough meta-analysis that included nine randomized controlled trials with 390 participants found no evidence of a significant impact of grape seed extract on LDL-C. More focused assessments of subpopulations and sophisticated lipid analysis have been carried out in additional studies, despite the fact that no overall effect was seen in this combined group. For example, one study found that when obese participants took grape powder supplements for three weeks, their plasma concentrations of large LDL-C and large LDL particles decreased, but the medication had no effect on the atherogenic small LDL particles.

C. Spirulina: Positive alterations in blood lipid profiles have been linked to spirulina supplementation. Total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) concentrations showed notable changes when Spirulina maxima was taken orally (4.5 g/day) for six weeks. Furthermore, taking 1 g of spirulina daily for 12 weeks decreased mean levels of triglycerides, LDL-C, and TC in people with dyslipidemia, but had no discernible impact on high-density lipoprotein cholesterol (HDL-C). These results appeared to be supported by a recent meta-analysis of seven randomized controlled trials that looked at spirulina. However, further carefully planned studies are required to elucidate the mechanism of action of spirulina supplementation in dyslipidemia and determine its impact on cardiovascular outcomes.[21]

Bioactive Dietary Compounds with Cardio protective Potentials

Plant-derived meals were previously tested for their vitamin C, E, and carotenoid content.

However, the benefits observed when testing them alone may be due to the synergistic activity of additional bioactives in source materials. The question of whether they should be consumed in a whole food diet or as a supplement remains unanswered. This will be examined further below. Bioactive compound families typically include multiple members, as discussed below.

1. Phytochemicals: Plant diets contain several bioactive substances called "phytochemicals." Phytochemicals with significant health benefits include carotenoids, phenolic compounds (flavonoids, phytoestrogens, phenolic acids), phytosterols and phytostanols, tocotrienols, organosulfur compounds, and nondigestible carbohydrates (dietary fiber). Soybeans, soybean derivatives (such as tofu), and red clover have high concentrations of isoflavones. Lignans are primarily found in flaxseed.[22]

2. Polyphenol compounds: Polyphenols have been shown in vivo to have antiatherosclerotic effects in the

early stages of atherosclerosis development, improve endothelial function and increase nitric oxide release (potent vasodilator), modulate inflammation and lipid metabolism(i.e., hypolipidemic effect), improve antioxidant status, and protect against atherothrombotic episodes such as myocardial ischemia and platelet aggregation (Perez-Jimenez and Saura-Calixto, 2008).[23]

3. Flavonoids: Plant-derived flavonoids are the most frequent polyphenols in the human diet, found in vegetables, fruits, and beverages including chocolate, tea, and wine. some isoflavones, such as lignans, mimic estrogens, which are nonsteroidal plant elements that cause biological responses similar to estrogen. They are found as minor components of dietary fiber in oilseeds, cereal grains, vegetables, fruits, and legumes. Phytoestrogens, like other phenolic chemicals, have antioxidant properties and can affect lipoprotein metabolism and vascular reactivity, similar to estrogens. Consuming flavonoids has been linked to lower cardiovascular and overall mortality rates in older Dutch adults.These properties include antioxidant activity, metal chelation for transitional elements like copper and iron, inhibition of platelet aggregation, modulation of eicosanoid generating enzymes in inflammatory cells, enhancement of nitric oxide synthesis, reduction of superoxide production, and benefits to lipid profile.[24]

4. Plant steroids and stanols: Plant sterols, also known as phytosterols, share structural and functional similarities with animal sterols, such as cholesterol. Plant stanols, also known as phytostanols, are a type of phytosterol that is totally saturated. Vegetable oils, nuts, seeds, and grains are dietary sources that may not have significant cholesterol-lowering effects. They have also been used in high-fat meals like margarines and salad dressings. Phytosterols and phytostanols prevent cholesterol absorption in the intestinal tract. Intake of stanols/sterols did not significantly impact HDL or VLDL levels. Sterols and stanols may enhance the effects of diets and cholesterol-lowering medications on LDLs. Concerns have been raised concerning margarines containing plant sterols and stanols, as they may increase energy intake when consumed more than 2g per day.[25]

5. Vitamin C: Vitamin C's antioxidant properties diminish tissue reactive oxygen species, preventing endothelial dysfunction, inhibiting smooth muscle proliferation, and lowering oxidized LDL cholesterol. Prospective studies have found inconsistent results regarding the effect of vitamin C, both dietary and supplementary, in CVD. Vitamin C can be a pro-oxidant when exposed to significant oxidative stress, despite its protective activity. Clinical investigations combining vitamin C, vitamin E, and β-carotene have yielded mostly negative results for CVD. Food's nutrients and bioactive substances can work with or against each other to provide health benefits.[26]

6. Carotenoids: Carotenoids can improve immune function and lower the risk of degenerative diseases as cancer, CVD, and cataracts. The physiological actions have been linked to antioxidant properties, notably the ability to quench singlet oxygen and interact with free radicals. Carotenoids, including lycopene and beta-carotene, are dietary antioxidants that lower oxidative stress and inflammatory indicators. Carotenoids may play a role in CVD, as evidenced by research linking increased intakes of fruits and vegetables to reduced risk.[27]

7. Vitamin E: Vitamin E is not only a free radical scavenger, but also an effective anti-inflammatory drug, particularly at high dosages. Evidence suggests an inverse relationship between plasma vitamin E and CVD[129], as well as a link between vitamin E intake and CHD risk. Clinical research has not supported the role of vitamin E supplementation in reducing CVD. Meta-analyses and systematic reviews of over 90 trials yielded comparable null findings. A recent dose-response meta-analysis found that high-dose vitamin E (≥400IU/day) increased the risk of total mortality. The negative effects of vitamin E may be attributed to using the appropriate form and/or dose.[28]

8. Antioxidant vitamin supplementation: A "dietary supplement" is a product that contains vitamins, minerals, herbs, or amino acids and is taken in pill, capsule, tablet, or liquid form. Nutraceuticals differ from dietary supplements in two ways: they should not only supplement the diet but also aid in disease prevention and treatment, and they can be consumed as regular foods or as the sole component of a meal or diet. Some supplements, such as marine n-3 FAs and niacin, can improve CVD risk factors. However, other supplements, such as B-vitamins (folate, vitamin B12, vitamin B6), antioxidants (vitamin E, selenium), have shown little effect on CVD mortality and morbidity, and may even have negative effects.[29]

CONCLUSION

Nutraceuticals can effectively prevent and control cardiovascular disorders by addressing several risk factors. Clinical and epidemiological research shows that omega-3 fatty acids, polyphenols, plant sterols, Coenzyme Q10, vitamins, probiotics, and herbal bioactives reduce cardiovascular morbidity and death. Combining nutraceuticals with balanced meals like the Mediterranean or DASH diets offers a safe, cost-effective, and comprehensive approach to cardiovascular health. However, difficulties such as low bioavailability, inconsistent product quality, and lack of standardized dose guidelines persist. Future research should prioritize large-scale, long-term clinical trials, precision nutrition strategies, and improved delivery technologies to maximize treatment effectiveness. Nutraceuticals offer a viable solution for cardiovascular prophylaxis and therapy, complementing traditional medicines and encouraging better lifestyles and quality of life. Novel

dietary approaches to cardiovascular protection are crucial in clinical research and practice.

Nutrition is a difficult research area, and it's unclear whether a specific dietary component or a combination of nutrients and practices contribute to cardio-protective benefits. The advanced Advancements in understanding disease processes and healthy diets have led to novel techniques for preventing and treating cardiovascular disease. Extensive scientific evidence shows that functional meals reduce inflammation and vascular reactivity. These effects are just as effective as pharmaceutical therapies, but safer. Future studies should include well-designed clinical trials to evaluate the potential additive and synergistic effects of functional foods on health outcomes, as many have great therapeutic potential.

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