



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

Impact Of Nutraceuticals in Managing Cardiovascular Diseases and Diabetes Mellitus

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ARTICLE INFO

Published: 02 Jan. 2025

Keywords:

Nutraceuticals, CVDs, DM,
Bioactive compound,
Antioxidant.

DOI:

10.5281/zenodo.14586261

ABSTRACT

Nutraceuticals, including dietary supplements, functional foods, and bioactive compounds derived from natural sources, hold immense potential in managing chronic diseases such as cardiovascular diseases (CVDs) and diabetes mellitus (DM). This review highlights their multifaceted roles, emphasizing therapeutic benefits and advantages over conventional pharmaceutical interventions. Nutraceuticals are broadly categorized into nutrients, herbals, enzymes, probiotics, and prebiotics, all of which contribute to health promotion and disease prevention. For CVDs, nutraceuticals target modifiable risk factors like hypertension, hyperlipidemia, and obesity. Bioactive substances such as omega-3 fatty acids, flavonoids, and Coenzyme Q10 exhibit anti-inflammatory and antioxidant properties, which help mitigate these risks. In diabetes management, nutraceuticals such as chromium, alpha-lipoic acid, fenugreek, cinnamon, and berberine have shown efficacy in improving glucose metabolism, enhancing insulin sensitivity, and reducing complications. Nutraceuticals are increasingly preferred due to their minimal adverse effects, cost-effectiveness, and ease of availability. They represent a natural, holistic approach to disease management, bridging the gap between nutrition and medicine. By addressing underlying causes and reducing dependence on costly pharmaceutical treatments, nutraceuticals offer a safer and sustainable alternative for individuals and healthcare systems worldwide. This review underscores their potential to transform chronic disease management, combining science and nature for improved health outcomes.


INTRODUCTION

Nutraceuticals, a term coined by Dr. Stephen DeFelice in 1989, are foods or parts of foods that

provide medical or health benefits, including the prevention and treatment of illness. They include medical foods, nutritional supplements, and dietary

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



supplements, and are marketed in concentrated forms such as pills, capsules, powders, and tinctures. Nutraceuticals are used as supplemental foods to provide long-term benefits and aid in the treatment of disease states. The global nutraceuticals market is growing, with an expected value of \$250 billion by 2018. Nutraceuticals cover

various therapeutic categories, including anti-arthritic, cold and cough, sleep disorders, digestion, and cancer prevention. They are recognized as beneficial sources of health promotion, especially for preventing life-threatening diseases like diabetes, cardiovascular diseases, renal, and gastrointestinal disorders.[1]

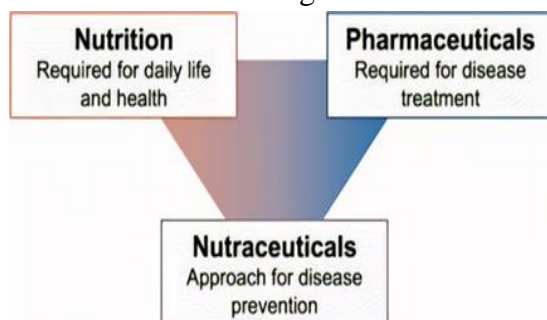


Figure No.1:- Concept of Nutraceuticals

Scope of Nutraceuticals: Nutraceuticals, such as dietary fiber, prebiotics, probiotics, polyunsaturated fatty acids, antioxidants, and herbal natural foods, are used to treat various diseases like obesity, cardiovascular diseases, cancer, osteoporosis, arthritis, diabetes, and cholesterol. They lead to a new era of medicine and health, with the food industry becoming a research-oriented sector. Dietary supplements are used to supplement calories, while functional foods offer health benefits beyond traditional nutrients, containing physiologically active ingredients from plant or animal sources.^[2]

Classification of Nutraceuticals: Nutraceuticals can be classified based on different criteria, such as their source, chemical composition, mode of action, and health benefits. Here are some common classifications:

❖ **Based On Products Available In Market:-**

I) Traditional Nutraceuticals: Natural, non-modified foods like tomatoes, grapefruit, guava, papaya, and water watermelon are rich in antioxidant properties, potentially preventing cancers, while conventional nutraceuticals are categorized according to their composition.

A) Chemical Constituents:

(i) Nutrients: Nutrients like amino acids, fatty acids, minerals, and vitamins play essential roles in maintaining health. Vitamins treat conditions like osteoporosis, while minerals prevent and strengthen bones. PUFAs regulate inflammation and brain function.

(ii) Herbals: Herbal nutraceuticals promote wellness and prevent chronic illnesses with anti-inflammatory, astringent, analgesic, antipyretic, and antiarthritic properties. Flavonoids and tannins help manage asthma, colds, stress, coughing, depression, and high blood pressure.

(iii) Phytochemicals: Phytochemicals, plant-based compounds like lutein and lycopene, are essential for human biochemical processes and neuroprotective, supporting brain chemical equilibrium and lowering cancer, heart disease, and neurological diseases risk.^[3]

B) Nutraceutical Enzymes:

Enzymes, essential for life, are sourced from microorganisms, plants, and animals. Consuming enzyme supplements can alleviate symptoms of medical diseases like blood sugar disorders, digestive issues, and obesity.

C) Probiotic Microorganisms:

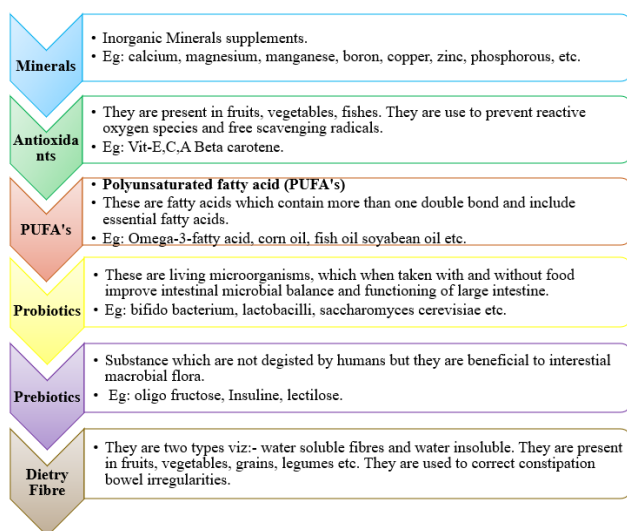
Probiotics are lifelong microorganisms that support healthy digestion and nutrition absorption, drive out pathogens, and create a beneficial symbiosis with the human gastrointestinal tract when ingested in moderation.

II) Non Traditional Nutraceuticals: Non-traditional nutraceuticals, artificially produced foods, enhance health and quality through biotechnology or agricultural breeding, categorized into fortified and recombinant nutraceuticals based on processing techniques.

A) Fortified Nutraceuticals: Supplements, such as cereals, milk, flour, and orange juice, are derived from agricultural breeding and are used to provide essential nutrients and nutraceuticals.

B) Recombinant Nutraceuticals: Recombinant nutraceuticals, produced through genetic engineering, enzyme/fermentation technology, and probiotic production, contain bioactive components and are used in energy-rich foods like bread, wine, and lactoferrin.^[4]

❖ **Based on food source:-** ^[5]



The Role of Nutraceuticals in Disease Management:

The role of nutraceuticals in following disease conditions:

- ❖ Cardiovascular diseases (CVD)
- ❖ Diabetes mellitus (DM)

Cardiovascular Diseases (CVDs):

Worldwide, cardiovascular diseases (CVDs) are the primary cause of death. It is commonly recognized that the primary causes of cardiovascular complications include major cardiovascular risk factors, including advanced age, hypertension, diabetes, hypercholesterolemia,

left ventricular hypertrophy, and heart failure. CVDs are diseases influenced by lifestyle choices and unmodifiable risk factors. Non-modifiable factors include gender, age, ethnicity, and family history. Modifiable factors include body weight, dietary habits, physical activity, alcohol consumption, stress, obesity, diabetes, hyperlipidemia, and hypertension.^[6] Dietary factors play a significant role in the pathophysiology of cardiovascular disease (CVD) and have been less thoroughly studied than traditional cardiovascular risk factors (Table:1).

Table No.1: Cardiovascular risk factor

Sr. No	Category	Examples
1.	Nonmodifiable risk factor	<ul style="list-style-type: none"> Advancing age Male gender Family history/genotype
2.	Metabolic risk factors	<ul style="list-style-type: none"> Hypertension

		<ul style="list-style-type: none"> ▪ Hyperlipidemia ▪ Diabetes mellitus ▪ Metabolic syndrome ▪ Obesity/overweight
3.	Lifestyle risk factors	<ul style="list-style-type: none"> ▪ Diet ▪ Smoking ▪ Physical activity
4.	Novel risk factors	<ul style="list-style-type: none"> ▪ Elevated homocysteine level ▪ Elevated lipoprotein (a) level ▪ Small dense LDL-C ▪ Elevated inflammatory marker levels ▪ Elevated hemostatic factors levels

❖ Types of Cardiovascular Diseases & Role of Nutraceuticals:

Hypertension: Hypertension (HTN), which is characterized as a diastolic blood pressure (DBP) of more than 90 mmHg or a systolic blood pressure (SBP) of more than 140 mmHg, is a serious and rapidly developing global health issue.

➤ Nutraceuticals in Hypertension:

i) Flavonoids: Flavonoids, found in various plants, have gained interest for their antioxidant properties and potential health benefits. They are found in cruciferous vegetables, onions, black grapes, red wine, grapefruits, apples, cherries, and berries. Flavonoids, including flavones, flavonones, silybin, flavonols, and rutin, play a significant role in treating cardiovascular diseases. They decrease platelet stickiness, suppress ACE, fortify capillaries, and lower estrogen-induced malignancies.^[7]

ii) Quercetin: Quercetin is an effective antihypertensive chemical that can scavenge blood pressure, maintain blood pressure levels, and act as an anti-inflammatory and antioxidant. It can also downregulate the autonomic nerve system, a primary source of hypertension. Quercetin can control blood volume by lowering fluid content and decreasing ENaC gene expression, which in turn reduces sodium reabsorption in the kidney.

iii) Omega-3 Polyunsaturated Fatty Acids (n-3 PUFAs):

A recent meta-analysis of 70 RCTs found that consuming omega-3 polyunsaturated fatty acids (0.3-15 g/day) for 4–26 weeks can reduce blood pressure by 4.5 mmHg and 3.0 mmHg in untreated hypertensive individuals and normotensive individuals, with EFSA stating that 3 g/day of EPA and DHA is necessary for the effect.^[8]

Heart Failure: Heart failure is a condition characterized by reduced myocardial contractility, affecting the heart's ability to pump enough blood to meet body needs. The frequency of heart failure is increasing as the population ages, with the most common causes being valvopathies, cardiomyopathies, hypertension, myocardial ischemia, and myocardial infarction.

➤ Nutraceuticals in Heart Failure (HF):

i) Hawthorn: Hawthorn extract, derived from *Crataegus monogyna* and *Oxyacantha*, is a nutraceutical therapy for cardiovascular health due to its bioactive ingredients, including antioxidants, inotropic agents, coronary vasodilators, and anti-inflammatory agents. Its flavonoids, particularly oligomeric procyanidins, have protective effects on the cardiovascular system. Hawthorn extract has been shown to improve endothelial calcium levels and lipid metabolism. It is recommended to be taken in two or three daily doses.^[9]

ii) D-Ribose: Heart diseases, such as heart failure, are more likely to occur when there is a deficiency in phosphate and ATP. D-ribose supplementation can raise ATP levels in an animal model of

ischemic injury, alleviating diastolic dysfunction caused by ischemia. A clinical trial showed that patients with NYHA II-IV improved tissue doppler velocity and early diastolic filling velocity in half of the patients after six weeks of D-ribose treatment.^[10]

iii) Coenzyme Q10: Coenzyme Q10 (CoQ10), a chemical compound isolated from beef hearts in 1957, is found in all body cells but is concentrated in mitochondria. It is a necessary cofactor for oxidative phosphorylation, leading to ATP synthesis. Myocardial mitochondria contain the highest concentration of CoQ10, which plays a pathogenic role in heart failure. Bioavailability varies based on factors like dosage, particle size, formulation, release technique, and mode of administration. Oral CoQ10 supplementation improves heart failure symptoms, including improved heart function and quality of life.

Atherosclerosis: Atherosclerosis is a chronic inflammatory disorder characterized by the accumulation of lipid-loaded fibrous plaques within the arterial wall, causing thrombus development. It affects the heart, brain, lower limbs, and intestines. Atherosclerosis is a major health issue in industrialized nations and is linked to significant diseases like angina pectoris, heart attacks, and stroke. Preventive measures include quitting smoking, reducing stress, eating well, exercising, maintaining blood pressure, and maintaining blood sugar levels.^[11]

➤ **Nutraceuticals in Atherosclerosis:**

i) Quercetin: Quercetin, found in various fruits and vegetables, has been shown to have anti-inflammatory properties, lowering CRP levels and preventing atherosclerosis. It also decreases low-density lipoprotein (LDL) levels and prevents macrophages from oxidizing LDL in obese individuals. These effects involve SIRT1 activation.

ii) Curcumin: Curcumin is a potent anti-atherosclerotic nutraceutical that lowers LDL and

HDL levels, resulting in a 12% drop in cholesterol in healthy men. It has potential pharmacodynamic mechanisms, including downregulating AR receptors in atherosclerosis. Curcumin has been shown to improve cholesterol and LDL levels in patients with acute coronary syndrome. Clinical research using 500 mg of curcumin showed a reduction in triglycerides and an increase in HDL-c levels, but total cholesterol and LDL-c levels remained unchanged.

iii) Brassica: Brassica, a substance with intriguing effects, has been shown to lower LDL oxidation levels in rats and total serum cholesterol without altering lipid profiles. Human studies have linked GST gene polymorphisms to brassica effects, with lipid profile improvement observed in GSTT-1-carrying participants. Clinical trials show significant reductions in cholesterol levels.

iv) Resveratrol: RES, when combined with other medications like statins, effectively addresses atherosclerotic disease by downregulating HMG-CoA reductase, lowering blood LDL cholesterol levels, and promoting antioxidant qualities. It also reduces hepatocyte LDL receptor expression, reducing smooth cell migration, and achieving a 20% ox-LDL and 4.5% LDL cholesterol drop.^[12]

Diabetes Mellitus (DM): Diabetes mellitus (DM) is a chronic metabolic disease causing high blood glucose levels due to insulin deficiency. It affects 2.8% of the global population and can lead to long-term complications. Type 2 diabetes is a common metabolic disease, often caused by insulin deficiency in pancreatic β -cells and loss of insulin secretory capacity. Diabetes is the most common cause of death among adults aged 20-79, with an estimated prevalence of 643 million by 2030 and 783 million by 2045. Nutraceuticals, which contain naturally occurring functional foods and bioactive phytochemicals, are being considered as a new approach to diabetes prevention and management.^[13]

Types of Diabetes Mellitus:



Diabetes can be divided into three main groups: type 1, type 2 and gestational diabetes.

1) Type 1 Diabetes Mellitus (T1DM): T1DM, also known as Insulin-Dependent Diabetes Mellitus (IDDM), is a type of diabetes caused by damage to pancreatic β -cells, resulting in insulin deficiency. Treatment involves insulin injections, and can affect young people.

2) Type 2 Diabetes Mellitus (T2DM): Non-insulin-dependent diabetes (NIDDM) is a metabolic disorder characterized by hyperglycemia, insulin shortage, and resistance, affecting glucose homeostasis and insufficient insulin production.

3) Gestational Diabetes Mellitus: Pregnant women who do not already have diabetes may develop gestational diabetes. At the conclusion of the third or the start of the fourth month of pregnancy, this typically occurs. Usually, after birth, this problem goes away. The body's utilization of glucose is impacted. In order to grow and provide energy, bodily cells need glucose as fuel. Obstetric blood sugar imbalances can pose a serious risk to the mother and unborn child.^[14]

➤ **Nutraceuticals in Diabetes Mellitus:** Nutraceuticals, traditionally containing minerals, proteins, carbohydrates, lipids, vitamins, and other nutrients, are often used for diabetic treatments due to their effectiveness, low adverse effects, and affordability.

❖ **Categories of nutraceuticals and their role in diabetes:**

Nutraceuticals are biological medicines that are non-specific and are used to control symptoms, prevent malignant processes, and promote wellness. These can be divided into the two main categories listed below.

a) Nutrients: Nutrients are substances, such as vitamins, minerals, amino acids, and fatty acids, that have been shown to have nutritional value.

b) Herbals: Plant materials in the form of extracts and concentrates.

a) Nutrients:

i) Chromium: A trace element called chromium may be required in diabetics. Supplemental chromium may help individuals with type 2 diabetes mellitus tolerate glucose better and become more sensitive to insulin, according to certain theories. A moderate but substantial increase in glycaemic control was observed in the latter group, according to a meta-analysis of randomized controlled trials examining the effects of chromium supplementation on glucose and insulin response in healthy adults and those with diabetes. The official stance of the American Diabetes Association is that there is conflicting information about the advantages of chromium supplementation in the treatment of diabetes.^[15]

ii) α -Lipoic Acid: Lipoic acid, found naturally, has a strong ROS scavenging action and antioxidant properties. It chelates transition metals, promotes antioxidant regeneration, and functions as a redox pair. It can increase insulin sensitivity by 18-20% in type 2 diabetes patients.

b) Herbals:

i) Fenugreek: Dried *Trigonella foenum-graecum* seeds, which belong to the Fabaceae family. Fenugreek seeds, rich in soluble fiber, protein, and flavonoids, are a popular herb for treating type 2 diabetes. They inhibit α -amylase activity, limit glucose uptake, slow intestinal transit, and delay digestion. Fenugreek also affects postprandial glucose absorption and boosts insulin secretion in pancreatic islets, according to in vitro tests.^[16]

ii) Cinnamon: Cinnamon, derived from the inner bark of *Cinnamomum Zeylanicum* and *Cinnamomum Cassia*, has medicinal benefits like anti-diabetes and insulin sensitivity. It inhibits intestinal sucrase, pancreatic amylase, and α -glucosidase activities, reducing carbohydrate digestion and absorption in diabetic rats.

iii) Curcuma Longa: Curcumin, a curcuminoid found in curcuma Longa, has anti-diabetic benefits. It inhibits glucose synthesis in diabetic millitus rats by increasing AMPK expression. Curcumin also enhances liver glycogen storage and glucokinase activity, suppressing glucose-6phosphatase and PEPCCK enzymes. It also decreases glycogen synthase phosphorylation in insulin-resistant L6 myotubes.

iv) Berberine: Berberis aristata, a plant in the Ranunculaceae family, contains compounds like berberine, palmatine, oxyacanthine, columbamine, berbamine, resins, tannins, and flavonoids. Berberine activates AMPK, improving insulin sensitivity and glucose metabolism in type 2 diabetes, reducing blood glucose levels during fasting.^[17]

CONCLUSION:

This review highlights the information about nutraceuticals are a highly efficient way to control diabetes mellitus and cardiovascular illnesses. They offer a natural, holistic approach that has major advantages over traditional pharmaceutical treatments. These bioactive substances, which come from foods and natural products, help to regulate blood sugar levels, enhance insulin sensitivity, and prevent complications from diabetes in addition to supporting cardiovascular health by lowering cholesterol, raising blood pressure, and decreasing inflammation.

Nutraceuticals are particularly beneficial because they can provide these health advantages with fewer adverse effects than many synthetic medications. For prolonged usage, this gives them a more secure choice. They are also more readily available and cost-effective, which makes them a desirable alternative for both consumers and healthcare systems, particularly in environments with limited resources. Nutraceuticals offer a complementary approach to normal medical treatments by promoting preventative care and improving general well-being. This allows for a

lasting and inexpensive bridge between nutrition and medicine. Thus, nutraceuticals represent a promising future in chronic disease management, reducing the dependency on costly pharmaceuticals while providing safer, more natural therapeutic options for individuals suffering from cardiovascular diseases and diabetes mellitus.

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HOW TO CITE: Wajid Khan Yunus Khan*, S. V. Ganjiwale, S. J. Dighade, Atif Ahemad Shakeel Ahemad, Impact Of Nutraceuticals in Managing Cardiovascular Diseases and Diabetes Mellitus, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 01, 94-101. <https://doi.org/10.5281/zenodo.14586261>

