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NUTRACEUTICALS & HUMAN HEALTH: A COMPREHENSIVE REVIEW

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ABSTRACT

The nourishing elements known as nutraceuticals are biologically active and have the potential to preserve maximum health and benefits. There are a mixture of nutrition and medications. These goods are crucial for the continued advancement of therapeutics as well as the maintenance of human health care. In addition to their medicinal effects and safety profile, nutritional supplements have gained prominence for their nutritional advantages. The use of nutraceuticals for services like illness prevention and promotion is expanding rapidly. In addition to nutrition, nutraceuticals have been utilised as a support therapy for the prevention and treatment of a number of diseases, such as to lessen the negative effects of radiotherapy and chemotherapy for cancer. Other nutraceutical supplements and micronized dietary products with enhanced health advantages are produced as a result of nanotechnology. The most recent significant results (clinical trials) on nutraceuticals that demonstrate the therapeutic effects of 'nutraceuticals' bioactive compounds on a variety of ailments are also reviewed in this review article.

KEYWORDS: Nutraceutical, cardiovascular diseases, nutrition, cancer prevention, skin treatment.

1. INTRODUCTION

Nutraceuticals are defined as "specially designed preparations," created to meet certain dietary needs and or provide preventive healthcare. In addition to a supplemental diet, nutraceuticals are the formulation of nutrient(s) that aid in the prevention and treatment of some diseases. The words "nutrition" and "pharmaceutical" were combined to form the phrase "nutraceutical," which was coined by Dr. Stephen De Felice in 1989. These are foods—or portions of foods—that have a variety of health advantages, such as the ability to treat and/or prevent disease. From anticipating dietary deficits to focusing on human health and the prevention and treatment of chronic illnesses, nutrition science has advanced to new heights. Literature of recent years emphasizes on redefining the concept of nutraceuticals, taking into consideration the efficacy, safety and toxicity of these products. Food products are nourishing substances that are used orally, topically, or in other ways to support life, give energy, and encourage growth. The separation of nutrients from these food products is now widely accepted and employed. The first step in distinguishing between food/dietary supplements and nutraceuticals is the selection of an epidemiological target, which is then followed by efficacy and safety studies that clarify the mode of action. Nutritional supplements should have a solid safety profile with less unwanted side effects and better bioavailability if there is sufficient clinical proof. The distinction between two types of formulations can be made on the basis of claims, even if the same substances may function as a nutraceutical or food supplement. Nutraceuticals include individual pro- and pre-biotic meals as well as mixes of both However, in order to prevent their out-of-control use and negative side effects, nutraceuticals must be administered and prescribed, and they must be closely managed. To increase the efficacy and bioavailability of drug compound-based nutraceuticals, several researchers have investigated them. Different statins have been utilised in the prevention of cardiovascular disorders even in pregnant women due to their safety and effectiveness. For the treatment of diabetes mellitus and hypertension, or as an adjunct to standard drug therapy, nutraceuticals with an effective safety profile and well-established influence on pregnancy may be an appropriate therapeutic choice. Potentially successful prospects for innovative nutraceuticals include calcium, omega-3 polyunsaturated fatty acids, vitamin D, folic acid, resveratrol, alpha-lipoic acid, zinc, and probiotic supplements.[1-4]

Recent analysis growth of neutraceuticals in market

According to a recent analysis, the global market for nutraceuticals is expected to grow, with a chance of up to $340 billion by 2024. From 2016 to 2024, the cumulative annual growth

rate (CAGR) for nutraceuticals is predicted to be 7.2%. This increase in the nutraceuticals-based industry's growth is attributed to a number of factors, including a rise in the demand for these products, increased public knowledge of the health advantages of nutrition, and an incremental rate seen in the healthcare graph.[5-6]

Approximately 90% of the global nutraceutical industry is now accounted for by Europe, the United States, and Japan. The market is anticipated to grow from $247 billion in 2019 to $336 billion in 2023 at a CAGR of 8%. Now that the global market has reached maturity, businesses in the nutraceutical industry are focusing more on emerging markets, particularly those in Asia Pacific, including India. Only 2% of the worldwide nutraceutical market was accounted for by the Indian market in 2017. It is projected to grow at a CAGR of 21% to $11 billion by 2023. India is anticipated to own at least 3.5% of the worldwide market by 2023.[7,8]

Every industry is being impacted by the COVID-19 virus. At this time, it is difficult to estimate the long-term effects. In the wake of the COVID-19 epidemic, the world economy is still in shambles, and its effects on international trade and the nutraceuticals industry are becoming more pronounced, with a rapid decline in product supply despite high demand. Because 75–80 percent of the raw materials used in nutraceuticals in North America, Europe, and Asia Pacific were obtained from China, the nutraceutical business is unable to close the gap between high demand and limited supply. The production of nutraceuticals has decreased as a result of the factory halt in China and the sudden recessive conditions in native regions. Due to their high nutritional benefits, dietary supplements have seen a sharp increase in consumer demand.[9-19]

Clinical trials on animals or *in vitro* are required in the pharmaceutical industry to confirm a compound's effects. However, as people's awareness of health-related issues and how food can either directly or indirectly contribute to maintaining good health and preventing diseases has increased in recent years, the composition of food has been scientifically studied and validated (Figure 1).[20-21]

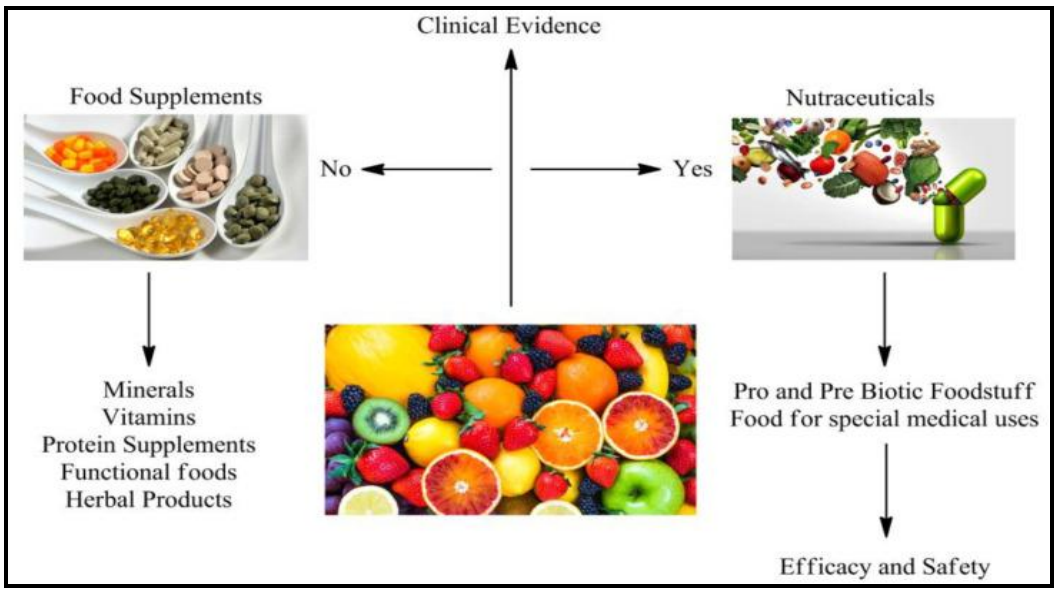

Fig. 1: Composition of food maintain good health.

A wide range of therapeutic areas, including the treatment of cancer, depression, diabetes, cholesterol, blood pressure, and painkillers, can benefit from the use of nutraceuticals, including the treatment of cough and cold, anti-arthritis, digestion, sleeping difficulties, and pain relief. In order to determine how diverse nutraceuticals can show to be significant in the pharmaceutical industry, the research and development sectors for nutraceuticals are operating at their top levels. Standardisation of the ingredients, cautious protocol formulation, and implementation of clinical studies are all necessary due to scientific requirements for nutraceuticals that will have an impact on the industry and the health of consumers. Nutraceuticals and their use as potent medicinal supplements have seen a significant increase in awareness over the past ten years. The use of nutraceutical medicine in complementary and alternative medicine is now recognised.[22-35]

2. Nutraceuticals And Human Health

Nutraceuticals support better health, well-being, and immune system control, preventing and curing a wide range of illness shown in (Figure. 2).[36] There are a variety of diseases that can be treated with the help of nutraceuticals which are discussed below:

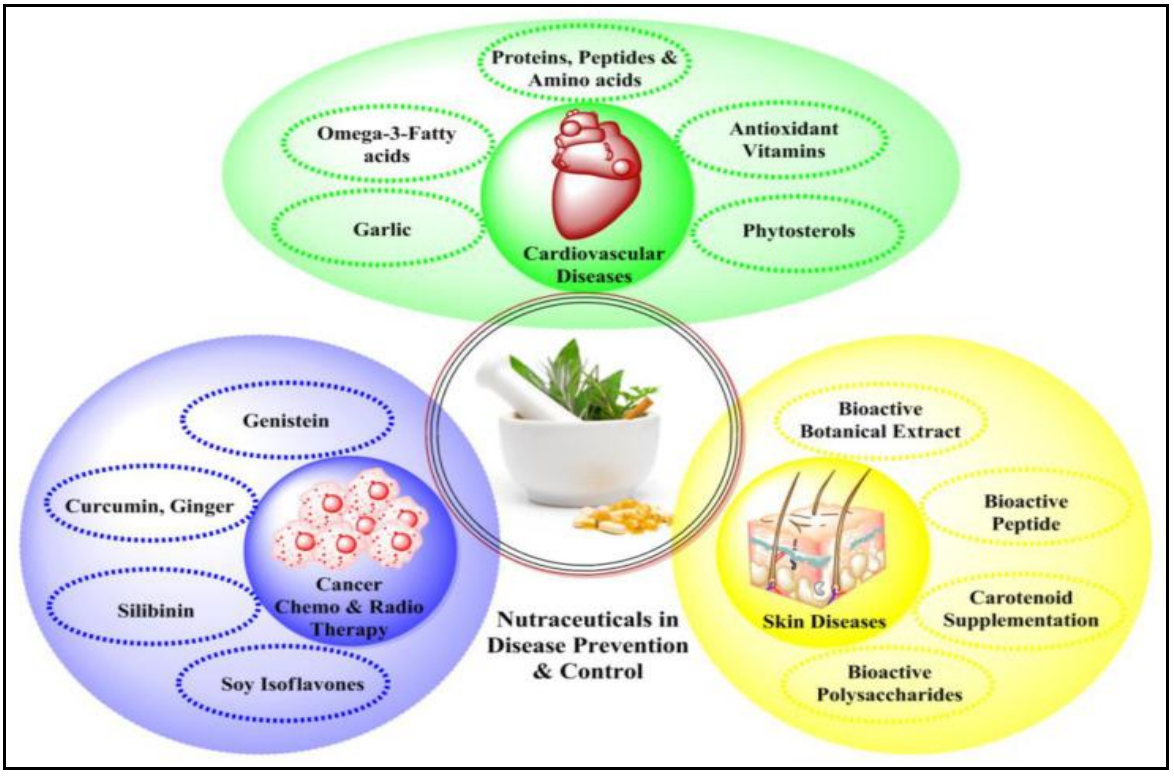

Fig. 2: Nutraceuticals support better health,control immune system and prevention of disease.

2.1 Nutraceuticals in Cardiovascular Diseases

Cardiovascular diseases stand out among all other illnesses for having considerable risk factors that can be mitigated by nutritional supplementation. Nutraceuticals can be employed in the treatment of cardiovascular illnesses, according to a large body of research. The blood arteries and the heart's functionality are the two main organs affected by cardiovascular diseases (CVDs). As one of the leading causes of death, CVDs account for around 30% of fatalities worldwide each year. Dietary supplements can be roughly categorised as those used to treat arrhythmias, congestive heart failure, angina, hypertension, and hyperlipidemia. They have been shown to be helpful in risk management and prevention of cardiovascular illnesses.

Below is a discussion of some of the nutraceuticals and dietary supplements that are utilised in the management and prevention of CVDs.[37-46]

Allicin and Alliin

Elevated levels of plasma triglycerides and blood cholesterol are linked to ischaemic heart disease and atherosclerosis. Allium sativum is naturally antihyperlipidemic, and it works by significantly reducing endogenous cholesterol synthesis and removing large amounts of

cholesterol and its byproducts from the faeces. This results in a more favourable HDL to LDL ratio. If stomach acids can protect them, allicin and alliin can affect cholesterol levels. Thirteen placebo-controlled trials including 781 participants were used to evaluate the effects of garlic supplementation on serum cholesterol. In addition to having anti-hyperlipidemic properties, garlic also has some natural antihypertensive effects.[47-49]

Omega-3Fatty Acids

Polyunsaturated fatty acids (PUFAs), from which omega-3 fatty acids are formed, are found in marine sources. Cardiovascular disorders are treated and prevented in large part by docosahexaenoic acid (DHA) and marine omega-3 eicosapentaenoic acid (EPA). In one study, the diet and reinfarction experiment (DART), a randomised trial comprising 2033 men post-myocardial infarction, found that taking fish oil supplements decreased mortality rate by 29% for a period of 2 years. Fish oil consumption significantly reduced cardiovascular disease deaths by 30%, unexpected deaths by 45%, and overall mortality by 20%. Recent clinical trial studies have revealed that exercise can help reduce the risk of heart arrhythmias.[50-51]

Soy Isoflavones

With potential medical benefits like antihyperlipidemic, antihypertensive, antihyperglycemic, antioxidant, anticancer, anti-inflammatory, anti-obesity, and neuroprotective activities that support the biological plausibility for observational associations, soy proteins and isoflavones are significant nutrients. Clinical trial results clearly show that soy protein ingestion lowers blood cholesterol levels in people. According to a study, participants who had a diet reduced in saturated fat had a lower risk of developing coronary heart disease. The lipid profiles weren't affected by soy isoflavone.[52-53]

Proteins, Peptides and Amino Acids

Heart disorders and hypertension go hand in hand. The main treatment for the illness has been ACE (angiotensin converting enzyme) inhibitors, however these medications include adverse effects such hypotension, high potassium levels, reduced renal function, coughing, and skin rashes. Casein and whey protein from milk contain ace inhibitors that are natural. Animal studies have also shown that these milk-derived proteins have antihypertensive properties. In clinical studies where a statistically significant hypotensive impact has been noted, the same has been reported.[54-55]

Antioxidant Vitamins

In the treatment of chronic conditions including cancer and cardiovascular disease, antioxidants have been proposed as viable supplements. By limiting the negative effects of free radicals, they lessen LDL-cholesterol oxidation. Antioxidant vitamins are found in significant quantities in vegetables, fruits, fish, and fixed oils. These vitamins act by inhibiting the creation of oxygen free radicals or by trapping them. There is evidence that CHD patients who consume a lot of antioxidants had lower rates of morbidity and mortality, according to several epidemiologic research. Antioxidant vitamins C and E found in supplements aid in CHD prevention. However, ß-carotene supplementation can have negative effects and is therefore not advised. According to the National Health and Nutrition Examination Survey-I cohort research, vitamin C intake lowers the incidence of CHDs.[56]

2.2 Nutraceuticals in Cancer Chemo- and Radiotherapy

Radiotherapy and chemotherapy are common forms of cancer treatment, but they come with a number of difficulties and major side effects, including pain, exhaustion, nausea, vomiting, diarrhoea, and hair loss. Systemic cytotoxic chemotherapy and radiotherapy are not very effective at promoting patient survival because some malignancies are highly resistant to chemo- and radiotherapy. In this instance, several combination therapies cover an effective cancer treatment strategy. Similarly, a number of plants and natural supplements have been found to lessen the negative effects of chemotherapy and radiotherapy. Therefore, these should be taken in conjunction with radiotherapy or chemotherapy to lessen adverse effects and increase the efficacy of the treatment. Zhang and his colleagues investigated the combined effects of chrysin and apigenin in 2021 by inhibiting the P38-MAPK/AKT pathway activity in colorectal cancer. Chrysin and apigenin both significantly increased apoptosis while significantly decreasing clone number, migration, and invasion in both colorectal cancer (CRC) cell lines when used at a concentration of 25 M. Chrysin and apigenin both dramatically reduced p-P38 and p-AKT levels. A P38 agonist called anisomycin successfully counteracted the tumor-inhibiting effects of apigenin and chrysin. By inhibiting the P38-MAPK/AKT pathway, apigenin (25 M) and chrysin (25 M) exhibited a synergistic effect on reducing the proliferation and metastasis of CRC cells.[57-63]

Curcumin from Turmeric

A powerful nutraceutical for the treatment of cancer is curcumin. Curcumin has been shown in pre-clinical tests to decrease carcinogenesis at every stage, including angiogenesis,

metastasis, and proliferation, in a variety of malignancies, including pancreatic, colorectal, prostate, gastric, and hepatic cancer. When used in conjunction with chemo- and radiotherapies to treat cancer, it is significantly more successful.[64-65]

Ginger

Ginger is a natural supplement that is anti-mutagenic, antioxidant, and anti-inflammatory and is known to lessen the negative effects of chemotherapy and radiation. These characteristics of ginger are what make it a useful radio-protector. Ginsenoside Rf and Ginseng and its polysaccharides are useful in lowering the side effects of cancer treatment therapies, which is reported to produce a 50% less risk in the recurrence of cancer, leading to a loss in the doses of morphine in cancer patients.[66]

Genistein

A strong isoflavone with promising anti-carcinogenic capabilities is genistein. According to in vitro research, some substances must be consumed in higher concentrations than are typically found in food to have the same anticancer effects. As a result, it is challenging to produce the intended effect at the tumour site, which makes us believe that the mechanism of delivery is a crucial aspect that must be taken into account in in vivo investigations and clinical trials. The non-toxicity of the natural ingredients is a key consideration when formulating a remedy. However, it has been discovered that some substances are more effective if given early in life, and genistein is one of them.[67-68]

2.3 Nutraceuticals for Skin Treatment

The skin is the largest organ in the body and provides defence against various pathogens, UV rays, and toxins as well as partaking in sensitivity. Skin plays a significant protective role for the body, but it can also experience changes like immunological dysfunction, photoaging, and inflammation that can be harmful to human health. With the use of nutraceuticals, a feasible strategy can be established to alleviate skin-related illnesses and delay or reduce premature skin ageing. These nutraceuticals may include carotenoids, bioactive peptides, bioactive polysaccharides, and plant extracts. In multiple human studies, supplementation with these compounds showed reduced indications of ageing and protection against UV-radiation-induced ageing.[69-70]

Bio-Active Peptides

From a wide range of dietary proteins, including both plant and animal proteins, bioactive peptides have been identified. The most popular sources of animal protein are eggs, milk (casein and whey), and meat. Common plant sources of bioactive peptides include soy, oat, pulses (chickpea, bean, pea, and lentil), canola, wheat, flaxseed, and hemp seed. Because of their improved bioavailability and solubility, peptides utilised for aesthetic purposes are typically generated from collagen and act as nutraceutical formulations.[71-72] It has often been shown in a carefully controlled research of the bioactive collagen peptide (BCP)-containing drug VERISOL®. In this trial, individuals were given VERISOL® or a placebo for 8 weeks, and skin wrinkles were measured both before and after the therapy. After 8 weeks of treatment, it was seen that BCP significantly reduced the volume of eye wrinkles in comparison to placebo. Pig origin and Peptan F Other fish-derived nutraceuticals with collagen peptides, such as Peptan P, are used to delay the onset of ageing by successfully preserving the moisture content of the skin's layers. A recent study showed that using the nutraceutical supplement Celergen® enhanced skin characteristics without increasing the risk of oxidative damage, demonstrating the safety and efficacy of the product.This nutraceutical is based on a marine collagen peptide derived from deep sea fish, grape skin, coenzyme Q10 and leutonin.[73-74]

Bio-Active Polysaccharides

These polymers, which are made of sugar, serve as structural support and a source of energy. They exist in a variety of monosaccharide combinations, physicochemical structures, and living forms, including plants, fungi, mammals, and prokaryotes. The Glycosaminoglycans from the marine origin are the most beneficial of them for the formulations of nutraceuticals. N-acetylglucosamine or N-acetylgalactosamine, an unbranched disaccharide (repeating) unit of amino sugar, and glucuronic or iduronic acid, a uronic acid, are the building blocks of these.[75-76]

Imedeen® DermOne®, which contains certain protein fractions in addition to the glycosaminoglycans and served as dietary supplements for skin care, was used in a human trial of the formulations comprising these. In the experiment, 10 women received 90 days of treatment with 500 mg of the drug Imedeen®. Dryness, brittleness of hair and nails, wrinkles, and mottling were among the parameters assessed. All of these symptoms were shown to improve after 90 days, and observations revealed skin thickness and supplements.[77]

Carotenoids

These are naturally occurring pigments that are present in diverse plants, photo-synthetic microorganisms, and algae. These have a tetra terpenoid structure that is linear. These can be discovered in organic foods including fruits, vegetables, and other foods. The most popular dietary carotenoids include -carotene, -carotene, -cryptoxanthin, lutein, zeaxanthin, and lycopene. These carotenes are used for skin care, including UV protection and anti-ageing. Probiotics and carotenoids have been linked to a reduction in skin cancer risk and a modulation of early skin UV impact indicators. A carotenoid supplement including lutein, beta-carotene, and alpha-carotene has been shown to be helpful in photoprotection. Similar to this, it has been suggested that a combination of beta-carotene, lutein, and lycopene carotenoids can prevent erythema. It functions as a cofactor for the production of collagen fibres and inhibits the creation of elastin in fibroblasts, limiting the buildup of this protein that is so prevalent in skin that has been exposed to light damage. It functions synergistically with vitamin E, utilising its mechanism of transformation. The primary lipophilic antioxidant, vitamin E, is present as tocopherols. It interacts with peroxyl radicals and stops them from oxidising lipids containing polyunsaturated fatty acids. Additionally, it is amply demonstrated that its application in avoiding photodamage, sunburn, atopic dermatitis, etc.[78-81]

2.4 Nutraceuticals as Specialized Medical Products

The legal rationale states that dietary supplements and foods used for certain medical conditions are considered specialized medicinal items. These dietary supplements should be governed by numerous national protocols, frequently issued by the "Ministry of Agriculture" and/or "Ministry of Health" of various countries around the world, as well as regulatory organization like the "European Food Safety Authority" and the "U.S. Food and Drug Administration."

The use of nutritional supplements as biological therapies to regulate symptoms, prevent disease, and promote wellbeing is known as nutraceuticals.[82-85] Flow chart outlining the function of nutraceuticals in illness prevention and health promotion is shown in Figure 3. The uses of several nutraceuticals for health promotion is outlined in Table 1.

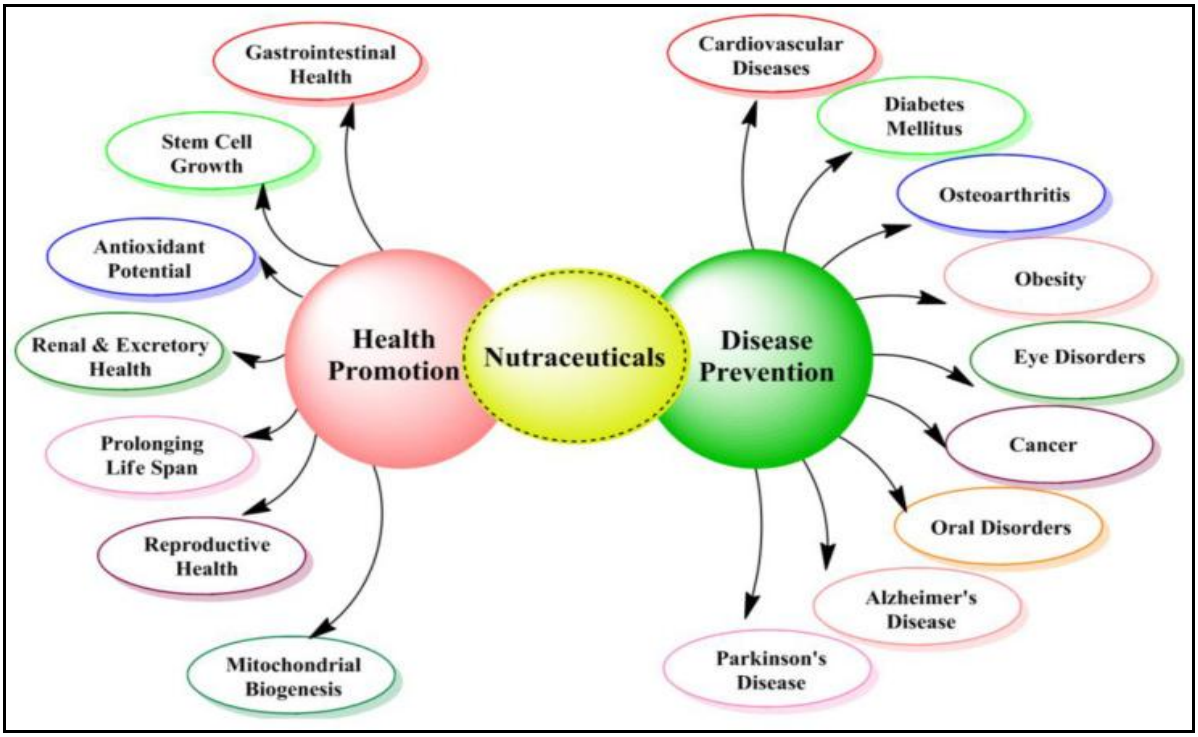

Fig. 3: Function of nutraceuticals in illness prevention and health promotion.

Table 1: List of nutraceutical used in health promotion.

Water Soluble Vitamins	Vitamin C	Wound healing, Antioxidant
	Vitamin B1	Carbohydrate metabolism, Neurological function
	Vitamin B2	Energy metabolism, Nerve function
	Vitamin B3	Brain function
	Vitamin B6	Convert proteins to energy
	Vitamin B12	Formation of RBC's, Synthesis of amino acids Metabolism of fat, protein and carbohydrate
	Folic acid	Formation of RBC's, Formation of genetic material of cells
	Pantothenic acid	Intraneuronal synthesis of acetylcholine Synthesis of cholesterol, steroids, and fatty acids
Fat Soluble Vitamins	Vitamin A	Cancer, Skin disorder, Healthy vision Antioxidant
	Vitamin D	Absorption of calcium, Formation of bones and teeth
	Vitamin E	Boost immune system, Antioxidant
	Vitamin K	Blood clotting
Minerals	Calcium	Maintaining bone strength, blood clotting
	Iron	Oxygen transport, Energy production
	Magnesium	Healthy nerve and muscle function and bone function
	Phosphorus	Phosphorylation process, Genetic material
	Copper	Heart functioning, Iron absorption

	Iodine	Functioning of thyroid gland
	Chromium	Diabetes
	Selenium	Antioxidant
	Zinc	Sperm production, wound healing
Herbals	Aloe vera	Anti-inflammatory, Wound healing
	Evening primrose oil	Treatment of atopic eczema
	Garlic	Anti-bacterial, Anti-fungal
	Ginger	Carminative, Anti-emetic
	Ginseng	Adaptogen
	Green tea	Cell mediated immunity, Antioxidant

3. CONCLUSION

In order to ensure integrated medical support, nutraceuticals are a potentially expanding sector that work in both the nutrition and medical treatment domains. These may serve as dietary supplements, prevent illnesses like CVD, support and treat different types of cancer, and provide other health advantages. As a result, the nutraceutical industry today has a comprehensive understanding of and perception of the potential success of nutrients that have an impact on people in healthcare. Currently, it's believed that medications should be used to provide medical care. The use of emerging technologies, including the use of genetically modified foods in the food sector and nutraceuticals based on nanotechnology, etc., results in better medical care and health advantages, which has further accelerated the growth of the nutraceuticals revenue market and Scientific research supports.

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