Nutraceuticals in Various Diseases

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Nutraceuticals are the nourishing components (hybrid of nutrition and pharmaceuticals) that are biologically active and possess capability for maintaining optimal health and benefits. These products play a significant role in human health care and its endurance, most importantly for the future therapeutic development. Nutraceuticals have received recognition due to their nutritional benefits along with therapeutic effects and safety profile. Nutraceuticals are globally growing in the field of services such as health care promotion, disease reduction, etc.

cardiovascular diseases interactions nutrition

1. Introduction

Nutraceuticals are characterized as ‘specially designed preparations’, formulated with the aim of fulfilling specific dietary requirements and/or offer preventive health care. Nutraceuticals are the formulation of nutrient/nutrients which helps in prevention and treatment of some diseases, in addition to a supplement diet. Nutraceutical is a term given by Dr. Stephen De Felice in 1989 and came from two words “nutrition” and “pharmaceutical”. These are foods or a part of foods that are beneficial in providing various health benefits including the treatment and/or prevention of the disease. Science of nutrition has increasingly achieved new horizons, starting from the anticipation of deficiencies in nutrients to prominence on human health and prevention and treatment of chronic ailments. Terms ‘nutraceuticals’, ‘food supplements’, ‘dietary supplements’ have evolved after the concept was originated by Dr. De Felice. There is no sharp demarcation between food supplements and nutraceuticals given by regulatory authorities. 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 eaten, drunk or otherwise taken to sustain life, provide energy and promote growth. Currently, isolation of nutrients from these food products are well recognized and used. The starting point to differentiate food/dietary supplements and nutraceuticals is the identification of an epidemiological target, followed by safety and efficacy studies that understand the mechanism of action. One approach to differentiate these two types of formulations is describing ‘food supplements’ as agents to compensate deficiencies in micro- or macronutrients; in addition, the use of a “nutraceutical” in the treatment of a pathological disease must be supported by strong scientific evidence [1]. With adequate clinical evidence, nutritional supplements should have a strong safety profile with few undesirable side effects and better bioavailability. There is a very fine line of demarcation between two type of formulations: the same ingredients may work as a nutraceutical or food supplement, but may be demarcated on the basis of claims. Nutraceuticals include single or combinations of pro- and pre-biotic foodstuff and food for special medical uses; and food supplements includes single or combinations of mineral, vitamins, protein supplements, functional foods and herbal products. By prolonging or eliminating the need for pharmaceuticals in subjects to fit for an alternative nonpharmacological treatment to a pathological condition, the incorporation of nutraceuticals into daily diet may aid in the prevention of pathological disorders. There are claims that foods including spices and herbs possess the tendency to decrease the risk of many diseases and can be highly beneficial in improving the quality of life [2]. There is a plethora of benefits that nutraceuticals have provided, including their promising results in the prevention and treatment of complicated diseases. However, there is a need of administration and prescription of nutraceuticals and they should be strictly regulated in order to prevent their uncontrollable use and side effects [3]. Several researchers have studied drug compound-based nutraceuticals to improve the efficacy as well as bioavailability. The safety and efficacy of various statins have been used in the prevention of cardiovascular diseases even in pregnant women. Nutraceuticals with an effective safety profile and well-established impact onpregnancy might be a suitable therapeutic option for preventing diabetes mellitus and hypertensive disorders, or as an adjuvant to therapy with standard medications. Calcium, omega-3 polyunsaturated fatty acids, vitamin D, folic acid, resveratrol, alpha-lipoic acid, zinc, inositol, and probiotic supplements are potentially proven candidates as novel nutraceuticals [4]. Researchers have evaluated the nutraceutical associated with the drug compound ezetimibe for patients atrisk of elevations of statin level, which further leads to cardiovascular diseases [5]. The use of a novel nutraceutical in blend with non-steroidal anti-inflammatory drugs (NSAIDs) has been proven a potential candidate for osteoarthritis, thus improving its efficacy and safety for commercial use [6].

The market remains robust and ever-growing for nutraceuticals such as antioxidants; omega-3 fatty acids; plants such asalgae, aloe vera, seaweed, and wheatgrass; teas and herbs such asginseng and Echinacea. A recent survey suggested that the nutraceutical market is expanding globally and the probability states that it may reach up to $340 billion by the year 2024. The compound annual growth rate (CAGR) of nutraceuticals is estimated to be 7.2% in the year 2016 to 2024. This increment in the growth of the nutraceuticals-based industry is associated with various factors such as a rise in demand for nutraceuticals, an awareness among people for the benefits of nutrition and an incremental rate observed in the healthcare graph [7][8]. Currently, Europe, USA and Japan account for ˃90% of the total global nutraceutical market and the global market is supposed to reach $336 billion by 2023 from $247 billion in 2019 at a CAGR of 8%. With this attainment of maturity of global markets, now the focus of nutraceutical players has been shifted towards developing economies, especially those across Asia Pacific, including India. The Indian market had only 2% market share of total global nutraceutical market in 2017. It is estimated to reach $11 billion by 2023, increasing at a CAGR of 21%. By 2023, India is also expected to hold at least 3.5% market share of the global market [9][10].

The COVID-19 virus is having a knock-on effect for every industry. The long-term repercussions are hard to predict as of yet. In a post-COVID-19 pandemic situation, the global economy is still struggling and its impact on the global trade and nutraceuticals market is rising with rapid deterioration in the supply of products irrespective of high demands. Nutraceutical industry is not able to bridge the gap between high demand and low supply as 75–80% of raw material used in nutraceuticals was sourced from China in North America, Europe and Asia Pacific. Due to China’s manufacturing shutdown, and the sudden recessive conditions in native regions, the nutraceutical production has reduced. The sharp surge in demand was observed for dietary supplements from consumers, as they provide a strong immune function and decrease possible health threats [11].

However, an officially shared and accepted definition of nutraceuticals is missing; these are also referred as ‘pharma food’—a powerful toolbox that is beyond the diet but before the drugs. Various formulations containing macronutrients (required in large amounts, e.g., omega-3 fatty acids, magnesium, potassium and calcium) [12], micronutrients (required in lesser amounts, e.g., minerals or vitamins) [13] and phytochemicals that are present in the food source [14] and are available at drug stores. Further, probiotics [15], minerals [16], polyunsaturated fatty acids [17], carotenoids [18], amino acids and proteins [19], vitamins [20], dietary fibers [21], spices and phytochemicals [22] have also become part of these formulations. Nutraceuticals exist as various types and may range from herbal products to isolated nutrient diets and may go up to existing genetically modified foods [23][24][25]. Plant foods such as vegetables, whole grains and vitamins are rich in dietary phytochemicals. Dietary supplements are consumed as such, or as isolated active ingredients. These phytochemicals are immensely diverse and these include carotenoids [26], phenolics [27], alkaloids [28], organosulfur [29] and nitrogen containing compounds [30]. However, these products may not be substantiated by scientific data on their safety, efficacy and effect on health and/or pathological conditions.

In the pharmaceutical industry, it is mandatory to do clinical tests on animals or in vitro for the verification of a compound’s effects. On the contrary, in nutrition, there was no such method in the past for the verification of effects of foods in preventing or treating diseases. In recent years, however, the food composition has been scientifically tested and verified as people are becoming more and more aware of health-related issues and how food can directly or indirectly be responsible for maintaining proper health and preventing diseases (**Figure 1**) [31][32].

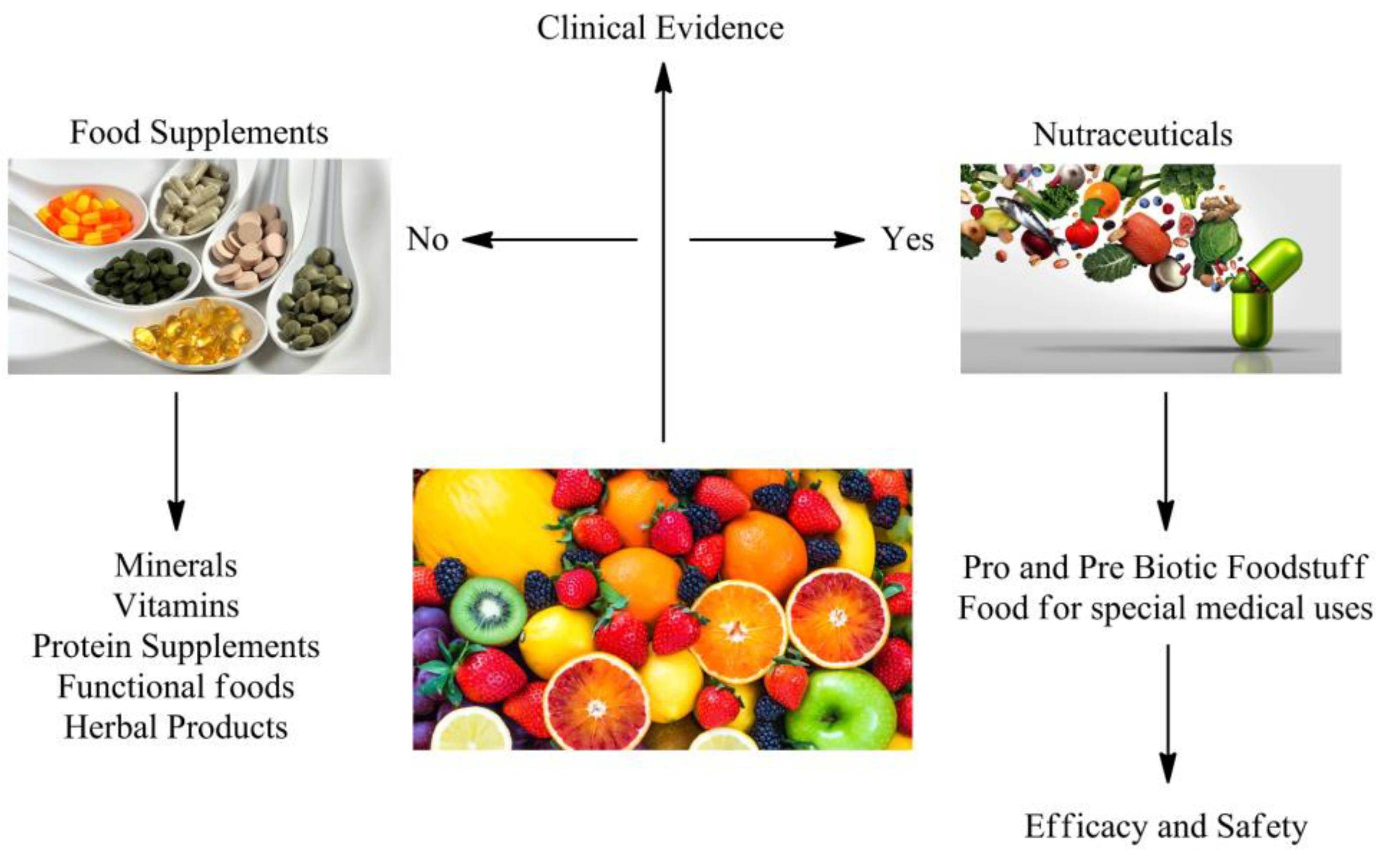

Figure 1. Potential roles of nutraceuticals.

Nutraceuticals provide their benefits in a wide range of therapeutic areas such as cough and cold [33], anti-arthritis [34], digestion [35], sleeping disorders [36] and treatment of cancers [37], depression [38], diabetes [39], cholesterol [40], blood pressure [41] and pain killers [42]. The research and development sectors for nutraceuticals are working at their peaks to discover how various nutraceuticals can prove to be of significance in the pharmaceutical industry. Scientific needs for nutraceuticals demand standardization of the constituents and cautious development of protocols and implement clinical studies which will form the foundation for consumer health and impact on nutraceutical companies [43][44].

In the last 10 years, a huge growth has been observed in the awareness of nutraceuticals and their use as powerful therapeutic supplements. Nutraceutical medicine has now been accepted as a part of Complementary and Alternative Medicine (CAM) and, thus, it has been incorporated as a new branch of CAM [45][46].

Due to dynamic action of nutraceuticals (nutritional and medicinal action), their popularity amongst general public and healthcare providers has increased over medicines.

2. Nutraceuticals in Various Diseases

Nutraceuticals help enhance health, wellbeing and modulating immunity, thus preventing and treating various diseases and health issues (**Figure 2**) [47]. There are a variety of diseases that can be treated with the help of nutraceuticals which are discussed below:

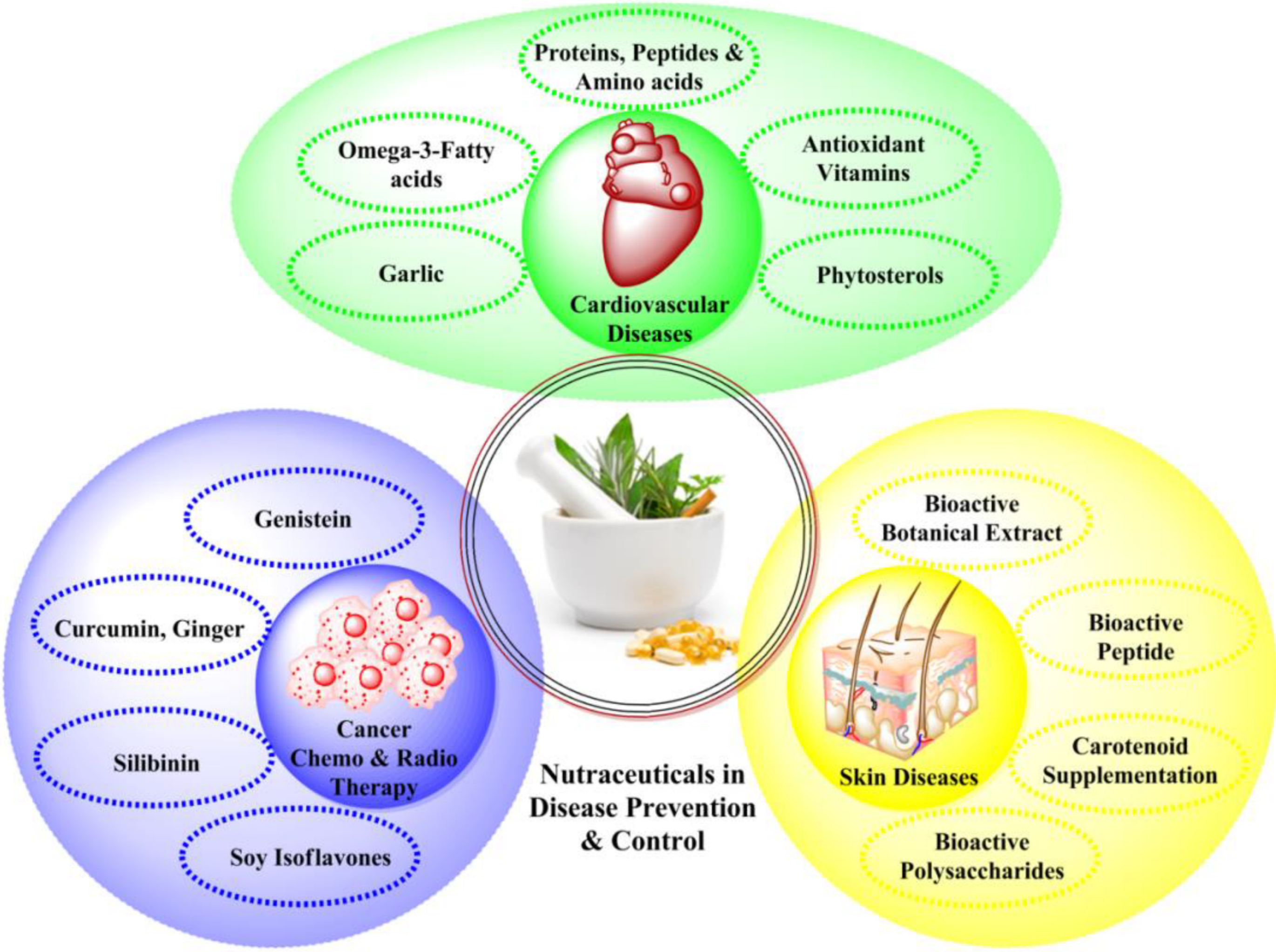

Figure 2. Nutraceuticals and Dietary Supplements in various diseases.

2.1. Nutraceuticals in Cardiovascular Diseases

Among all other diseases, cardiovascular diseases reveal significant risk-related factors acquiescent to nutraceutical intervention [48]. There is significant evidence indicating that nutraceuticals can be used in cardiovascular diseases [49][50].

Cardiovascular diseases (CVDs) mainly affect the blood vessels and the functioning of the heart. CVDs are one of biggest causes of mortality, as they account for about 30% of deaths all over the world annually [51]. Dietary supplements have been proven to be beneficial in risk management and prevention of cardiovascular diseases and can be classified broadly into the ones used in the treatment of arrhythmias [52], Congestive heart failure [53], angina [54], hypertension [55] and hyperlipidemias [56][57]. Some of the nutraceuticals and dietary supplements that are used for the treatment and prevention of CVDs are discussed below.

2.1.1. Allicin and Alliin

Ischemic heart disease and atherosclerosis are associated with elevated levels of plasma triglycerides and blood-cholesterol are associated with. *Allium sativum* is antihyperlipidemic in nature and it exerts its effects by the elimination of cholesterol and its end-products in high amounts in the feces and by decreasing the cholesterol synthesis endogenously [58]. This helps in producing more favorable ratio of HDL and LDL. Allicin and alliin can effect cholesterol levels, if these can be protected by gastric acids. Garlic supplementation on serum cholesterol was assessed using thirteen placebo-controlled trials concerning 781 patients. Garlic also has some inherent antihypertensive effect, apart from being antihyperlipidemic [59][60].

2.1.2. Omega-3Fatty Acids

Omega-3 fatty acidsare derived from marine sources and are called polyunsaturated fatty acids (PUFAs). Docosahexaenoic acid (DHA) and Marine omega-3 eicosapentaenoic acid (EPA) plays a critical role in the treatment and prevention of cardiovascular diseases. In one study, it has been reported that intake of fish oil supplements reduced mortality rate by 29% for over a period of 2 years in the diet and reinfarction trial (DART), which was a randomized trial involving 2033 men post-myocardial infarction. Consumption of fish oil led to a noteworthy reduction in unexpected demises by 45%, cardiovascular diseases deceased by 30% and a 20% decrease in overall mortality. According to the recent clinical trial studies, it has been found that the risk of cardiac arrhythmias is decreased with the help of omega-3 fatty acids, and they also improve the health of the patients suffering from plaque formation caused by atherosclerosis. Omega-3 fatty acids enhance the electrical-stability of heart cells, thereby extending its relative refractory period and helping treat arrhythmias [61][62].

2.1.3. Soy Isoflavones

Soy proteins and soy isoflavones are important nutrients with potentially medicinal benefits such as antihyperlipidemic, antihypertensive, anti-hyperglycemic, antioxidant, anticancer, anti-inflammatory, anti-obesity and neuroprotective activities that support the biological plausibility for observational associations. It is evident from clinical study reports that consumption of soy protein reduces serum cholesterol levels in humans [63]. In addition, USFDA has evidenced that 25g of soy proteins or isoflavone per day intake showed a lowering of blood pressure in postmenopausal women. Moreover, soy proteins exert favorable effects on the serum lipid concentrations, especially in hypercholesterolemic patients. In a study, subjects fed with a diet low in saturated fat leads to the decrease in risk of coronary heart disease. Soy isoflavone had no effects on the lipid profiles [64]. Further a study reported significant reduction of the ratio of LDL to HDL after intake of new soy products, having high levels of isoflavones, cotyledon soy fiber and soy phospholipids (Abaco and Abalon) [65].

2.1.4. Proteins, Peptides and Amino Acids

Hypertension is associated with cardiovascular diseases. ACE (angiotensin converting enzyme) inhibitors have been a chief line of therapy to treat the condition, but these drugs lead to side effects such as hypotension, elevated levels of potassium, impaired renal function, coughing and skin rashes [66]. Natural, ACE inhibitors are found in casein and whey protein derived from milk. It is also evidenced from animal studies that these milk-derived proteins exert antihypertensive effects. The same has been reported in clinical studies where a statistically significant hypotensive effect has been observed [67].

2.1.5. Antioxidant Vitamins

Antioxidants have been used as potential supplements in chronic diseases such as cardiovascular diseases and cancer. They reduce LDL-cholesterol oxidation by counteracting the damaging effects of free radicals. Vegetables, fruits, fish and fixed oils contain antioxidant vitamins in large volumes, which works by preventing the formation of oxygen free radicals or by entrapping them. It has been evidenced in some epidemiologic studies of CHD patients on a diet of large quantities of antioxidants that they result in fewer incidences of morbidity and mortality. Supplements having antioxidant vitamins C and E help in preventing CHD. However, supplementation with ß-carotene can produce adverse effects and, thus, is not recommended. The National Health and Nutrition Examination Survey-I cohort study observed that risk of CHDs decreases in vitamin C intake, which was found in the observation of over 10 years in American men and women of age group of 25–74 years, in which subjects were randomized with diverse combinations of 10 nutritional supplements for over five years [68].

2.1.6. Phytosterols

Phytosterols are structurally similar to cholesterol. They tend to compete for absorption through the small intestine. These are found naturally in vegetable oils, seeds, nuts, grains, wood pulp, etc. [69]. Intake of phytosterols led to increased hepatic uptake of LDL, reduced blood LDL levels, and reduced absorption of cholesterol. Studies have indicated up to 15% reduction in LDL levels by intake of plant sterols [70]. Plant sterols are derived from natural grains such as soy, sunflower and corns. Various studies evidenced that the consumption of 2–3 g/day of plant sterols/stanols tend to reduce LDL cholesterol levels up to 20%; although, there is substantial variation amongst individuals [71].

2.2. Nutraceuticals in Cancer Chemo- and Radiotherapy

Radiotherapy and chemotherapy are conventional therapies for cancer therapy but have serious side effects and various complications (e.g., pain, fatigue, diarrhea, vomiting, nausea and hair loss) [72][73]. There are some cancers that are highly resistant to chemo- and radiotherapy and, because of this, systemic cytotoxic chemotherapy and radiotherapy are not very operative at cultivating patient subsistence [73][74]. In this situation, various combination therapies overlay an efficient means to treat cancer. Likewise, there are a variety of plants and natural supplements that are observed to reduce side effects of radiotherapy and chemotherapy. Thus, these should be used in the combination with radio- or chemotherapy for the reduction of side-effects and to augment treatment effectiveness. Proliferation of cells leading to cancer results in the need to treat, and the nutraceutical industry is evolving to treat the needs of the consumers. The evolution of the nutraceutical industry can be recognized as it has now reached disease prevention after it started from health promotion. A plethora of currently used herbs and phytochemicals are safe pharmacologically and have been proven to be potent nutraceuticals in suppressing tumor progression, alleviating the disadvantages of radio- and chemotherapy and increasing the sensitivity of these therapies [75][76]. Caponio and his team evaluated the effects of the phenolic compounds found in Aglianico Grape pomace (GP) on colorectal cancer cell lines at varying stages of development after subjecting them to an in vitro digesting model. Aglianico GP extract was found to have strong effects on cell proliferation and apoptosis, as well as on other cellular processes. A substantial upregulation of Bax, as well as the Bax/Bcl-2 ratio and caspase-3, was observed in both HT29 and SW480 cells. UHPLC-DAD analysis revealed that anthocyanins, phenolic acids, and flavonoids were the primary components responsible for the elevated (total phenolic content) TPC and antioxidant activity in the Aglianico GP digested extract [77]. In 2021, Zhang and his co-workers studied the combined effect of chrysin and apigenin by suppressing the activity of P38-MAPK/AKT pathway in colorectal cancer. Apigenin and chrysin, both at 25 µM, substantially inhibited clone number, migration and invasion, while increasing apoptosis in both colorectal cancer (CRC) cell lines. Additionally, chrysin and apigenin significantly suppressed p-P38 and p-AKT. Anisomycin, a P38 agonist, effectively mitigated the tumor-inhibiting action of apigenin and chrysin. Together, apigenin (25 µM) and chrysin (25 µM) had a synergistic impact in limiting the proliferation and metastasis of CRC cells by suppressing the P38-MAPK/AKT pathway [78].

2.2.1. Curcumin (Diferuloyl-Methane) from Turmeric (Curcuma Longa)

Curcumin has been classified as a commanding nutraceutical for cancer treatment. Pre-clinical studies with curcumin suggest that it inhibits carcinogenesis in different types of cancers, such as pancreatic, colorectal, prostate, gastric and hepatic cancer; in addition, it has been able to suppress it at every step, that is, angiogenesis, metastasis and proliferation. It is much more effective when it is in combination with the chemo- and radiotherapies for cancer treatment [79][80].

2.2.2. Ginger

Ginger is an antimutagenic, antioxidant and anti-inflammatory nutraceutical and is known to diminish the side effects of radio and chemotherapy. It is these properties of ginger that provide helpful radio-protector activity. A reported loss in the doses of morphine in cancer patients is seen with the help of Ginsenoside Rf and Ginseng and its polysaccharides are helpful in reducing the side effects of cancer treatment therapies, which has reported to cause a 50% less risk in the recurrence of cancer [81].

2.2.3. Genistein

Genisteinis a potent isoflavone and has promising anti-carcinogenic properties. In vitro studies have shown that there are a few components that exert their antitumor effects only at higher concentrations that are not possible to achieve at normal dietary consumption [82]. Thus, it is difficult to achieve the desired effect at the tumor site, which leads us into thinking that the mode of delivery is a very important factor that needs to be considered in in-vivo studies and clinical trials. For a therapy to be formulated, the non-toxicity of the natural components is a very important factor. Nevertheless, it has been found that some compounds are more potent if administered early in life and Genistein is one of them [83].

2.3. Nutraceuticals in the Treatment of Prostate Cancer (PCa)

Prostate canceris the most common type of cancer and has been recorded as the second leading cause of mortality by cancer in American males. It has been noticed that men descendent from United States and Africa have the highest prostate cancer mortality rates compared to those of European descent. Although current strategies of treatment are quite potent and effective, there are always opportunities of resistance towards disease and progression to metastasis and many more that may develop over time. Therefore, more effective and non-toxic therapeutic approaches are required to overcome these major hurdles and provide proper management and treatment of this disease. Thus, in this regard, various potential safe nutraceuticals are available as effective anti-PCa agents. Evidently, execution of nutraceuticals might help in the development of precision in the design of the medicines and reduce the toxicities associated with chemotherapy and decrease the resistance of disease and have the potential of treating the disease in both localized and advanced stages. Some of the nutraceuticals that can potentially be used as treatment are discussed below [84][85].

2.3.1. Silibinin

Silibinin that is, flavanolignan from milk thistle “Silybummarianum” seeds have potent anti-carcinogenic effects for a plethora of tumors including PCa. A pre-clinical animal model shows significant anticancer activity of silibinin in the treatment of PCa, and phase II clinical trials bioavailability studies have also been evaluated. There is still a need of larger clinical trials to be performed to confirm the biological efficacy and effectiveness of silibinin as a nutraceutical for effective clinical management of advanced or localized form of PCa [86][87].

2.3.2. Soy Isoflavones

Soy Isoflavones are members of the polyphenolic flavonoid family, mainly found in soybeans, red clover, kudzu root, etc., and are widely used in cuisines from Asia and Africa. Clinical studies have proven some benefits against the disease PCa with the help of Soya Isoflavones as it has a marked effect on inflammatory signaling and insulin. Among others there have also been reports in which Isoflavones have shown immuno-modulatory properties in the plasma of asymptomatic bio-chemically-recurrent PCa patients. It was found out that the high concentration of genistein in plasma was linked to a 69% reduction in the risk of future development of PCa in Chinese patients. If isoflavones are administered short term, such as for a period of 6 weeks, they show an inhibitory effect in the cell cycle of prostate tumor and also shows apoptotic-associated signaling; however, it does not have any influence on the levels of testosterone, PSA, free testosterone and total cholesterol in patients suffering from PCa. A clinical trial performed for 6 months showed that the intervention of soy protein had no effect on molecular markers determining proliferation and apoptosis, i.e., EGFR, Bax:Bcl-2, Bax:PCNA ratios in patients with high-risk and low-grade PCa. On the contrary, soy protein (alcohol-washed) intake decreased the tissue levels of Bax and PCNA in comparison with patients receiving milk protein treatment [88][89]. Recently, Zhu and his team reported that the potential cholesterol-reducing effects of soy protein isolate were enhanced by glycation with soy soluble polysaccharide at higher degrees of glycation (DG) [90].

2.4. Nutraceuticals for Skin Treatment

The skin is known to be the body's largest organ and it offers protection against all sorts of microorganisms, ultraviolet radiations and chemicals also participating in sensitivity. As a result of having a major role in protecting the body, skin may face alterations, such as immune dysfunction, photo-aging and inflammation, which may result in harm on human health [91]. A potential strategy of delaying or diminish pre-mature ageing of the skin and alleviation of skin-related disorders can be found with the help of nutraceuticals. These nutraceuticals can be bioactive peptides, bioactive polysaccharides, botanical extracts, carotenoids, etc. Supplementation with these products in several human trials has evidenced fewer signs of ageing and also protection against UV-radiation ageing [92].

2.4.1. Bio-Active Peptides

Peptide moieties are the combination of two or more amino acids and are short sized with low molecular weight (<3 kDa), and some may perform important biological actions thatare termed bioactive peptides. Bioactive peptides have been isolated from a wide variety of dietary proteins, including plant and animal. Eggs, milk (casein and whey), and meat proteins are the most common sources of animal protein. Soy, oat, pulses (chickpea, bean, pea and lentil), canola, wheat, flaxseed and hemp seed are common plant sources for bioactive peptides [93]. Peptides that are used for cosmetic purposes are usually derived from collagen and typically serve as nutraceutical formulations because of their increased bioavailability and solubility [94]. It has typically been observed in a controlled study of VERISOL®, which contains bioactive collagen peptide (BCP). In this study VERISOL® and a placebo were given to subjects for 8 weeks and skin wrinkles were measured before the treatment and after 8 weeks. It was observed that BCP promoted a significant decrease in the eye-wrinkle volume in comparison to placebo after a period of 8 weeks of treatment. Not only this, BCP intake showed an increase in the content of elastin and procollagen type1 along with an increase in the fibrillin content. Thus, this treatment reduced wrinkles and has encouraging effects on skin matrix synthesis [95].

Peptan F and porcine origin Peptan P are some other nutraceuticals of fish origin containing collagen peptides used to slow aging by effectively maintaining the moisture content within skin layers. Recently, a study indicated improved skin properties without risk of oxidative damage by use of a nutraceutical product Celergen®, proving it a safe and effective supplement. This nutraceutical is based on a marine collagen peptide derived from deep sea fish, grape skin, coenzyme Q10 and leutonin [96][97].

2.4.2. Bio-Active Polysaccharides

These are sugar-based polymers that have the energy storage and structural functions. They are present in life forms such as plants, fungi, animals and prokaryote organisms having diverse monosaccharide combinations, physicochemical properties and structures. The most useful of them for the nutraceutical formulations is the Glycosaminoglycans from the marine origin. The basic unit of these are- an un-branched disaccharide (repeating) unit of amino sugar called *N*-acetylglucosamine or *N*-acetylgalactosamine and an uronic acid called glucuronic or iduronic acid [98][99]. A human trial of the formulations containing these was conducted using Imedeen® DermOne®, these contain some protein fractions as well along with the glycosaminoglycans and served as dietary supplements for skin care. In addition to the protein the supplement contained zinc gluconate and vitamin C which are relevant for skin care. In the trial conducted, 10 women were treated with an amount of 500 mg of Imedeen® for a period of 90 days. Parameters evaluated were, dryness, brittleness of hair and nails, wrinkles and mottles. It was seen that after 90 days, all these signs were improved, and observations established skin thickness and elasticity [91].

2.4.3. Bio-Active Botanical Extracts

These extracts are multifaceted mixtures of various compounds having diverse structures and origin. Since long times they are being used and reviewed. Polyphenols are one of the key natural compounds with cosmetic applications with a plethora of families and structures. These are plant-based micronutrients available from diet. These are beneficial as support therapy in the prevention of diseases and also improved the outcome of diseases. Various polyphenols have significantly different bioavailability and the most abundant polyphenols in our diet possess the maximum concentration of active metabolites in target tissues. Their composition and proportion vary depending on the procedure of extraction and families [100]. Pycnogenol® is a formulation being made with the help of these and is rich in catechins, flavonoids and procyanidins (B1, B2, B3, B7 C1 and C2), also, they contain phenolic acids such asferulic acid and caffeic acids. It is also confirmed to have several effects such as cholesterol lowering and cardiovascular benefits because of its antidiabetic, anti-inflammatory and antioxidant properties [101][102][103].

2.4.4. Carotenoids

These are naturally occurring pigments found in algae, photo-synthetic bacteria and various plants. These have linear tetra terpenoid structure. These are found in natural sources such as fruits, vegetables etc. α-carotene, β-carotene, β-cryptoxanthin, lutein, zeaxanthin, and lycopene are the most commonly used dietary carotenoids [104]. These carotenoids are used for skin health such as anti-ageing and photo protection of skin. The probiotics and carotenoids are reported for decreasing the skin damage due to UV-exposure and also in modulating early skin biomarkers of UV effects. A Carotenoid mixture supplement of α-carotene, β-carotene and lutein are proved effective in photo protection. Similarly, a mixture of beta-carotene, lutein and lycopene carotenoids is reported for protection against erythema. The vitamin C and E is studied for the photoprotective effect and found to be effective in skin health care [105]. Vitamin C is a hydrophilic vitamin, commonly taken in large doses via consuming various food products with the intent of inhibiting the formation of carcinogenic nitrous metabolites. It acts as a cofactor for the synthesis of collagen fibers and inhibits the biosynthesis of elastin in fibroblasts thereby preventing its accumulation, which is highly present in photo-damaged skin. In combination with vitamin E, it acts synergistically working with its mechanism of transformation. Vitamin E is the main lipophilic antioxidant and is found in the form of tocopherols. It binds with peroxyl radicals, thereby preventing lipid peroxidation of polyunsaturated fatty acids. In addition, itsuse for preventing photodamage, sunburn, atopic dermatitis, etc., is clearly evidenced [106][107].

2.5. Nutraceuticals as Specialized Medical Products

According to the legal basis, dietary foods and enhancements for distinct medical purposes are specialized medical products. These dietary supplements should be regulated according to the regulatory agencies such as ‘European Food Safety Authority’ and the ‘U.S. Food and Drug Administration’, in addition to numerous national protocols issued most often by the ‘Ministry of Agriculture’ and/or ‘Ministry of Health’ of various countries around the world [108].

Nutraceuticals are non-specific biological therapies used to promote wellness, prevent malignant processes and control symptoms. **Figure 3** shows a flow chart indicating role of nutraceuticals in health promotion and disease prevention.

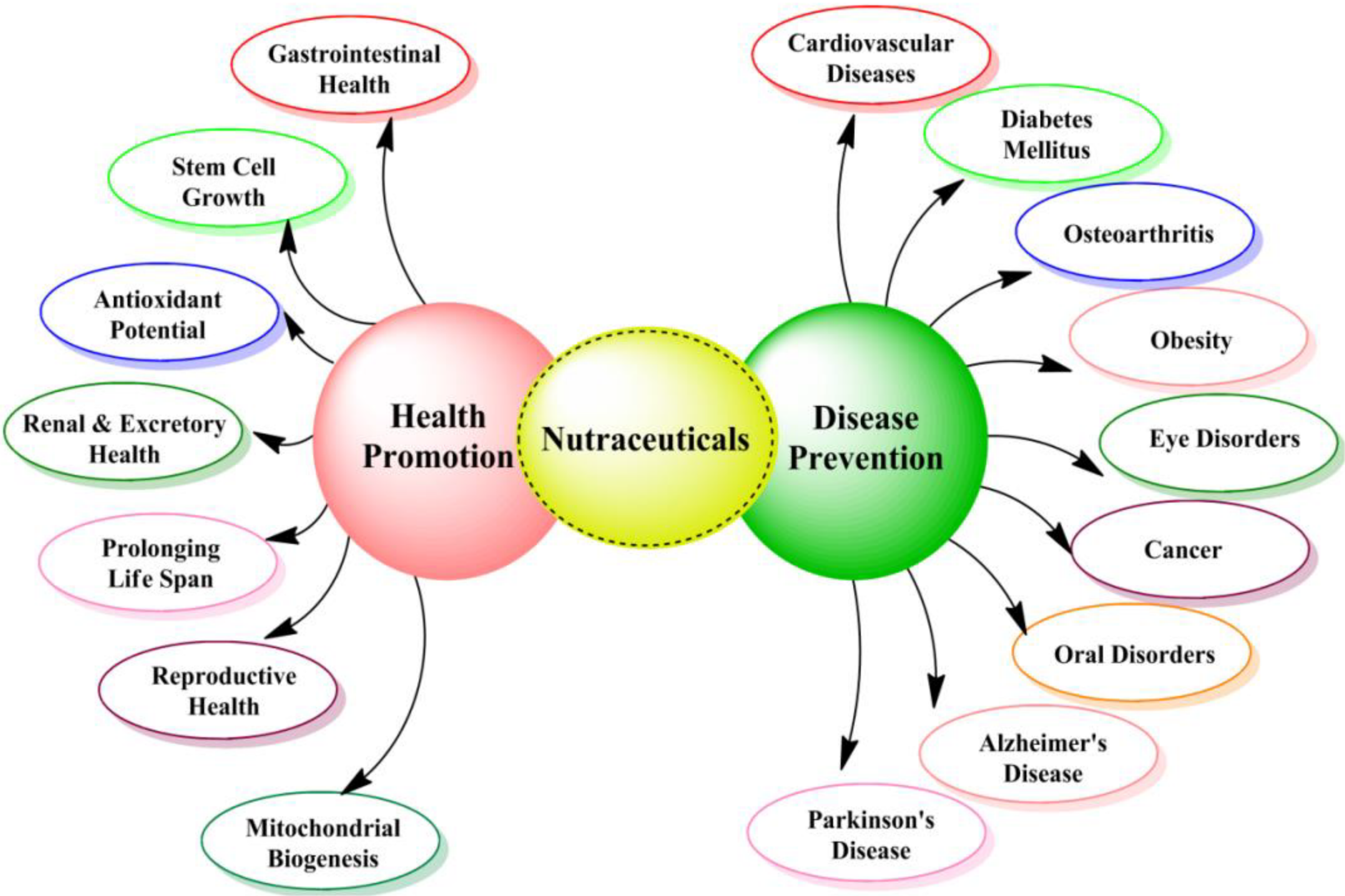

Figure 3. Role of nutraceuticals in disease prevention and health promotion.

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