

## OUTLOOK ON EMERGING TRENDS OF NUTRACEUTICALS FOR TREATMENT

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### ABSTRACT

Nutraceuticals are food ingredients that have the potential to offer a variety of health benefits and are used to cure or prevent a diverse range of diseases. In contrast to medicines, which are pure unitargeted and utilised at very high concentrations, nutraceuticals are multitargeted mixtures. Nutraceuticals are considered to be a component of food and shouldn't be viewed as a type of pharmaceuticals or drug formulation. Now that nutraceuticals have less side effects and contraindications than chemical therapies, people are becoming more interested in them. In the prevention and occurrence of many diseases caused by unhealthy eating and lifestyle choices, nutraceuticals are anticipated to deliver positive results. This article's goal is to educate readers about the use of nutritional supplements in the treatment of various diseases.

**KEYWORDS:** Nutraceuticals, Medicinal food, Probiotics, Dietary supplements, Biocatalyst.

### Abbreviation

CAM- complementary and alternative medicine, FDA- Food and Drug Administration, TNF-tumour necrosis factor, NK Cells-natural killer cells, AD- Alzheimer's disease, SDAT-senile dementia of Alzheimer's type, PDDAT-primary degenerative dementia of Alzheimer's type, CVDs- cardiovascular diseases, PUFA-polyunsaturated fatty acid, CLA-conjugated linoleic acid, MC-*Momordica charantia*, OA-osteoarthritis, AA-arachidonic acid, EPA-ecosapentaenoic acid, DHA-docosahexaenoic acid.

### 1). INTRODUCTION

Numerous studies have revealed that dietary patterns are one of the prominent factors contributing to the

development of medical problems like cardiovascular disease, diabetes, gallstones, neurodegenerative disorders, cataract, and so many others.<sup>[1]</sup> A number of different types of pathological conditions with a highly complex aetiology make up neurological illness.<sup>[2]</sup> In 1989, DeFelice merged the terms "nutrition" and "pharmaceutical" to develop the terminology "nutraceutical," which again was initially defined as "a food (or edible part of the plant) that provides health or relevant information, including the diseases prevention and/or treatment (figure 1)."<sup>[3]</sup>



Fig 1. Term Nutraceuticals.

Any substance that is a food or a component of food that offers medical or health advantages, including the prevention and treatment of disease, is a nutraceuticals, as per Dr. Stephen DeFelice. The terminology

"nutraceutical" is a combination of both pharmaceuticals and nutrition for instance a food that is naturally rich in nutrients, including such as spirulina, garlic, soy or a specific food ingredient like salmon's omega-3 oil.

Nutraceuticals also go by the terms Medicinal foods, dietary supplements, and nutritional supplements. Various dietary supplements, isolated nutrients and Reinforcement, 'designer' food production, herbal items as well as processed foods like grains, pulses and soups. They have attracted a lot of interest due to its stated safety and possible nutritional and therapeutic benefits.<sup>[4]</sup>

Nutraceuticals were initially considered as natural foods that might offer the daily sufficient amount of energy and the advantages of nutraceuticals in treating various nutritional illnesses, using the supplements for self-prescription. There has been a greater rise in the public's awareness with the recognised idea of nutraceutical medicine in different areas. nutraceuticals are effective therapeutic supplements of "complementary and alternative medicine"(CAM). Hippocrates, the well-known as the father of medicine, offered "Let food be thy medicine" about 2000 years ago.<sup>[5]</sup> Approximately 3.1% of the Western Countries recognised to be at risk for neurodegenerative illnesses, are between the ages of 70 and 79. In India, 0.7% of people in similar age groups have disorder incidence. The main cause of the disparity depending on the ingestion of various substances, people have various eating and lifestyle patterns. People have depend on spices and natural items since the dawn of time for healing various illnesses, with outstanding outcomes.<sup>[6]</sup>

Nutraceuticals are defined by the American Nutraceutical Association as a food or its product which have health-promoting characteristics. They range from nutritional supplements for the diet to genetically engineered foods, herbal remedies, drinks, soups, fruits, vegetables, and processed foods, also including cereals etc.<sup>[7]</sup> Vitamins, minerals, and amino acids are the vital factors of nutraceutical, along with more than a thousand other.

The earliest civilizations that provided proof of the efficient utilisation of food products. Indians are also affected by medical treatment and ailments and a fact that has even been supported for 5000 years by Ayurveda, Sumerians, Egyptians, and Chinese also.<sup>[8]</sup> The significant potential for both plant-based and animal-based nutraceuticals good chance for the food industries to develop new foods goods in the future. Studies on nutrition are now starting to focus on the Foods' abilities to protect against illness and prevent disease are explored<sup>[9]</sup> isolated nutrients, herbal items, nutritional supplements, and diets are instances of nutraceuticals. "Designer" meals and processed goods, like cereals, soups, and drinks, that have undergone genetic engineering. Definitely, many of these compounds have important physiological properties and beneficial to biological systems.<sup>[10]</sup>



Fig 2. Concept of nutraceutical benefit.

## 2). The Ideology of Nutraceuticals

In the process of creating pharmaceuticals, it is necessary to have the results or outcomes of clinical tests from research and testing on animals. As opposed to that, in this instance of nutrients, there was no way to verify it for foods in the past in preventing illnesses. In yet, as food composition has changed recently scientific evidence that it causes lifestyle-related illnesses and has developed into societal problem.<sup>[11]</sup> Nutraceuticals were first thought of as natural foods that might offer the daily necessary amount of energy health up required in the body until the year 1990. For instance, various food enterprises originated in the early 19th century to season salt with iodine in order to avoid goitre. This is an example of an attempt to design a useful component. Later, with rising awareness of the benefits of nutraceuticals in treating various nutritional problems, using the supplements for self-prescription. There has

been a tremendous increase in public awareness of with the recognised idea of nutraceutical medicine as a new approach. Nutraceuticals are powerful therapeutic supplements of "Complimentary and Alternative medicines" (CAM) (figure 2). Hippocrates, the well-known father of medicine, recommended "Let food be thy medicine medicine be thy food," almost 2000 yrs ago highlighting the connections between diet and health in general and in particular between healthy eating choices and their medicinal advantages. Nutraceuticals are defined as pure extracted phytomolecules, although semi-purified plant products are not considered to be normal food is referred to as functional food.<sup>[12]</sup>

### 3). Categories of nutraceuticals or nutritional supplements<sup>[13]</sup>

In general, biological therapies called nutraceuticals are used to control symptoms, prevent disease, and promote wellness. The groupings for them are follows:

#### (a) Nutrients

Things with well-established nutritional purposes, like vitamins, minerals, and amino acids, and fatty acids, their related health advantages. The vitamins that are water, fat, and antioxidant-soluble are the most well-known nutrients. Antioxidant use, whether through dietary intake or supplementation, has been linked to a wide range of possible advantages. Antioxidants, may be helpful in preventing cancer and cerebrovascular disease in general.<sup>[14]</sup>

Parkinson's disease may be avoided by eating a diet high in vitamin E. Dehydroascorbic acid, a type of vitamin C that has undergone oxidation, can easily pass the blood-brain barrier, according to research by Agus et al. Some believe that these results have significance because they could lead to an increase in the absorption of antioxidants in the central nervous system. The capacity for enhancing Alzheimer's disease therapy. Jialal and Fuller discovered that combining Taking vitamin E, C, and beta carotene has helped to reduce low density lipoprotein oxidation and the ensuing atherosclerosis.<sup>[15]</sup>

#### (b) Herbal

Herbs are as old as human civilization, and they have a vast array of treatments for both acute and chronic illnesses. In order to ensure our health, now we have numerous efficient ways and we should thanks to the thousands of years of gathered herbal knowledge. B-sitosterols, which are present in Saw Palmetto berries, cernilton (pollen extract), and other herbal extracts. A clinical evaluation of the *African plum*, *Pygeum africanum*, for the treatment of benign prostatic hyperplasia.<sup>[16]</sup>

#### (c) Dietary Supplements

Dietary supplements, commonly referred to as food supplements or nutritional supplements, are preparations that are meant to make up for nutrients such as vitamins, minerals, fibre, fatty acids, or amino acids that are either lacking from a person's diet or are not ingested in appropriate amounts.<sup>[17]</sup>

Ingredients in supplements can include organ tissues, amino acids, enzymes, vitamins, minerals, herbs, botanicals or other food ingredients. They are offered in many dose forms, such as pills, extracts, capsules, liquids, powders, and concentrates.<sup>[18]</sup>

#### (d) Traditional Nutraceuticals or Food-Based Nutraceuticals

This category comprises food items that are derived entirely from nature without being altered from their natural component state. Fruits, vegetables, cereals, meat, fish, eggs, and dairy products are among these give advantages past merely nutritional.<sup>[19]</sup>

#### (e) Probiotic

Microbes that are "probiotics", term coined by the scientist Metchnikoff. With regard to the physiology of the stomach and intestines, they are quite beneficial. They have antibacterial qualities and support the elimination of harmful intestinal flora. A balanced diet promotes both physical and mental wellness. Consuming probiotics has revolutionised the way gastrointestinal diseases are treated. Following these findings, probiotics have also been introduced for use as dietary supplements, including probiotic beverages and pills. Consequently, contemporary probiotics assert their efficacy in all medical disorders, including everything from diarrhoea to neurological issues like depression and Alzheimer's and their therapeutic efficacy are contested. Probiotic research is urgently needed. According to published studies, there is a dearth of study on their safety. It is challenging to distinguish probiotics' advantages from their disadvantages and contraindications. In situations where people with weakened immune systems are at significant risk for infection, probiotics may have a mild therapeutic effect on the body.<sup>[20,21]</sup>

#### (f) Nutraceuticals biocatalyst

Cells produce protein structures called enzymes or biocatalysts. They accelerate metabolic processes and are particularly helpful for gastrointestinal disorders such gastric reflux disease, constipation, diarrhoea etc. Supplemental enzymes give the least benefits to neurological health. Although recently, some treatments to remedy uncommon illnesses like Hunter syndrome, Gaucher disease, etc. Considering how cost-effective they are both plant and animal sources may be used to get. The ingestion of food-based nutraceuticals offers a huge variety of benefits. Nutraceuticals made from food sources like dairy, carotenoids, ginger, garlic, and turmeric are considerably healthier and may give our bodies, all the critical nutrients they need. Those are commonly accessible in food stores and stop the worsening of serious life-related problems like even cancer and diabetes. A good diet can be the key to maintaining excellent mental health, which is a priority and most desirable choice for neuro-protection. They also have certain drawbacks though majority. The safety of food-based nutraceuticals is an emphasised drawback. There is still an urgent need to investigate that Prior to being made available on the market for eating in raw forms, functional foods are tested for safety. Unless a certain amount is consumed, and all chemicals are poisonous. It is obvious that a diet that is extremely effective against cancer can also be cardio toxic. So, it is advised to administer the desired dose.<sup>[22, 23, and 24]</sup>

#### (g) Non Traditional Nutraceutical

Alternative Nutraceuticals are foods created by the breeding of agricultural goods and nutrients, such as calcium-fortified orange juice, cereals fortified with vitamins and minerals, etc. Cultural anthropologists have successfully developed strategies, altered the nutrient

content of crops, and conducted additional study is being done to enhance the nutritional quality of crops.<sup>[25,26]</sup>

#### (h) Fortified or Additive Nutraceutical

These are the kinds of nutraceutical that are created through agricultural breeding to improve nutrition, such as minerals in cereals, calcium, folic acid, and iron in flour, among others. Cholecalciferol-fortified milk is used to treat vitamin D deficiency, among other conditions.<sup>[27,28]</sup>

#### (i) Recombinant Nutraceuticals

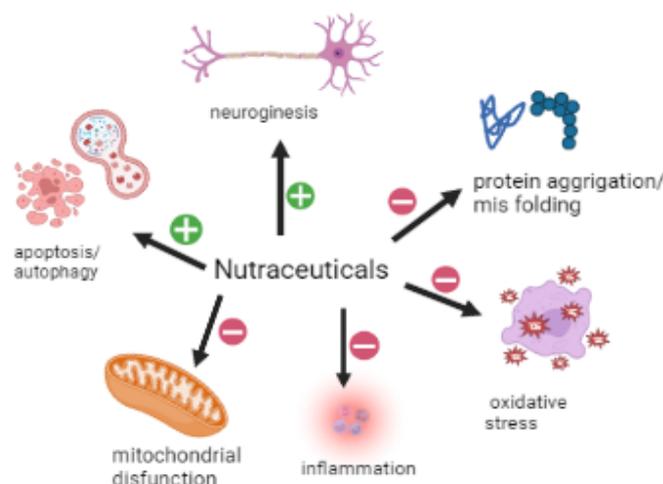
Recombinant nutraceuticals are those obtained by the incorporation of biotechnology in food items. These nutraceuticals are among the most often utilised types and they include the nutrient extraction from specific food items like dairy, cheese, and bread. To obtain the enzyme that utilised at optimal doses, has therapeutic benefits.<sup>[29,30]</sup> In order to increase the amount of nutrients in already existing food supplements and to increase the number of benefits in the same amount of food consumed, non-traditional nutraceuticals have arisen.

In the age of sedentary lifestyles, it has many benefits and is a blessing, but it also poses some risks. The Food

and Drug Administration (FDA) currently does not have regulations governing the production of nutraceuticals.<sup>[31]</sup>

#### (j) Based on the Mechanism of Action

To separate their function and evaluate their usage, nutraceuticals have been further categorised into antibacterial, antifungal, antioxidant, anti-inflammatory, and anti-obesity categories based on the therapeutic capabilities they exhibit. Many death related infections are caused by food-borne illnesses. Carsonic acid (terpenoids), quercetin (polyphenols) and other bioactive chemicals have all been employed as effective antibacterial therapies in the treatment of infectious diseases. They come from a variety of fruits and vegetables.<sup>[32]</sup> Due to their anti-inflammatory effects, nutraceuticals have been employed in a variety of inflammatory illnesses, and including rheumatoid arthritis (Figure 3).<sup>[33]</sup> Foods abundant in carotenoids, tocopherols and antioxidants have stronger anti-inflammatory properties. The antioxidant and free radical-scavenging abilities of nutraceuticals are well known. Its role in the treatment of other linked illnesses, such as obesity, is a result of its antioxidant action.<sup>[34]</sup>



**Fig 3. Mechanism of action: nutraceuticals inhibit the mitochondrial dysfunction, inflammation, oxidative stress, protein aggregation/mis-folding and stimulate autophagy/apoptosis and neurogenesis.**

#### 4). Curative use of nutraceuticals

##### i) Cancer

Additionally, it has been calculated that lifestyle modifications, such as proper eating, can save one-third of all cancer-related deaths.<sup>[35]</sup> There is a long history of using botanicals to treat cancer. Numerous cancer-fighting medications are derived from plants, such as the vinca species' alkaloids (vincristine and vinblastine) and the Pacific yew *Taxus brevifolia* (Taxol).<sup>[35]</sup> Despite advancements in medicine, cancer continues to be a major global health concern. Several plant extracts are used to cure and prevent cancer. Treatment for cancer patients may benefit from nutritional modification.<sup>[36]</sup> There is proof that cancer patients benefit from eating

foods that are comparatively low in simple carbs and moderate in high-quality protein, fibre, and fat (particularly lipids of the omega-3 fatty acid series).<sup>[37]</sup> Additionally, nutraceuticals may be useful in minimising the side effects of chemotherapy and radiation treatment as well as improve life circumstances by lowering cancer cachexia.<sup>[38]</sup> Early in-vitro research revealed that phytochemicals may counteract the tumorigenic effects of carcinogens by inhibiting their mutagenic activity and cell growth.<sup>[39]</sup> Even at very low concentrations, dietary bioactive chemicals may have a significant effect on how genes are regulated. A greater understanding of the disease's preventative mechanisms, such as those for obesity, diabetes, atherosclerosis, hypertension and

others, should result from ongoing study on the effects of nutraceuticals on gene expression cancer with dietary adjustments. Furthermore, it was discovered that phytochemicals regulate innate and adaptive immunity, protect against lipid peroxidation, and inflamed reactions.<sup>[40]</sup>

In fact, some cancer patients exhibit cachexia, which is characterised by major changes in their metabolism of carbohydrates, proteins, and fats and leads to poor quality of life, decreased therapeutic response, and shortened survival time. To correct these metabolic changes, nutritional modification may be helpful in the treatment of cancer patients. A useful technique for managing cancer and minimising the side effects of chemotherapy and radiation therapy is nutritional intervention.<sup>[41]</sup> Additionally, in patients with advanced cancer, nutraceuticals can greatly increase tumour necrosis factor (TNF) and natural killer cells (NK cells) function.<sup>[42]</sup>

### ii) Alzheimer's disease (AD)

The most prevalent type of dementia is Alzheimer's disease (AD), also known as senile dementia of the Alzheimer type (SDAT), primary degenerative dementia of the Alzheimer's type (PDDAT), or simply Alzheimer's. Due to the high level of oxidative stress that most chronic diseases come with, antioxidants are absolutely necessary in the treatment of practically all diseases antioxidant stress. A considerable number of studies have linked a high intake of dietary antioxidants to a lower risk of AD, which is crucial because preventing disease is far simpler than treating it. It is currently being investigated whether vitamin E actually decreases the course of AD. The patients were divided into two groups for assessment purposes: one group received treatment with 1000 IU of vitamin E and at least 5 mg of donepezil (Aricept), and the other group received no vitamin E at all. The results revealed that individuals undergoing permutation therapy degenerated at a markedly lower rate. Studies on food usage have produced similar results. Antioxidants are abundant in food and you consume an abundance of them. Everything from well-known flavonoids to antioxidants such as vitamin C and E.<sup>[43]</sup>

The antioxidant ALA also contributes to proper brain function. The biological traits and hallmarks of AD are oxidative stress and decreased energy. Strong antioxidant alpha lipoic acid helps the brain's ingestion and metabolism of glucose.<sup>[44]</sup> The compound of phosphatidyl serine is quite intriguing. The primary phospholipid in the brain, phosphatidyl serine, is responsible for the fundamental structure of the cell membrane. The oral supplement phosphatidyl serine improves neuronal membranes, cell metabolism, and certain neurotransmitters, including acetylcholine, nor-epinephrine, serotonin, and dopamine.<sup>[45]</sup>

### iii) Cardiovascular Disease

The costs of chronic conditions like cancer, diabetes, cardiovascular disease, and obesity are rising quickly over the world. About 59% of the 56.5 million global recorded fatalities in 2001 and 46% of the total burden of disease were attributable to chronic diseases. Hypertension (high blood pressure), coronary heart disease, and other conditions affecting the heart and blood vessels are together referred to as cardiovascular diseases (CVDs), heart attack, heart failure, cerebral vascular disease, stroke, disease of the peripheral arteries, etc. In 1999 CVD alone was responsible for one third of deaths worldwide and by 2010, it would be the primary contributor to dying in emerging nations.<sup>[46,47]</sup> Numerous studies have found that a diet high in fruits and vegetables protects against CVD.<sup>[48]</sup> In addition to physical activity, nutraceuticals such as antioxidants, dietary fibre, omega-3 polyunsaturated fatty acids (n-3 PUFAs), vitamins, and minerals are advised for the prevention and treatment of CVD. It has been shown that compounds like polyphenols found in grapes and wine change cellular signalling and metabolism, which is linked with a decrease in artery disease.<sup>[49]</sup> Onion, endives, cruciferous vegetables, black grapes, red wine, grapefruits, apples, cherries, and berries are abundant in flavonoids.<sup>[50]</sup>

### iv) Parkinson's disease

Parkinson's disease is a neurological ailment that causes muscle rigidity, shaking, and difficulty in walking as a result of nerve damage in certain areas of the brain.<sup>[51]</sup> Typically taking place in mid- to late-life. According to Canadian experts, dietary vitamin E may offer protection against Parkinson's disease.<sup>[52]</sup> A Decrease in the clinical indicators suggested that creatinine appeared to alter the characteristics of Parkinson's disease.<sup>[53]</sup>

### v) Obesity

Obesity is a complicated disorder that affects almost all ages and socioeconomic groups and has major social and psychological implications. Between 1980 and 2008, the prevalence of obesity roughly doubled globally. According to national estimates for 2008, around 23% of women and 20% of men in the WHO European Region were obese, while over 50% of both men and women in this region were overweight.<sup>[54]</sup> It is advised that weight loss programmes concentrate on obtaining a modest weight loss of 7–10% of the starting weight.<sup>[55]</sup> Pharmaceutical businesses already employ all of these strategies, but creating functional meals intended to help people control their weight may be a more appealing way to address the 61% of the population that is currently overweight or obese.<sup>[56]</sup> Nutraceuticals with possible anti-obesity qualities include conjugated linoleic acid (CLA), capsaicin, *Momordica charantia* (MC) and psyllium fibre.<sup>[57]</sup> The nutritional supplement's combination of glucomannan, chitosan, fenugreek, G Sylvester, and vitamin C dramatically lowered body weight and encouraged fat reduction in obese people.

Additional research is required to determine long-term efficacy and adverse effect potential.<sup>[58]</sup>

#### vi) Anti-inflammatory activities

Turmeric contains a polyphenol called curcumin (diferuloylmethane), which has anti-inflammatory, anti-carcinogenic and antioxidant effects. Top of Form Antitumor properties have been documented for beet roots, cucumber fruits, spinach leaves, and turmeric rhizomes. Gamma linolenic acid is used to treat inflammation and auto-immune illnesses. It can be found in green leafy vegetables, almonds, and vegetable oils such as evening primrose oil, blackcurrant seed oil, and hemp seed oil. In addition to being used to treat osteoarthritis, glucosamine and chondroitin sulphate also control gene expression and PGE2 production. A strong anti-inflammatory agent is cat's claw. *Uncaria guianensis*, which is traditionally used to treat wounds and *Uncaria tomentosa*, which has many medical applications and is most frequently found in supplements, are the two species of cat's claw that are known. 17 alkaloids, glycosides, tannins, flavonoids, sterol fractions, and other phytochemicals are abundant in cat's claw.<sup>[59]</sup>

#### vii) Adrenal Dysfunction

Natural herbs known as adaptogens have general, balancing effects on physiology; they only slightly alter regular bodily processes to promote generalised resilience to stresses.<sup>[60]</sup> Herbs including *Eleutherococcus senticosus*, *Ginkgo biloba*, *Ocimum sanctum*, *Panax ginseng*, and *Withania somnifera*, as well as the mushroom *Cordyceps sinensis*, are examples of adaptogens. Here is a brief explanation of each. Chinese herbal therapy has long employed *Eleutherococcus senticosus*, sometimes known as Siberian ginseng, to improve overall health, longevity, appetite and memory. It was made popular in Russia in the 1950s because *Panax ginseng* was quite expensive and scarce. Despite being only distantly related to it.<sup>[61,62]</sup>

The glycosides eleutherosides through *Eleutherococcus* are the active components, and they are recognised to provide anti-stress, anti-fatigue and immunomodulatory actions.<sup>[63]</sup> The Chinese have been using *ginkgo biloba* for thousands of years to treat a variety of illnesses, such as vertigo, short-term memory loss, and a lack of focus or vigilance.<sup>[64]</sup> Dementia development is slowed by neuroprotective qualities.<sup>[65]</sup> *Ginkgo* was efficient in lowering corticosterone levels in rats exposed to acute stress, but it had little to no effect and on rats exposed to chronic stress, according to a different study comparing acute and chronic stressors in rats treated with *panax*, *ginkgo*, or placebo.<sup>[66]</sup> It has been demonstrated that the Ayurvedic herb *Ocimum sanctum*, sometimes known as holy basil or tulsi, has anti-stressing properties.<sup>[66]</sup> Since ancient times, the herb *Withania somnifera*, also known as ashwagandha, Indian ginseng, or winter cherry, has been utilised in Ayurvedic medicine as an aphrodisiac, liver tonic, anti-inflammatory, and astringent.<sup>[67]</sup>

#### viii) Osteoarthritis

In United States 21 million individuals affected by most prevalent type of arthritis, is osteoarthritis (OA), a crippling joint illness. All kinds of arthritis resulted in direct and indirect health care expenses of over 86 billion USD in 2004. Increased weight can make existing issues worse by putting more strain on the joints.<sup>[68]</sup> These nutraceuticals appear to control gene expression and the creation of NO and PGE2, which provides a credible explanation for their anti-inflammatory characteristics. They also appear to have both nutritional and medicinal properties.<sup>[69]</sup>

#### ix) Stem Cell Therapy

Stem cell research has recently been proven to be useful in treating a number of disorders. Several researchers have examined the results of specific supplements for stem cell development and proliferative activity that could induce endogenous using stem cells to promote repair and regrowth, aims as replacement for stem cell transplantation.<sup>[70]</sup>

In comparison to human granulocyte macrophage colony-stimulating factor, Bickford et al. reported a dose-related effect of blueberry, green tea, catechin, carnosine and vitamin D3 on proliferation with human bone marrow. Additionally, combinations of nutrients can synergistically promote proliferation of human hematopoietic progenitors indicating yet another potential function or mechanism by which nutraceuticals function encourage the body's natural ability to repair person's body.<sup>[71]</sup> It is thought that nutritional factors during early development have long-term implications on adult health, illness risk, death rates and short-term effects on growth, body composition and bodily functioning. The formation and development of bone and the human neurological system depend on dietary intakes of minerals like Ca, P, Mg, Fe, Zn, I, F, and B as well as vitamins D and K.<sup>[72]</sup>

#### x) Apoptosis and Disease Prevention

Numerous epidemiological and animal model studies have hypothesised that nutraceuticals, primarily phytochemicals derived from dietary or medicinal plants like tea, garlic, ginger, soya bean, and others may have chemo preventive potential. We discuss the impacts of a few particular phytochemicals that fall under the following structural classes: stilbenes, carotenoids, flavonoids, or other substances containing sulphur.<sup>[73]</sup>

#### xi) Depression

Depression is a mental illness defined by a sad or gloomy mood along with a loss of interest in any social engagement, which impairs routine. With an annual incidence of 7%, its frequency is around 15%. Because a depressed individual is less productive and has a higher mortality risk, it places a significant financial burden on society. With growing data supporting their efficacy as a mono-therapy, folic acid and omega-3 fatty acids have typically proven successful in treating unipolar

depression. As a correlation between the quality of food and brain health and mood has been established and investigated, the nutrients from dietary products are essential for good brain functioning.<sup>[74]</sup>

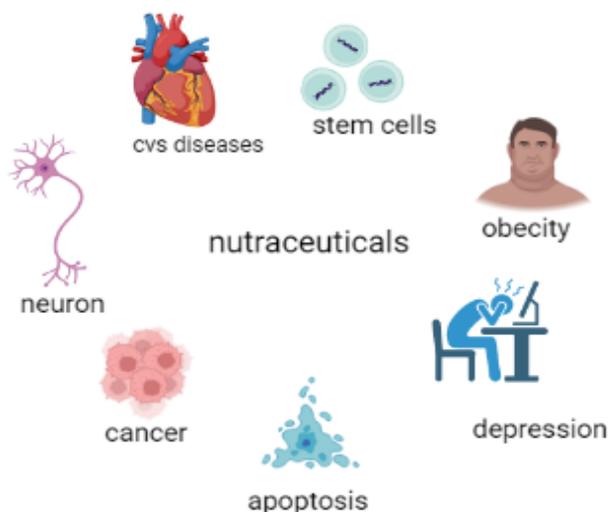
A whole-grain diet rich in nutrients can stimulate brain function and has consistently demonstrated results in the treatment of depression. These nutrients include zinc, folic acid, omega-3 fatty acids, and several other crucial macro and micronutrients (figure 4).<sup>[75]</sup>

### xii) Psychotic Disorders

Beyond the functional aspects that have been explored, nutritional supplements are essential for the treatment of mood disorders and psychotic illnesses like schizophrenia and bipolar disorder.<sup>[76]</sup> Omega-3 fatty acids and vitamins are two of the most often used nutraceuticals in psychosis. In the human body, there are

two primary forms of polyunsaturated fatty acids: those of the omega-3 series, obtained as alpha-linolenic acid, and those of the omega-6 series, such as arachidonic acid (AA), which are derived from linoleic acid. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are among the latter.<sup>[77]</sup>

Each of them is crucial for the life of the human body and forms part of the phospholipid cell membrane. They must, however, be received through diet because the body is unable to produce them. Omega-3 EPA and DHA have characteristics at the molecular level that are relevant to psychotic illnesses. Dopaminergic and serotonergic neurotransmission is enhanced. They lessen oxidative stress and micro-inflammatory symptoms. They alter how mitochondria, the primary source of oxidative stress function.<sup>[78]</sup>



**Fig 4: Nutraceuticals as health care.**

### 5). CONCLUSION

People are now turning to nutraceuticals. It is obvious that improving people's quality of life, which translates into raising health awareness among the populace, is a driving force behind the development of nutraceuticals. The present demographic and health trends are the main drivers of the global nutraceuticals market's expansion. Because of humans' constantly changing lifestyles, their antioxidant defence systems are frequently overworked, which leads to oxidative stress. Additionally, the antioxidant defence system levels significantly decline with ageing. Many plant components, including catechines, carotenoids, PUFA, polyphenols, etc., have proven to be quite useful in preventing and treating a variety of diseases, including inflammation, Parkinson's, GIT diseases, and others. Hence, nutraceuticals play an important role in disease prevention as well as promoting health.

### 6). Competing interest

No conflicting interest regarding this review paper.

### 7). REFERENCES

1. Smith-Warner, S. A., Elmer, P. J., Tharp, T. M., Fosdick, L., Randall, B., Gross, M., ... Potter, J. D. (2000). Increasing vegetable and fruit intake: randomized intervention and monitoring in an at-risk population. *Cancer Epidemiol Biomarkers Prev*, 9: 307-317.
2. Williams, R.J.; Mohanakumar, K.P.; Beart, P.M. Neuro-nutraceuticals: Further insights into their promise for brain health. *Neurochem. Int.*, 2016; 95: 1-3. [CrossRef] [PubMed]
3. Kalra EK. Nutraceutical- definition and introduction. *AAPS PharmSci.*, 2003; 5(3): E25.
4. Rajasekaran, A, Sivagnanam, G and Xavier R, Nutraceuticals as therapeutic agents. A Review. *Res J Pharm Sci Technol*, 2008; 1(4): 328-340.
5. Roudebush, P., Davenport, D. J., & Novotny, B. J. (2004). The use of nutraceuticals in cancer therapy. *Vet Clin N Am-Small*, 34(1): 249-269. <http://dx.doi.org/10.1016/j.cvsml.2003.09.001>

6. Bungau, S.G.; Popa, V.C. Between Religion and Science Some Aspects Concerning Illness and Healing in Antiquity. *Transylv. Rev.*, 2015; 24: 3–18.
7. Prakash, V.; Boekel. Nutraceuticals: Possible future ingredients and food safety aspects. In *Ensuring Global Food Safety*; Academic Press: Cambridge, MA, USA, 2010; 333–338.
8. Orlando, J.M. Behavioral Nutraceuticals and Diets. *Vet. Clin. Small Anim. Pract.*, 2018; 48: 473–495. [CrossRef][PubMed]
9. Nicoli MC, Anese M, Parpinel M (1999) Influence of processing on the antioxidant properties of fruits and vegetables. *Trends Food Sci Technol*, 10: 94–100.
10. Andlauer W, Furst P. Nutraceuticals: a piece of history, present status and outlook. *Food Research International*, 2002; 35: 171–6.
11. [www.medicinalfoodnews.com/vol01/issue2/japan.Functional foods in Japan](http://www.medicinalfoodnews.com/vol01/issue2/japan.Functional%20foods%20in%20Japan), *Medical Food News*, May 1997 No.6.
12. Roudebush, P., Davenport, D. J., & Novotny, B. J. (2004). The use of nutraceuticals in cancer therapy. *Vet Clin N Am-Small*, 34(1); 249–269. <http://dx.doi.org/10.1016/j.cvsm.2003.09.001>
13. Hathcock J. Dietary supplements: How they are used and regulated. *J. Nutrition*, 2001; 131: 1114–1117.
14. Mobarhan S. Micronutrient supplementation trials and the reduction of cancer and cerebrovascular incidences and mortality. *Nutr Rev.*, 1994; 52: 102–5.
15. Jialal I, Fuller CJ. Effect of vitamin E, vitamin C and beta carotene on the LDL oxidation and atherosclerosis. *Can J Cardiol*, 1995; 11: 97–103.
16. Clark LC, Combs Jr GF, Turnbull BW, Slate EH, Chalker DK, Chow J, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. *Nutritional Prevention of Cancer Study Group. JAMA*, 1996; 276: 1957–63.
17. Braeckman J. The Extract of *Serenoa repens* in the treatment of benign prostatic hyperplasia: a multicenter open study. *Curr Ther Res.*, 1994; 55: 776–85.
18. WWW.NCCA.M.NIH.GOV. National Institutes of Health National Center for Complementary and Alternative Medicine.
19. Bhaskarachary, K. Traditional Foods, Functional Foods and Nutraceuticals. *Proc. Indian Natl. Sci. Acad.*, 2016; 82: 1565–1577.
20. Gosálbez, L.; Ramón, D. Probiotics in Transition: Novel Strategies. *Trends Biotechnol*, 2015; 33: 195–196.
21. Zucko, J.; Starcevic, A.; Diminic, J.; Oros, D.; Mortazavian, A.M.; Putnik, P. Probiotic—Friend or foe? *Curr. Opin. Food Sci.*, 2020; 32: 45–49.
22. Putnik, P.; Gabrić, D.; Roohinejad, S.; Barba, F.J.; Granato, D.; Lorenzo, J.M.; Bursać Kovačević, D. Bioavailability and food production of organosulfur compounds from edible *Allium* species. In *Innovative Thermal and Non-Thermal Processing, Bioaccessibility and Bioavailability of Nutrients and Bioactive Compounds*; Francisco, J., Barba, J.M.A.S., Giancarlo Cravotto, J., Lorenzo, M., Eds.; Woodhead Publishing: Cambridge, UK, 2019; 293–308.
23. Poojary, M.M.; Putnik, P.; Bursać Kovačević, D.; Barba, F.J.; Lorenzo, J.M.; Dias, D.A.; Shpigelman, A. Stability and extraction of bioactive sulfur compounds from *Allium* genus processed by traditional and innovative technologies. *J. Food Compos. Anal.*, 2017; 61: 28–39.
24. Tapal, A.; Kaul Tiku, P. Nutritional and Nutraceutical Improvement by Enzymatic Modification of Food Proteins. In *Enzymes in Food Biotechnology*; Kuddus, M., Ed.; Academic Press: Cambridge, MA, USA, 2019; 471–481.
25. Singh, J.; Sinha, S. Classification, regulatory acts and applications of nutraceuticals for health. *Int. J. Pharma Bio Sci.*, 2012; 2: 177–187.
26. Sapkale, A.P.; Thorat, M.S.; Vir, P.R.; Singh, M.C. Nutraceuticals—Global status and applications: A Review. *Int. J. Chem. Pharm.*, 2012; 1: 1166–1181.
27. Ottaway, P.B. *Food Fortification and Supplementation: Technological, Safety and Regulatory Aspects*; Woodhead Publishing: Cambridge, UK, 2008.
28. treet, A. Food as Pharma: Marketing Nutraceuticals to India's Rural Poor. *Crit. Public Health*, 2015; 25: 361–372.
29. Williams, R.J.; Mohanakumar, K.P.; Beart, P.M. Neuro-nutraceuticals: The path to brain health via nourishment is not so distant. *Neurochem. Int.*, 2015; 89: 1–6.
30. Andlauer, W.; Fürst, P. Nutraceuticals: A piece of history, present status and outlook. *Food Res. Int.*, 2002; 35: 171–176.
31. Dietary Supplement Health and Education Act of 1994. Available online: [https://ods.od.nih.gov/About/DSHEA\\_Wording.aspx](https://ods.od.nih.gov/About/DSHEA_Wording.aspx) (accessed on 11 June 2020).
32. Gutiérrez-Del-Río, I.; Fernández, J.; Lombó, F. Plant Nutraceuticals as Antimicrobial Agents in Food Preservation: Terpenoids, Polyphenols and Thiols. *Int. J. Antimicrob. Agents*, 2018; 52: 309–315.
33. Al-Okbi, S.Y. Nutraceuticals of Anti-Inflammatory Activity as Complementary Therapy for Rheumatoid Arthritis. *Toxicol. Ind. Health*, 2014; 30: 738–749.
34. Cornelli, U. Antioxidant Use in Nutraceuticals. *Clin. Dermatol*, 2009; 27: 175–194.
35. Danaei, G., Vander Hoorn, S., Lopez, A. D., Murray, C. J., & Ezzati, M. (2005). Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. *Lancet*, 366: 1784–1793. [http://dx.doi.org/10.1016/S0140-6736\(05\)67725-2](http://dx.doi.org/10.1016/S0140-6736(05)67725-2)
36. Weisburger, J. H. (1999). Antimutagens, anticarcinogens, and effective worldwide cancer

- prevention. *J Environ Pathol Toxicol Oncol*, 18: 85-93.
37. Tuomisto, J. T., Tuomisto, J., Tainio, M., Niittynen, M., Verkasalo, P., Vartiainen, T., ... Pekkanen, J. (2004). Risk-benefit analysis of eating farmed salmon. *Science* 305, 476-477; author reply, 476-477. <http://dx.doi.org/10.1126/science.305.5683.476>
  38. Grimble, R. F. (2003). Nutritional therapy for cancer cachexia. *Gut*, 52: 1391-1392. <http://dx.doi.org/10.1136/gut.52.10.1391>
  39. Surh, Y. J. (2003). Cancer chemoprevention with dietary phytochemicals. *Nat Rev Cancer*, 3: 768-780. <http://dx.doi.org/10.1038/nrc1189>
  40. Issa, A. Y., Volate, S. R., & Wargovich, M. J. (2006). The role of phytochemicals in inhibition of cancer and inflammation: New directions and perspectives. *J Food Compos Anal*, 19: 405-419. <http://dx.doi.org/10.1016/j.jfca.2006.02.009>
  41. McCullough, M. L., & Giovannucci, E. L. (2004). Diet and cancer prevention. *Oncogene*, 23: 6349-6364. <http://dx.doi.org/10.1038/sj.onc.1207716>
  42. See, D., Mason, S., & Roshan, R. (2002). Increased tumor necrosis factor alpha (TNF-alpha) and natural killer cell (NK) function using an integrative approach in late stage cancers. *Immunol Invest*, 31: 137-153. <http://dx.doi.org/10.1081/IMM-120004804>
  43. Klatter ET, Scharre DW, Nagaraja HN, Davis RA, Beversdorf DQ. Combination therapy of donepezil and vitamin E in Alzheimer disease. *Alzheimer Dis Assoc Disord*, 2003; 17: 113-116.
  44. Hager K, Marahrens A, Kenklies M, Riederer P, Munch G. Alpha-lipoic acid as a new treatment option for Alzheimer type dementia. *Arch Gerontol Geriatr*, 2001; 32: 275-282.
  45. Engel RR, Satzger W, Gunther W, Kathmann N, Bove D, Gerke S, Munch U, Hippus H. Double-blind cross-over study of phosphatidylserine vs. placebo in patients with early dementia.
  46. Rissanen TH, Voutilainen S, Virtanen JK, Venho B, Vanharanta M, Mursu J and Salonen JT. Low Intake of Fruits, Berries and Vegetables Is Associated with Excess Mortality in Men: the Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study. *J Nutr.*, 2003; 133: 199-204.
  47. Temple WJ and Gladwin KK. Fruits, vegetables, and the prevention of cancer: Research challenges. *Nutrition*, 2003; 19: 467-470.
  48. Hu FB and Willett WC. Optimal diets for prevention of coronary heart disease. *JAMA*, 2002; 288: 2569-2578.
  49. German JB and Walzem RL. The health benefits of wine. *Annual Review of Nutrition*, 2000; 20: 561-593.
  50. Hollman PCH, Hertog MGL and Katan MB. Analysis and health effects of flavonoids, *Food Chem.*, 1996; 57: 43-46.
  51. Losso JN. Targeting excessive angiogenesis with functional foods and nutraceuticals *Trends in Food Science and Technology*, 2003; 14: 455-468.
  52. Latif S, Anwar F Ashraf M and Gilani AH. Moringa oleifera: a food plant with multiple medicinal uses. *Phytother Res.*, 2007; 21: 17-25.
  53. Brower V. A nutraceutical a day may keep the doctor away. *EMBO reports*, 2005; 8: 708-711.
  54. World Health Organization. Global Strategy on Diet, Physical Activity and Health 2010. <http://www.who.int/dietphysicalactivity/publications/facts/obesity/en/>.
  55. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA: Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*, 2005; 112: 2735-52.
  56. Hil JO, Peters JC: Biomarkers and functional foods for obesity and diabetes. *Br J Nutr*, 2002; 88: 213-18.
  57. Kasbia GS: Functional foods and nutraceuticals in the management of obesity. *Nutr Food Sci.*, 2005; 35: 344-51.
  58. Wood gate DE, Conquer JA: Prevalence of self-treatment with complementary products and therapies for weight loss: A randomized, cross-sectional Study in Overweight and Obese Patients in Colombia. *Curr Thera Res.*, 2003; 64: 248-62.
  59. Balch SA, Mckenney CB and Auld DL. Evaluation of gamma-linolenic acid composition of evening primrose (*Oenothera*) species Native to Texas. *Hort Science*, 2003; 38: 595-598.
  60. Brekhman II, Dardymov IV. New substances of plant origin which increase nonspecific resistance. *Annu Rev Pharmacol*, 1969; 9: 419-430.
  61. Deyama T, Nishibe S, Nakazawa Y. Constituents and pharmacological effects of *Eucommia* and *Siberian ginseng*. *Acta Pharmacol Sin.*, 2001; 22(12): 1057-1070.
  62. Bucci L. Selected herbals and human exercise performance. *Am J Clin Nutr.*, 2000; 72(2 Suppl): 624S-636S.
  63. No authors listed. Monograph. *Eleutherococcus senticosus*. *Alt Med Rev.*, 2006; 11(2): 151-155.
  64. Oyama Y, Chikahisa L, Ueha T, Kanemaru K, Noda K. Ginkgo biloba extract protects brain neurons against oxidative stress induced by hydrogen peroxide. *Brain Res.*, 1996; 712(2): 349-352.
  65. Rai D, Bhatia G, Sen T, Palit G. Antistress effects of Ginkgo biloba and Panax ginseng: a comparative study. *J Pharmacol Sci.*, 2003; 93(4): 458-464.
  66. Sembulingam K, Sembulingam P, Nanasivayam A. Effect of *Ocimum sanctum* Linn on noise induced changes in plasma corticosterone level. *Indian J Physiol Pharmacol*, 1997; 41(2): 139-143.
  67. Grandhi A, Mujumdar AM, Patwardhan B. A comparative pharmacological investigation of Ashwagandha and Ginseng. *J Ethnopharmacol*, 1994; 44(3): 131-135.
  68. Rice-Evans C Flavonoid antioxidants. *Curr Med Chem.*, 2001; 8: 797-807.

69. Kalioraa AC, Dedoussisa GVZ and Schmidt H. Dietary antioxidants in preventing atherogenesis. *Atherosclerosis*, 2006; 187: 1-17.
70. Gennero L, Mortimer P, Sperber K, Carloni G, Ponzetto A. Stem cells: an alternative to organ transplantation in chronic, degenerative and infectious diseases. *New Microbiol*, 2006; 29: 151-67.
71. Bickford PC, Tan J, Shytle RD, Sanberg CD, El-Badri N, Sanberg PR. Nutraceuticals synergistically promote proliferation of human stem cells. *Stem Cells Dev*, 2006; 15: 118-23.
72. Koletzko B, Aggett PJ, Bindels JG, et al. Growth, development and differentiation: a functional food science approach. *Br J Nutr*, 1998; 80: 5-45.
73. Alexander G, Kuang YC. Nutraceuticals, Apoptosis, and Disease Prevention. *Nutrition*, 2004; 20: 95-102.
74. Ceskova, E.; Silhan, P. Novel treatment options in depression and psychosis. *Neuropsychiatr. Dis. Treat*, 2018; 14: 741.
75. van der Burg, K.P.; Cribb, L.; Firth, J.; Karmacoska, D.; Sarris, J. Nutrient and genetic biomarkers of nutraceutical treatment response in mood and psychotic disorders: A systematic review. *Nutr. Neurosci.*, 2019; 1-17.
76. Cloutier, M.; Aigbogun, M.S.; Guerin, A.; Nitulescu, R.; Ramanakumar, A.V.; Kamat, S.A.; DeLucia, M.; Duffy, R.; Legacy, S.N.; Henderson, C. The economic burden of schizophrenia in the United States in 2013. *J. Clin. Psychiatry*, 2016; 77: 764-771.
77. Brown, H.E.; Roffman, J.L. Emerging treatments in schizophrenia: Highlights from recent supplementation and prevention trials. *Harv. Rev. Psychiatry*, 2016; 24: e1-e7.
78. Sarris, J.; Logan, A.C.; Akbaraly, T.N.; Amminger, G.P.; Balanzá-Martínez, V.; Freeman, M.P.; Hibbeln, J.; Matsuoka, Y.; Mischoulon, D.; Mizoue, T.; et al. Nutritional medicine as mainstream in psychiatry. *Lancet Psychiatry*, 2015; 2: 271-274.