

Breaking Ground in Nutraceutical Medicine: Recent Advancements and Promising Trends**Dharmendra Singh¹, Arsh Chanana², Pooja Gupta³, Akhilesh Patel⁴, Vani Madaan⁵, Ravindra Pal Singh⁶**^{1,2,3,4,5,6} Department of Pharmaceutics, NIMS Institute of Pharmacy, NIMS University Rajasthan.

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Abstract

Nutraceutical have emerged as a vital frontier in healthcare, offering innovative solutions that bridge the gap between food and pharmaceuticals. Nutraceuticals are mainly characterized into dietary products supplements and functional foods that provide the body with medical or health benefit. This article review provides a comprehensive overview of the recent advancements in nutraceutical medicines, focusing on their potential to revolutionize the way we approach health and well-being. We delve into cutting-edge research and clinical studies that highlight the efficacy of nutraceuticals in preventing and managing various health conditions. The review also explores the evolving regulatory landscape and consumer trends shaping the nutraceutical industry. As we navigate the ever-expanding landscape of nutraceutical medicine, this review sheds light on the promising developments and challenges that lie ahead, emphasizing their potential to reshape the future of healthcare. Nutraceuticals are dietary supplements that have shown to provide biological advantages or to offer some defence against long-term illnesses. Nutraceutical have become a billion-dollar industry in US, Europe and Japan with multiple factors contributing to the growth of nutraceutical industry in India. The Indian nutraceutical industry has been growing at 25% annually during the pandemic.

Keywords: Nutraceutical, Nutraceutical Industry, Healthy diet, functional foods, supplements.

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Introduction

Nutraceuticals are substances that have the potential to be classified as foodstuff or a food ingredient that, beyond its typical nutritious worth, offer health advantages such as disease prevention. Nutraceuticals are unique foods that have elements or compounds added for physiological or therapeutic effects in addition to their usual nutritional value. Natural products, dietary supplements, specific diets, and refined foods like grains or soups, and drinks are all referred to as "nutraceuticals". These goods serve as medicines in addition to being dietary supplements.[1,2]

Nutraceuticals can be seen as a very valuable instrument for preserving wellness because they fight a variety of diseases and improve quality of life in the process. Rapid expansion, advancements in research, quality control, and regulation will all be essential to improving currently available goods. The most popular types of nutraceuticals and functional meals are offered as conventional folk remedies. The widespread use of nutraceuticals and supplements as food additives may be deceiving consumers about their eating patterns, leading to an imbalance in the intake of macro- and micronutrients. It's crucial to remember,

nevertheless, that the laws pertaining to nutraceuticals are currently unclear yet loose. [3, 4, 1]

Two words make up the term nutraceuticals 1989 saw the founding and chairman of the Foundation of Innovation Medicine, Stephen L. Defelice, invented the phrase "nutrient and pharmaceutical." "Nutrient" is a nourishing component which profoundly impact on person wellbeing that basically found in foods and pharmaceutical is a medicinal drug. Nutraceuticals are mainly categorized into dietary products, functional foods and supplements that provides the body with clinical or medical advantages such as illness prevention and treatment. So exactly Nutraceuticals are supplements obtained from food source which offers extra health advantages beyond general fundamental nutrition.[6,1,7] Products containing nutraceuticals may include a combination of different substances or one or more nutrients. Herbal products could be added as well. Nutraceuticals can prolong life, delay aging, prevent chronic illnesses, improve overall health, and support the functions and structure of the body. They may lessen the risk of acquiring chronic

illnesses, control symptoms, and enhance general wellbeing. Nutraceuticals are typically not protected by patents, in contrast to medications. Despite the fact that both medicinal and nutritional substances have the potential to cure or stop illness.[5,8,1]

Anything that includes any of the following dietary ingredients—minerals, vitamins, amino acids, botanicals or medicinal herbs, dietary substances to supplement daily intake, or a combination of these components—such as concentrates, metabolites, constituents, extracts, or their combinations—is considered a dietary supplement.⁴ A subset of these dietary supplements called nutraceuticals is utilized for health reasons other than basic nutrition. In the current review, new concepts regarding nutraceuticals are presented, with a focus on how these items can alter specific diseases. A lot of work has gone into this presentation. Highlighting herbal nutraceuticals that help with disorders include obesity, allergies, diabetes, cancer, heart disease, inflammation, and Parkinson's disease that are linked to oxidative stress has been the main focus.[9,10]

Recent Trends and Developments in Nutraceutical

Nutraceuticals are a novel idea and a catch-all word for nutrient-dense supplements that have health advantages above and above their basic nutritional content. A number of bioactive ingredients, such as food extracts or extracts enhanced with phytochemicals, have been created and sold as pharmaceutical formulations in the last several decades in the form of capsules, solutions, powders, gels, etc.

Epidemiological research indicates a somewhat positive correlation between the phytochemical components of nutraceuticals and improved health. Similarly, natural chemicals originating from plants and other sources have shown promise in producing a pool of molecules that could have therapeutic qualities. This pool of molecules is expected to continue producing new medications for some time to come.[11]

The nutraceutical business has had an unanticipated global upsurge and is presently valued at billions of dollars. Before the 2019 coronavirus illnesses pandemic (COVID-19), the worldwide nutraceutical business was estimated to be worth approximately USD 385 billion (EUR 315 billion) in 2017 and was projected to reach approximately USD 563 billion by 2022 (EUR 458 billion).

It is expected that the nutraceutical business will continue to develop, providing new chances for creative items predicated on customer desire for foods that enhance wellbeing, as health awareness

and lifestyle modifications spread throughout the world.[12]

Demand for nutraceuticals worldwide: The nutraceutical market is divided into three primary segments: functional foods, dietary supplements, and herbal/natural goods. Dietary supplements (21.6% annually growth) and natural/herbal goods (13.5% annual growth) were the two fastest-growing industry segments.[13]

The nutraceutical business has seen the emergence of major food and pharmaceutical companies, the market is becoming more competitive. Furthermore, a number of food companies launched their nutraceutical divisions in an effort to diversify their product offerings.[11,12]

Nutraceuticals have a bright and promising future as they continue to bridge the gap between nutrition and pharmaceuticals to revolutionize the healthcare industry.

Nutraceuticals have a great deal to offer in terms of managing health conditions and promoting wellbeing because of their personalized interventions, technological advancements, integration with conventional medicine, and benefits for preventive health. To guarantee consumer awareness, safety, and efficacy, however, cooperation between industry stakeholders, healthcare providers, and regulatory bodies is necessary for them to reach their full potential. Nutraceuticals will surely play a crucial role in our quest for optimum health and wellness as we adopt a holistic approach to treatment.[14,11]

Here are some trends that were notable in the nutraceutical industry:

1. Personalized Nutrition

"The tailoring of medical treatment to the individual characteristics of each patient." is the definition of the personalized nutrition given by the President Council of Advisors on Science and Technology. This refers to the capacity to divide people into subpopulations that vary in how they react to a given treatment or in how susceptible they are to a certain disease, not the actual process of creating medications or customized medical equipment for a patient.[15]

This allows us to focus therapeutic or preventive actions on individuals who will benefit, sparing others who won't, in terms of cost and adverse effects. Nutraceutical product customization to meet the demands of each person based on lifestyle, genetics, and medical conditions has become more popular. Businesses are using AI algorithms and technology like DNA testing to develop customized supplement regimens. [16, 17, 15]

2. Plant-Based Nutraceuticals

Plant polyphenols have garnered significant attention as one of the most prevalent and plentiful chemical substances. Additionally, scientific interest in plant-derived functional meals has been continuously increasing due to their numerous favorable benefits on human health. Fruits, vegetables, cereals, tea, coffee, and other plants all naturally contain plant polyphenols. These compounds have a wide range of complicated structures, but can be broadly categorized as flavonoids, anthocyanins, phenolic acids, and tannins. They often contain phenolic rings as the monomer. [18, 19]

Herbal nutraceuticals help to prevent and treat acute and chronic diseases that are brought on by poor nutrition, which in turn helps to maximize life expectancy and standard of living. The evolution in nutraceuticals will usher in a novel era in medical and wellness, where research within the food sector will be directed toward the pharmaceutical industry. The goal of this review is to better understand nutraceuticals derived from various medicinal plants and their specific indications for treating various diseases. [18, 19, 20]

3. Digital Health and Nutraceutical Apps

It is anticipated that digital apps will offer a fresh perspective on users' health and wellness. The goal of apps is to empower users and sponsors to take proactive measures for both public and individual well-being. Software urge users are granted access to commonly recognize medical and wellness of people information in order to gain a better understanding of their conditions. [21, 22]

They might have more fruitful conversations with healthcare professionals as a result. More organized information collection on the state of health and wellbeing is facilitated by well beings and medical apps. Technology is contributing to the nutraceutical industry by creating digital platforms and apps. With the aid of these tools, users can monitor their diet, establish health objectives, and get tailored suggestions for nutraceutical supplements. [23, 24, 21]

Innovations in Formulations

Numerous techniques have been utilized to group nutraceuticals according to discrete criteria. Initially, the classifications for nutraceuticals were established based on how unique they were: traditional and non-traditional. Second, there are four kinds of nutraceuticals that can be distinguished by their chemical composition: nutrients, herbals, medical food, functional food, and dietary supplements.

Thirdly, potential and established categories for nutraceuticals were determined based on their

proven safety and effectiveness. Fourth, the structures of the Nutraceuticals have been categorized according to the study of herbal remedies and compounds. Last but not least, there are other categories that depend on extra elements like bioavailability, uses, and more. [26, 27]

Oversupply of food items Pharmacokinetics, pharmacodynamics, immunogenicity, biorecognition, nonspecific toxicity, and efficacy are all improved by NDDS. There are several routes to deliver NDDS, such as transdermal, transmucosal, sublingual, oral, and more. Nutraceutical formulations have made extensive use of a variety of novel delivery systems, such as conjugation systems, chitosan-based delivery systems, micelle-based delivery systems, nanoencapsulation, nanofibers, liposomes, phytosomes, nanoparticles, emulsions, nano emulsion, microspheres, dendrimers, and others. [29, 28, 32]

Also, consumers are expecting more from formulations that contain nutraceuticals. In order for the dietary supplement and health product industries to stay competitive and relevant, this is causing change and presenting new challenges. As food has been used as medicine for millennia, even though the term "nutraceutical" is relatively new, the category represents one of the longest-lasting therapeutic trends in the history of healthcare. [29, 30]

More people than ever are aware that eating a healthy diet can lead to overall wellbeing and improved health. More convenient ways to supplement diets and greater health value are what consumers are demanding from product options. Additionally, a wide range of conditions are being managed or treated by people using nutraceuticals. The COVID-19 pandemic, according to industry analysts, increased consumer demand for goods that promote improved physical and mental health. [31, 66, 29]

Nutraceutical in disease prevention and control

When it comes to lowering the chance of contracting certain diseases and its after effects, nutraceuticals are essential. It prolongs life, delays the onset of non-communicable diseases, improves physiological processes, and slows down aging. [34]

Nutraceuticals hold great potential for improving human health and preventing illness. All age groups accept them widely because of their superior quality, safety, efficacy, and ability to promote and cure disease. The most recent movement in medicine and health is toward nutraceuticals, which has ushered in a new era. In India, it is still in its early stages. However, we have to say that "food is your medicine" and

"taking the right nutraceuticals every day can keep

the medicine away" in this hype-era.[35,36]

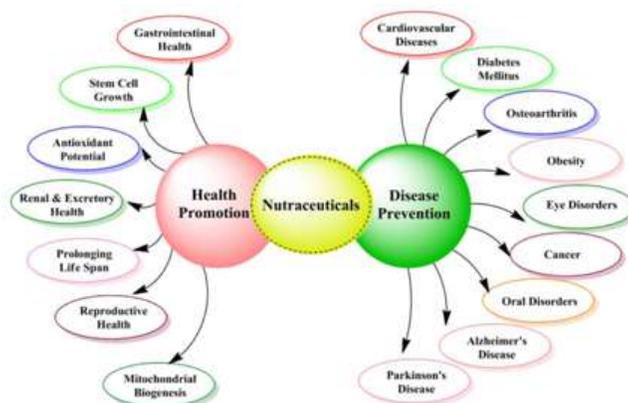


Figure 1: Nutraceutical in disease prevention and control [37]

Using scholarly search engines like Medline, PubMed, and Google Scholar, we looked up recently published articles examining many different aspects of Nutraceuticals as a substitute to prescription drugs. Among The terminology employed were allergy, Parkinson's illness, cancer, diabetics, heart disease, immune system, andInflammatory reactions.[37]

1. Allergy and Nutraceuticals

An allergy is an allergic reaction having an immune system that is hypersensitive. An allergic response is typically the result of the immune system of a person respond to a normally harmless substance. One type of antibody called immunoglobulin E causes mast cells and basophils, two types of white blood cells that cause allergies, to become hyperactive.. An inflammatory reaction that can be uncomfortable or even dangerous is the result of this reaction.[40]

Low-density lipoprotein (LDL-C) is shielded from damage by a substance known as especially by blood vessels. Heart disease is mostly caused by LDL-C, and quercetin scavenges free radicals and functions as an antioxidant. People with diabetes have an increased risk of oxidative stress-related blood vessel damage. This substance is therefore beneficial for these patients additionally.[41,42]

2. Alzheimer's Disease and Nutraceuticals

Memory loss with Alzheimer's disease is the least prevalent reason. The illness ultimately results in death, and there is currently no recognized treatment.

Early-onset Alzheimer's is less common and can manifest much sooner than Alzheimer's disease (AD), which is often diagnosed in persons over 65. In 2006, 26.6 million people suffered as a result worldwide, and by 2050, 1 in 85 people are expected to be impacted.[43]

There is a nearly 2:1 ratio of women to men who are affected. Numerous lines of evidence point to a potential connection between oxidative stress and AD, among other neurodegenerative illnesses. Antioxidant nutrients like β -carotene, turmerin, lutein, lycopene, and curcumin can prevent oxidative harm and therefore have beneficial effects on certain diseases. Nutraceuticals are becoming more and more popular due to the belief that they can delay the onset of cognitive declines like Alzheimer's. Numerous recently published studies demonstrate the beneficial effects of various nutraceutical plants on AD, learning, or memory, including *Zizyphus jujube* and *Lavandula officinalis* [44,45]

3. Diabetes and Nutraceuticals

Significant changes have been made to the way of life, including a moderate 7% weight loss and regular 2.5 hours of physical activity per week. Thus, a diet's daily calorie intake should consist of less than 10% saturated fats, less than 30% total fat, 15%–20% protein, 50 g of moderate sugar, and 45%–60% carbohydrates.[11]

A metabolic condition called diabetes is brought on by insufficient insulin production, which prevents the body from using carbohydrates. The pancreatic islets of Langerhans' beta cells naturally produce the hormone insulin. Diabetes can be classified into two types: type I and type II. By 2035, 592 million people worldwide are predicted to have type II diabetes. The management and prevention of diabetes are significantly aided by nutraceuticals and dietary supplements. Garlic, ginseng, fenugreek, onion, *Gymnema sylvestre*, *Pleurotus ostreatus* (mushroom), omega-3 fatty acids, cinnamon, L-carnitine, berberine, and α -lipoic acid are a few supplements that have shown promise against diabetes.[47,49]

4. Renal Disorders

The kidneys control every person's health and homeostasis. Conditions related to infection or inflammation, nephrotoxicity, ischemia or hypoxia, cancer, or abnormalities in metabolism can all interfere with the kidneys' ability to function normally. Research on the application of food substances to regulate renal health is continuous, both in vitro and in vivo, because of the adverse consequences and hefty cost of pharmaceutical therapies for renal disorders. Astragalus Membranaceus or Astragalus Mongholicus (Astragalosides), Blue-green algae (Spirulina spp.), Licorice (Glycyrrhiza glabra), Milk Thistle (Silybum marianum), Neem (Azadirachta indica), and Rhubarb (Rheum spp.) are a few natural products that are effective for renal disorders.[11,47]

5. Hepatic Disorders

The liver's distinct physiology, anatomy, and metabolism make it vulnerable to a wide range of toxic, infectious, immune-mediated, metabolic, and carcinogenic causes.

Through antineoplastic, anti-inflammatory, antioxidant, or proliferative processes, a variety of nutraceuticals have been proposed to support the liver's healthy operation (Gwaltney-Brant, 2016). Numerous nutraceuticals have been studied for their possible liver advantages; however, further investigation is necessary to ascertain the therapeutic usefulness of these natural products. [46, 47, 11]

Bioactive compounds in nutraceuticals

Natural systems are abundant in bioactive substances especially in plants, which can produce phenolics, flavonoids, caffeine, carotenoids, and a host of other compounds. Because of their various biological activities, different Bioactive substances has the capacity to alter or change the course of life.[38]

1. Polyphenol

In recent decades, the organic compounds known as polyphenols, which are abundant in plants, have gained attention in the field of nutrition. Consuming polyphenols may be essential for maintaining good health since they regulate metabolism, weight, chronic illness, and cell division, according to an increasing amount of research.

Currently, over 8,000 polyphenols have been identified; however, their effects on health, both short- and long-term, remain incompletely understood. Numerous polyphenols have demonstrated their anti-inflammatory and antioxidant properties in human, animal, and epidemiological investigations. These attributes could be beneficial in treating or preventing

diseases like cancer, obesity, neurological illnesses, and cardiovascular disease.[52,53,54]

Resveratrol, phenolic acids, and flavonoids are just a few of the many substances that make up polyphenols, which are present in plants. They show antioxidant qualities and been connected to a number of well-being advantages, such as counter-inflammatory and cardiovascular benefits. Berries, tea, red wine, and dark chocolate are foods high in polyphenols.[50,51]

2. Carotenoids

The following natural carotenoids (CARs) are being investigated as possible candidates in the food, feed, nutraceuticals, and cosmeceutical industries: A number of substances have been identified, including zeaxanthin, lutein, astaxanthin, bixin, norbixin, capsanthin, lycopene, and β -apo-8-carotenol-ester. Carotenoids are well recognized for their contribution to immunological and ocular health. Carrots, sweet potatoes, spinach, and tomatoes are examples of sources. Three main areas of CAR research are being explored further: [55, 56, 57]

- Natural source CAR production and downstream processing optimization;
- Summarization for improved both chemical and physical characteristics.
- Studies on the preclinical, clinical, and epidemiological effects of CARs on wellness.[56]

3. Omega-3 Fatty Acids

Polyunsaturated fats omega-3, or PUFAs, important for human nutrition and well-being. Only minute amounts of Omega-3 PUFA are produced by the body. Marine sources are often the source of omega-3 PUFA. The world's growing population has led to increased consumer awareness of proper nutrition, yet traditional sources are exhausted and cannot meet the need for Omega-3 PUFA in aquaculture and the human diet. Polyunsaturated fats with omega-3 content take part in the metabolic process that start the inflammatory resolution phase. [58]

Supplemental treatment for COVID-19-associated heart problems may use omega-3 polyunsaturated fats (PUFAs), which are recommended in therapeutic regimens aimed at averting the "cytokine storm." They are often included in nutritional formulas supporting heart and brain function. [59, 60]

4. Probiotics and Prebiotics

It is beneficial for human nutrition and health to take prebiotics and probiotics. Prebiotics are substances that probiotics can use and ferment, enabling them to support intestinal probiotic

metabolism and reproduction for overall health. Numerous illnesses, such as inflammatory bowel disease, allergic responses, and irritable bowel syndrome, intestinal, respiratory, and urogenital infections, have been demonstrated to benefit from probiotic usage as a therapeutic intervention or prevention of these ailments. Live bacteria known as probiotics can improve health when consumed in large enough doses. Because of their beneficial effects on gut health, they are frequently added to nutraceuticals. Conversely, prebiotics are indigestible fibres that support the development of good gut flora. [61, 62]

5. Glucosinolates

Plant nitrogen-containing natural products include the class of thioglucosides known as Glucosinolates, which can be present in veggies that are cruciferous like cabbage, lettuce, leek, and okra, had research for possible anti-cancer effects. Chop or chew these vegetables to release the glucosinolates, which then break down into bioactive compounds like sulforaphane. glycosinolates. Thus far, there is very little evidence linking intact glucosinolates to biological activity. The biological activity of the products of glucosinolate hydrolysis has long been of interest, drawing attention to the process. The range of activities exhibited by the breakdown products of common glucosinolates has been extensively studied, encompassing allelopathic, antiparasitic, antimicrobial, and antineoplastic impact. [63]

6. Phytosterols

For the past 50 years, phytosterols have been used as drugs to lower blood cholesterol. They have proven to be secure and efficient. Phytosterols were first introduced as a pharmaceutical formulation, but they are now included in a wider range of foods. Although concerns have occasionally been raised about their safety, no negative effects have been noticed as of yet, even at the current usage level. They are frequently included in functional meals and supplements meant to control cholesterol levels. [64]

7. Curcumin

The worlds of science and medicine as well as cooking have both shown a great deal of interest in turmeric. Turmeric is a spice that has anti-inflammatory and antioxidant qualities. Its active ingredient is curcumin. Nutraceutical formulations for joint health, cognitive function, and general well-being frequently contain it. Anxiety, rheumatoid arthritis, metabolic syndrome, oxidative and inflammatory illnesses, and hyperlipidemia can all be treated with it.

Additionally, it might help manage muscle soreness and inflammation brought on by exercise,

enhancing recovery and performance in those who participate in physical activity. [65]

Clinical Studies and Evidence

Clinical Studies in Nutraceuticals and Dietary Supplements provides in-depth details on every important topic as well as research that is supported by evidence regarding nutraceuticals and dietary supplements. The most interesting aspect of this article is how it examines a crucial idea while highlighting current findings and advancements in the realm of nutritional supplements and nutraceuticals to cure a range of illnesses, including neurological dysfunction, cancer, heart disease, renal and hepatic issues, and issues affecting the mother and foetus. [67, 68]

Maternal and Fetal Health

Pregnancy progression, embryogenesis, fetal growth and survival, and the perinatal phase are all aided by the mother's health and placental development. Pregnancy-related complications can be minimized for mother and child by providing the right nutrition for the mother before, during, and after. Maternal complications like iron deficiency anemia, restricted intrauterine growth, short for gestational age (SGA) newborns (IUGR), preeclampsia, and preterm labor (PTL) can result from any micronutrient deficiency (WHO, 2016). Dietary supplements and nutraceuticals are therefore advantageous for the health of both the mother and the fetus. [68]

Even though there aren't many clinical studies on nutraceuticals that improve mother and child health, those that are carried out always produce promoting and successful results that support the idea of using nutraceuticals safely.

Bacopa monnieri has long been used as a stimulant and healer; porridge containing Terminalia chebula, Cuminum cyminum, Cedrus deodara, and Sida retusa was used as a pain reliever; and garlic was used for postpartum care. [68, 69]

Cardiovascular Diseases

The onset of cardiovascular diseases is attributed to atherosclerosis, arterial vessel hardening, and endothelial lining inflammation. It has been demonstrated through clinical and preclinical research that dietary supplements and nutraceuticals control the expression of genes and proteins, which alters endogenous metabolic pathways and homeostasis and lowers the risk of cardiovascular illnesses.

Nutraceuticals are effective in treating cardiovascular diseases while having the fewest negative effects, according to numerous successful clinical trials. Elevated blood pressure levels suggest a higher risk of cardiovascular disease. The

majority of antihypertensive patients who take medication for the same experience certain side effects, which decrease patient adherence. Because they don't have any negative side effects, preference is given to natural substances with therapeutic potential.[70]

Treatments for vascular disorders and antihypertensive medications, such as Oleuropeina (*Olea Europaea*), are possible thanks to polyphenolic compounds. For eight weeks, a group of fifty participants were given a combination of nutraceuticals, which included extract from rice with red yeast, coenzyme Q10, berberine, folic acid, policosanol, folic acid, and astaxanthin. This study proved that the combination of nutraceuticals was able to lower low-density lipoprotein (LDL) cholesterol by 21.1% and total cholesterol by 12.8%.

Cancer

Chinese and Indian medicines have been used for their anticancer properties since ancient times. These medicines are derived from plants and animals. Many studies demonstrate that dietary supplements and nutraceuticals have little to no negative effects while being effective against cancer. The characteristics of an antioxidant of nutraceuticals, like vitamins, carotenoids, polyphenolic compounds, and glucosinolates, have been the subject of much research because they may help prevent cancer.

Genistein, apigenin, epigallocatechin gallate (EGCG), luteolin, curcumin, quercetin, tannic acid, and chrysin are plant-derived polyphenols that have been shown to exhibit inhibiting effect of proteasomes. These polyphenols have the power to overcome chemoresistance to a wide range of chemotherapeutic drugs not only does it work well against a wide range of tumours. [71, 68]

Bone Health

For the purpose of preventing bone loss, the FDA suggests specific nutraceuticals and dietary supplements that have anti-inflammatory properties, minimal side effects, and are reasonably priced. They include gambogic acid, plubagin, butein, cardamonin, embelin, diosgenin, genistein, resveratrol, curcumin, and cercetin. These all-natural supplements slow down or reverse osteoporosis and also modify cell signalling pathways.

A study of seventy-two people, double-blind and placebo-controlled, demonstrated the efficacy of combining acetyl-11-keto-beta-boswellic acid and high molecular weight hyaluronic acid in a nutraceutical for the treatment of osteoarthritis in the knee. [72]

Neurological Disorders

Nutraceuticals are becoming more and more well-known as health-promoting substances with minimal negative effects. It is presently helpful in treating and preventing brain conditions like Alzheimer's and Parkinson's, and Huntington's disease. Numerous neurological illnesses may benefit from the use of nutraceuticals such as ω -3 FA (DHA/EPA/ALA), resveratrol, curcumin, coenzyme Q10 (CoQ10), and epigallocatechin-3-gallate.

An open-label preclinical study using a mouse model of age-related degeneration of neurons found that nutraceuticals improved mood (neuropsychiatric inventory and AD CS-Activities of daily living) and cognitive performance (dementia rating, clock drawing) with no negative side effects.

Another multisite clinical trial with ninety participants showed that, within three months of comparing the nutraceutical formulation to a placebo, dementia patients (aged 45–73) showed statistically improved executive function, which increased further over the next six months.[73,68]

Conclusion

Supplemental foods and nutraceuticals are powerful health-promoting agents that work to enhance well-being. If they come from natural sources, dietary supplements are included in the category of nutraceuticals. There is a need to conduct a large number of evidence-based studies to demonstrate the long-term safety and quality of these beneficial effects, as there are very few clinical studies on them. Larger-scale, longer-term studies that demonstrate efficacy against a range of diseases must be incorporated into clinical research in order to determine which nutraceuticals are the most economical and risk-reducing.

References

1. Puri, V., Nagpal, M., Singh, I., Singh, M., Dhingra, G.A., Huanbutta, K., Dheer, D., Sharma, S.A. and Sangnim, T., 2022. A comprehensive review on nutraceuticals: therapy support and formulation challenges. *Nutrients*, 14(21), p.4637.
2. Santini, A. and Novellino, E., 2018. Nutraceuticals-shedding light on the grey area between pharmaceuticals and food. *Expert Review of Clinical Pharmacology*, 11(6), pp.545-547.
3. Bagchi, D. and Nair, S. eds., 2016. Developing new functional food and nutraceutical products. Academic Press.
4. Fernandes, S.D., Narayana, R.C. and Narayanan, A.V., 2019. The emergence of India as a blossoming market for nutraceutical supplements: An overview. *Trends in food science & technology*, 86, pp.579-585.

5. Sosnowska, B., Penson, P. and Banach, M., 2017. The role of nutraceuticals in the prevention of cardiovascular disease. *Cardiovascular diagnosis and therapy*, 7(Suppl 1), p.S21.
6. Mazza, A., Nicoletti, M., Lenti, S., Torin, G., Rigatelli, G., Pellizzato, M. and Fratter, A., 2021. Effectiveness and safety of novel nutraceutical formulation added to ezetimibe in statin-intolerant hypercholesterolemic subjects with moderate-to-high cardiovascular risk. *Journal of medicinal food*, 24(1), pp.59-66.
7. Singh, J. and Sinha, S., 2012. Classification, regulatory acts and applications of nutraceuticals for health. *International Journal of Pharma and Bio Sciences*, 2(1), pp.177-187.
8. Smarta, R.B., 2017. Paradigm shift from pharmaceuticals to nutraceuticals. *Nuffoods Spectrum*.
9. Coopers, P.W., 2013. Food as pharma: As wellness products evolve, the distinction between food and medicine blurs. *R & C Worlds Express*.
10. Srivastava, S., Sharma, P.K. and Kumara, S., 2015. Nutraceuticals: A review. *J. Chronother. Drug Deliv*, 6, pp.1-10.
11. Nasri, H., Baradaran, A., Shirzad, H. and Rafieian-Kopaei, M., 2014. New concepts in nutraceuticals as alternative for pharmaceuticals. *International journal of preventive medicine*, 5(12), p.1487.
12. Hardy, G., 2000. Nutraceuticals and functional foods: introduction and meaning. *Nutrition*, 16(7-8), pp.688-689.
13. Zhao, J., 2007. Nutraceuticals, nutritional therapy, phytonutrients, and phytotherapy for improvement of human health: a perspective on plant biotechnology application. *Recent patents on biotechnology*, 1(1), pp.75-97.
14. Chopra, A.S., Lordan, R., Horbańczuk, O.K., Atanasov, A.G., Chopra, I., Horbańczuk, J.O., Józwick, A., Huang, L., Pirgozliev, V., Banach, M. and Battino, M., 2022. The current use and evolving landscape of nutraceuticals. *Pharmacological research*, 175, p.106001.
15. Abrahams, E. and Silver, M., 2009. The case for personalized medicine. *Journal of diabetes science and technology*, 3(4), pp.680-684.
16. US Food and Drug Administration, 2009. Table of valid biomarkers in the context of approved drug labels.
17. Wells, R.C., 2009. A new President, a new Congress and the path to personalized medicine. *Personalized Medicine*, 6(3), pp.235-239.
18. Zhang, Z., Li, X., Sang, S., McClements, D.J., Chen, L., Long, J., Jiao, A., Jin, Z. and Qiu, C., 2022. Polyphenols as plant-based nutraceuticals: health effects, encapsulation, nano-delivery, and application. *Foods*, 11(15), p.2189.
19. Brower, V., 1998. Nutraceuticals: poised for a healthy slice of the healthcare market?. *Nature biotechnology*, 16(8), pp.728-731.
20. Asif, M. and Mohd, I., 2019. Prospects of medicinal plants derived nutraceuticals: A re-emerging new era of medicine and health aid. *Progress in Chemical and Biochemical Research*, 2(4), pp.150-169.
21. Powell, A. and Torous, J., 2020. A patient-centered framework for measuring the economic value of the clinical benefits of digital health apps: theoretical modeling. *JMIR Mental Health*, 7(10), p.e18812.
22. Henson, P., Wisniewski, H., Hollis, C., Keshavan, M. and Torous, J., 2019. Digital mental health apps and the therapeutic alliance: initial review. *BJPsych open*, 5(1), p.e15.
23. Oldenburg, B., Taylor, C.B., O'Neil, A., Cocker, F. and Cameron, L.D., 2015. Using new technologies to improve the prevention and management of chronic conditions in populations. *Annual review of public health*, 36, pp.483-505.
24. Siemensma, G., Anderson, A. and Gorton, C., 2023. Government-supported clinical knowledge and information resource portals are key to ensuring quality, safe health care and evidence-based practice—the Australian context. *Australian Health Review*, 47(5), pp.596-601.
25. Helal, N.A., Eassa, H.A., Amer, A.M., Eltokhy, M.A., Edafiogho, I. and Nounou, M.I., 2019. Nutraceuticals' novel formulations: the good, the bad, the unknown and patents involved. *Recent patents on drug delivery & formulation*, 13(2), pp.105-156.
26. Ruchi, S., 2017. Role of nutraceuticals in health care: A review. *International Journal of Green Pharmacy (IJGP)*, 11(03).
27. Petrovska, B.B., 2012. Historical review of medicinal plants' usage. *Pharmacognosy reviews*, 6(11), p.1.
28. Chopra, A.S., Lordan, R., Horbańczuk, O.K., Atanasov, A.G., Chopra, I., Horbańczuk, J.O., Józwick, A., Huang, L., Pirgozliev, V., Banach, M. and Battino, M., 2022. The current use and evolving landscape of nutraceuticals. *Pharmacological research*, 175, p.106001.
29. Xiang, Y.Z., Shang, H.C., Gao, X.M. and Zhang, B.L., 2008. A comparison of the ancient use of ginseng in traditional Chinese medicine with modern pharmacological experiments and clinical trials. *Phytotherapy Research*, 22(7), pp.851-858.
30. Nasri, H., Baradaran, A., Shirzad, H. and Rafieian-Kopaei, M., 2014. New concepts in

- nutraceuticals as alternative for pharmaceuticals. International journal of preventive medicine, 5(12), p.1487.
31. Shinde, N., Bangar, B., Deshmukh, S. and Kumbhar, P., 2014. Nutraceuticals: A Review on current status. Research journal of pharmacy and technology, 7(1), pp.110-113.
 32. Kalra, E.K., 2003. Nutraceutical-definition and introduction. Aaps Pharmsci, 5(3), p.25.
 33. Dutta, S., Ali, K.M., Dash, S.K. and Giri, B., 2018. Role of nutraceuticals on health promotion and disease prevention: A review. Journal of Drug Delivery and Therapeutics, 8(4), pp.42-47.
 34. Keservani, R.K., Kesharwani, R.K., Vyas, N., Jain, S., Raghuvanshi, R. and Sharma, A.K., 2010. Nutraceutical and functional food as future food: A review. Der Pharmacia Lettre, 2(1), pp.106-116.
 35. Rajasekaran, A., Sivagnanam, G. and Xavier, R., 2008. Nutraceuticals as therapeutic agents: A Review. Research Journal of Pharmacy and Technology, 1(4), pp.328-340.
 36. Das, L., Bhaumik, E., Raychaudhuri, U. and Chakraborty, R., 2012. Role of nutraceuticals in human health. Journal of food science and technology, 49, pp.173-183.
 37. <https://encyclopedia.pub/entry/38118> source on 11nov2023.
 38. Sharma, K., Mishra, K., Senapati, K.K. and Danciu, C. eds., 2021. Bioactive Compounds in Nutraceutical and Functional Food for Good Human Health. BoD—Books on Demand.
 39. Siró, I., Kápolna, E., Kápolna, B. and Lugasi, A., 2008. Functional food. Product development, marketing and consumer acceptance—A review. Appetite, 51(3), pp.456-467.
 40. Kalra, E.K., 2003. Nutraceutical-definition and introduction. Aaps Pharmsci, 5(3), p.25.
 41. Zhao, J., 2007. Nutraceuticals, nutritional therapy, phytonutrients, and phytotherapy for improvement of a human health: a perspective on plant biotechnology application. Recent patents on biotechnology, 1(1), pp.75-97.
 42. Chauhan, B., Kumar, G., Kalam, N. and Ansari, S.H., 2013. Current concepts and prospects of herbal nutraceutical: A review. Journal of advanced pharmaceutical technology & research, 4(1), pp.4-8.
 43. Corbo, M.R., Bevilacqua, A., Petrucci, L., Casanova, F.P. and Sinigaglia, M., 2014. Functional beverages: the emerging side of functional foods: commercial trends, research, and health implications. Comprehensive reviews in food science and food safety, 13(6), pp.1192-1206.
 44. Zeisel, S.H., 1999. Regulation of "nutraceuticals". Science, 285(5435), pp.1853-1855.
 45. Hardy, G., 2000. Nutraceuticals and functional foods: introduction and meaning. Nutrition, 16(7-8), pp.688-689.
 46. Khosravi-Boroujeni, H., Mohammadifard, N., Sarrafzadegan, N., Sajjadi, F., Maghroun, M., Khosravi, A., Alikhasi, H., Rafieian, M. and Azadbakht, L., 2012. Potato consumption and cardiovascular disease risk factors among Iranian population. International journal of food sciences and nutrition, 63(8), pp.913-920.
 47. Khosravi-Boroujeni, H., Sarrafzadegan, N., Mohammadifard, N., Sajjadi, F., Maghroun, M., Asgari, S., Rafieian-Kopaei, M. and Azadbakht, L., 2013. White rice consumption and CVD risk factors among Iranian population. Journal of health, population, and nutrition, 31(2), p.252.
 48. Shirzad, H., Burton, R.C., Smart, Y.C., Rafieian-kopaei, M. and Shirzad, M., 2011. Natural Cytotoxicity of NC-2+ Cells Against the Growth and Metastasis of WEHI-164 Fibrosarcoma. Scandinavian journal of immunology, 73(2), pp.85-90.
 49. Roohafza, H., Sarrafzadegan, N., Sadeghi, M., Rafieian-Kopaei, M., Sajjadi, F. and Khosravi-Boroujeni, H., 2013. The association between stress levels and food consumption among Iranian population. Archives of Iranian medicine, 16(3), pp.0-0.
 50. Cory, H., Passarelli, S., Szeto, J., Tamez, M. and Mattei, J., 2018. The role of polyphenols in human health and food systems: A mini-review. Frontiers in nutrition, 5, p.370438.
 51. Lecour, S. and T Lamont, K., 2011. Natural polyphenols and cardioprotection. Mini reviews in medicinal chemistry, 11(14), pp.1191-1199.
 52. Pérez-Jiménez, J., Neveu, V., Vos, F. and Scalbert, A., 2010. Identification of the 100 richest dietary sources of polyphenols: an application of the Phenol-Explorer database. European journal of clinical nutrition, 64(3), pp.S112-S120.
 53. Crowe, K.M. and Francis, C., 2013. Position of the academy of nutrition and dietetics: functional foods. Journal of the Academy of Nutrition and Dietetics, 113(8), pp.1096-1103.
 54. Singh, A., Holvoet, S. and Mercenier, A., 2011. Dietary polyphenols in the prevention and treatment of allergic diseases. Clinical & experimental allergy, 41(10), pp.1346-1359.
 55. Carotenoids: Dietary Sources, Extraction, Encapsulation, Bioavailability, and Health Benefits—A Review of Recent Advancements.
 56. Wang, P.Y., Fang, J.C., Gao, Z.H., Zhang, C. and Xie, S.Y., 2016. Higher intake of fruits, vegetables or their fiber reduces the risk of type 2 diabetes: A meta-analysis. Journal of diabetes investigation, 7(1), pp.56-69.

57. Aune, D., Giovannucci, E., Boffetta, P., Fadnes, L.T., Keum, N., Norat, T., Greenwood, D.C., Riboli, E., Vatten, L.J. and Tonstad, S., 2017. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality—a systematic review and dose-response meta-analysis of prospective studies. *International journal of epidemiology*, 46(3), pp.1029-1056.
58. Jump, D.B., Depner, C.M. and Tripathy, S., 2012. Omega-3 fatty acid supplementation and cardiovascular disease: thematic review series: new lipid and lipoprotein targets for the treatment of cardiometabolic diseases. *Journal of lipid research*, 53(12), pp.2525-2545.
59. Darwesh, A.M., Sosnowski, D.K., Lee, T.Y., Keshavarz-Bahaghighat, H. and Seubert, J.M., 2019. Insights into the cardioprotective properties of n-3 PUFAs against ischemic heart disease via modulation of the innate immune system. *Chemico-biological interactions*, 308, pp.20-44.
60. Oliver, L., Dietrich, T., Marañón, I., Villarán, M.C. and Barrio, R.J., 2020. Producing omega-3 polyunsaturated fatty acids: A review of sustainable sources and future trends for the EPA and DHA market. *Resources*, 9(12), p.148.
61. You, S., Ma, Y., Yan, B., Pei, W., Wu, Q., Ding, C. and Huang, C., 2022. The promotion mechanism of prebiotics for probiotics: A review. *Frontiers in Nutrition*, 9, p.1000517.
62. Sender, R., Fuchs, S. and Milo, R., 2016. Are we really vastly outnumbered? Revisiting the ratio of bacterial to host cells in humans. *Cell*, 164(3), pp.337-340.
63. Abdel-Massih, R.M., Debs, E., Othman, L., Attieh, J. and Cabrerizo, F.M., 2023. Glucosinolates, a natural chemical arsenal: More to tell than the myrosinase story. *Frontiers in Microbiology*, 14, p.113020.
64. Kritchevsky, D. and Chen, S.C., 2005. Phytosterols—health benefits and potential concerns: a review. *Nutrition Research*, 25(5), pp.413-428.
65. Rani, L., Thapa, K., Kanojia, N., Sharma, N., Singh, S., Grewal, A.S., Srivastav, A.L. and Kaushal, J., 2021. An extensive review on the consequences of chemical pesticides on human health and environment. *Journal of cleaner production*, 283, p.124657.
66. Braithwaite, M.C., Tyagi, C., Tomar, L.K., Kumar, P., Choonara, Y.E. and Pillay, V., 2014. Nutraceutical-based therapeutics and formulation strategies augmenting their efficiency to complement modern medicine: An overview. *Journal of Functional Foods*, 6, pp.82-99.
67. Evans, M., Lewis, E.D., Antony, J.M., Crowley, D.C., Guthrie, N. and Blumberg, J.B., 2022. Breaking new frontiers: Assessment and re-evaluation of clinical trial design for nutraceuticals. *Frontiers in Nutrition*, 9, p.958753.
68. Gopi, S., Amalraj, A., Nair, A. and Chandradhara, D. eds., 2022. *Clinical Studies on Nutraceuticals and Dietary Supplements*. CRC Press.
69. Ronis, M.J., Pedersen, K.B. and Watt, J., 2018. Adverse effects of nutraceuticals and dietary supplements. *Annual review of pharmacology and toxicology*, 58, pp.583-601.
70. Mueller, C., 1999. The regulatory status of medical foods and dietary supplements in the United States.
71. Garcia-Cazarin, M.L., Wambogo, E.A., Regan, K.S. and Davis, C.D., 2014. Dietary supplement research portfolio at the NIH, 2009–2011. *The Journal of nutrition*, 144(4), pp.414-418.
72. AlAli, M., Alqubaisy, M., Aljaafari, M.N., AlAli, A.O., Baqais, L., Molouki, A., Abushelaibi, A., Lai, K.S. and Lim, S.H.E., 2021. Nutraceuticals: Transformation of conventional foods into health promoters/disease preventers and safety considerations. *Molecules*, 26(9), p.2540.
73. Budsberg, S.C., 2015. Evidence for use of nutraceuticals in osteoarthritis—Is “Joint juice” insane quackery or is the internet right. In *Pacific Veterinary Conference*, Long Beach July.