



Potential Benefits of Nutraceuticals for Oxidative Stress Management

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Abstract

Oxidative stress is an unbalanced redox state caused due to high concentration of reactive species and comparatively a very lower concentration of endogenous antioxidants in the body. When established, oxidative stress can disrupt cell structure and protein conformation and even damage genetic materials. Considering the degree of damage that oxidative stress can cause and the lack of promising treatment, preventing its onset is the best possible solution. Nutraceuticals, food or their extract that provides an added health benefit along with nutrition, can be used to prevent oxidative stress. An entire class of nutraceuticals are known for their inherent antioxidant properties, which can be included in our daily diet to prevent the occurrence of oxidative stress. Regulatory consumption of nutraceuticals can maintain a stable redox state, and thus prevents oxidative stress. In addition to managing oxidative stress, nutraceuticals can also help to control conditions like diabetes, neurodegeneration, cancer, organ inflammation, cardiovascular diseases, and other such conditions which are caused due to cellular oxidation. This review highlights the potential nutraceutical effect of several food and supplements which with further research along with genetic analysis can pave the road for nutrigenomics.

Keywords Antioxidants · Anti-inflammatory · Parkinson’s disease · Cancer · COVID-19 · Reactive oxygen species

Introduction

Rigvedic texts such as Ayurveda underline the importance of plants, herbs, spices, and foods in disease cure and prevention to maintain a healthy lifestyle (Patwardhan 2014). The words of Hippocrates “let food be thy medicine and medicine be thy food” indicates that the science of modern medicine also agrees with the concepts written in Ayurveda (Das et al. 2012). Both concepts help to promote the act of prevention from diseases through proper and scientific intake of food instead of looking for a cure. These ideas developed the process of nutritional therapy and the introduction of nutraceuticals which helped people with a path for disease prevention. As coined by Stephen de Felice, “nutraceuticals are food or food extracts that provide additional medical or health benefits including prevention or/and treatment of a disease” (Ansari et al. 2013). Nutraceuticals, an amalgamation of **nutrition** and **pharmaceuticals**, do not have patent protection unlike pharmaceutical compounds (Nasri et al. 2014). The key theory

of nutritional therapy is that apart from being served for energy and nutrients, food also provides health benefits (Ansari et al. 2013).

Nutraceuticals are a collective group of bioactive compounds, dietary fibers, probiotics, and prebiotics found in food. In this age where pathogens are developing resistance toward antimicrobials and the associated side effects of medicinal drugs, nutraceuticals are catching the eyes of public (AlAli et al. 2021). Nutraceuticals help in restabilizing a proper digestion, and absorption of minerals and vitamins to prevent their deficiency, detoxify cells, inhibit harmful biochemical reactions, facilitate the growth of beneficial microbiota, and excrete out waste (Ansari et al. 2013; Zhou et al. 2020). Nutraceuticals show antioxidant, anti-aging, and anti-cancerous properties, and enhance biochemical processes and structures (Nasri et al. 2014; Zhou et al. 2020). They also induce immunomodulatory, enhance immune response, augment phagocytosis, and prevent hypersensitivity, and reduce auto-immune response (Carr and Maggini 2017; AlAli et al. 2021). Nutraceuticals can help to prevent and cure diseases related to the heart, neurodegeneration, ailments caused due to oxidative stress, and contemporary lifestyle disorders like diabetes, hypertension, and cancer (Das et al. 2012; Sachdeva et al. 2020).

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Effects of nutraceuticals have undergone several studies which have conferred that the consumption of nutraceuticals is safe. The active ingredients which are the soul of nutraceutical efficacy may have a toxic profile but when administered in controlled dosage do not intoxicate an individual. This pool of beneficial bioactive compounds present in nutraceuticals provide a synergistic and elevated health impact (AlAli et al. 2021). What makes nutraceuticals popular is their effective widespread immune enhancement, ease of availability, affordability, and high tolerance in individuals (Kim and Kim 2010). Consumers' belief in nutraceuticals is increasing due to its high efficacy and thus they are being used as preventive self-medication for day-to-day diseases and for several chronic diseases like diabetes (AlAli et al. 2021).

This review deals with different types of nutraceuticals based on their origin, function, and structure, their demand, and regulation. Further it highlights different health issues caused due to oxidative stress in different parts of our body. Finally, it emphasizes on the potential source of nutraceuticals which can be used as method to prevent the onset of different diseased states caused due to oxidative stress.

Search Strategy

Search keywords associated with potential nutraceutical compounds for managing oxidative stress and related issues were used in the following order: nutraceuticals/types of nutraceuticals/nutraceuticals and oxidative stress/oxidative stress/nutraceuticals and cancer/nutraceuticals and neurodegeneration/nutraceuticals and cardiovascular diseases/nutraceuticals and liver/nutraceuticals and muscle fatigue/Ayurveda/Ayurvedic prebiotics/Nutraceuticals demands. The following list of biological databases were used to search the data for writing this article: PubMed, PubMed Central, Google Scholar, Springer, Science Direct, Wiley Online Library, LiebertPub, Nature. Time filter was used to retrieve articles from 2015–2021 in PubMed.

Traditional and Conventional Nutraceuticals

According to the origin and availability, all the naturally occurring sources build the class of traditional nutraceuticals. It comprises of all the fruits, herbs, vegetables, and other such foods which inherit additional health benefits along with the nutritional attribute in their naturally existing form. Depending on their structure and function, these can be grouped into different sub-classes as functional foods, carotenoids, dietary supplements, fatty acids, herbs, prebiotic, and probiotics, as summarized in Fig. 1 (AlAli et al. 2021).

Functional Food

These are the foods which are consumed as a routine or as a part of a local tradition of the people and are easily found in that locality (Lau et al. 2012). It includes cereal crops, pulses, lentils, fruits, dairy products, meat, nuts, and beans (Sikand et al. 2015). The presence of different active ingredients in functional foods improves the status of health and facilitates disease prevention by providing the necessary controlling inflammatory and inherent antioxidant properties (Alkhatib et al. 2017). The most common one is the widely consumed cereal crop rice. Nutritionally it contains carbohydrates, low amount of fat, and salt. Depending on the variety of rice, it may contain vitamins like niacin, vitamin D, thiamine, and riboflavin, and mineral like iron and calcium. Rice is also gluten free, and the presence of dietary fibers and resistant starch makes up the environment for a healthy gut microbiome growth (Bhat and Riar 2015). Tomato is another functional food which contains lycopene. It shows anticancerous activity for lung and prostate cancer and reduces blood pressure. Soyabean contains saponins which have antioxidant properties and enhances enzyme activity and immune response (Singh et al. 2017).

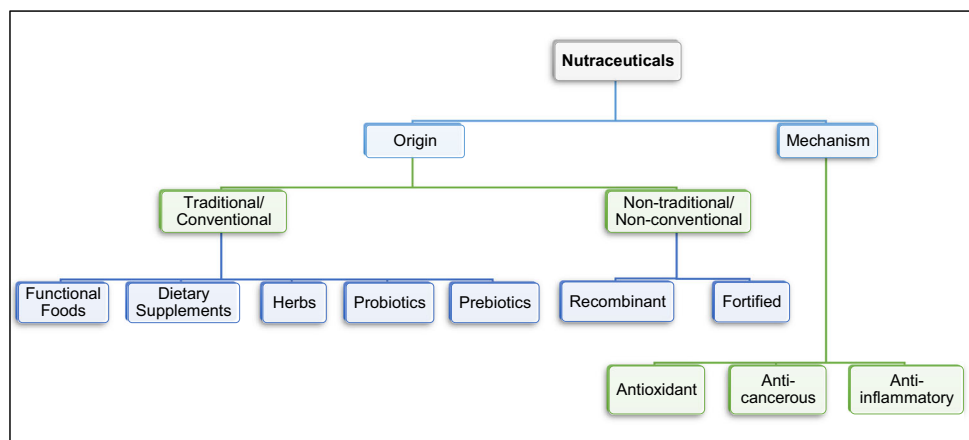
Dietary Supplements

These products are the extracts or a part of the food source which aid in maintenance of a better health in an individual (Bailey et al. 2013). They serve as an additional sources of nutrients which help to overcome nutrient deficiency and improve the overall health (Garg et al. 2018). The dietary supplements can be taken as a liquid solution, powder, tablets, and capsules and can be consumed with or without prescription with an assigned dosage (Gupta et al. 2010). They serve as a source of minerals like iron and calcium, omega-3, and vitamins like vitamin A, and C (Helal et al. 2019). Iron is used as a dietary supplement to increase the ATP production and blood oxygen supply (Gupta et al. 2010). Folic acid promotes erythropoiesis and maintains healthy neural tubes when taken as a dietary supplement (Ansari et al. 2013).

Herbs

Herbs are the shortest form of plants which do not develop into wooden form. Their leaves, roots and stems are formulated into a solution or are dried to use as a medication. Many of the herbs which are used as a source of aroma in cooking inherit antioxidant properties (Embuscado 2015). *Aloe vera* (L.) Burm.f., Xanthorrhoeaceae, is used as an herbal remedy for its antioxidant and wound healing properties. Garlic and ginger also show similar properties like aloe vera and in addition they also reduce cholesterol (AlAli et al. 2021).

Fig. 1 Different classes of nutraceuticals according to their origin and mechanism



Probiotics

Probiotics are defined as a “group of live microorganisms which are non-pathogenic and when administered in adequate amount confers an additional health benefit to the host” (Hill et al. 2014). The two prominent probiotic genera are *Bifidobacterium* and *Lactobacillus*. They are involved in maintaining a healthy gut microbiome while being a part of it. They also aid in digestion, relieving inflammation, and cancer prevention (Kechagia et al. 2013).

Prebiotics

“Prebiotics serve as the food for probiotics”. Prebiotics generally are a type of carbohydrate like galacto-oligosaccharide and inulin. These are food components which cannot be digested by the stomach and intestinal juices but are degraded by the bacterial enzymes. Thus, bacteria present in the gut use them as a source of nutrition. However, these components have a negative impact on the pathogenic species, so they are also helpful in preventing gut dysbiosis. They also aid in stabilizing the gut health by subsiding inflammation and cellular oxidation (Al-Sheraji et al. 2013).

Non-traditional Nutraceuticals

Non-traditional nutraceuticals are the type of nutraceuticals which are engineered or produced by humans artificially like recombinant nutraceuticals and fortified nutraceuticals (Garg et al. 2018; AlAli et al. 2021). All the food products which are synthesized using various methods and are not available naturally are termed as non-traditional nutraceuticals. Breeding techniques or biotechnological approaches are used to cultivate a nutrient-enriched product (Fig. 1) (AlAli et al. 2021).

Fortified Nutraceuticals

These are the foods whose nutritional value is increased by chemically adding additional nutritional components. These additives can be nutrients or vitamins which help to improve overall health status and prevent conditions like anaemia (Gupta et al. 2010). For example, adding calcium into orange provides a support in controlling glucose level in blood (Sui et al. 2016).

Recombinant Nutraceuticals

Using recombinant DNA techniques, nutritional value of a food is increased by genetically adding an extra nutrient gene. The added gene codes for an extra nutrient which is naturally not present in that food (Drake et al. 2017). In golden kiwi, the added genes code for an upregulation of ascorbic acid, lutein, and carotenoid production which enhances immunity. It also increases the level of vitamins, fibers, and potassium (Skinner et al. 2011).

Antioxidant Nutraceuticals

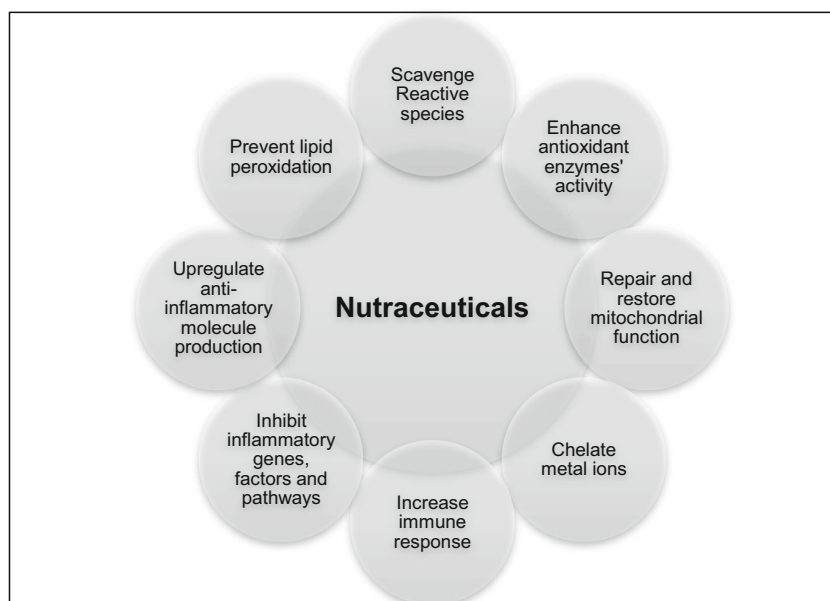
Nutraceuticals are associated with many health benefits which are achieved by employing different mechanisms. Thus, they can also be divided according to the mechanism of action they use to cure a particular ailment (AlAli et al. 2021). All the nutraceuticals which possess antioxidant activity are clubbed together under antioxidant nutraceuticals. Our body has several antioxidant compounds and enzymes which keep the level of reactive species in check. It includes vitamin C, zinc, selenium, vitamin E, and enzymes like glutathione peroxidases and catalases whose primary job is to scavenge reactive species. However, if a situation arises where the reactive species overpowers the defense of endogenous enzymes, nutraceuticals can provide an external source of antioxidants to the

body. Fruits, nuts, vegetables, and some supplements serve as the best and affordable source for nutraceuticals containing antioxidants. All these are a rich source of minerals, vitamins, and phytochemicals. For example, beet root contains betalain which prevents oxidative damage of LDLs. Lignans and isoflavone present in dried fruits like dates lower reactive species levels and increase insulin production in diabetic patients. Nuts like walnut, pistachio, and pecans also have antioxidants which inhibit free radicle accumulation (AlAli et al. 2021). Figure 2 represents the general mechanism nutraceuticals use to suppress oxidative stress.

Anticancer and Anti-inflammatory Nutraceuticals

Bioactive compounds present in nutraceuticals have shown potential for prevention as well as treatment of different types of cancer. During cancerous state, nutraceuticals can prevent its further spread either by inducing apoptosis and autophagy or by inhibiting proliferation, DNA-alkylation, cancer signaling pathways, and metastasis. Presence of high concentration of fibers in prebiotics lowers the risk of colon cancer due to the production of high amount of short-chain fatty acids which induces the growth of healthy gut microbiota. Use of probiotics to establish a healthy gut microbiota to treat colon cancer and associated inflammation is widely under practice. Vitamin D upregulates the expression of DNA damage inducible gene and growth arrest gene when it binds to vitamin D-receptor. This initiates anti-angiogenesis and apoptosis in cancer cells. Resveratrol suppresses the cell signals in STAT-3 and NF- κ B pathways which prevent cancer proliferation and metastasis (AlAli et al. 2021).

Fig. 2 General mechanism adapted by nutraceuticals against oxidative stress



Inflammation is associated with chronic diseases like cardiovascular diseases, diabetes, pulmonary infections, and cancer as a secondary effect, but it can also occur individually. Treating inflammation especially the once associated with chronic diseases depends on extensive use of drugs. As a result, their treatment becomes expensive and dose dependent with a chance of producing side effects and drug resistance. Switching to nutraceuticals for treatment and even preventing inflammation is a solution which eliminates the abovementioned drawbacks associated with drug treatment. Probiotics are known to prevent inflammation in the gut by managing a healthy gut microbiota and inhibiting inflammatory pathways and cytokines; prebiotics assist them in doing so (AlAli et al. 2021). Curcumin possesses many health benefits including inhibiting the activity of inflammatory cytokines (Nair et al. 2010). Polyunsaturated fats elevate the level of anti-inflammatory markers while suppressing the pro-inflammatory markers (Panahi et al. 2012).

Oxidative Stress: Why It Is an Issue

The human body utilizes many biochemical reactions to properly regulate the processes required to keep it up and running all the time. One such process is oxidation which is used in many biochemical processes inside the body including respiration and immunity. The components that carry out oxidation in the body are the reactive species of oxygen and nitrogen. Hydrogen peroxide, hydroxyl radical, superoxide radical, and dioxygen (singlet), along with α -oxygen, form the group “reactive oxygen species (ROS),” and nitroxyl anion, peroxy-nitrite, and nitrosonium cation are examples of “reactive nitrogen species (RNS)” (Martínez and Andriantsitohaina 2009;

Pizzino et al. 2017). These reactive species are a byproduct of the different metabolic reactions and superoxide radicals serve as the precursor for the generation of most ROS, while RNS are derived from nitric oxide radical (Martínez and Andriantsitohaina 2009; Hayyan et al. 2016).

The production of these reactive species majorly occurs in mitochondria from where they head out to take part in metabolic processes or in immune response. Enzymatic reactions taking place during respiration, phagocytosis, and synthesis of prostaglandins are responsible for the synthesis of these reactive species. Oxidases like NADPH oxidase along with peroxidases produce superoxide radicals. Xanthine oxidase and the myriad of other oxidases generate hydrogen peroxide. Nitric oxide synthase generates nitric oxide radicals during arginine being oxidized to citrulline. Also, exposure of cells to ionizing radiations or organic compounds reacting with oxygen can also generate reactive oxygen species, called non-enzymatic production (Pizzino et al. 2017). Reactive species generated through cellular respiration also contribute to the count of total reactive species concentration (Talib et al. 2020).

Endogenous sources like inflammation, infection and their respective immune response, aging, intensive exercise, stress, and related mental issues induce the production of reactive species. Production of reactive free radicals is also activated by the degradation of exogenous compound and contaminants which upon exposure penetrate the body. The list includes contaminants like alcohol, cigarette smoke, heavy metals, recycled oils, smoked meals, or the environment pollutants along with drugs like gentamycin, cyclosporin, and several chemical solvents (Pizzino et al. 2017). After their synthesis, reactive species when present in regulatory moderate amount take part in cellular synthesis. Also, when synthesized by the phagocytes, they become a part of the immune system and degrade the pathogenic cellular constituent by oxidation. Nitric oxide radical acts as an intracellular signaling molecule and takes part in innate immune response (Pacher et al. 2007; Pizzino et al. 2017).

When the human body fails to regulate the amount of these reactive species, they start to accumulate in the cells and tissues causing a state of stress. This state of non-equilibrium between the generation and purging of reactive species inside the human body which leads to degradation of biomolecules and cellular structure is called oxidative stress. The presence of excessive amount of hydroxyl radical along with peroxynitrite (NO_3^-) disrupts lipoproteins and cell membrane, thus generating mutagenic substance. Changes in protein conformation due to oxidative stress cause a loss in protein function and enzymatic activity (Halliwell 2007; Pizzino et al. 2017). Oxidative stress also changes the guanine residue to 8-oxo-2'-deoxyguanosine in the DNA leading to epigenetic loss and mutagenesis (Nishida et al. 2013). These phenomena can lead to aging and, various degenerative and chronic ailments in the

heart, lungs, brain and, cancer and, lifestyle disorders like mental stress, hypertension and diabetes (Reuter et al. 2010; Talib et al. 2020). The damage due to oxidative stress can be seen in almost every part of the body as shown in Fig. 3, and the intensity of this damage depends on the concentration of the reactive species present in a particular location.

Reactive Species in Brain

For Parkinson's and other neuro-degrading diseases, oxidative damage to DNA and protein and low levels of glutathione serve as trigger point for their onset (Young et al. 2007; Gutierrez-Mariscal et al. 2020). Oxidative stress can cause nerve cell damage and makes dementia severe. In Alzheimer's disease, protein oxidation generates toxic peptide called β -amyloid which is the primary cause of the disease (González-Guardia et al. 2015). Lower mitochondrial activity due to oxidative damage and the increased oxidative stress can cause Parkinson's disease (Muthukumaran et al. 2018). Oxidative stress can also affect the memory, and emotions of a person thus creating a state of depression and memory loss (Pizzino et al. 2017).

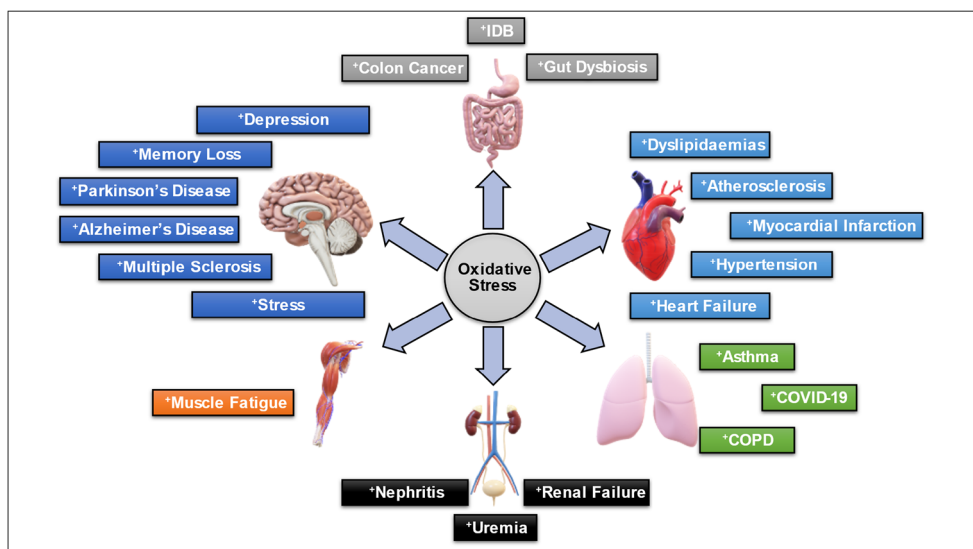
Reactive Species in Lungs

Presence of high concentration of reactive species in lungs is associated with chronic pulmonary inflammation. Their presence upregulates the production of NF- κ B, and the activity of pathways with kinases. The increased oxidative stress in lungs can cause pulmonary diseases like asthma and COPD, and in severe cases, it can be life-threatening (Pizzino et al. 2017). In COPD inflammation, cell death and disruption of pulmonary barrier due to the presence of reactive species became an essential cause of the disease (Di et al. 2016).

Reactive Species in Heart

Although being a secondary cause, oxidative stress acts as trigger for many heart-related diseases. The improper mitochondrial function in the heart leads to the production of large concentration of reactive species which causes inflammation and endothelial dysfunction causing dyslipidemias and heart failure (Gutierrez-Mariscal et al. 2020). In myocardial infarction, the presence of high reactive species concentration reduces functioning of myocardium and induces cell death (Ulla et al. 2017). These reactive species can also oxidize the LDL present in the blood which then accumulates along with the foam cells. The accumulated lipids then develop into plaques which leads the development of atherosclerosis (Pizzino et al. 2017).

Fig. 3 Diseases caused due to oxidative stress in different organ systems. Abbreviations: IBD, inflammatory bowel disease; COPD, chronic obstructive pulmonary disease



Reactive Species in Kidneys

The upset of equilibrium towards reactive species causes a whole lot of trouble in the kidneys like renal failure, nephritis, and uremia. The presence of reactive species in the kidneys causes the accumulation of inflammatory cytokines and cells as well as transcription factors required to maintain the course of inflammation. At first, reactive species causes inflammation in the nephrons followed by degeneration of organ or its function due to the large amount of fibrotic tissue formed due to oxidative stress (Pizzino et al. 2017).

Reactive Species in Cancer

Oxidative DNA damage is one of the causes that trigger cancer. On the molecular level, oxidative stress generates carcinogenic hydrolyzed nucleotide bases as a by-product of DNA oxidation. They can hamper cell growth due to the induced cell mutation and change the transcriptomic profile. Modification in the structure of the DNA like DNA-protein cross-linking, base lesions and strand breaks can also be caused by oxidative stress. It can also activate the dormant oncogenes and induce chromosomal aberrations. All these alterations related to the DNA due to oxidative stress serve as a promoter for cancer development (Pizzino et al. 2017).

Why “Prevention Is Better Than Cure”

Maintaining adequate level of reactive species inside the body is an utmost necessity to prevent oxidative stress. It is facilitated by the human body through the secretion of antioxidant enzymes catalases, peroxidases, and superoxide dismutase. Our body also circulates antioxidant molecules like vitamin E, vitamin C, selenium, and zinc (Deponete 2013). If the offset

of the equilibrium between the antioxidants and reactive species occurs, it will lead to several ailments including cancer. Some of them like Alzheimer’s disease and other neurodegenerative diseases, CVDs, and renal failure can be very severe and life-threatening. If detected at an early stage, these diseases can be cured but the overall cost of medications and treatment of many of the induced diseased states poses a heavy burden on the pocket. In induced severities like that of cancer, treatments can be even more difficult. For curing the oxidative stress–induced cancer, pro-oxidant therapy is under consideration. However, this attempt is like a double-edged sword as a slight increase in the administered dose will lead to increased oxidative stress.

Polyphenols are known to show antioxidant properties, but they can also be used as pro-oxidant. Cancer cells have a high amount of transition metals, which by using with polyphenols undergo Fenton reaction to produce reactive species. The produced reactive species then inhibits cell proliferation and division, inducing cytotoxic and apoptotic effects on the cancer cells. Another pro-oxidant under consideration is the water-soluble vitamin ascorbic acid. Just like polyphenols, it undergoes Fenton reaction using metal ions to produce reactive species. These then cause DNA damage in the cancer cells which lack the proper protective mechanisms like DNA repair enzymes, and cause cell disruption (Pizzino et al. 2017). This approach is very strict in terms of administration due to the chance of an increased diseased state. Increased level of pro-oxidant can start damaging the normal cell DNA and cause cell death.

If the treatment is expensive or can have serious complications, the best way to deal with the disease is to prevent its onset. A preventive measure can re-establish the equilibrium between antioxidants and reactive species concentration before it leads to a diseased state. The easiest preventive measure for oxidative stress is to include nutraceuticals with

antioxidant potential in one’s daily routine either as a part of the diet or as a supplement. They can serve as an essential external source of antioxidants required by our body to maintain a steady state to prevent oxidative stress just like the endogenous antioxidants. If the extended effect of the oxidative stress is diagnosed at an early stage, consumption of nutraceuticals can also help in reducing the effect of the induced disease or to cure it to some extent. Table S1 consists of the list of potential nutraceuticals for the prevention of diseases caused due to oxidative stress in different organ systems.

Regulation and Demand

Even though they are food items, the claim of having an additional health benefit requires that nutraceuticals should have a proper regulation. They must undergo efficacy, quality, and safety testing, and should be a demand of the market. All of this is taken care by “Food and Drug Administration, FDA,” which also looks over the nutrition labelling of foods through “Nutrition Labelling and Education Act, 1990”. FDA maintains a secure environment for food safety and innovation and prevents misconducts in development and manufacturing of products on international level (Ansari et al. 2013). Nations have also adopted their own regulatory principles regarding nutraceuticals like “Dietary Supplement and Health Education Act, 1994” in USA, and “Food and Nutrition Safety Act, 2006” in Poland (AlAli et al. 2021). India has also adopted “Food Safety and Standard Act” in 2006 to set a parallel set of regulations to international standards, and to improve the food industry (Fig. 4) (Ansari et al. 2013). The Brazilian Health Regulatory Agency (Anvisa) is linked to the Ministry of Health, part of the Brazilian National Health System (SUS) as the coordinator of the Brazilian Health Regulatory System (SNVS) and is responsible for regulating various products that are present in our daily lives (Bagchi 2008).

Health benefit along with safety and feasibility are the factors which have helped nutraceuticals gain consumers’ trust. In 2007, the global investment in nutraceuticals was \$379.061 billion which by calculations will be doubled in the next 10 years (Sachdeva et al. 2020). Functional foods, herbal products, and dietary supplements are the three components that make up nutraceuticals (Das et al. 2012). “Associated Chambers of Commerce and Industry of India, ASSOCHAM” released a report about the increase in demand of individual heads of nutraceuticals for the period between 2015 and 2022 in India. Functional foods’ market will receive approximately three times the demand increasing it from 2.8 billion USD to 8.5 billion USD during this period. Dietary supplement market will also show triple their sales, from 1.8 billion USD to 5.2 billion USD during the same period. A rise in sales from \$600 million to \$1700 million for the herbal products shows the same trend as the other two components (Sachdeva et al. 2020).

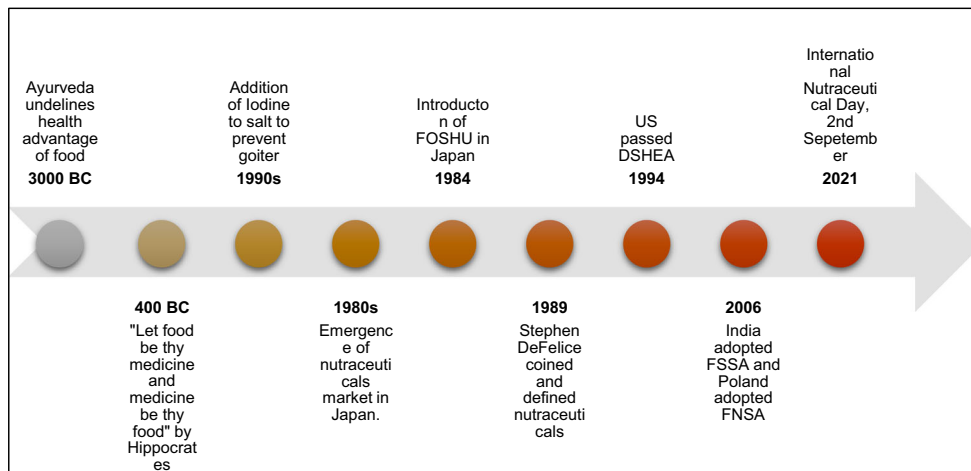
Challenges to Overcome

Nutraceuticals provide an effective and sustainable prevention approach but the fact of them having a toxic profile cannot be ignored. Any alteration with prescribed consumption may turn out to be fatal (Riccioni et al. 2018). Also, most of the claimed nutraceuticals have not gone through complete safety assessment due to lack of required means to do so. The presence of bioactive compounds pool poses a difficulty in analysis of pharmacokinetic properties of the testing nutraceuticals (Pirillo and Catapano 2015). Though nutraceuticals are cost-effective initially, as compared to medications, when taken for a prolonged time, they do dig up a hole in the pockets.

Even though we lack the proper data on every nutraceutical and the overall effects of each of the bioactive components present in them, some of them are a possible source of genotoxicity. They can cause mutations and lesions in DNA,

Fig. 4 History of progression and regulation of nutraceuticals.

Abbreviations: FOSHU, food for specific health uses; DSHEA, Dietary Supplement Health and Education Act; FSSA, Food Safety and Standard Act; FNSA, Food and Nutrition Safety Act



apoptosis, and even cancer. Danthron, found in *Aloe vera*, is reported to induce stomach cancer due DNA damage, increased mitochondrial permeability, and apoptosis (Sehgal et al. 2013; AlAli et al. 2021). Also, being chemical in nature, nutraceuticals can be cross reactive to some drugs like anticoagulants, immunomodulator, and chemotherapeutics and be antagonistic to their functions (Pirillo and Catapano 2015). The pool of bioactive compounds may also have some alkaloids like pyrrolizidine which can alter cell division, and induce carcinogenesis, and cellular dysfunction. Sources of nutraceuticals can also be contaminated from heavy metals, microorganisms, and toxins which degrade the quality of the nutraceuticals and can also turn out to be life-threatening (Gul et al. 2016).

The Present and the Future

Individuals are now more inclined towards a healthy diet so that they can prevent the disease onset through the food they eat rather than relying on drugs for treatment. This belief and the assistance of internet regarding the benefits of different nutraceuticals have increased their demand in the last 20 years. Though self-medication can sometimes turn out to be dangerous, with the detailed information on the internet and with experts' help it is a trend now. Keeping this trend in mind and the fact that drug development is a costlier venture, companies will shift to producing new and cost-effective nutraceutical products. Meanwhile, an increased government funding can be expected for quality and safety assurance of nutraceuticals and research to check their efficiency against life-threatening diseases. Just like personalized medicine, nutrigenetics can be developed to analyze the difference in response to the administered nutraceutical between two genetically different individuals to suggest a personalized nutraceutical. A broader field of nutrigenomics can also be established for understanding the nutraceutical's influence on transcription and translation after genomic interaction to devise the best preventive method (AlAli et al. 2021).

Conclusion

Nutraceuticals are the food sources like fruits, nuts, meat, vegetables, herbs, dietary supplements, and dairy products which inherit additional health benefits along with known nutritional value. It follows the path of nutrition therapy which aims to promote the act of prevention from disease through proper and scientific intake of food instead of looking for a cure. Health benefits of nutraceuticals which are wide include anti-inflammatory, immunomodulation, cell detoxification, proper digestion, mineral absorption, anti-aging, and anti-tumorigenesis. As such, there is a class of nutraceuticals which

solely contains a collection of food items possessing antioxidant activity.

Oxidative stress attacks our body from the inside through reactive species like hydroxyl ion, superoxide radical, and many others just like a slow acting poison. These active redox species occur due to a disbalanced equilibrium between reactive species and endogenous antioxidants; oxidative stress can serve as a precursor of many chronic diseases. Preventing oxidative stress and its associated diseases is a better choice than curing it after its onset to safeguard our body from sustaining an organ damage due to that disease. Also, if the disease has taken its hold on the body and its detection is rather late, the damage due to that disease will be incurable and even life-threatening. The fact that we rely more on treatment of a disease rather than taking the required preventive measure has also unfolded the pandemic of drug-resistant pathogens. Preventive measures such as nutraceuticals on the other hand aim to effectively eliminate such onsets and are comparatively an affordable option. It is due to this effectiveness and cost-efficiency that nutraceuticals have gained people's trust to an extent that their demand has doubled in the last decade. With the development of sufficient techniques and research, the positive aspects of nutraceuticals can be clearly demonstrated and cure for many diseases will be served to us at the dining table.

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Declarations

Competing Interests The authors declare no competing interests.

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