



Research Journal of Pharmaceutical, Biological and Chemical Sciences

Nutraceuticals: A Functional Food as the Anti-Aging Drug and Neuroprotective Agent.

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ABSTRACT

Since its history in food science, nutraceuticals have been placed at the thin boundary separating the food substances and pharmaceuticals. There have been various developments in the research works on nutraceuticals, which revealed many of its important roles in disease prevention and control. The most popular of which is the role of nutraceuticals as an anti-aging substance by virtue of its antioxidant activity which enables it to be a potent free radical scavenger in human physiological system. The free radicals are responsible for the generation of dead cells and gradually results in aging related disease. Other role of nutraceuticals has been found as a functional food and neuroprotectant. It has been reported in various research works that nutraceuticals plays a role in prevention of Alzheimer's disease, Parkinson's disease and other sensory diseases. The nutraceuticals are still being kept under the rules and regulation of food products. The marketing of nutraceuticals does not need the efficacy of documents like that for the pharmaceutical drugs. There have been very few or negligible report for the side effects of nutraceuticals, making it as a most desirous consumable food or drug in future.

Keywords: Nutraceuticals, Neuroprotectant, Antioxidant, Anti-aging, Functional Food.

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INTRODUCTION

Nutraceuticals have been recently introduced in the pharmaceutical market as a health supplement. There have been various approaches to prove nutraceuticals helpful in curing many health problems such as Osteoarthritis, Alzheimer's disease, headache, intestinal problems, diabetes, and inflammations and many more. The term "Nutraceutical" was coined from "nutrition" and "pharmaceutical" in 1989 by Dr. Stephen De Felice, and is defined as "a food (or part of a food) that provides medical or health benefits, including the prevention and/or treatment of a disease [1]. This definition is mostly being used for literature purposes and in marketing, there is no regulatory definition of nutraceuticals. Also, the above definition concerns only human beings and not animal and pets [2]. Most of the times, there are no legally recognizable indications for nutraceuticals because there is no requirement of official proof of efficacy to market them. The manufacturers have to necessarily conduct an extensive scientific study to get the official permission for marketing medicinal products like anti – inflammatories and antibiotics, but this is not true for nutraceuticals. They do not require an official evidence of efficacy to market the Nutraceutical products [3]. The modern food market is inclined towards the effort of conceptualizing the term "optimal nutrition", which aims at optimizing the daily food intake of a person in terms of nutrients and non – nutrients, and other food products for the maintenance of a sound health. The modern consumers have a strong belief to modify their diet and use nutraceuticals and food supplement to improve personal health and reduce healthcare cost [4]. In the words of Diplock, "A functional food must remain food and it must demonstrate its effect in amounts that can normally be expected to be consumed in the diet: it is not a pill or a capsule, but part of the normal food pattern" [5]. The Dietary Supplement Health and Education act, 1994, expands the definition of nutraceuticals to include minerals, vitamins, amino acids, herbs and food supplements for human diet [6]. The term "food supplement" is globally more prominent when compared to the term "Nutraceuticals". Over 470 food supplements and nutraceuticals are available currently with documented health benefits [7]. Seeing the short term and long term side effects of chemical drugs, these nutraceuticals and functional foods are becoming more popular among the current population. This results into a new research on finding alternative therapies preferably with the help of functional foods [8]. Nutraceuticals differs from the chemical drugs in the fact that it does not require any clinical trials which is of utmost importance in the case of chemical drugs. Health Canada defines the term as, "A nutraceutical is a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with food. A nutraceutical is demonstrated to have a physiological benefit or provide protection against chronic disease." Nutraceuticals have the potency to act as the antioxidant compound, antimicrobial agent and functional food, simultaneously [9-11].

Reactive oxygen species

There has been extensive research in recent years on the role of reactive oxygen species in diseases associated with aging and the essentiality and benefits of antioxidative nutraceuticals in the prevention of diseases and boosting of healthy aging. Oxygen is one of the essential constituent of living organisms. The production of reactive oxygen species such as superoxide anion, hydrogen peroxide, hydroxyl radicals, and singlet oxygen is inexorable

in aerobic metabolism of the body. Scientists have pointed out that antioxidant nutraceuticals provided from regular diets quench the reactive oxygen species or are required as cofactors for antioxidant enzymes. Nutraceuticals play important roles in the prevention of a number of age-related diseases and are essential for healthy aging. Health-conscious consumers have made antioxidative nutraceuticals the popular trend in the food industry worldwide in recent years [12].

Antioxidants – natural and synthetic

With the advancement of research in the field of antioxidants, apart from their natural forms scientists have developed a number of synthetic antioxidants which have either replaced or supplemented natural form of antioxidants. Ironically antioxidants are not always adequate or safe for a long period as they themselves are oxidized and their utility recedes with time. Nevertheless antioxidants have potent uses for a plausible time. As observed, consumers prefer natural antioxidants over synthetic antioxidants, mostly for emotional reasons. The universal Western daily diet contains approximately 1 g natural antioxidants even without added antioxidants for lipid stabilization. Cereals, fruits, vegetables, and beverages are some of the sources of naturally found antioxidants. Only a part of the natural antioxidants is absorbed and utilized as free-radical scavengers in vivo. Since synthetic antioxidants are less active, natural antioxidants should be supplemented in higher amounts. However, the actual activity depends on particular conditions and food compositions. Nevertheless, the addition of additional antioxidants is still inconsequential when compared with the dietary supply of native antioxidants. The safety limits of natural antioxidants are yet to be completely known, but they are hardly safer than synthetic antioxidants [13].

Health effects of antioxidants and ROS

Antioxidants have a profound role in health and diseases of humans like oxidative injury causing oxidative-stress. Some of the considerable beneficial roles include those in prevention of ageing induced disease and treatment. The chemical antioxidants, protects the cells against oxidative stress by a combination of several antioxidant enzymes [14]. Oxidative stress is thought to play a role in the development of a wide range of diseases including Alzheimer's disease [15], Parkinson's disease [16], rheumatoid arthritis [17] and neurodegeneration in motor neuron diseases [18]. In most of these cases, it is uncertain if oxidants set off the disease, or if they are produced as a secondary consequence of the disease and from general tissue damage [19]. Toxicity associated with high doses of water-soluble antioxidants such as ascorbic acid is less of a concern since these can be excreted rapidly in urine. Very high doses of some lipid soluble antioxidants may have harmful long-term effects. On the other hand, antioxidants are commonly used as medications to treat various forms of brain injury. Targeted antioxidants may lead to better medicinal effects. For overall life expectancy, it has even been implied that reasonable levels of oxidative stress may increase lifespan in the worm *Caenorhabditis elegans*, by inducing a protective response to increased levels of reactive oxygen species [20]. However, even though unclear, antioxidant supplements do not show increase life expectancy in humans [21]. The evidence for benefits from antioxidant supplementation in strenuous exercise is ambiguous. Then again, there are substantial evidence that one of the variations resulting from exercise is a

strengthening of the body's antioxidant defenses, especially the glutathione system, to monitor the increased oxidative stress [22].

Current work

Recent research on antioxidants and reactive oxygen species have shown that the vast majority of agents used to kill cancer cells work through either directly or indirectly provoking reactive oxygen species that block key steps in the cell cycle. Studies show that since mesenchymal cancers evolve from their epithelial cell progenitors, they necessarily possess much-heightened amounts of antioxidants that effectively block otherwise highly effective oxidant therapies [23].

Aging is the process of accumulation of various health hazardous chemicals in the body, such as free radical and reactive oxygen species, with growing age and resulting in an increase in the risk of diseases and eventually leads to death. The oxidation products from various biomolecules such as nucleic acids, lipids, proteins, sterols, and sugars are found to increase with age in the animal body. In case of plants, they have indefinite life span or a very long life span when compared to the life span of animals and this can be related to the presence of various antioxidants in the green parts of the plant whereas the animal body does not have any integral mechanism to synthesize antioxidant enzymes. Thus, considering the facts and data's of previous research on the antioxidant species, it can be stated that the most promoting factor for aging is the concentration of reactive oxygen species and free radicals, such as singlet oxygen, hydroxyl radicals, and hydrogen peroxide and superoxide anions. The aging process accelerates with the increase in oxidative stress because the level of prooxidants increases against antioxidants. The antioxidative nutraceuticals can be used for reducing the cause of aging, which are free radicals and reactive oxygen species. These nutraceuticals can decrease the level of ROS (Reactive Oxygen species) and free radicals, leading to the deceleration of aging process and hence eventually the increase of life span. From the previous researches, it has been reported that the levels of antioxidant enzymes and their activities are much higher in long living species than short living ones. Few examples of antioxidant enzymes include superoxide dismutase, glutathione peroxidase and catalase. Also, it has been found that vitamin E in elderly people (of age more than 65 years) are lower than that found in younger adults. At the same time, it has also been proved that the consumption of optimal amounts of vitamin E and A has increased the life span of animals [24]. Antioxidant nutraceuticals find their use in inhibiting or reducing the synthesis of free alkyl radical in the initiation step and break the free-radical chain reaction in the propagation step during lipid oxidation. The antioxidative nutraceuticals may be the antioxidative enzymes, metal chelators, hydrogen donating compounds and singlet oxygen quenchers. The antioxidative enzymes (Table 1) include catalase, superoxide dismutase and glutathione peroxidase/ reductase and their role is to convert the reactive oxygen species into non-reactive oxygen molecules [25].

Classification of nutraceuticals

With respect to obligation of nutraceuticals, they should be classified in two ways, namely potential nutraceuticals and established nutraceuticals. A potential nutraceutical is one that holds a guarantee of a particular health or medical assistance. It only becomes an

established one after there are sufficient clinical data to validate the promised benefit. However, unfortunately the overwhelming majority of nutraceutical products are in the 'potential' category, waiting to become established [26]. The food products used as nutraceutical are categorized as [27] Probiotic, Prebiotic, Dietary fiber, Omega 3 fatty acid and Antioxidant.

Table 1: Antioxidative enzymes/proteins

Proteins / Enzymes	Function
Superoxide dismutase	Superoxide removal
Catalase	Hydroperoxide removal
Glutathione peroxidase	Hydroperoxide removal
Glutathione disulfide reductase	Oxidised glutathione reduction
Glutathione – S – Transferase	Lipid Hydroperoxide removal
Methionine sulfoxide reductase	Repair oxidised Methionine residues
Peroxidase	Decomposition of hydrogen peroxide and lipid Hydroperoxide

The future of nutraceuticals

An increasing alertness about fitness and health, sparked by media has urged the majority of people to lead healthy lifestyle. The expanding nutraceutical market reveals that consumers are searching minimally processed food with extra nutritional benefits. This development has triggered expansion in the nutraceutical markets globally. Its incredible growth has significance in the food, pharmaceutical, healthcare, and agricultural industries.

Future demand of nutraceutical will vary on consumer perception in regards to the relationship between disease and diet. Although nutraceuticals have significant promise in the advancement of human health and disease prevention, health professionals, nutritionists and regulatory toxicologist should strategically work together to plan for regulations to provide the ultimate health and therapeutic benefit to the mankind. Long-term clinical studies are required to scientifically demonstrate the nutraceuticals in various medical conditions. The synergy of nutraceuticals with food and drugs is another area, which should be acknowledged. The effect of different processing methods on the biological availability and adequateness of nutraceuticals remains to be resolved. As like drugs, there should be strict regulatory controls over nutraceuticals also [28].

Marketing

The U.S. Congress, in the Dietary Supplement Health and Education Act (DSHEA) pioneered a structure for supervision of dietary supplements. Labeling is regulated by the FDA to limit health claims, but cannot entitle to insist on stringent studies establishing safety before marketing. This creates a considerable potential risk to the health of the public. It is favored that a new category of dietary supplements, i.e. "nutraceuticals," should be well-established for supplements which can be administered at doses that exceed normal human exposure to these elements in foods. Regulations should require that these nutraceuticals be assessed safe before they are marketed [29].

Nutraceuticals as antioxidants used as neuroprotective agents

There are several chemical classes of nutraceuticals found in a variety of foods. Some nutraceuticals like epigallocatechin 3-gallate (EGCG) from green tea and resveratrol from

grapes are well known, whereas others are predominantly unfamiliar to the lay user. Even though these compounds are structurally divergent, each of them has been known to show neuroprotective and antioxidant properties. The intrinsic free radical scavenging activities of these nutraceutical antioxidants imply that they may have probable utility in reducing neuronal oxidative stress and neurodegeneration. As shown in the figure 1, the characteristic of nutraceuticals to alter key pro-survival kinase pathways potentially plays a significant role in their neuroprotective actions.

Modulation of pro-survival protein kinase pathways by nutraceuticals.

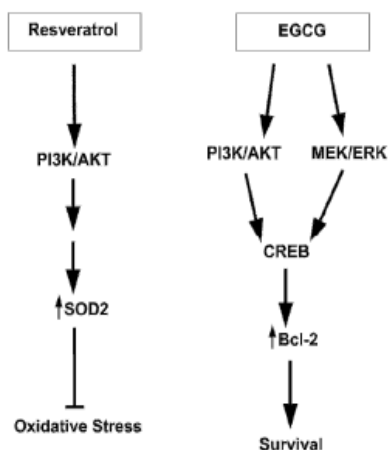


Figure 1: Modulation of pro-survival protein kinase pathways by nutraceuticals

There are strong scientific facts to support that nutraceutical antioxidants can be developed as novel therapies for neurodegenerative diseases. Many of these natural antioxidants are not only effective scavengers of free radicals but also act as modulators of pro-survival or pro-apoptotic signaling pathways. Result of which, these compounds may have a greater potential for therapeutic success than drugs with only one mechanism of action. Nutraceutical antioxidants may be the best options for these patients in the short term since they are subject to fewer regulations than traditional pharmaceuticals and therefore, could be made available to patients much more rapidly than new prescription drugs [30].

CONCLUSION

The overall role of nutraceuticals in the prevention of human diseases can be viewed from the figure 2. It serves as an antioxidant, neuroprotectant and functional food, simultaneously. Natural antioxidants can be used for the manufacturing of nutraceuticals, which will prove to be a better functional food as compared to the already present functional food in the market. The nutraceuticals have very little or no side effects in addition to the profound effect on the cell metabolism. These features of nutraceuticals make it a potent food substance to be used by all age groups. There is a need of government regulation and industrial initiatives for commercializing the nutraceuticals and promoting health of humankind.

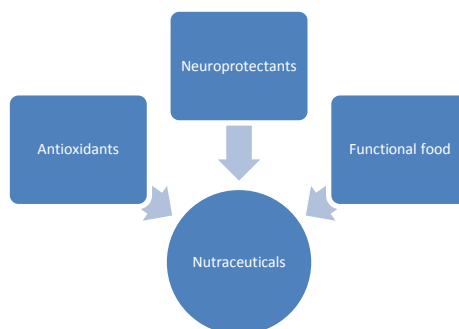


Figure 2: The various roles of antioxidants in human health and diseases.

ACKNOWLEDGEMENT

The authors are thankful to the Chancellor, VIT University, Dr. G. Viswanathan for his kind infrastructural support and encouragement during the work. The author would also like to thank the Vice Presidents and Vice Chancellor, VIT University, for their immense support during the work.

REFERENCES

- [1] Brower V. *Nat Biotechnol* 1998; 16: 728 – 731
- [2] Zeisel SH. *Science* 1999; 285: 185 – 186
- [3] JM Vandeweerd, et al. *J Vet Inter Med* 2012; 26: 448 – 456
- [4] Arai S. *British J Nutr* 2002;88(Suppl 2):S139 – 43
- [5] Diplock AT, Aggett PJ, Ashwell M, Borner F, Fern EB, and Roberfroid MB. *British J Nutr* 1999;81:S1–S27
- [6] Stauffer JE. *Cereals Food World* 1999; 44(2): 115 – 116
- [7] Brower V. *Nat. Biotechnology* 1999; 16: 728 – 731
- [8] Summet Gupta, Devesh Chauhan, Kritika Mehla, Preeti Sood and Anroop Nair. *J Basic Clin Pharm* 2010;1(2).
- [9] Alok Prakash, Kanupriya Mathur, Ankita Vishwakarma, Suneetha Vuppu and Bishwambhar Mishra. *Int J Pharm Sci Rev Res* 2013;5(1):131-135.
- [10] Ramalingam C, et al. *Int J Drug Dev Res* 2013;5(1): 310 – 320.
- [11] Alok Prakash, Shampa Sen, Rishabh Dixit. *Int J Pharm Sci Rev Res* 2013;22(1):107 – 111.
- [12] J Lee, N Koo, DB Min. DOI: 10.1111/j.1541-4337.2004.tb00058.x
- [13] Jan Pokorný. *European J Lipid Sci Technol* 2007;109(6):629–642.
- [14] Sies, Helmut. *Exp Physiol* 1997;82(2):291–5.
- [15] Wood-Kaczmar A, Gandhi S, Wood N. *Trends Mol Med* 2006;12(11):521–8.
- [16] Hitchon C, El-Gabalawy H. *Arthritis Res Ther* 2004;6(6):265–78.
- [17] Cookson M, Shaw P. *Brain Pathol* 1999;9(1):165–86.
- [18] Valko M, Leibfritz D, Moncol J, Cronin M, Mazur M, Telser J. *The Int J Biochem Cell Biol* 2007;39(1):44–84.
- [19] Schulz TJ, Zarse K, Voigt A, Urban N, Birringer M, Ristow M. *Cell Metab* 2007;6(4): 280–93.
- [20] Green GA. *Evid Based Med* 2008;13(6):177.



- [21] Leeuwenburgh C, Fiebig R, Chandwaney R, Ji L. Am J Physiol 1994;267 (2 Pt 2): R439–45.
- [22] Oxidants, antioxidants and the current incurability of metastatic cancers; Jim Watson; January 9, 2013, 3(1) doi: 10.1098/rsob.120144 Open Biol. January 2013
- [23] Teoh CY, Davies KJA. Free Rad Res 2001;36: 8 – 12.
- [24] dillard CJ, German JB. J Sci Food Agric 2000; 80: 1744 – 56
- [25] Wildman REC. 2001. Classifying nutraceuticals. In: Wildman REC, editor, Handbook of nutraceuticals and functional foods, Boca Raton, Fla. : CRC Press. P 13 – 30
- [26] De Felice L Stephen. Trends in Food Sci Tech 1995; 6:59-61
- [27] Kokate CK, Purohit AP, Gokhale SB. Nutraceutical and Cosmaceutical. Pharmacognosy, 21st edition, Pune, India: Nirali Prakashan, 2002; p 542-549
- [28] Manisha Pandey, Rohit K Verma, Shubhini A Saraf. Nutraceuticals: new era of medicine and health: Vol.3 Issue 1, January-March 2010
- [29] Science 17 September 1999: Vol. 285 no. 5435 pp. 1853-1855
DOI: 10.1126/science.285.5435.1853
- [30] Natalie A. Kelsey, Heather M Wilkins and Daniel A Linseman. Molecules 2010;15: 7792-7814.