CURRENT TRENDS AND FUTURE PROSPECTIVE OF NUTRACEUTICALS IN HEALTH PROMOTION

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ABSTRACT

Nutraceutical is a term derived from “nutrition” and “pharmaceutics.” The term is applied to products that are isolated from herbal products, dietary supplements (nutrients), specific diets, and processed foods such as cereals, soups, and beverages that other than nutrition are also used as medicine. It is a pharmaceutical alternative which claims physiological benefits. In the US, "nutraceuticals" are largely unregulated, as they exist in the same category as dietary supplements and food additives by the FDA, under the authority of the Federal Food, Drug, and Cosmetic Act Nutraceuticals are treated differently in different jurisdictions. Under Canadian law, a nutraceutical can either be marketed as a food or as a drug; the terms "nutraceutical" and "functional food" have no legal distinction referring to "a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with food [and] is demonstrated to have a physiological benefit or provide protection against chronic disease." The terms "nutraceutical" and 'bioceutical' are not defined by US law. Depending on its ingredients and the claims with which it is marketed, a product is regulated as a drug, dietary supplement, food ingredient, or food. In the global market, there are significant product quality issues. Nutraceuticals from the international market may claim to use organic or exotic ingredients, yet the lack of regulation may compromise the safety and effectiveness of products. Companies looking to create a wide profit margin may create unregulated products overseas with low-quality or ineffective ingredients. Nutraceuticals are products derived from food sources that are purported to provide extra health benefits, in addition to the basic nutritional value found in foods. Depending on the jurisdiction, products may claim to prevent chronic diseases, improve health, delay the aging process, increase life expectancy, or support the structure or function of the body.

Keywords- Nutraceutical, Physiological benefit, Pharmaceutic, aging.

I INTRODUCTION

Our understanding of the relationships between food, physiological function and disease has progressed in recent years, particularly over the past decade. The National Academy of Sciences report, Diet and Health [1],[2] Health Canada's Nutrition Recommendations2 and, more recently, two reports on dietary reference intakes for nutrients [3],[4] have led the way in making chronic disease prevention a key objective of nutrition recommendations. At the same time, Canadians have been taking greater control over their health, exploring alternative or traditional medicines, complementary therapies and natural health products. There has been a growing interest in the role that nutrition plays in our state of well being. As public knowledge of this field has evolved, manufacturers have sought to fulfill a consumer appetite for products derived from foods that could be used to promote good health. The result has been the development and marketing of a growing spectrum of products called "nutraceuticals" and "functional foods."

II CLASSIFICATION OF NUTRACEUTICALS

A. Dietary supplements

In the United States, the Dietary Supplement Health and Education Act (DSHEA) of 1994 defined the term "dietary supplement": "A dietary supplement is a product taken by mouth that contains a 'dietary ingredient' intended to supplement the diet. [5]The 'dietary ingredients' in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. [6] Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders."[7]

Dietary supplements do not have to be approved by the U.S. Food and Drug Administration (FDA) before marketing, but companies must register their manufacturing facilities with the FDA and follow current good manufacturing practices (cGMPs). With a few well-defined exceptions, dietary supplements may only be marketed to support the structure or function of the body, and may not claim to treat a disease or condition, and must include a label that says: "These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." The exceptions are when the FDA has reviewed and approved a health claim. In those situations the FDA also stipulates the exact wording allowed.

B. Functional foods

Functional foods are fortified or enriched during processing and then marketed as providing some benefit to consumers. Sometimes, additional complementary nutrients are added, such as vitamin D to milk.

Health Canada defines functional foods as "ordinary food that has components or ingredients added to give it a specific medical or physiological benefit, other than a purely nutritional effect."[11] In Japan, all functional foods must meet three established requirements: foods should be (1) present in their naturally occurring form, rather than a capsule, tablet, or powder; (2) consumed in the diet as often as daily; and (3) should regulate a biological process in hopes of preventing or controlling disease.

Table 1: Herbal Health Drink Formulation

Plant Neutraceutical Concentrate	Quantity per litre
Ashwagandha concentrate	400 mg
Brahmi concentrate	400 mg
Tulsi concentrate	200 mg
Ginger concentrate	200 mg
Awala concentrate	400 mg
Shatavari concentrate	100 mg
Gokharu concentrate	100 mg
Arjuna concentrates	100 mg
Giloy concentrate	100 mg
Safed musli concentratev	100 mg
Aloe vera concentrate	100 mg

Haldi concentrate	50 mg
Sugarcane	100ml

Table 2: Common herbal and Phytochemical products.

Plant	Therapeutic activity
Aloe vera gel (Aloe vera L. N.L. Burm.)	Dilates capillaries, anti-inflammatory, emollient, wound
Garlic (Allium sativum L.)	healing properties
Ginger (Zingiber officinale Rosc.)	Antibacterial, antifungal, antithrombotic, hypotensive,
Tinospora cardifolia	fibrinolytic, antihyperlipidemic,
Piper nigrum (Kalimirchi)	Anti-inflammatory
Withania somnifera (Ashwagandha)	Carminative, antiemetic, cholagogue, positive inotropic,

Table 3: Common nutrients and their associated health benefits [8]

Plant Neutraceutical Components	**Health benefits**
Fat Soluble Vitamins Vitamin A Vitamin D Vitamin E Vitamin K	Antioxidant, essential, for growth and development, maintains healthy vision, skin and mucous membranes, may aid in the prevention and treatment of certain Cancers and in the treatment of certain skin disorders. • Essential for formation of bones and teeth, helps the body absorb and use calcium • Antioxidant, helps form blood cells, muscles, lung and nerve tissue, boosts the • immune system • Essential for blood clotting
Water Soluble Vitamins Vitamin C Vitamin B1 Vitamin B2 Vitamin B3 Vitamin B6 Vitamin B12 Folic acid Pantothenic acid	• Antioxidant, necessary for healthy bones, gums, teeth and skin, helps in wound healing, may prevent common cold and attenuate its symptoms •Helps to convert food in to energy, essential in neurologic functions • Helps in energy production and other chemical processes in the body, helps maintain healthy eyes, skin and nerve function • Helps to convert food in to energy and maintain proper brain function • Helps to produce essential proteins and convert protein in to energy • Helps to produce the genetic material of cells, helps with formation of red blood cells, maintenance of central nervous system and synthesize amino acids and is involved in metabolism of fats, protein and carbohydrates • Necessary to produce the genetic materials of cells, essential in first three months of pregnancy for preventing birth defects, helps in red blood cell formation, protects against heart disease • Aids in synthesis of cholesterol, steroids and fatty acids, crucial for intraneuronal synthesis of acetylcholine
Dietary Nucleotides	• Nucleotides have been demonstrated to affect a number of immune functions and health rejuvenation
Minerals Calcium Iron Magnesium Phosphorous	• Essential for building bones and teeth and maintaining bone strength, important in nerve, muscle and glanddular functions • Helps in energy production, helps to carry and transfer oxygen to

	tissues • Essential for healthy nerve and muscle function and bone formation, may help prevent premenstrual syndrome (PMS) • Essential for building strong bones and teeth, helps in formation of genetic material, energy production and storage
Trace elements Chromium Cobalt Copper Iodine Selenium Zinc	• With insulin helps to convert carbohydrates and fats into energy • Essential component of vitamin B , but ingested cobalt is metabolized in vivo to form the B12, coenzymes • Essential for hemoglobin and collagen production, healthy functioning of the heart, energy production, absorption of iron from digestive tract • Essential for proper functioning of the thyroid • Antioxidant, essential for healthy functioning of the heart muscle • Essential for cell reproduction, normal growth and development in children, wound healing, production of sperm and testosterone
Vitamin like compounds Biotin L- Carnitine Choline Vitamin F Inositol Taurine	• Required for various metabolic functions • Oxidation of fatty acids, promotion of certain organic acid excretion and enhancement of the rate of oxidative phosphorylation • Lipotropic agent used to treat fatty liver and disturbed fat metabolism • Involved in proper development of various membranes and synthesis of prostaglandins, leukotrienes and various hydroxy fatty acids • Lipotropic agent necessary for amino acid transport and movement of potassium and sodium • Aids in retinal photoreceptor activity, bile acid conjugation, white blood cell antioxidant activity, • CNS neuromodulation, platelet aggregation, cardiac contractility, sperm motility, growth and insulin activity

Table 4 : List of Marketed Neutraceutical Products [9]

Product	Category	Manufactures
Coral calciumTM	Calcium supplement	Nature's answer, Hauppauge, NY, USA
Weight smart	Nutritional supplement	Bayer corporation, Morristown,NL, USA
Omega womanTM	Immune supplement	Wassen, Surrey, U.K.
Appetite InterceptTM	Appetite suppressant	Natrol, Chatsworth, CA, USA
Chaser®	Hangover supplement	Living essentials, Walled lake,MI, USA
Rox	Energy drink	Rox America, Spartanburg, SA, USA
Mushroom optimizeTM	Immune supplement	Jarrow formulas, Los Angeles, CA, USA
Biovinca®	Neurotonic	Cyvex nutrition, Irvine, CA, USA
ProplusTM	Nutritional supplement	Campbell soup company, Camden,NJ, USA
Snapple-a-day®	Meal replacement bevera	Snapple beverage group, White Plains, NY, USA
WelLifeTM	Amino acid supplement	Daesang America Inc.,Hackensach, NJ, USA

PNer plusTM	Neuropathic pain supplement	NeuroHelp, San Antonio, Texas, USA
Olivenol®	Dietary supplement	Cre Agri, Hayward, CA, USA
Threptin Diskettes®	Protein supplements	Raptakos, Brett & Co. Ltd., Mumbai, India
GRD®	Nutritional supplement	Zydus Cadila Ltd. Ahmedabad, India
Proteinex®	Protein supplement	Pfizer Ltd., Mumbai, India

III Future of Nutraceuticals

A) Allergy and nutraceuticals

Allergy is a hypersensitivity disorder of the immune system. An allergic reaction usually occurs when a person's immune system reacts to normally harmless substances. Allergic reactions are distinctive because of excessive activation of certain white blood cells called mast cells and basophils by a type of antibody called immunoglobulin E. This reaction results in an inflammatory response which can range from uncomfortable to dangerous. [10]

Quercetin protects low-density lipoprotein (LDL-C) from becoming damaged, especially to blood vessels. LDL-C is an underlying cause of heart disease and quercetin acts as an antioxidant and scavenges free radicals. Diabetic patients are at higher risk of blood vessel damage from oxidative stress. Therefore, quercetin is beneficial in these patients, too.

B) Alzheimer's disease and nutraceuticals

Alzheimer's disease (AD) is the most common form of dementia. There is no cure for the disease and eventually leads to death. Most often, AD is diagnosed in people over 65 years of age, although the less-prevalent early-onset Alzheimer's can occur much earlier. There were 26.6 million sufferers worldwide in 2006 and is predicted to affect 1 in 85 people globally by 2050 [11]

Women are more affected in comparison to men, at a ratio of almost 2:1. Several lines of evidence suggest that oxidative stress might be related to a number of neurodegenerative disorders including AD. Nutraceutical antioxidants such as curcumin, lutein, lycopene, turmerin and β-carotene may exert positive effects on specific diseases by combating oxidative stress. The growing trends in nutraceutical usage are due to the belief that these compounds are able to postpone the development of dementias such as AD.There are several recently published papers showing the positive effects of different nutriceutical plants such as *Zizyphus jujube*, *Lavandula officinalis* on AD, learning or memory.

C) Cardiovascular diseases and nutraceuticals

Worldwide, the prevalence of CVD and the researches in this area is increasing. CVD is a term which is used for disorders of the heart and blood vessels and includes coronary heart disease (heart attack), peripheral vascular diseases, cerebrovascular disease (stroke), hypertension, heart failure, and so on. It is believed that low intake of vegetables and fruits is associated with a high mortality in CVD.Majority of the CVD are preventable. Many studies have reported a protective role for a diet rich in vegetables and fruits against CVD.

Nutraceuticals in the form of vitamins, minerals, antioxidants, dietary fibers and omega-3 polyunsaturated fatty acids (*n*−3 PUFAs) together with physical exercise are recommended for prevention and treatment of CVD. The molecules such as polyphenols alter cellular metabolism and signaling, which is believed to reduce arterial disease.

Flavonoids are widely distributed in vegetables, onion, endives, cruciferous, grapefruits, apples, cherries, pomegranate, berries, black grapes, and red wine, and are available as flavones, flavanones and flavonols, playing a major role in prevention and curing the CVD. Flavonoids block the angiotensin-converting enzyme, block the cyclooxygenase enzymes that break down prostaglandins, and prevent platelet aggregation. They also protect the vascular system that carries oxygen and nutrients to cells.Anthocyanins, tannins (proanthocyanidins), tetrahydro-β-carbolines, stilbenes, dietary indoleamines, serotonin and melatonin, in plant foods are hypothesized to impose health benefits. Orange juice containing pulp is rich in flavonoids. Hesperidin is a flavanone glycoside which is classified as a citrus bioflavonoid. Citrus sinensis and tangelos are the richest dietary sources of hesperidin. The peel

and membranous parts of lemons and oranges have the highest hesperidin concentrations. Hesperidin is used for the treatment of venous insufficiency and hemorrhoids.

Flavonoid intake was significantly inversely associated with mortality from coronary heart disease and the incidence of myocardial infarction. Flavonoids in regularly consumed foods may reduce the risk of death from coronary heart disease, especially in elderly people.

The rhizome of zingiber officinalis is a common condiment for various foods and beverages. It has a long history of medicinal use and has a positive effect on CVD. Ginger has potent antioxidant and antiinflammatory activities and recently it has been recommended for various diseases including hypertension and palpitation. This plant has a good protective effect on toxicity of synthetic drugs, too.

Phytosterols compete with dietary cholesterol by blocking the uptake as well as facilitating its excretion from the body. Hence, they have the potential to reduce the morbidity and mortality of CVD. Phytosterols occur in most plant species and although green and yellow vegetables contain significant amounts of sterols, their seeds concentrate them.

Buckwheat seeds possess phytosterols, flavonoids, flavones, proteins and thiamin-binding proteins, etc., Buckwheat proteins lower blood cholesterol and hypertension.Dietary fibers have also cholesterol-lowering property with beneficial effects in prevention and alleviation of CVD and diabetes.

Fatty acids of the omega-3 series (*n*−3 fatty acids) present in fish are dietary components affecting plasma lipids and the CVD, like arrhythmias. Octacosanol, present in whole grains, fruits and leaves of many plants, has lipid lowering property, with no side-effects.

D) Cancer and nutraceuticals

Cancer has emerged as a major public health problem in developing countries. According to the World Cancer Report the cancer rates are increasing and it would be 15 million new cases in the year 2020 that is, a rise in 50%. A healthy lifestyle and diet can help in prevention of cancer.Carotenoids are a group of phytochemicals responsible for different colors of the foods. They have antioxidant activities and effective on cancer prevention. Recent interest in carotenoids has focused on the role of lycopene in human health, especially in cancer disease.

Plants rich in daidzein, biochanin, isoflavones and genistein, also inhibit prostate cancer cell growth. Because of the unsaturated nature of lycopene it is considered to be a potent antioxidant and a singlet oxygen quencher. Lycopene concentrates in the prostate, testes, skin and adrenal where it protects against cancer. The linkage between carotenoids and prevention of cancer and CAD, heightened the importance of vegetable and fruits in human diet.

Lycopene contained vegetables and fruits exert cancer-protective effect via a decrease in oxidative stress and damage to DNA. Lycopene is one of the major carotenoids and is found exclusively in tomatoes, guava, pink grapefruit, water melon and papaya.

β-carotene has antioxidant activity and prevents cancer and other diseases. Among the carotenes, β-carotene has the most antioxidant activity. Alpha-carotene possesses 50–54% of the antioxidant activity of β-carotene, whereas epsilon carotene has 42–50% of the antioxidant activity.

Chronic inflammation is associated with a high cancer risk. Chronic inflammation is also associated with immune-suppression, which is a risk factor for cancer. Ginseng is an example of an antiinflammatory molecule that targets many of the key players in the inflammation-to-cancer sequence.

Nowadays, phytochemicals with cancer-preventive properties have been on high attention. Chemopreventive components in fruits and vegetables, among other beneficial health effect, have potential anticarcinogenic and antimutagenic activities. A broad range of phyto-pharmaceuticals with a claimed hormonal activity, called “phyto-estrogens,” is recommended for prevention of prostate and breast cancers.

Citrus fruit flavonoids are able to protect against cancer by acting as antioxidants. Soyfoods are a unique dietary source of isoflavones, the polyphenolic phytochemicals exemplified by epigallocatechin gallate from tea, curcumin from curry and soya isoflavones possess cancer chemopreventive properties. Soybean seems to offer protection

against breast, uterine, lung, colorectal, and prostate cancers. β-carotene found in yellow, orange, and green leafy vegetables and fruits such as tomatoes, lettuce, oranges, sweet potatoes, broccoli, cantaloupe, carrots, spinach, and winter squash has anticancer activity.

Saponins are reported to possess anti mutagenic and antitumor activities and might lower the risk of human cancers, by preventing cancer cells from growing. Saponins are phytochemicals which can be found in peas, soybeans, and some herbs with names indicating foaming properties such as soapberry, soapwort and soapbark. They are also present in tomatoes, potatoes, alfalfa, spinach, and clover. Commercial saponins are extracted mainly from *Yucca schidigera* and *Quillaja saponaria*

REFERENCES

[1] Sarris, Jerome; Murphy, Jenifer; Mischoulon, David; Papakostas, George I.; Fava, Maurizio; Berk, Michael; Ng, Chee H. (2016). "Adjunctive Nutraceuticals for Depression: A Systematic Review and Meta-Analyses". *American Journal of Psychiatry*. **173** (6): 575–587

[2] Banach, Maciej; Patti, Angelo Maria; Giglio, Rosaria Vincenza; et al. (2018). "The Role of Nutraceuticals in Statin Intolerant Patients". *Journal of the American College of Cardiology*. **72** (1): 96–118.

[3] *"Supplement Makers Touting Cures for Alzheimer's and Other Diseases Get F.D.A. Warning". The New York Times. 11 February 2019. Retrieved 2019-05-11.*

[4] *"Labeling & Nutrition". The Food and Drug Administration, US Department of Health and Human Services. 5 October 2016. Retrieved 2016-10-11.*

[5] "Nutraceuticals / Functional Foods and Health Claims on Foods: Policy Paper". Health Canada. June 24, 2013. Retrieved January 30, 2014

[6] *Committee on the Framework for Evaluating the Safety of the Dietary Supplements (2005). "Committee Change". Dietary Supplements: A Framework for Evaluating Safety. Institute of Medicine. p. 21*

[7] National Research Council (USA), 1989. Committee on Diet and Health. Diet and Health: implications for reducing chronic disease risk. Washington. National Academy Press

[8] Institute of Medicine, 1997. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride, Standing Committee on the Scientific Evaluation of Dietary reference intakes, Food and Nutrition Board, Washington, D.C., National Academy Press.

[9] Institute of Medicine, 1998. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6 , Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Washington, DC, National Academy Press.

[10] Shibamoto, Takayuki; Kanazawa, Kazuki; Shahidi, Fereidoon; et al., eds. (2008). *Functional Food and Health*. ACS Symposium. p. 993.

[11] "Glossary - Biotechnology". Hc-sc.gc.ca. 2006-03-23. Retrieved 2011-06-03