

NUTRACEUTICALS AND FUNCTIONAL FOODS IN HEALTH PROMOTION AND DISEASE RISK MANAGEMENT

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Received: June 08, 2011; Accepted: July 01, 2011

Abstract- Plants play an important role in the daily life, which are essential not only for food, shelter and clothing but also for recreation world is colorful because of diversified flora of dye yielding plants. Plants are one of the most important resources of human foods and medicines. Rapidly increasing knowledge on nutrition, medicine, and plant biotechnology has dramatically changed the concepts about food, health and agriculture, and brought in a revolution on them. Nutritional therapy and phytotherapy have emerged as new concepts and healing systems have quickly and widely spread in recent years. Strong recommendations for consumption of nutraceuticals, natural plant foods, and the use of nutritional therapy and phytotherapy have become progressively popular to improve health, and to prevent and treat diseases. With these trends, improving the dietary nutritional values of fruits, vegetables and other crops or even bioactive components in folk herbals has become targets of the blooming plant biotechnology industry. This review attempts to display and remark on these aspects. It summarizes the progress made on nutraceuticals, nutritional therapy, phytonutrients, phytotherapy, and their related epidemiological investigations and clinical studies. It also covers markets of these health-promoting products and disease-preventing or healing systems, as well as regulations behind them that direct the development of biotechnology study and application. Finally, related patents are listed and briefly analyzed, regarding of plant biotechnological research and progress on transgenic crops to improve nutritional value, phytotherapy efficiency, or to produce pharmaceutically important secondary metabolites or high-valued protein medicines such as vaccines and antibodies. In the case of plant foods, phenolics and polyphenolics constitute a main group of compounds that render beneficial effects, in part, due to their antioxidant potential, among other mechanisms of action.

Keywords: Nutraceuticals, clinical trial, metabolic engineering, phytonutrients, plant biotechnology.

INTRODUCTION

About 2000 years ago, Hippocrates correctly emphasized "Let food be your medicine and medicine be your food". Currently there is an increased global interest due to the recognition that "nutraceuticals" play a major role in health enhancement.

The term "Nutraceutical" was first coined by Dr. Stephen L. Defelice as "a product isolated or purified from foods and sold in medicinal forms. They have physiological benefit" Nutraceutical is a combination of 2 words

1. Nutrition and
2. Pharmaceutical.

Nutraceuticals are food product that provides health as well as medical benefits; including the prevention and treatment of disease. Phytochemicals and antioxidants are two specific types of nutraceuticals. Research has proved that foods with phytochemicals may help to provide protection from diseases such as cancer, diabetes, heart disease, and hypertension,

e.g., carotenoids found in carrots. Antioxidants may be helpful in avoiding chronic diseases, by preventing oxidative damage in our body. Over the last 20 years, numbers of Nutraceuticals are available for self-medication or for sale. There has been a boom in sale of Nutraceutical because of -

1. Adverse effects of pharmaceuticals
2. Increased tendency of patients for self-medication
3. Aging population e.g. - arthritis

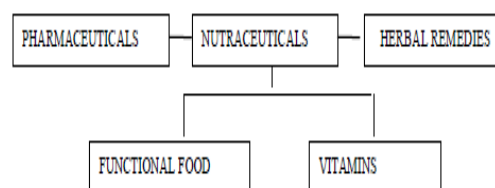


Fig. 1-

CLASSIFICATION OF NUTRACEUTICALS

Nutraceutical is a term used to describe product obtained from food sources that provides extra health benefits as well as basic nutritional value present in food. There are different types of products that come under the class of nutraceuticals.

DIETARY SUPPLEMENTS

A dietary supplement is a product that contains nutrients derived from food products. The "dietary ingredients" present in these products are: metabolites, vitamins, minerals, vitamins, herbs, and amino acids.

FUNCTIONAL FOODS

Functional foods are designed foods which provide enriched foods close to their natural state to consumer, rather than manufactured dietary supplements in liquid or capsule form. A process of making enriched food is called Nutrification. Functional foods provide required amount of vitamins, fat, carbohydrate, amino acid etc to body. Established requirement that functional food should possess are-

- (1) They should be in their naturally-occurring form,
- (2) They should be an essential part of our daily diet,
- (3) Should regulate a biological process in hopes of preventing or controlling disease.⁶

RELATIONSHIP BETWEEN NUTRACEUTICALS, FOOD AND MEDICINE

Figure 1 shows the relationship between nutraceuticals, food and medicine. Pharmaceuticals are usually classified as medicines by law.

1. Herbal remedies may be classed as medicines because of their perceived risk with selfmedication e.g.-Digitalis
2. Functional food are closely related to nutraceuticals consumed as a part of normal diet, e.g. Carotenoids
3. Vitamins are classed as medicine but are freely available

NUTRACEUTICAL AND HEALTH

1. JOINT DISEASE

Joint diseases affect people of all ages mainly the elderly. Main joint diseases are:-

Osteoarthritis- Degenerative damage and loss of the articular cartilage of the joint due to loss of protein substance between the bones of joints.

Rheumatoid Arthritis- Rheumatoid arthritis (RA) is a chronic, inflammatory disorder that may affect many an organs and tissues but principally affect joints. In this condition inflammatory synovitis produced that causes destruction of articular cartilage.

Nutraceutical use

A-Glucosamine and Chondroitin

Glucosamine is a precursor to a molecule called a glycosaminoglycan-this molecule is used in the formation and repair of cartilage.

Source-bovine or calf cartilage

Glucosamine sulphate in several European countries used as first line of treatment for arthritis. There side effects and contraindications are less but diabetics need to be careful as glucosamine might have an effect on insulin resistance. Glucosamine sulphate stimulates the production of hyaluronic acid in joint fluid. Hyaluronic acid relieves pain and improves mobility by repairing damaged cartilage. In vitro experiment of Glucosamine has shown a dose dependent increase in proteoglycan after administering it.

It is marketed usually as hydrochloride or sulfate salt. Both compounds have anti inflammatory effects. Combination of Glucosamine and Chondroitin are available.

Chondroitin is the most abundant glycosaminoglycan in cartilage and is responsible for the resiliency of cartilage.

B -Methylsulfonyl Methane

Methylsulfonyl Methane (MSM) is sold as nutritional and dietary supplement often used in combination with glucosamine and Chondroitin for helping to treat or prevent. MSM is the oxidized form of dimethyl sulfoxide; a natural organic form of sulfur. Both this compound used for pain and inflammation. MSM has advantage over DMSO as it is odourless and does not cause skin irritation. MSM provide source of sulfur for the formation of the cartilage matrix or the antioxidant system.

2. CARDIOVASCULAR DISEASE

Cardiovascular disease, affect the heart and circulatory system. In cardiac heart disease, atherosclerotic plaques form on the inner surface of arteries, which narrow the lumen and reduced the blood flow. There are many Nutraceutical which are beneficial in the prevention or symptom reduction of CHD. For example - soy protein, isoflavonoid and flax lignan.

A-Black and Green Tea

Tea contains catechin derivative, amino acid theanine (shown reduced in blood pressure in hypertensive rats. Black and green tea both show equal activity in total plasma antioxidant status after single dose. But some study show green tea to be more effective than black. Tea polyphenols have anti-inflammatory, antithrombotic and antiplatelet properties and effective in lowering risk of developing CHD and MI.

C-Flaxseed and Fish Oil

is also very beneficial in cardiovascular heart disease. Flax seed contain lignans and fiber which involve in cardiac protection.

BIOTECHNOLOGY ON PLANT NUTRITION FOR HUMAN HEALTH

Biotechnology is the technique utilizing various living organisms to produce desired products or to carry out tasks for purposes of human being. The oldest biotechnology may be fermentation of microorganisms to make breads and soups. The new technology can use genetically modified organisms, such as transgenic plants or engineered bacteria, to benefit human beings. Now, scientists are using genetic or metabolic engineering to increase crop yields and certain nutrients (like vitamins, minerals, and essential amino acids or fatty acids) and medicinal compounds, or even produce vaccines, antibodies, or medicines that are traditionally generated by animals or human body. Many current biotechnologies applied in agriculture, food science, and medicine, are focused on human health. After decades of development, biotechnology has created a number of results such as various new cultivars either by traditional crossing or transgenic breeding. Super-rice that exhibits high yields has been invented by Chinese scientists, Golden Rice with high levels of the pro-vitamin A carotenoid, beta-carotene, was invented by Swiss and German scientists, and many other crops have been invented with improved agricultural traits such as drought-, salt-, insect-, or disease-resistance, that have also significantly improved yields of many crops. Dietary nutrient deficiencies, e.g., lack of vitamin A, I, Fe or Zn, are a major source of morbidity (increased susceptibility to disease) and mortality worldwide. These deficiencies especially affect children by impairing their immune systems and normal development and causing disease and ultimately death.

The best way to avoid micronutrient deficiencies is dietary supplements or diets rich in vegetables, fruits and animal products. Another approach is eating more nutrient enhanced staple foods, such as sweet potatoes or Golden Rice, which are rich sources of pro-vitamin A.

ENGINEERING PLANTS FOR IMPROVED NUTRITIONAL VALUE

Currently, due to the lack of enough knowledge about usage, outcome, and safety of many nutraceuticals, phytonutrients, as well as their corresponding therapies, many efforts have been put on these studied. However, from many aspects of nutritional value including quality and quantity, our food pantries is very limited in supplying adequate nutrients for

human being, as indicated by an investigation. Therefore, how to produce the nutritional products in plant foods is becoming a major issue. Increasing contents and qualities of many desired nutrients in plant foods is a huge metabolic engineering project. Manipulation of biosynthetic or metabolic pathways and overproduction of nutrients such as vitamins, minerals, long-chain polyunsaturated fatty acids, and other phytonutrients including flavonoid, terpenoid, and alkaloid in crops or medicinal plants have made a number of successes. These engineered crops have been one of the most expected breakthroughs in plant biotechnology.

VITAMINS

There is much information about the essential roles of various vitamins in maintaining normal metabolism and health status. Deficiency of any kind of vitamins can cause distinguishable clinical symptoms. Scientific knowledge about vitamin metabolism and functions are well accumulated. Therefore, most nutraceutical or nutritional therapy products contain some vitamins, such as common vitamins like vitamin A, vitamin Bs, vitamin C, vitamin D, and vitamin E. A large portion of vitamin sources for human beings is from plant foods, plant biotechnology thus has been used for improvement of contents of vitamins in crops. An excellent example is "Golden Rice", a transgenic rice with a high level of the pro-vitamin A b-carotenoid in its grains. Currently, absorption studies with Golden rice are being carried out with humans, to test the efficiency of absorption and conversion of beta-carotene into vitamin A. Overproduction of b-carotenoid has also achieved in other crops. Vitamin B is most water soluble enzyme cofactors, playing essential roles in numerous physiological and cellular processes. Plant foods provide a major portion of vitamin Bs for humans. Engineering vitamin Bs production in plants and microorganisms have been studied. Yet due to diverse and complex structures and biosynthetic pathways, success on it is still limited. For example, cobalamin (Vitamin B12) belongs to the same class of compounds as heme and chlorophyll with a complicated structure. Its biosynthesis that may require around 30 enzymes remains one of most enigmatic and exigent metabolic pathways in nature. Biotin (Vitamin H) biosynthetic pathway is not clear yet. A genetic engineered tomato lines could increased their folate content by up to 10-fold compared with control, suggesting a great promise in application. The dairy starter bacterium *Lactococcus lactis* has the potential to synthesize both folate (vitamin B11) and riboflavin (vitamin B2). The engineered *Lactococcus lactis* strains produce more riboflavin or folate. Vitamin C is essential to prevent disease associated with connective tissue and to

improve cardiovascular and immune cell functions, and it is also used to regenerate vitamin E. In contrast to most animals, humans cannot synthesize ascorbic acid. Vitamin C, therefore, must be obtained from dietary sources. With increased understanding of vitamin C biosynthetic pathway, metabolism, and regulations, transgenic vegetables with improved vitamin C level have been generated. Vitamin C levels also can be increased through strategies to change the recycling of vitamin C in plants. A genetically engineered maize line with Vitamin C biosynthetic gene successfully increased vitamin C level by up to 100-fold. Tocopherols and tocotrienols, known as vitamin E, are important lipophilic antioxidants for animals and humans. Vitamin E has been touted as a panacea for age-related diseases, including cardiovascular disease and Alzheimer's disease and, thus, the demand for this nutraceutical has increased dramatically in recent years. Different strategies to engineer the vitamin E content in photosynthetic bacteria and plants have been reported. Metabolic engineering of vitamin E production in important crops such as soybean seeds is under going. Transgenic expression of the barley HGGT (homogentisic acid geranylgeranyl transferase) in *Arabidopsis thaliana* leaves resulted in a 10- to 15-fold increase in total vitamin E antioxidants (tocotrienols plus tocopherols). Overexpression of the barley HGGT in corn seeds resulted in an increase in as much as 6-fold increase in tocotrienol and tocopherol content. Expectations using these metabolic engineered plant foods could be realized in near future. These vitamin-overproducing crops, such as soybean and barley, not only increase nutritional value of foods, but also can make such foods as good medicines served for vitamin-deficient people.

MINERALS

Ca, I, Zn, Fe, Mn, Mg, and other mineral elements are essential components for human health. Deficiency of any one of these minerals may cause serious health problems. Dietary Ca, Zn, Fe, and other minerals are taken from both meats and plant foods. Due to various reasons, mineral deficiencies, mainly Ca, Zn, and Fe deficiencies, are the major health problems in developing countries, particularly for infants and children. Zn or Fe deficiency causes poor growth, impaired immune function, and delayed mental development. Although numerous mineral supplements or mineral-containing nutraceuticals are available on the market, poor absorption of Ca, Zn, and Fe by the humans significantly limits effectiveness of these supplements. Many reasons, such as dietary habits, lipids and vitamin cofactors, or mineral-mineral interactions during absorption, as well as health status of individual, can influence their absorption.

Nevertheless, increasing dietary Ca, Fe, and Zn in plant foods is an important strategy to enhance mineral nutrition. Therefore, it is important to know mechanisms by which plants take up these ions and accumulate in plant cells in the bio-available forms rather than precipitated salts or crystals. Oxalate or phytate forms of Ca, Zn, or Fe could dramatically decrease the bioavailability of dietary minerals and inhibit the absorption of these minerals by humans. Using biotechnology to modify crops or vegetable plants to decrease oxalate or phytate levels (or completely remove them) could increase the availability and absorption of these minerals.

FLAVONOIDS

As multiple benefits of eating flavonoid-rich plant foods for human health are well documented, increasing particular bioactive flavonoid species in plant foods has become of great interest. Genetically modified tomatoes contain high levels of flavonols such as quercetin, kaempferol, and glycosides and flavones such as luteolin, lycopene and luteolin-7-glucoside in their peel tissue, resveratrol level in *Brassica napus* seed has also dramatically increased. Consumption of these transgenic tomatoes has been shown to yield certain health benefits in mice. On the other hand, flavonoids are highly consumed bioactive phytonutrients that are taken daily in large amounts by humans. Most flavonoids from flavonoid-rich foods are extensively metabolized by human body, which can affect their antioxidant capacity. Flavonoids are absorbed from the gastrointestinal tracts of humans and animals and excreted either unchanged or as flavonoid metabolites in the urine and feces. It is assumed that the large increase in plasma total antioxidant capacity observed after the consumption of flavonoid-rich foods may not be caused by the flavonoids themselves, but likely by the increased levels of uric acid. In addition to flavonoids, fruits and vegetables contain many macro- and micronutrients that may directly or indirectly affect their absorption, activity, and metabolism. Absorption and metabolism of most plant secondary metabolites can occur either inside the gut (such as by microorganisms) or inside liver cells by P450 enzymes.

TERPENOIDS

Terpenoids are the most diverse and largest class of plant natural products with wide industrial application, as provitamin A, vitamin E, flavors, pharmaceuticals, perfumes, insecticides, and anti-microbial agents. Metabolic engineering of terpenoids in plants has proven to be a fascinating effort. Monoterpenes are major flavors used by humans. Peppermint oil is a popular flavoring agent or fragrance component in cosmetics and food products. Engineering peppermint

oil production in transgenic peppermint plants with improved productivity has been achieved. Coenzyme Q is an electron transfer terpenoid in the respiratory chain. It is a lipid-soluble antioxidant and is a very popular food supplement. Recently, genetic engineering of the coenzyme Q production in plants has been tried. Other valuable terpenoid compounds that have been modified include the introduction of β -carotene to tomato fruits and rice and zeaxanthin to potato tubers. Tomato is a major food crop and the principal source of the carotenoid lycopene. Epidemiological studies have clearly shown the great benefits of consumption of tomato to human health due to tomato carotenoids, mainly lycopene, β -carotene, and lutein [203,204]. Tomato carotenoid levels have thus become important nutritional quality parameters and agricultural traits [204]. Metabolic engineering tomato carotenoids have been extensively studied and some achievements have been made. Related patents including methods of terpenoids for disease treatment, transgenic plants with increased pro-Vitamin A (Golden Rice) and Vitamin E.

CONCLUSION

Nutraceuticals are currently receiving recognition as being beneficial in coronary heart disease, obesity, diabetes, cancer, osteoporosis and other chronic and degenerative diseases such as Parkinson's and Alzheimer's diseases. Evidences indicate that the mechanistic actions of natural compounds involve a wide array of biological processes, including activation of antioxidant defenses, signal transduction pathways, cell survival-associated gene expression, cell proliferation and differentiation and preservation of mitochondrial integrity. It appears that these properties play a crucial role in the protection against the pathologies of numerous age-related or chronic diseases. It is very imperative that the nutrients found in many foods, fruits and vegetables are responsible for the well-documented health benefits. For example, lutein and zeaxanthin prevent cataracts and macular degeneration; β -carotene and lycopene protect the skin from ultraviolet radiation damage; lutein and lycopene may benefit cardiovascular health, and lycopene may help prevent prostate cancer. Because of these and other marked health benefits of these, it must be taken regularly and to reduce the risk factors like high cholesterol, high blood pressure and diabetes. Some of the most popular nutraceutical products marketed today are botanicals such as St. John's wort, echinacea, ginkgo biloba, saw palmetto, and ginseng. Many industries manufacture and market the nutraceuticals, where the side effects (especially consumed in large quantities) of these nutraceuticals not reported or often unproven. In order to have

scientific knowledge about the nutraceuticals, publics should be educated, where recommended daily doses of these nutraceuticals should be known by each consumer. With the rapidly increasing interest in the nutraceutical revolution, we need to establish a vibrant nutraceutical research community which is absolutely necessary to convert the majority of potential nutraceuticals to established ones thereby truly delivering their enormous benefits to all of us. The list of nutraceuticals being studied is changing continually and reflects ongoing research, market developments and consumer interest.

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Table 1- Nutraceutical used in various diseases

Disease	Nutraceuticals
Eye health	Lutein and Zeaxanthin
Mental health	Phosphatidylserine Docosahexaenoic Soy isoflavones
Sleep enhancement	Melatonin
Cancer prevention	Tea, Lycopene, flaxseed, coenzyme Q10
Bone health	Melatonin, L-carnitine
Skin health	Tea, soy isoflavones, coenzyme Q10, Glucosamine, melatonin
Oral health	Pycnogenol, coenzyme Q10