Nutraceuticals, Nutritional Therapy, Phytonutrients, and Phytotherapy for Improvement of Human Health: A Perspective on Plant Biotechnology Application

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Abstract: 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.

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

INTRODUCTION

Obtaining adequate nutrients from various foods plays a vital role in maintaining normal function of the human body. With recent advances in medical and nutrition sciences, natural products and health-promoting foods have received extensive attention from both health professionals and the common population. New concepts have appeared with this trend, such as nutraceuticals, nutritional therapy, phytonutrients, and phytotherapy [1-3]. These functional or medicinal foods and phytonutrients or phytomedicines play positive roles in maintaining well being, enhancing health, and modulating immune function to prevent specific diseases. They also hold great promise in clinical therapy due to their potential to reduce side effects associated with chemotherapy or radiotherapy and significant advantages in reducing the health care cost [4]. The original idea in these concepts goes back three thousand years ago. Hippocrates (460–377 BC), the well-recognized father of modern medicine, stated "Let food be thy medicine and medicine be thy food" to predict the relationship between appropriate foods for health and their therapeutic benefits [3]. The truth in this saying is widely recognized today.

Since the start of the industrial age, lifestyles of human beings have dramatically changed. Increasing work and living speed, longer work schedules, and various psychological pressures have pushed people into various fast-eating cultures with more instant and tasty meals, but decreased quantity and quality in nutrients. At the same time, industrialization has caused numerous air and water pollutions, and soil and food contamination because of extensive use of various chemicals, heavy metals, electromagnetic waves, and other potentially harmful man-made items. These problems have led to an increased incidence of diabetes, obesity, various cancers and vascular diseases, physiological problems, as well as other degenerative diseases. The raised demands for health care have dramatically increased the cost of medical care. Now, more and more people realize that a healthy body is more important than money or work in their lives. Therefore, people have tried to achieve a better quality of life by eating more vegetables, fruits, and other plant foods, taking dietary supplements or nutraceuticals, or using nutritional therapy or phytotherapy to replace chemotherapy or radiotherapy [3, 5, 6].

In this background, with increasing demands for nutraceuticals, phytonutrients and their therapeutic services, manufacturers, marketers, and related licensed professionals have grown up accordingly. Scientific studies also have expanded to these areas and have given supports to many of these products and therapeutic services. Furthermore, plant biotechnologists have put lots of effort to engineer plants and crops in order to improve their nutritional value. There are already many plant biotechnological products, which are patented in an increasing number and diversity. This review attempts to summarize the recent progress on these new health care concepts, as well as the marketing and regulations about nutraceuticals, nutritional therapy, phytonutrients, and phytotherapy. Epidemiological studies or

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clinical trials on these nutritional products and therapeutic practices are included. Particularly, some pending or issued patents on plant biotechnology for improving nutritional value of plant foods or phytonutrients are highlighted.

NUTRACEUTICALS

The term "Nutraceutical" combined from "Nutrition" and "Pharmaceutical" in 1989 by Dr. Stephen DeFelice, is defined as food or part of a food that provides medical or health benefits [7]. Nutraceuticals also refer to natural functional/medical foods or bioactive phytochemicals that have health promoting, disease preventing or medicinal properties. These nutraceuticals normally contain the required amount of vitamins, lipids, proteins, carbohydrates, minerals, or other necessary nutrients, depending on their emphases [8, 9]. The concepts of nutraceuticals, functional or medical foods, or dietary supplements are confusing and most often they can be used interchangeably. These concepts may be distinguished by their description from different points of view, e.g. functional food is a more general term to emphasize foods with specific or strong purposes [3,10]; Dietary supplements have more defined health roles such as vitamins, minerals, herbs or other botanicals, amino acids, and other dietary substances intended to supplement the diet by increasing the total dietary intake of these ingredients [11]. Dietary supplements are not intended to treat or cure disease [12], whereas nutraceuticals more emphasize the expected results of these products, such as prevention or treatment of diseases [3, 8].

Various nutraceuticals are used in nutritional therapy, which is mainly based on scientific research and with more clear information about chemical structures, biological functions, clinical information, and quality control [13]. Although most nutraceuticals currently used are known vital nutrients for the human body, many details such as dose, drug-drug interaction, nutraceutical-drug interaction, and their effects on individuals under certain health conditions remain elusive [9]. It is normally assumed that keeping proper nutrient balance is required to maintain a healthy status of the human body, and that excess intake of any nutrient may not benefit or even can be harmful to health. Increasing knowledge from food chemistry, nutritional, and clinical studies is providing more insight into our understanding of biological functions, usage, and potential adverse effects of nutraceuticals [8,9]. This advanced knowledge could also help to standardize manufacturing processes and clinical practices and at the same time could add more value to nutraceutical markets [14]. Some selected patents on nutraceuticals are listed in Table **1** with corresponding therapy methods in patents [15-53].

NUTRITIONAL THERAPY

Nutritional therapy is a healing system using dietary therapeutics or nutraceuticals as a complementary therapy. This therapy is based on the belief that foods can not only be sources of nutrients and energy but could also provide medicinal benefits. In other words, foods can be medicine if they were properly prepared. Both a long folk history of foods, along with modern scientific research, continue to extend the idea about functional foods or nutraceuticals. Nutritional therapy mainly uses functional food, nutraceuticals, and dietary supplements to promote the body's natural healing based on knowledge from food sciences, clinical nutrition studies, and epidemiological studies [54]. According to nutraceutical and nutritional therapy theory, it achieves this goal by using efficacy of such nutraceuticals in detoxifying the body, avoiding vitamin and mineral deficiencies, and restoring healthy digestion and dietary habit. Although many health problems require specific medications, many other conditions such as some degenerative and chronic diseases can be relieved alternatively with nutritional therapy. These disorders may range from chronic fatigue, energy loss, insomnia, and osteoarthritis, to backache, skin complaints, and asthma [2]. A comprehensive nutritional therapy always tries to employ as many health-affecting factors as possible to improve the overall health conditions of an individual. It depends not only on balanced dietary nutrients, but also enough exposure to sunlight, fresh air, pure water, proper exercise and rest, emotion and self-control, to build up a healthy human immunity. The immune system is a basic and essential part of the disease-defense system. Even in clinical settings, nutritional therapy gets more and more attention in helping recovery of various kinds of patients [54]

PHYTONUTRIENTS

The term phytonutrients refer to plant nutrients with particular biological activities in supporting human health. This concept not only covers the human foods derived from agricultural products, but mainly refers to phytonutrients which act as modifiers of physiological function [1]. As compared with the concepts such as functional foods, dietary supplements, and nutraceuticals, phytonutrients emphasize more specifically natural bioactive compounds from plants with general benefits to human health, which become closer to or even overlap with phytomedicines. The wide use of phytonutrients reflects a fact that nutrition science has advanced beyond the treatment of deficiency syndromes to reduce disease risk. Food nutrients are no longer evaluated only in terms of macronutrient and micronutrient levels. Contents of some biologically active compounds are becoming more important.

Almost every nation has traditional folk medicines or folk remediation with medicinal plants [1]. Plants as natural medicines to benefit humans have a long history, particularly in some nations such as China, India, Egypt, and Greece. Thousands of years of using plants have accumulated numerous information and experiences in different nations worldwide about use of medicinal plants and their functions or toxicities [55]. The secondary metabolites of plants provide humans with numerous biologically active products, which have been used extensively as food additives, flavors, colors, insecticides, drugs, fragrances, and other fine chemicals. These plant secondary metabolites include several classes such as terpenoids, flavonoids, and alkaloids, have diverse chemical structures and biological activities, and exist widely in different crops such as rice, wheat, maize, and soybean. Therefore, these natural compounds as dietary components have considerable impact on human health. Plant foods rich in dietary fiber have well-addressed benefits to people, such as improving digestive system health,

Table 1. Patents for Nutraceuticals

Authors	Patents No.	Titles and main achievement
Shyur LF, Yang NS, Kang PL, Sun SJ, Wang SY	US7033617	Use of *Anoectochilus formosanus* plant extracts and their derived fractions as herbal medicines or nutraceutical supplements for chemoprevention or treatment of human malignancies
Fan W, Bohlmann JA, Trinkle JR, Steinke JD, Hwang KO, Henning JP	*US7049433	Glucosamine and method of making glucosamine from microbial biomass
Falco SC, Cahoon RE, Hitz WD, Kinney AJ, Rafalski JA	US6451581	Plant branched-chain amino acid biosynthetic enzymes
Udell RG	US20060003947A1	Soft gel capsules containing polymethoxylated flavones and palm oil tocotrienols
Wolfram S, Loon van LJC	*WO06077202A1 EP1633208A1	Novel nutraceutical compositions
Romero T, Miller P	WO06020091A3 WO06020091A2	Dietary supplements containing extracts of cinnamon and methods of using same to promote weight loss
Whittle B, Hart PM	WO06016170A3 WO06016170A2	Premixes, flour enriched with same, mineral supplemented foodstuff and methods of manufacture thereof
Shen BJ, Ghosh P	*AU20020112A4 WO03062279A1 JP2005519914T2 EP1476471A1 CA2474269AA ZA0406621A NZ0534760A	Nutraceuticals for the treatment, protection and restoration of connective tissues (D2)
Raju GG	*US20050282894A1 US20050282904A1	Hydroxycitric acid compositions, pharmaceutical and dietary supplements and food products made therefrom, and methods for their use in reducing body weight
Boreyko BK, Wang Y	US20050266018A1	Nutraceuutical compositions with mangosteen
Garrity AR, Morton JC, Morrison P, de la Huerga V	US20050196511A1 MX5004564A EP1562619A2	Nutraceutical mangosteen tea
Triplett DG, Weatherspoon JB, Wang PY	US20050181105A1	Producing hollow tubular fibers from legume hulls and utilizing such fibers for enhancing flavors and aromas and imparting time-release capabilities for pharmaceuticals and nutraceuticals
McGrew GN, Barkalow DG, Johnson SS, Record DW, Patel MM, Yatka RJ, Greenberg MJ, Witkewitz DL, Song JH.	*US6949264	Nutraceuticals or nutritional supplements and method of making
McKee D, Karwic A	US20060134294A1 WO06063219A2	Product and method for oral administration of nutraceuticals
Andreoni V, Benedtti A, Canzi E, Ciappellano S, Fumagalli M	WO05118776A1 EP1602716A1	Selenium-enriched biomass, method for pretreating thereof and probiotic and nutraceutical products including said biomass
Pushpangadan P, Prakash D	*US20060147561A1 US7014872	Herbal nutraceutical formulation for diabetics and process for preparing the same
Bagchi D	US20060105965A1	Method for enhancing energy levels and reducing the effects of stress using nutraceutical formulations
Gaudout D, Megard D, Inisan C, Esteve C, Lejard F	US20060073223A1 US7041322	Phloridzin-rich phenolic fraction and usethereof as a cosmetic, dietary or nutraceutical agent

(Table 1) Contd….

Authors	Patents No.	Titles and main achievement
Butters DE, Davis CKC, McGeary RP, Powanda MC, Rainsford KD, Whitehouse MW	US6761913 US6352728	Extracts of celery seed for the prevention and treatment of pain, inflammation and gastrointestinal irritation
Cravotto G	US20050234127A1	Long chain unsaturated oxygenated compounds and their use in the therapeutical, cosmetic and nutraceutical field
Matkin JR, Wang S, Li C, Huang W	US20060013842A1	Natural mixture of long-chain fatty alcohols and long-chain fatty acids, its obtension from animal and vegetable waxes and its nutraceutical uses
Watkins JM, Takaki MA	WO06069020A1 US20060134132A1	Protective barriers for micronutrients, phytochemcials, and nutraceuticals
Wahlqvist ML, Wattanapenpaiboon N	WO06053379A1	Improved nutraceutical composition
Bell SJD	WO06050368A2 WO06050368A3	Therapeutic calcium phosphate particles in use for aesthetic or cosmetic medicine, and methods of manufacture and use
Centore R, Berna M, Giovannone D	WO06048911A3 WO06048911A2	Pharmaceutical or nutraceutical compositions containing chromium or iron complexes of alpha-lipoic acid
Bagchi D, Preuss HG, Kothari SC	*****EP1438038A1 EP1438038A4	Method and composition for preventing or reducing the symptoms of insulin resistance syndromes
Mercati V	*****US20060147560A1	Pharmaceutical, nutraceutical, dietetic and nutritional compositions based on vegetable fibres
Cha A, Englenman EG	WO06002096A2 WO06002096A3	Low does of L-citrulline for treating diseases
Macfarlane G, Macfarlane S, Furrie E, Cummings J	US20060115465A1	Treatment of gastrointestinal disorders
McCleary EL	US20060110477A1	Composition and methods for supporting and promoting healthy sexual faction and prevention and treatment of sexual dysfunction
Chaung HC, Huang CS, Lee FY, Lin TC	US20060083799A1 WO06020246A1	Anti-hypersensitive inflammation and anti-allergy activities of *Zingiber zerumbet* (L) Smith
Angellotti C	EP1607096A3 EP1607096A2	Nutraceutical composition containing milk enzymes useful as synbiotic
Mukhtar H, Bhat MS	US20060062745A2 S20050201956A1	Lupeol anti-tumor agent and uses thereof
Raederstoff D, Teixeira SR, Weber P	*CN1694695A US20060165671A1 WO04041257A2 JP2006508096T2 AU3293592AH	Novel nutraceutical compositions comprising epigallocatechin gallate
Nafisi-Movaghar K, Svanoe TT, Seroy WA	*US5912363	Method for extraction of proanthocyanidins from plant material
Darland GK, Lukaczer DO, Liska DJ, Irving TA, Bland JS	US6210701	Medical food for treating inflammation-related diseases
Ghai G, Boyd C, Csiszar K, Ho CT, Rosen RT	US5955269	Methods of screening foods for nutraceuticals

(Table 1) Contd….

Authors	Patents No.	Titles and main achievement
Lukaczer DO, Darland GK, Liska DJ, Irving TA. Bland JS	US6352712	Dietary supplements for treating fatigue-related syndromes
Guthrie N, Kurowska EM, Manthey JA, Horowitz S, Horowitz RM	US6987125	Compositions and methods of treating, reducing and preventing cardiovascular diseases and disorders with polymethoxyflavones

reducing the risk of heart disease, and preventing weight gain [56]. This is another reason why eating plant foods helps to maintain overall health. Exploration of new phytonutrients and increasing useful phytonutrient levels in plants have led to many patents registered Table **2** which also include methods of phytotherapy for particular treatments [57-80].

PHYTOTHERAPY

Phytotherapy mainly refers to using medicinal plants or herbals to prevent or cure diseases or to improve health conditions. Most phytotherapies are developed from folk medicinal plants. This concept is a summary for evidence-based healing system that is practiced by people widely all over the world. Compared with nutritional therapy, phyto-therapy is more complicated because of use of many phyto-nutrients with diverse chemical structures and biological activities. Most phytotherapy strategies are ahead of the scientific basis and without strict controls in quality, safety, and efficiency [1,81]. However, phytotherapy has a long history and has been used worldwide. Some phytotherapy strategies have been well recognized since they have been extensively studied in chemistry and pharmacology and are partly proven by clinical trials [1]

Phytotherapy relies on more phytonutrients with the discovery that many plant food components can not only modify physiological function but also aid in medical practices such as drug delivery. Epidemiological studies have shown protective effects of plant-based diets on cardiovascular diseases and cancers, as well as other wide aspects of health problems such as obesity and diabetes [1, 82, 83]. In particular, a close correlation has been suggested between dietary flavonoid intake and decreased mortality from coronary heart disease, partly due to the inhibition of low density lipoprotein (LDL) oxidation and reduced platelet aggregability by flavonoids [83]. Dietary intake of flavonoids ranges between 23 mg/day estimated in The Netherlands (mainly tea, onions, apples, and red wine) and 170 mg/day estimated in the USA. The consumption of 30 to 50 mg per day of soy isoflavones in the traditional eastern diet may help lower the incidence of breast cancer [1]. Bioactive compounds normally occur in small quantities in plant foods as nutritional constituents. Biochemistry and phytochemistry studies have identified the exact bioactive compounds, such as flavonoids, alkaloids, terpenoids, phytoestrogens, and other classes of phytochemicals [84]. Some natural products with specific and strong biological activities have been developed into medicines applied to chemotherapy, such as vincristine and taxol. Almost all plant foods have specific natual products with certain bioactivity [84]. Hydroxytyrosol from olives and olive oil is a potent antioxidant. Resveratrol found in nuts and red wine has strong antioxidant, antithrombotic, anti-inflammatory, and anti-carcinogenesis activities. Lycopene from tomatoes and other fruits is a potent antioxidant carotenoid protective against prostate and other cancers and inhibiting tumor cell growth in animals. Organosulfur compounds in garlic and onions even have more multifunctional benefits to human health. Isothiocyanates in cruciferous vegetables, and monoterpenes in citrus fruits, cherries, and herbs have anticarcinogenic actions in experimental models, as well as cardioprotective effects. Naringenin (4´,5´,7-hydroxy-flavanone) found in grapefruit can slow hepatic detoxi-fication of prescription drugs like cyclosporine and thus potentially help prevent rejection of transplanted organs [1]. All these examples are just a small portion of science-based phytonutrient and nutritional therapy recommendations. Many other plants, not used as foods, are now being studied for their potential as phytonutrients or phytotherapy mate-rials. Cruciferous vegetables such as cabbage, cauliflower, and broccoli possess unique phytochemicals able to modify the metabolism of estrogen. Supplemental use of such phytochemicals as dietary indole diindolylmethane from these vegetables provides nutritional support to enhance the beneficial action and safety of estrogen. Various phyto-estrogens act both as antioxidants, estrogen agonists and antagonists with multiple effects on anticancer benefiting [82]. An optimal "estrogen balance" has implications for cancer prevention and successful aging in both women and men. The Federal Food and Drug Administration (FDA) seldom makes recommendations for nutraceuticals or phytonutrients. But in 2001, FDA approved the claim that soluble fiber from foods such as oat may reduce cholesterol and the risk of heart disease. Dietary fiber nutraceutical has been showed to reduce cholesterol level and maintain weight, therefore has promising benefits to obesity and diabete patients [56].

MARKETS

Synthetic drugs and pharmaceuticals based on extensive safety, efficacy, mechanistic and clinical studies have significantly contributed to improvement of overall human health. However, a large number of these drugs have been withdrawn from the marketplace due to various toxicities and other adverse effects [3]. Now people are greatly concerned about how their health care is managed and priced. More and more people are frustrated with expensive high-tech generated modern medicines with potential harmful side-effects. The unaffordable medicines, increased

Table 2. Patents for Phytonutrients and Phytotherapy

Authors	Patents No.	Titles and main achievement
Moady N, Moady M	USRE39199	Antipsoriatic compositions, method of making, and method of using
Pushpangadan P, Rawat AKS, Rao CV, Srivastava SK, Kharton S	US20060141069A1	Synergistic antipyretic formulation
Drieu K, Papadopoulos V	US7078434	Use of ginkgo extract
Kreuter MH, Wagner HKM, Tittel G	US7074436	Method for the production of Phyllanthus extracts
Jones BC	US7060303	Use of purslane to treat facial wrinkles
VailIII WB anning, Vail ML	US7048953	Methods and apparatus to prevent, treat and cure infections of the human respiratory system by pathogens causing severe acute respiratory syndrome (SARS)
Thornton SP, Troyer E	US7029712	Treatment for dry eye syndrome
Romancyzk Jr Leo J, Basak A, Townsend CA	US7015338	Synthetic methods for preparing procyanidin oligomers
Lin CH, Chuang HS	*US7015248	Use of abietic acid and derivatives thereof for inhibiting cancer
Trant AS	US6989164	Method and composition for improving male fertility health
Aleksandrovna KD, Gennad'evna AS, Viktorovna GA, Glebovich PV, Nikolaevnapt, Leonidovna ZK, Viktorovna NJ	RU2276607C2	Agent for treatment of stomach ulcerous disease of stress genesis
Franchesko DP	*RU2274470C2; WO03013561A1; US20050008711A1; JP2005511494T2; EP1414473B1	Oral compositions for treatment disorders in head skin hair part
Valentinovich NS, Anatol'evich LV, Dmitrievna SN, Vladimirovich KT	RU2274469C2	Medicinal preparation "vita-plant"
Cherukuri RSV, Cherukuri RC, Cherukuri A, Natarajan K	*US20060083700A1	Use of a novel phytonutrient rich bioactive concentrate (Ri-ActiveTM) for the prevention and treatment of cardiovascular disease, diabetes and other health disorders.
Alekseevna PE	RU2271215C1	Method for detoxification and rejuvenation of body
Tonikovich OE, Jur'evich PA, Andreevna AO, Grigor'evna DE, Sergeevnaaz, Olegovna PE	*RU2270686C2	Method for preparing hepatoprotective and hypocholesterolemic agent
Kaloeva TV, Kaloeva AM	RU2266127C2	Method for preparing ointment for erysipelas treatment
Agarval RK, Agarval A	RU2264224C2	Improved vegetable composition possessing anti-allergic property and method for its preparing
Mikhaljlova TM, Tankhaeva LM, Sambueva ZG, Olennikov DN, Tsyrenzhapov AV, Nikolaeva GG, Nikolaeva SM, Bodoev NV	RU2264211C1	Method for preparing 1-hydroxy-2,3,5-trimethoxyxanthone possessing cholagogic and hepatoprotective action
VUTKE VG, Jarri K, Kristoffel V, SHPENGLER B, POP M.	RU2263505C2	Using belamcanda chinensis extract as estrogen-like organ-selective medicinal preparation without uterotropic effect
Theuer RC	US6051235	Ginger-containing baby-food preparation and methods therefor
Feldmann M, Malfait AM, Gallily R, Mechoulam R	US6410588	Use of cannabinoids as anti-inflammatory agents
Wakabayashi K, Moriyama H	*US6562793	Antiallergic agent
Paiva NL, Hipskind JD	*US6974895	Transgenic legume plants modified to produce resveratrol glucoside and uses thereof

clinical expense, failures of modern medicines on many important diseases, as well as more and more effective nutritional therapies available have expanded the nutraceuticals market. Nutraceuticals and nutritional therapy have emerged from the food and drug industry and the phytonutrient and dietary supplement market, and have become complementary ways to promote human well being. Generally, the use of nutritional therapy, nutraceuticals, and phytotherapy results from several reasons including (1) high-priced modern medicines with limited success on many degenerative diseases, such as osteoarthritis, which have driven people to look for alternatives to modern drugs with potential harmful side effects; (2) evidence-based phytotherapy in many nations is still very popular, and more customers begin to try nutritional supplements to prevent illness. (3) growing knowledge from nutritional research and pharmacological or epidemiological studies have suggested a close relationship between nutritional therapy or nutraceutical intake and the promotion of health conditions.

In addition, the expansion of markets for nutraceuticals, nutritional therapy, and phytotherapy have also been due to the relatively loose regulations on the marketing of these products or the practicing of these therapies [11,6,85]. In the United States, FDA established very detailed laws about drugs and foods to regulate pharmaceutical and food manufacturing, marketing and clinical practices and activities. However, there is still no clear regulation on food supplementation, nutraceuticals, or phytotherapy [12]. The Federal Food, Drug, and Cosmetic Act does not provide a statutory definition of functional foods, and FDA thus has no authority to establish a formal food in conventional form as a nutraceutical, dietary supplement, or a medicinal food [12,86]. Although many governments have started to establish more complete and restrictive regulations on the market, this situation potentially has allowed companies and nutritional professionals to pursue large and potential profits from nutritional and phytotherapy markets. Over 158 million Americans regularly consume dietary supplements to maintain and/or improve their health. Dietary supplements (alone) reached a reported $20.5 billion in sales in 2004. The market for functional foods reached a reported $24.5 billion in 2004 in the United States. The global markets for dietary supplements and functional foods reported $63.3 billion and $71.9 billion in sales, respectively, in 2004 [3]. With the increasing markets, the team of nutrition professionals is also expanding to provide services on nutrition therapy or nutrition practice for health promotion or disease treatment. In the United States, two kinds of nutrition professionals, nutritionists and dietitians, are recognized by the government. Many registered dietitians practice medical nutrition therapy, which requires their advanced knowledge and skilled treatments. Many registered nutritional therapists declare importance and special success of nutritional therapy, and they try hard to demonstrate the beneficial role of health foods, nutraceuticals, nutritional therapy in health promotion, disease prevention and treatment. Their activities directly led to rapid growth of functional foods, nutraceuticals, and nutritional therapy or phytotherapy markets in the United States and worldwide. The preference for the discovery and production of new nutraceuticals over pharmaceuticals is well seen in pharmaceutical and biotechnology companies [4,13]. Some pharmaceutical and biotechnology companies commit major resources to the discovery of nutraceuticals.

REGULATIONS

The governmental administration of food and drugs in many countries such as the United States of America (http://www.cfsan.fda.gov/list.html), Canada (http://www.hc-sc.gc.ca/index_e.html), European Union (http://www.emea.eu.int), China (http://www.sfda.gov.cn/cmsweb/web portal), and India (http://mohfw.nic.in/), have strict regulations on food and drugs in terms of manufacturing, servicing, and marketing, and usage [3,8,86]. But not all has a complete regulation on nutraceuticals and phytonutrients as well as their therapies. Many countries are making corresponding laws, or complementary regulations, or addressing issues with new explanations [87-89]. The legislation for the marketing of functional foods in the European Union (EU) was in legislative process [88]. Particularly, the safety-basis of nutritional or phytotherapy products are based on risk analysis. In Europe, scientific risk assessment is performed by the European Food Safety Authority and risk management is performed by the European Commission. Canadian government provides some guidelines for evidence-based clinical practice of clinical nutrition support, enteral or parenteral nutrition for ill adults [90].

The more detailed regulations on nutraceuticals, phytonutriton or phytotherapy, or nutritional therapy are being worked out through consultations with expert panels who can provide descriptions of regulatory hurdles for these products and practices, Good Manufacturing Practice (GMP) compliance, Generally recognized as safe (GRAS) status, analytical methods and validation [3,8,86]. For instance, a workshop on "Natureceuticals, Nutraceuticals, Herbal Botanicals, Psychoactives: Drug Discovery and Drug-Drug Interactions" was held recently to discuss several of these topics [91]. Various government-supported projects study on improvement of nutritional professional services for the public. For example, studies indicated that dietitians' ability to incorporate an evidence-based approach is largely determined by their education and training, work experience, and professional association involvement [92]. Therefore, advanced education and training is important for dietitians to participate in nutritional services, contribute to knowledge discovery, translation, and outreach to improve the nutritional status and health of populations [93]. In addition, databases for nutraceuticals, phytonutrients, or nutritional therapy or phytotherapy have also grown and are available to serve the public [94-97].

CLINICAL STUDY ON NUTRITIONAL THERAPY

Many clinical trials have been carried out to investigate nutritional supplementation (therapy) on various health problems. An oral nutritional supplementation (a complete nutritional supplement with 223 subjects) for older acutely ill patients showed improved nutritional status and led to a statistically significant reduction in the number of non-elective readmissions [98]. One small-scale study showed that enteral nutritional supplementation is effective in improving nutritional intake and status in stroke patients who do not have swallowing difficulties [99].

Clinical trials on treatment of severe chronic hepatitis and posthepatic cirrhosis with nutritional support has been carried out [100]. Results show that nutritional support treatment could obviously improve the nutritional status of these patients, and was helpful to ameliorate the liver function of the patients with severe chronic hepatitis. A preliminary clinical trial on effectiveness of a combined therapy with vitamin B12, folate, erythropoietin, and orally and intravenously administered iron on premature infants suggests that this combined therapy is more effective in stimulating erythropoiesis than each single treatment [101]. There is enough evidence to prove that an appropriate nutritional contribution is related to less morbidity and mortality. A recent clinical trial has shown the effectiveness of enteral supplement with glutamine, arginine, and omega-3 fatty acid on acute severe pancreatitis [102].

Using osteoarthritis as an example, it can be demonstrated how nutraceuticals work and conflicts occur between nutraceuticals and pharmaceuticals. Osteoarthritis is a very common degenerative and chronic disease. Causes and mechanisms for this disease are very diverse and complicated, and there is no specific and effective medicine for osteoarthritis. On the other hand, many successful examples can be found about excellent effects of nutraceuticals on this disease, with broad acceptance by patients. Nutritional factors can be expected to exert favorable influences on pathophysiological processes in osteoarthritis. Such processes include oxidative damage, cartilage matrix degradation and repair, and chondrocyte function and responses in adjacent bone. Micronutrients for which preliminary evidence of benefit exist include vitamin C and vitamin D. In addition, numerous nutraceuticals that may influence osteoarthritis pathophysiology–including glucosamine, chondroitin, S-adenosylmethionine, ginger and avocado/soybean unsaponifiables have been tested in clinical trials (for review and references therein, see [103]). Although many clinical trials show very significant effects of glucosamine, chondroitin sulfate, and collagen hydrolysate on relieving osteoarthritic symptoms, studies in the United States also have revealed that a number of preparations contain significantly lowere dosages than what is claimed for the included nutritional components (normally glucosamine, 1500 mg, and chondroitin sulfate, 1200 mg, daily) [104]. Therefore, dietary supplementation and nutraceuticals used in conjunction with non-steroidal, anti-inflammatory drugs may benefit patients with these joint disorders. Goggs *et al*. [105] and Ameye *et al*. [106] systematically examined many human clinical trials that evaluated the effects of nutritional compounds on osteoarthritis. Among all reports about randomized human clinical trials in osteoarthritis that investigated the effects of oral interventions with glucosamine and chondroitin sulfate on osteoarthritis [104], good evidence was found for avocado soybean unsaponifiables; moderate evidence was found for methylsulfonylmethane and SKI306X, a cocktail of plant extracts. Limited evidence was found for the Chinese plant extract Duhuo Jisheng Wan, cetyl myristoleate, lipids from green-lipped mussels and plant extracts from *Harpagophytum procumbens*. Therefore, it is concluded that scientific evidence exists for some specific nutritional interventions to provide symptom relief to osteoarthritic patients [104]. Even with wide acceptance of nutritional therapy by osteoarthritis patients, these nutraceuticals are not FDA-evaluated or recommended for the treatment of osteoarthritis. The scientific and medical community remains skeptical about the effects of nutrition for osteoarthritis. They are only available as health food supplements due to the number of studies on toxicity, particularly with respect to long-term evaluations on such therapy is still limited [104]. Such safety reasons affecting the use of these nutraceuticals have driven more scientific studies on it.

Strong evidence shows that early enteral feeding of patients with nutritional therapy reagents prevents infections in a variety of traumatic and surgical illnesses. Dietary supplementation with glutamine appears to lower the risk of post-surgical infections and the ingestion of cranberry products has value in preventing urinary tract infections in women [107]. Investigations suggest that the use of dietary supplements (vitamins, minerals, and nutraceuticals) as one of many healthy behaviors can generally enhance one's health status, such as lowering cardiovascular risk [108]. In support of enteral feedings for patients admitted to intensive care units, a medical nutrition therapy protocol was proposed on the basis of clinical outcomes from clinical practices to enteral feeding of critically ill patients [109].

CLINICAL STUDY ON PHYTOTHERAPY

It is well known that health benefits are associated with diets containing different bioactive phytochemicals or nutraceutical compounds [1]. For example, consumption of a large amount of grapes and its products such as wine have contributed to the low risk of chronic diseases, such as coronary heart disease and certain cancers [110]. The increasing knowledge about polyphenols such as stilbenes and anthocyanins, and condensed tannins such as proanthocyanidins, dietary indoleamines like melatonin and serotonin from grape and wine and their biological effects further support the health benefits of consumption of grape and their products due to their bioactive chemical diversity [110]. OPC (oligomeric proanthocyanidins) is a combination of plant derived bioflavonoids. OPC is patented by Professor Jacques Masquelier of the University of Bordeaux (France). It is made from a combination of grape seed, pine bark and red wine extracts in addition to bilberry and citrus extracts. OPC has been marketed for many years in Europe and USA as a nutraceutical or phytotherapy product with strong antioxidant and anti-aging agents. Oxidative stress-caused lipid peroxidation can be involved in the etiology of atherosclerosis, cardiovascular diseases, and cancer. The soy isoflavone phytoestrogens, genistein and daidzein, and a daidzein metabolite equol produced by intestinal microflora have potent antioxidant activity. Particularly, equol is an inhibitor of low density lipoprotein (LDLs) oxidation taking place in the arterial intima. Therefore, intake of soy-derived antioxidants provides protection against oxidative modification of LDL, and helps to reduce the risk of atherosclerosis, cardiovascular disease, and cancer [111,112]. Also, soy isoflavones are thought to be cardioprotective due to their structural similarity to estrogen. A randomized, double-blind, placebo-controlled, cross-over study with thirty healthy postmenopausal women indicated that 8 weeks consumption of cereal bars enriched with 50 mg soy

isoflavones/d increased plasma nitrite and nitrate concentrations and improved endothelium-independent vasodilation in healthy postmenopausal women [113]. There are continuously increasing numbers of breast cancer patients in Western societies, relative to Asian countries. Investigations suggest that the likely contributory factor to this difference may be that Asian women take a vegetarian diet with higher intake of legumes and other plant foods containing a variety of lignans, dietary fibres, and isoflavonoids, which act as nature's sex hormone modulators and provide oestrogenic effects and an anti-oestrogenic competitive effect [114].

Compared to plant-derived drugs that often consist of one single natural compound in combination with other minor chemicals, herbs or phytotherapy materials often contain multiple bioactive components with multiple targets during intake and therapy. Phytotherapy strategies using herbal drug combinations with superior efficacy and lesser side effects in comparison with single isolated constituents of plant extracts has been repeatedly assessed clinically as well as pharmacologically [115]. Recently, a summary of main aspects from a Health Technology Assessment report on Traditional Chinese Medicine (TCM) in Switzerland concerning effectiveness and safety was given [116]. TCM training and practice for physicians in Switzerland are officially regulated. A multicomponent herbal preparation, STW 5, has been clinically proved effective for the treatment of patients with functional dyspepsia and irritable bowel syndrome [117]. Just like many other Chinese herbal medicines are obtained from various plants and contain complex extracts with different active substances, this phytomedicine is a combination of nine plant extracts with different active constituents. The clinical efficacy of this multicomponent herbal preparation questions the current trend of highly targeted drug molecules that usually target one single receptor population while it has not been shown that a single receptor group plays a pivotal role for the control of symptoms. Hijikata *et al*.[118] evaluated the effectiveness of traditional Chinese herbal formulation Bu-yang-huan-wu-tang, for treating epilepsy stemming from cerebrovascular dysfunction. Decrease of seizure frequency and severity in all three epileptic patients was achieved with Bu-yang-huan-wu-tang therapy according to the principles of Traditional Chinese Medicine theory. This treatment mainly relied on the resolution of blood stagnation in cerebrovascular systems. Blood stagnation is an important underlying pathology of many disease processes [118].

Allergic rhinitis is the most frequently occurring immunological disorder. Current therapies are far from satisfactory. A traditional Chinese polyherbal formulation Aller-7 comprising seven medicinal herbal extracts was assessed in a multicenter clinical trial for treatment of allergic rhinitis with 545 patients [119]. Results show that Aller-7 is well tolerated and efficacious in patients with allergic rhinitis without any serious adverse effect [119]. Similarly, another formulation was also studied in clinical trial and appears to offer symptomatic relief and improvement of quality of life for some patients with seasonal allergic rhinitis [120]. The efficacy and safety of the butterbur leaf extract Ze 339 were tested by Swiss scientists on patients with seasonal allergic rhinitis [121]. In an open postmarketing surveillance study, symptoms of seasonal allergic rhinitis improved in 90% of patients (580 patients). Butterbur leaf extract Ze 339 was confirmed by 3 GCP trials and 2 postmarketing surveillance trials to be safe and efficacious in the treatment of patients with seasonal allergic rhinitis [121]. All these studies clearly suggest that muticomponent traditional herbals can offer a very efficacious and better therapeutic option to patients in many diseases. However, a lack of information on the phytochemistry and pharmacological section of phytochemicals, or the synergistic effects of phytotherapies may eventually threaten and damage the customers and market [115]. Advances in drug synergy research using standardized plant extracts may open the chance to use extract combinations for the treatment of diseases as chemotherapeutics have in the past.

On the other hand, negative effects of some diets have also been investigated to gain scientific understanding. High dietary fat consumption is associated with endothelial activation in men and this detrimental effect is likely attributable to the saturated fatty acid content of the diet [122]. Higher intake of trans fatty acids has been associated with a higher risk of cardiovascular disease, as indicated by adverse effect on both lipid profile and endothelial function [123-125]. Mozaffarin group established a link between trans fatty acid intake and high risks of coronary artery disease and diabetes in women by indicating that dietary intake of trans fatty acid is associated with systemic inflammation in generally healthy women, as reflected by higher tumor necrosis factor α-receptor concentrations and higher interleukin 6 and C-reactive protein concentrations in women [124].

NUTRACEUTICALS AFFECT HUMAN BEING FROM STEM CELL

Recently the significant potentials and promising application of stem cell research has been an extremely hot topic in medicine. Stem cell transplantation is assumed to be able to cure many diseases [126]. Some researchers also have investigated the effects of certain nutraceuticals on stem cell growth and proliferation, which could stimulate endogenous stem cells to reach healing and regenerating goals, as an alternative to stem cell transplantation. Bickford *et al*. [127] reported a dose-related effect of blueberry, green tea, catechin, carnosine, and vitamin D_3 on proliferation with human bone marrow as compared with human granulocyte-macrophage colony-stimulating factor, and combinations of nutrients can synergistically promote proliferation of human hematopoietic progenitors, suggesting another potential role or mechanism by which nutraceuticals promote health and healing capability of human body.

Although any mediation including herbs during pregnancy needs to be carefully checked [128], the effects of nutraceuticals on pregnant women, development and differentiation of the infants and young children are essential for health of new generations [10]. It is believed that nutritional factors during early development not only have short-term effects on growth, body composition and body functions but also exert long-term effects on health, disease and mortality risks in adulthood [10]. There are indications for some beneficial effects of nutraceuticals such as antioxidant vitamins, essential amino acids, and polyunsaturated fatty acids in infant foods on the developing immune response. Actually, mineral intakes such as Ca, P, Mg, Fe,

Zn, I, F, and B, as well as vitamins D and K are important for the growth and development of bone and human nervous system [10]. Collaboration of clinicians, epidemiologists and basic scientists in an EU funded research project (www. metabolic-programming.org) on the relationship between early nutrition and later health should provide further insights into metabolic programming and help to transfer scientific progress into clinical practice [129].

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 [130]. 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 heath.

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 [131,132], 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 [130]. 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 [131,133].

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 [134]. 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. Most newly designed nutraceutical formulas listed in Table **1** for various purposes contain quite lots of different vitamins.

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 β-carotenoid in its grains [132]. 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 [131]. Overproduction of β-carotenoid has also achieved in other crops [133].

Vitamin Bs are 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 [135,136]. Yet due to diverse and complex structures and biosynthetic pathways, success on it is still limited [137,138]. 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 [137]. Biotin (Vitamin H) biosynthetic pathway is not clear yet [138]. A genetic engineered tomato lines could increased their folate content by up to 10-fold compared with control, suggesting a great promise in application [136]. 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 [135,139].

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 [140]. A genetically engineered maize line with Vitamin C biosynthetic gene successfully increased vitamin C level by up to 100-fold [140].

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 [141]. 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 [142]. 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 [143]. 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 [144]. 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 [145,146], resveratrol level in *Brassica napus* seed has also dramatically increased [147]. Consumption of these transgenic tomatoes has been shown to yield certain health benefits in mice [148]. Table **3** lists some patents related usage of flavonoids as phytonutrients for various health-promoting and disease-prevention or treatment, as well as production of particular flavonoids in plants [149-195].

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 [196]. 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 pro-vitamin A, vitamin E, flavors, pharmaceuticals, perfumes, insecticides, and anti-microbial agents. Metabolic engineering of terpenoids in plants has proven to be a fascinating effort [197, 198]. 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 [199]. 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 [200]. Other valuable terpenoid compounds that have been modified include the introduction of β-carotene to tomato fruits and rice [201] and zeaxanthin to potato tubers [202]. 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 heath 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 has been extensively studied and some achievements have been made [205,206]. Related patents [132, 207-216] including methods of terpenoids for disease treatment, transgenic plants with increased pro-Vitamin A (Golden Rice) and Vitamin E are listed in Table **4**.

LONG-CHAIN POLYUNSATURATED FATTY ACIDS (LCPUFAs)

Dietary essential fatty acids and LCPUFAs are critically important for fetal and infant development because of their

Table 3. Patents on Flavonoids

Authors	Patents No.	Titles and main achievement
Miller G, Brown LA, Del Balzo U, Flaim S, Boddupalli S, Wang B	US7034054	Methods for the prevention and treatment of cerebral ischemia using non-alpha tocopherols
Guthrie N, Kurowska EM, Manthey JA, Horowitz S, Horowitz RM	US6987125	Compositions and methods of treating, reducing and preventing cardiovascular disease and disorders with polymethoxyflovones
Rosenbloom RA	US7083813	Methods for the treatment of peripheral neural and vascular ailments
Romanczyk Jr LJ, Schmitz HH	US6998417	Compositions for, and methods of, treating atherosclerosis
Huang R	WO06026905A1	A use of phyto-flavonoid compounds for preparing medicament against avian influenzal virus
Guthrie N	*WO05115377B1 WO05115377A1	Functional foods comprising flavonoids and tocotrienols and methods thereof
Fukumoto S, Tsuruhami K; Mori S.	WO06070810A1	Antioxidant material, antideterioration agent and food or beverage
Xu, G, Boyd TJ, Hao Z, Viscio D, Gaffar A, Mello SV, Arvanitidou ES, Prencipe M	WO06069210A2	Oral care compositions containing flavonoids and flavans
Trivedi HM, Xu T,	WO06068973A2	Methods for use of oral care compositions containing free-B-ring flavonoid anti-oxidants
Han BH, Kang SS, Son KH	WO06001665A1	Composition for preventing or treating acute or chronic degenerative brain diseases including flavonoid derivatives
Rojas Castaneda P	WO06004386A1 WO06004386C1	Use of *Ginkgo biloba* extract for the preparation of a medicine that is used to treat Parkinson's disease
Gutierrez-Uribe JA, Serna-Saldivar SRO, Moreno-Cuevas JE, Hernandez-Brenes C, Guajardo-Touche EM	*WO05107780C1 US20060024394A1 WO05107780A2 WO05107780A3	Cancer cell growth inhibition by black bean (*Phaseolus vulgarisl* extracts)
Caldwell ST, Bennett CJ, Hartley RC, McPhail DB, Duthie GG	*U20060137207A1	Flavonoid compositions as therapeutic antioxidants
Nair MG. Wang H, Strasburg GM, Booren AM, Gray JI	US6623743	Method for the use of cherry isolates providing antioxidant phytoceutical or nutraceutical benefits
Tehoharides TC	US20060013905A1	Anti-inflammatory compositions for treating multiple sclerosis
Guthrie N	US20060013902A1	Pharmaceutical products for treating neoplastic disease and inflammation
Kelly GE	US6987098	Healthy supplement
Pandol SJ, Gukovskaya A	US6953786 WO05099721A2	Compositions comprising plat-derived polyphenolic compounds and inhibitors of reactive oxygen species and methods of using thereof
Guthrie N	*US20060013861A1	Functional foods comprising flavonoids and tocotrienols and methods thereof
Johnson CD	US20060040001A1 WO06014878A1	Nutritional compositions and methods for treating or preventing osteoporosis
Zabrecky G	US7078064	Compositions and methods useful for treating and preventing chronic liver disease, chronic HCV infection and non-alcoholic steatohepatitis
Koffas M, Leonard E, Yan Y, Chemler J	WO06010117A2 WO06010117A3 US20060019334A1	Production of flavonoids by recombinant microorganisms
Dixon RA, Steele CL	US7038113	Genetic manipulation of isoflavonoids

(Table 3) Contd….

Authors	Patents No.	Titles and main achievement
Spangenberg G, Sawbridge TI, Ong EK, Emmerling M	NZ0531985A	Manipulation of flavonoid biosynthesis in Trifolium repens (white clover), Lolium perenne(ryegrass) and Festuca (fescue)
Briskin RA	US7025994	Dietary compounds useful for the reduction of pathological codntions and the promotion of good health
Cavazza C	EP1128822B1 EP1128822A1	Antioxidant composition comprising propionyl L-carnitine and a flavonoid against thrombosis and atherosclerosis
Chan, PK, Mak MS, Wand Y	US20050220910A1 WO05096704A3 WO05096704A2	Cholesterol lowering combination
Rosenbloom RA	US20050239721A1	Methods for the treatment of peripheral neural and vascular ailments
Medical Research and Education Trust, The	GB0520247A0 GB2415905A1 WO04080474A1 US20050032882A1 DE10394175T5 AU3269928AA	Botanical extract compositions with anticancer or phytoestrogenic activity comprising prenyl flavonoids
Iiiek B, Fischer, Horst B	EP1669067A2	Flavonoids for cystic fibrosis therapy
Rodriguez GC, Whitaker RS	US7053074	Prevention of ovarian cancer by administration of a Vitamin D compound
Schwartz GK, Albino AP	US7045495	Combination of bryostatin and paclitaxel for treating cancer
Florio VV	US6136795	Dietary regimen of nutritional supplements for relief of symptoms of arthritis
Briskin RA	US7025994	Dietary compounds useful for the reduction of pathological conditions and the promotion of good health
Romancyzk Jr LJ, Basak A, Townsend CA	US7015338	Synthetic methods for preparing procyanidin oligomers
Andrei DC	RO0120531B1	Pharmaceutical composition for the treatment of chronic psoriasis
Andrei C	RO0120529B1	Antioxidant composition based on natural extracts for treating psoriasis
Chen S	GB2415905A1	Botanical extract compositions with anticancer or phytoestrogenic activitycomprising prenyl flavonoids
Watkins JM, Takaki MA	US20060134132	Protective barriers for micronutrients, phytochemicals, and nutraceuticals
Gutierrez-Uribe JA, Serna-Saldivar SRO, Moreno-Cuevas JE, Hernandez-Brenes C, Guajardo-Touche EM	WO05107780A3 WO05107780A2	Cancer cell growth inhibition by black bean (*Phaseolus vulgarisl*) extracts
Udell RG, Israel K	US20060051435	Nutritional supplement for body fat reduction
Ziegler R	US20050181076A1	Compositions and methods for treatment of diabetes
Miller PJ, Steele C, Kerr K	US6903136	Food supplements containing 4-hydroxyisoleucine and creatine
Kahol AP, Singh T, Tandon S, Gupta MM, Khanuja SPS	US6833143	Process for the preparation of a extract rich in bacosides from the herb *Bacopa monniera*
Mower TW, Harmon MC, Bawden JC, Banks DR, Young JJ	US20060093685	High mineral content dietary supplement
Pushpangadan P, Prakash D	US20060147561	Herbal nutraceutical formulation for diabetics and process for preparing the same
Magnuson BA, Giusti MM, Malik M, Zhao C	US20060159781	Anthocyanin-rich compositions and methods for inhibiting cancer cell growth

Table 4. Patents on Terpenoids

Authors	Patents No.	Titles and main achievement
Potrykus I, Beyer P	*AU776160B2	Method for improving the agronomic and nutritional value of plants.
Jeong TS, Lee WS; Kim HC, Choi YK, Kim JR, An SJ, Im KR, Jang KC, Moon OS, Son JS.	WO05084141A2 WO05084141A3	Novel abietane diterpenoid compound, and composition comprising extract of torreya nucifera, or abietane diterpenoid compounds or terpenoid compounds isolated from them for prevention and treatment of cardiovascular disease
Coughlan SJ.	US7071381	Plant vitamin E biosynthetic enzyme
Ernst H, Henrich K, Keller A.	US20060106257A1	Method for producing carotenoids
Andrei C	RO0120529B1	Antioxidant composition based on natural extracts for treating psoriasis
Mechoulam R, Maor Y, Hanus L, Horowitz M	WO05123051A3 WO05123051A2	Resorcinol derivatives for lowering blood pressure
Shewmaker CK, Bhat BG, Venkatramesh M, Rangwala SH, Kishore GM, Boddupalli SS	*US6653530	Methods for producing carotenoid compounds, tocopherol compounds, and specialty oils in plant seeds
Shewmaker CK	US6972351	Methods for producing carotenoid compounds and specialty oils in plant seeds
Hanada M, Iwai H, Fujigasaki J	US6960350	Antifungal fragrance composition
Wallace WH	US6949582	Method of relieving analgesia and reducing inflammation using a cannabinoid delivery topical liniment
Drake RG, Bird CR, Schuch W	WO9746690	Enhancement of tomato phytoene synthase gene expression with a modified DNA.

essential roles in cellular growth and metabolism, and membrane structure and function [217,218]. It has been suggested that inadequacy of LCPUFAs may lead to a failure to accomplish a specific component of brain growth and irrevocable damage because both the brain and the retina are rich in arachidonic acid and docosahexaenoic acid and rely on them for their normal functions [217]. Most infant formulas contain dietary essential fatty acids and LCPUFAs as supplements, except for various vitamins and minerals. Both epidemiologic and clinical studies have demonstrated that dietary omega-3 type polyunsaturated fatty acids decrease the risk of cardiovascular disease [219]. Sources of plant-derived LCPUFAs include flaxseed, flaxseed oil, walnuts, canola oil, and soybean oil [219]. Plant oils that are used for human consumption are comprised essentially of five main fatty acids, the saturated palmitic and stearic acids, monounsaturated oleic acid, and the polyunsaturated linoleic and α-linolenic acids [220]. Significant advances have been made recently in developing higher plants that synthesize LCPUFAs. These efforts have the potential to eventually provide safe, affordable and renewable plant sources of these important nutritional fatty acids, such as arachidonic acid, eicosapentaenoic acid and docosahexaenoic acid [221,222]. More recently, eicosapentaenoic acid and docosahexaenoic acid have been produced in *Brassica juncea* with a high-yield [223]. Several patents are listed in Table **1**.

ESSENTIAL AMINO ACIDS

Among 20 amino acids that are used in protein biosynthesis, several amino acids are called essential amino acids for all mammals because mammals cannot synthesize them by themselves but have to take up from plant foods or other food sources. Due to important roles of essential amino acids, many nutraceutical formulas also contain these amino acids (Table **1**). L-Arginine is an essential amino acid for infants and growing children, as well as for pregnant women. L-arginine is essential for the synthesis of creatine, urea, polyamines, nitric oxide, and agmatine. Arginine may be considered an essential amino acid in sepsis; rats receiving arginine-supplemented parenteral nutrition showed an increased ability to synthesize acute phase proteins when challenged with sepsis. L-arginine also exerts antihypertensive and antiproliferative effects on vascular smooth muscles. In addition to lysine and threonine, sulfur-containing amino acids such as methionine and cystine are also essential for human being. Glutamine is considered a conditionally essential amino acid in metabolic stress. Depletion of plasma and muscle glutamine is observed in acute burn injury and contributes to muscle wasting, weight loss, and infection. Glutamine supplementation has been shown to benefit to patients and reduces the rate of mortality and length of stay [224]. Elevating the levels of essential amino acids in staple foods such as wheat, rice, corn, and other plants has been studied for many years [225]. Related patents for engineered crops [226-240] with increased storage proteins of good essential amino acid sources have been issued as listed in Table **5**.

TRANSGENIC PLANTS TO PRODUCE PHARMACEUTICALLY IMPORTANT PROTEINS

The production of proteins, such as vaccines, antibodies, and other pharmaceutically important proteins in plants has been studied for over fifteen years [241, 242]. Affordable and reliable vaccines are some of the most powerful weapons

Table 5. Patents for Seed Nutrition and Composition

Authors	Patents No.	Titles and main achievement
Kirihara JA, Hibberd KA, Anthony J	*US6960709 US20060112443A1	Method for altering the nutritional content of plant seed
Anderson PC, Chomet PS, Griffor MC, Kriz AL	*US6515201 US6118047 US6118047	Anthranilate synthase gene and method of use thereof for conferring tryptophan overproduction
Chieko O, Yuji J, Takao K, Tetsuya M, Daisuke I	*US2002100074	Method for producing transformed plant having increased glutamic acid content
Chui CFC, Falco SC, Rice JA, Knowlton S	*US5939599	High sulfur seed protein gene and method for increasing the sulfur amino acid contact of plants
De Clercq A, Krebbers E, Vandekerckhove J, Gander E, Van Montagu M	US5589615 CA2000661	Process for the production of transgenic plants with increased nutritional value via the expression of modified 2S storage albumins
Falco SC, Allen SM, Anderson SL, Rafalski JA	US6338966 US6548280	Genes encoding sulfate assimilation proteins
Falco SC, Keeler SJ, Rice JA,	US5559223	Synthetic storage proteins with defined structure containing programmable levels of essential amino acids for improvement of the nutritional value of plants
Grimm B, Tanaka R	*US6624342	Manipulation of tocopherol content in transgenic plants
Falco SC, Keeler SJ, Rice JA	US5773691 US6459019	Chimeric genes and methods for increasing the lysine and threonine content of the seeds of plants
Galili G, Shaul O, Perl A	US5367110	Transgenic plants overproducing threonine and lysine
Gengenbach BG, Somers DA, Bittel DC, Shaver JM, Sellner JM	US5545545	Lysine-insensitive maize dihydrodipicolinic acid synthase
Glassman KF, Barnes LJ, Pilacinski WP	US5258300	Method of inducing lysine overproduction in plants
Hoffman LM	US5576203	Modified 7S legume seed storage proteins
Laberge S, Vezina LP, Yelle S, Benmoussa M, Simard R, Page M,	CA2248396	Improved starchy flours
Lund A	WO06069017A2	Transgenic plants with enhanced agronomic traits

for human beings to fight against diseases. However, due to the high costs of traditional vaccines (production, maintenance and delivery), people in many developing countries who are most in need of the various kinds of vaccines still cannot use them. In past years, plant biotechnologists have been able to produce recombinant vaccines in transgenic plants in the laboratory. Significant advantages are associated with the production of medicinal proteins in transgenic plants over traditional production ways. These include the fact that they are edible oral vaccines, are inexpensive due to "on site" production, and are safer due to no other undesired pathogenic antigens. The number and variety of successfully produced vaccines in transgenic plants, proven by vaccine effectiveness tests, are continuously increasing, including heat-labile toxin B subunit of *E. coli* (LTB) [243], Hepatitis B surface antigen [244, 245], respiratory syncytial virus F protein [246], measles virus haemagglutinin [247] and norwalk virus capsid protein [248]. A multi-component oral vaccine against acute gastro-enteric diseases [249] has been successfully expressed in plants and delivered orally in animals or humans to determine their immunogenicity. Scientists from Stanford University generated a therapeutic vaccine produced from tobacco plants, which prevented the growth of non-Hodgkin's lymphoma cells in laboratory mice and enabled the animals to survive the disease. However, there are still problems in commercial production of pharmaceutically important proteins. Such problems include low productivity of target proteins, quality and homogeneity of the final product [250].

One of the major limitations of the expression of recombinant antigens in transgenic plants is low yield of expressed proteins that is not sufficient to confer total

protection in humans. Although antibodies can be expressed with yields reaching 8% of total soluble protein [251], most examples of recombinant antigen production are low and rarely exceed 0.4% of total soluble proteins [241]. The low yield mainly results from poor expression, rapid degradation, or wrong targeting. Yet, researchers have used chloroplast transformation to increase non-glycoproteins (often bacterial antigens), and have achieved yield of somatostatin for more than 7 % total soluble proteins [252]. Because of the presence of plant-specific glycan, many vaccines that are glycoproteins could not be properly processed with the glycosylation machinery in plant cells and therefore are not immunogenic in mice [253]. Co-overexpression of some mammalian glycosylation processing enzymes such as glycosyl-transferases11 with vaccine-producing plants may help to gain their activity or antigenicity [254-292]. It is expected that production of pharmaceutically important proteins in plants will realize its largest potential eventually (Table **6** and **7**).

Table 6. Patents for Vaccine Production in Transgenic Plants

Authors	Patents No.	Titles and main achievement
Arakawa T, Langridge WHR, Yu J	*WO0155169	Transgenic plant-based vaccines (cholera vaccine)
Brandle J, Babiuk L, Rymerson R,	WO0194392	Recombinant subunit proteins from porcine parovirus produced in plants
Brandle J, Erickson L, Rymerson R, Yoo D, Zhang J	CA2221843	Porcine reproductive and respiratory syndrome oral vaccine production in plants
Lam DM-K, Arntzen CJ	US5612487	Anti-viral vaccines expressed in plants
Curtiss RIII, Cardineau G A	*US5654184, US5679880 US5686079	Oral immunization by transgenic plants
Boffey SA, Jones H, Slater RJ, Arokiaraj P, Cheong KF, Wan AR, Wan Y, Yeang HY	US5580768	Method for the production of proteins in plant fluids
Griot-Wenk ME, Goff SA, Heifertz PB, Tuttle AB	WO0020612	Therapeutically active proteins in plants
All BP, Howard JA	US2002058312 US20050166290A1	Expression cassettes and methods for delivery of animal vaccines
Koprowski H, Yusibov V, Hooper DC, Modelska A	US6042832 US6448070	Polypeptides fused with alfalfa mosiac virus or ilarvirus capsid
Van Rooijen G, Deckers H, Heifertz PB, Briggs SP, Dalmia BK, Del Val G, Zaplinski S, Moloney M	WO0250289	Methods for the production of multimeric proteins and related compositions
Russell DR, Fuller JT, Miller MJ	US6140075	Method for producing antibodies and protein toxins in plant cells, Monsanto, (tobacco cell culture)
Russell DR, Fuller JT	US6080560	Method for producing antibodies in plant cells
Lam, D. M., Arntzen, C. J.,	US5484719	Vaccines produced and administered through edible plants
McCormick AA, Tuse D, Reinl SJ, Lindbo JA, Turpen TH	US7084256	Self antigen vaccines for treating B cell lymphomas and other cancers
Daniell, Henry	US20030204864A1	Pharmaceutical proteins, human therapeutics, human serum albumin, insulin, native cholera toxic B submitted on transgenic plastids
Langridge WHR, Arakawa T	US20020055618A1 US20050044588A1	Methods and substances for preventing and treating autoimmune disease
Arntzen, CJ, Lam DMK	*US20030138456A1 US20050232949A1 US20040166121A1 US20010053367A1	Vaccines expressed in plants

(Table 6) Contd….

Authors	Patents No.	Titles and main achievement
Buetow DE, Korban SS, Sandhu J, Krasnyanski SF	US20050129704A1	Plant-derived vaccines against respiratory syncytial virus
Daniell H	*US20060117412A1	Pharmaceutical proteins, human therapeutics, human serum albumin insulin, native cholera toxic B submitted on transgenic plastids
Seki T, Fujiyama K	US6998267	Method for manufacturing glycoproteins having human-type glycosylation

Table 7. Patents for Antibody Production in Plants

Authors	Patents No.	Titles
Hein MB, Hiatt A	*US7037722, US7005560 US6995014 US6417429	Transgenic plants expressing assembled secretary antibodies
Hein MB, Hiatt AC, Fitchen JH	US6251392	Epithelial cell targeting agents
Hein MB, Hiatt A, Ma JKC	EP946717A1, WO9742313A1 CA 2252454, US5959177	Transgenic plants expressing assembled secretory antibodies
Hein MB, Hiatt AC	US7101688	Method of producing heteromultimeric mammalian proteins in plants
Hein MB, Hiatt AC, Fitchen JH	US6440419	Novel epithelial tissue targeting agent
Hein MB, Hiatt AC, Fitchen JH	WO9920310A1	J-chain and analogues as epithelial cell targeting conjugates
Hall, G., Bascomb, N., Bossie, M.,	WO02101006	Production of proteins in plants
Conrad U, Fieldler U, Phillips J, Artsaenko O.,	US6403371 WO972900A1	Cassettes for the expression of storable proteins in plants
Van Rooijen G, Deckers H, Heifertz PB, Briggs SP, Dalmia BK, Del Val G, Zaplinski S, Moloney M	WO0250289	Methods for the production of multimeric proteins and related compositions
Russell DR, Fuller JT, Miller MJ	*US6140075	Method for producing antibodies and protein toxins in plant cells
Russell DR, Fuller JT	US6080560	Method for producing antibodies in plant cells
Lehner T, Ma JKC, Hiatt AC	CA2208783AA	Methods for producing immunoglobulins containing protection proteins in plants and their use
Hiatt AC, Ma JKC, Lehner T, Mostov KE,	*US6046037, WO9621012A1 EP807173A1, CA2209783AA	Method for producing immunoglobulins containing protection proteins in plants and their use
McDonald KA, Jackman AP, Trexler MM	US7045354	Process for scaled-up production of recombinant proteins using transgenic plant suspension cultures
Hiatt AC, Hein MB, Fitchen JH	US6391280, US6045774	J chain polypeptide targeting molecule linked to an imaging agent (anti-cancer antibodies)

(Table 7) Contd….

Authors	Patents No.	Titles
Hiatt AC, Hein MB	US5639947	Compositions containing glycopolypeptide multimers and methods of making same in plants
Hiatt AC, Hein MB	US5202422	Compositions containing plant-produced glycopolypeptide multimers, multimeric proteins and method of their use
Huang N, Rodriguez RL, Hagie FE	US6991824	Expression of human milk proteins in transgenic plants

ABSORPTION AND METABOLISM OF NUTRACEUTICALS AND PHYTONUTRIENTS

Since the purpose of consuming nutraceuticals and phytonutrients is to incorporate them into our body and to allow them to build overall health and to treat some diseases, we assume that our bodies could absorb these important compounds as much as possible. However, many important nutraceuticals and phytonutrients are not fully absorbed in the human body. This conclusion is based on studies of the absorption of several nutrients; however, the exact percent absorption of most nutraceuticals and phytonutrients has yet to be determined. Information on their metabolism in the human body is also lacking. Therefore, absorption and metabolism of all nutrients and health-beneficial phytonutrients in humans, needs to be investigated. For some nutrients, improving their rate of absorption may be a more important target than enhancing their production, since a current bottleneck in alleviating nutrient deficiencies is the poor absorption.

Even for such important and common nutraceuticals as vitamins, which have been discovered for almost two centuries, their absorption and metabolism from food sources are not fully understood. For water-soluble vitamins such as Vitamin C and Vitamin Bs that are very essential for maintaining normal functions, their absorption rate and metabolism capability is relatively high and easer to study. Fat-soluble vitamins such as Vitamin A, E, D, K, are not so easy to study for absorption and metabolism from food sources are not well understood. Human can not synthesize Vitamin A, and it is mainly obtained from animal foods, but for many developing countries, such as China, where people eat more plant foods, Vitamin A is primarily obtained from plant foods that contain various pro-vitamin A carotenoids. Intestinal absorption and metabolism of carotenoids in cell culture models have been studied [293]. Beta-carotene-15,15'-oxygenase was identified as a key enzyme in the conversion of carotenoids to vitamin A. Recently, Tang *et al*.[294] reported the absorption of beta-carotene from spinach and carrot foods by using intrinsically labeled beta-carotene. Conversion ratio of spinach beta-carotene was 20:1 and carrot beta-carotene was 14:1 in adult subjects. The absorption, metabolism, and active forms of many plant secondary metabolites in humans remain to be determined.

CURRENT & FUTURE DEVELOPMENTS

Although nutraceuticals and phytonutrients have significant promise in the promotion of human health and disease prevention, health professionals, nutritionists and regulatory toxicologists also could strategically work together to plan appropriate regulations to provide the ultimate therapeutic benefits to mankind [12,86]. The nutraceutical, phytonutrient, and phytotherapy markets are still not well regulated [6,11,85]. Concerns from scientists, professionals, and customers continuously arise, due to increases in the use of these products and therapies. Quality, safety, long-term adverse effects, and toxicity are primary concerns. For manufacturing processes of nutraceuticals and phytonutrient products, quality controls such as the composition and contents of active constituents in natural plants, and maintenance are critically important. To establish product safety and efficacy, extensive safety studies including acute, subacute, subchronic, chronic and long-term toxicity studies, reproductive toxicology, as well as supplementation studies in animals and clinical trials in humans are necessary. The safety assessment of botanicals and botanical preparations in food and food supplements is complicated and should at least involve the characterization and quality of the material, its quality control; the intended use and consequent exposure; toxicological information, and risk evaluation [55, 295]. Although these concerns exist, governments, scientists, nutritional professionals, and other related parties are making great efforts to build the nutritional product and therapeutic system markets. Advances in biotechnology at different levels will greatly enhance these markets, as well as other technologies in diagnosis, product quality control, service style, etc. In this era of genomics, cDNA oligonucleotide microarray technology has emerged as a powerful tool. The potential of this technology in diagnostics is promising. Similar to DNA fingerprint technology and epigenetic studies, the technology may someday be able to identify each individual's genetic background and accordingly nutrient conditions. Based on this information, nutrition professionals could prescribe an improved dietary supplement for the individual. The DNA microarray technology may be used to examine the safety and efficacy of drugs, chemicals, food supplements and nutraceuticals [296]. With advances of analytic technique, now it is feasible to do metabolic screening on the newborns to predict or find out possible metabolic diseases, which may be treated with particular nutritional therapy or phytotherapy [297]. For plant biotechnology, although concerns about unintended effects of transgenic crops or plants on humans and the environment is warranted, stopping the use of these beneficial biotechnological products only because of unproven worries is unfortunately misguided. In summary, agricultural, food,

and biomedical biotechnology continue growing as a non-stop to change our life, the potential is high that one day our foods will also serve as medicines.

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