



Scholars Research Library

Der Pharmacia Lettre, 2010; 2 (1) 106-116
(<http://scholarsresearchlibrary.com/archive.html>)



Nutraceutical and Functional Food as Future Food: A Review

Raj K. Keservani^{*1}, Rajesh K. Kesharwani³, Narendra Vyas¹, Sarang Jain¹, Ramsaneh Raghuvanshi¹, Anil K. Sharma²

¹Rajeev Gandhi College of Pharmacy, Bhopal, India

²Delhi Institute of Pharmaceutical Sciences and Research, New Delhi

³Bioinformatics Division, IIIT, Allahabad, India

Abstract

In recent years there is a growing interest in nutraceuticals which provide health benefits and are alternative to modern medicine. Nutrients, herbals and dietary supplements are major constituents of nutraceuticals which make them instrumental in maintaining health, act against various disease conditions and thus promote the quality of life. The explosive growth, research developments, lack of standards, marketing zeal, quality assurance and regulation will play a vital role in its success or failure. In India the most common forms of functional foods and nutraceuticals are available as traditional Indian Ayurvedic Medicines (IAM); these are marketed under different brand names. India is the home of a large number of medicinal herbs, spices and tree species that have a substantially large domestic market with no major foreign competition at present. However, it is important to note that there are no strict pharmaceutical regulations on Ayurvedic and nutraceutical health products in India. In India and China have large populations, in particular in rural, remote and inaccessible areas which are totally dependent upon herbal remedies and other naturally available bioresources which they use to treat common ailments, and as general preventive and protective medications. In the global marketplace nutraceuticals and functional foods have become a multi-billion dollar industry and estimates within Canada suggest that the Canadian nutraceutical and functional food industry has potential to grow to \$50 billion US. Japan is the second largest market in the world for nutraceutical products after the United States. Its nutraceutical market has exhibited a steady average growth rate of 9.6% per annum.

Key Words: Nutraceuticals, functional Food, future food.

Introduction

The interest in nutraceuticals and functional foods continues to grow, powered by progressive research efforts to identify properties and potential applications of nutraceutical substances, and coupled with public interest and consumer demand. The principal reasons for the growth of the functional food market are current population and health trends. Across the globe, populations are aging. Life expectancy continues to rise, as does the contribution made by older individuals to the total population. Also, obesity is now recognized as a global issue as its incidence continues to climb in countries throughout the world. In the U.S., approximately 62% of the adult population is classified as overweight (based on body mass index (BMI)), and more than half of those adults are classified as obese. Heart disease continues to be a primary cause of death, responsible for 32% of deaths in the U.S., and cancer, osteoporosis, and arthritis remain highly prevalent. As of this writing, the International Obesity Task Force reports that the incidence of obesity in the majority of European countries has increased by 10 to 50% in the last 10 years. People can optimize the health-promoting capabilities of their diet by way of supplementation and by consuming foods that have been formulated or fortified to include health-promoting factors. Another reason for the growing trend in functional foods is public education. People today are more nutrition-savvy than ever before, their interest in health-related information being met by many courses of information. [1]

1. Nutraceuticals and Functional Food

The term nutraceutical is a hybrid or contraction of nutrition and pharmaceutical. Reportedly, it was coined in 1989 by DeFelice and the Foundation for Innovation in Medicine. [2] Restated and clarified in a press release in 1994, its definition was "any substance that may be considered a food or part of a food and provides medical or health benefits, including the prevention and treatment of disease. Such products may range from isolated nutrients, dietary, supplements and diets to genetically engineered 'designer' foods, herbal products, and processed foods such as cereals, soups, and beverages. [3]

According to the International Food Information Council (IFIC), functional foods are "foods or dietary components that may provide a health benefit beyond basic nutrition." [4] The International Life Sciences Institute of North America (ILSI) has defined functional foods as "foods that by virtue of physiologically active food components provide health benefits beyond basic nutrition." [5] Health Canada defines functional foods as "similar in appearance to a conventional food, consumed as part of the usual diet, with demonstrated physiological benefits, and/or to reduce the risk of chronic disease beyond basic nutritional functions." The *Nutrition Business Journal* classified functional food as "food fortified with added or concentrated ingredients to functional levels, which improves health or performance. [6] Functional foods include enriched cereals, breads, sport drinks, bars, fortified snack foods, baby foods, prepared meals, and more."

The *Nutrition Business Journal* states that it uses the term nutraceutical for anything that is consumed primarily or particularly for health reasons. Based on that definition, a functional food would be a kind of nutraceutical. [7] On the other hand, Health Canada states that nutraceuticals are a product that is "prepared from foods, but sold in the form of pills or powders (potions), or in other medicinal forms not usually associated with foods. A nutraceutical is demonstrated to

have a physiological benefit or provide protection against chronic disease.” [6] Based on this definition and how functional foods are characterized, as noted previously, nutraceuticals would be distinct from functional foods.

2. Nutraceutical factor

Depending upon one’s interest and/or background, the appropriate organizational scheme for nutraceuticals can vary. For example, cardiologists may be most interested in those nutraceutical substances that are associated with reducing the risk factors of heart disease. Specifically, their interest may lie in substances purported to positively influence hypertension and hypercholesterolemia and to reduce free radical- or platelet-dependent thrombotic activity. Nutraceutical factors such as n-3 fatty acids, phytosterols, quercetin, and grape flavonoids would be of particular interest. Meanwhile, oncologists may be more interested in those substances that target anticarcinogenic activities. These substances may be associated with augmentations of microsomal detoxification systems and antioxidant defenses, or they may slow the progression of existing cancer. Thus, their interest may lie in both chemoprevention and potential adjunctive therapy. The anticarcinogenic triterpene limonin is lipid-soluble and intensely bitter, somewhat limiting its commercial use as a functional food ingredient. [8] However, the glucoside derivative of limonin, which shares some of the anticarcinogenic activity of limonin, is water soluble and virtually tasteless, thereby enhancing its potential use as an ingredient. [9]

3. Food and non-food sources of nutraceutical factors

One of the broader models of organization for nutraceuticals is based upon their potential as a food source to humans. Here nutraceuticals may be separated into plant, animal, and microbial (i.e., bacteria and yeast) groups. One interesting consideration with this organization system is that the food source may not necessarily be the point of origin for one or more substances. An obvious example is conjugated linoleic acid (CLA), which is part of the human diet, mostly as a component of beef and dairy foods. However, it is actually made by bacteria in the rumen of the cow. Therefore, issues involving the food chain or symbiotic relationships may have to be considered for some individuals working with this organization scheme. Because of fairly conserved biochemical aspects across species, many nutraceutical substances are found in both plants and animals, and sometimes in microbes. For example, microbes, plants, and animals contain choline and phosphatidylcholine. This is also true for sphingolipids; however, plants and animals are better sources. Also, linolenic acid (18:3 ω -3 fatty acid) can be found in a variety of food resources including animal flesh, despite the fact that it is primarily synthesized in plants and other lower members of the food chain. Table 1 presents some of the more recognizable nutraceutical substances grouped according to food-source providers.

Nonfood sources of nutraceutical factors have been sourced by the development of modern fermentation methods. For example, amino acids and their derivatives have been produced by bacteria grown in fermentation systems. The emergence of recombinant-genetic techniques has enabled new avenues for obtaining nutraceutical compounds. These techniques and their products are being evaluated in the arenas of the marketplace and regulatory concerns around the world. An example is the production of eicosapentaenoic acid (EPA) by bacteria. This fatty acid is produced by some algae and bacteria. The EPA derived from salmon are produced by algae and are later incorporated in the salmon that consume the algae. EPA can now be produced by non-EPA producing bacteria by importing the appropriate DNA through recombinant methods.

[¹⁰] The ability to transfer the production of nutraceutical molecules into organisms that allows for economically feasible production is cause for both optimism and discussion concerning regulatory and popular acceptance.

Table 1. Examples of nutraceutical substances grouped by food source

Plants	Animal	Microbial
α -Glucan	Conjugated Linoleic Acid (CLA)	<i>Saccharomyces boulardii</i> (yeast)
Ascorbic acid	Eicosapentaenoic acid (EPA)	<i>Bifidobacterium bifidum</i>
γ -Tocotrienol	Docosahexenoic acid (DHA)	<i>B. longum</i>
Quercetin	Spingolipids	<i>B. infantis</i>
Luteolin	Choline	<i>Lactobacillus acidophilus</i> (LC1)
Cellulose	Lecithin	<i>L. acidophilus</i> (NCFB 1748)
Lutein	Calcium	<i>Streptococcus salvarius</i> (subs. <i>Thermophilus</i>)
Gallic acid	Coenzyme Q ₁₀	
Perillyl alcohol	Selenium	
Indole-3-carbonol	Zinc	
Pectin	Creatine	
Daidzein	Minerals	
Glutathione		
Potassium		
Allixin		
δ -Limonene		
Genestein		
Lycopene		
Hemicellulose		
Lignin		
Capsaicin		
Geraniol		
β -Ionone		
α -Tocopherol		
β -Carotene		
Nordihydrocapsaicin		
Selenium		
Zeaxanthin		
Minerals		
MUFA		

4. Nutraceutical Factors In Specific Foods

In an organization model related to the one above, nutraceuticals can be grouped based upon relatively concentrated foods. This model is more appropriate when there is interest in a particular nutraceutical compound or related compounds, or when there is interest in a specific food for agricultural/geographic reasons or functional food-development purposes. For example, the interest may be in the nutraceutical qualities of a local crop or a traditionally consumed food in a geographic region, such as pepper fruits in the southwestern United States, olive oil in Mediterranean regions, and red wine in Western Europe and Northern California.

Table 2. Examples of foods with higher content of specific nutraceutical substances

Nutraceutical Substance/Family	Foods of Remarkably High Content
Allyl sulfur compounds	Onions, garlic
Isoflavones (e.g., genestein, daidzein)	Soybeans and other legumes, apios
Quercetin	Onion, red grapes, citrus fruit, broccoli, Italian yellow squash
Capsaicinoids	Pepper fruit
EPA and DHA	Fish oils
Lycopene	Tomatoes and tomato products
Isothiocyanates	Cruciferous vegetables
β-Glucan	Oat bran
CLA Beef and dairy	Beef and dairy
Resveratrol	Grapes (skin), red wine
β-Carotene	Rosemary
Catechins	Teas, berries
Adenosine	Garlic, onion
Indoles	Cabbage, broccoli, cauliflower, kale, brussels sprouts
Curcumin	Tumeric
Ellagic acid	Grapes, strawberries, raspberries, walnuts
Anthocyanates	Red wine
3-n-Butyl phthalide	Celery
Cellulose	Most plants (component of cell walls)
Lutein, zeaxanthin	Kale, collards, spinach, corn, eggs, citrus
Psyllium	Psyllium husk
Monounsaturated fatty acids	Tree nuts, olive oil
Inulin, Fructooligosaccharides (FOS)	Whole grains, onions, garlic
Lactobacilli, Bifidobacteria	Yogurt and other dairy
Catechins	Tea, cocoa, apples, grapes
Lignans	Flax, rye

There are several nutraceutical substances that are found in higher concentrations in specific foods or food families. These include capsaicinoids, which are found primarily in pepper fruit, and allyl sulfur (organosulfur) compounds, which are particularly concentrated in onions and garlic. Table 1.3 provides a listing of certain nutraceuticals that are considered unique to certain foods or food families. One consideration for this model is that for several substances, such as those justnamed, there is a relatively short list of foods that are concentrated sources. However, the list of food sources for other nutraceutical substances can be much longer and can include numerous seemingly unrelated foods. For instance, citrus fruit contain the isoflavone quercetin, as do onions, a plant food seemingly unrelated. Citrus fruit grow on trees, whereas the edible bulb of the onion plant (an herb) develops at ground level. Other plant foods with higher quercetin content are red grapes but not white grapes, broccoli (which is a cruciferous vegetable), and the Italian yellow squash. Again, these foods appear to bear very little resemblance to citrus fruit or onions for that matter. On the other hand, there are no guarantees that closely related or seemingly similar foods contain the same nutraceutical compounds. For example, both the onion plant and the garlic plant are perennial herbs arising from a rooted bulb and are also cousins in the lily family. However, although onions are loaded with quercetin, with some varieties containing up to 10% of their dry weight of this flavonoid, garlic is quercetin-void.

5. Mechanism of action

Another means of classifying nutraceuticals is by their mechanism of action. This system groups nutraceutical factors together, regardless of food source, based upon their proven or purported physiological properties. Among the classes would be antioxidant, antibacterial, antihypertensive, antihypercholesterolemic, antiaggregate, anti inflammatory, anticarcinogenic, osteoprotective, and so on. Similar to the scheme just discussed, credible Internet resources may prove invaluable to this approach. [11, 12] Examples are presented in Table 3.

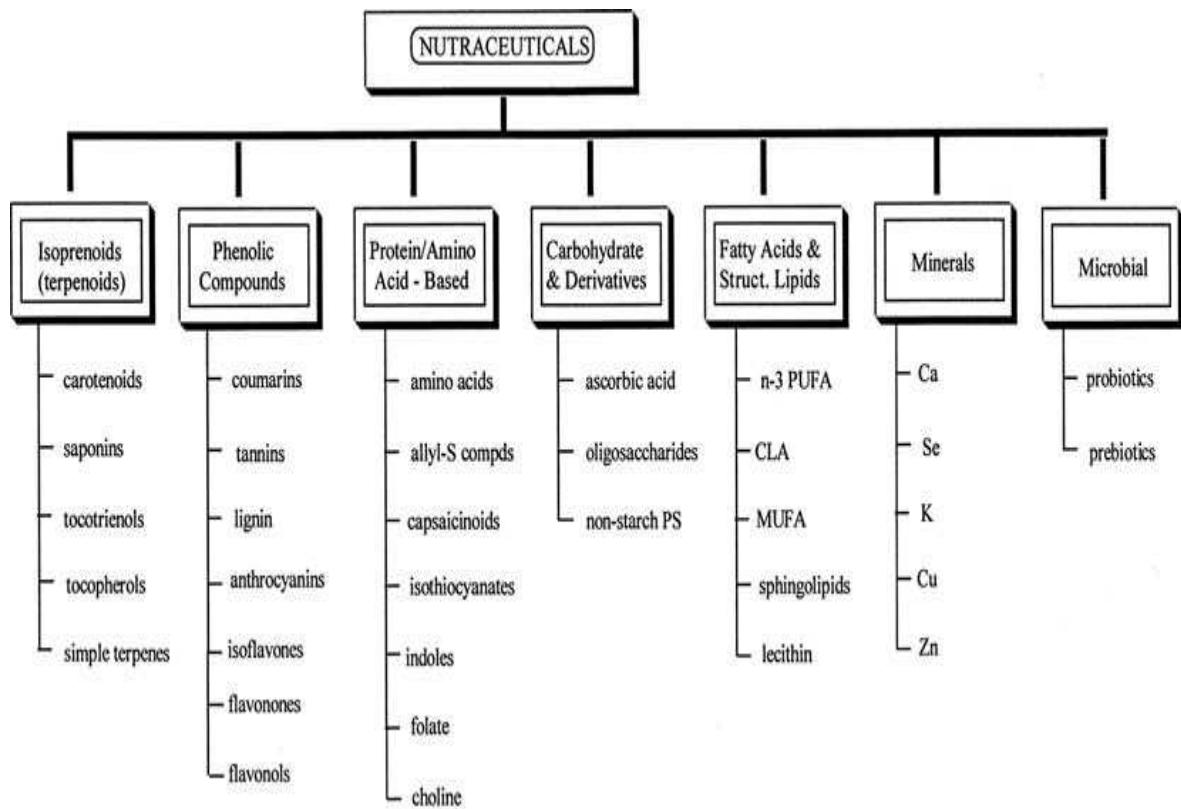
Table 3. Examples of nutraceuticals grouped by mechanisms of action

Anticancer	Positive Influence on Blood Lipid Profile	Antioxidant Activity	Anti inflammatory	Osteogenetic or Bone Protective
Capsaicin	α -Glucan	CLA	Linolenic acid	CLA
Genestein	γ -Tocotrienol	Ascorbic acid	EPA	Soy protein
Daidzein	δ -Tocotrienol	β -Carotene	DHA	Genestein
α -Tocotrienol	MUFA	Polyphenolics	GLA (gamma-linolenic acid)	Daidzein
γ -Tocotrienol	Quercetin	Tocopherols		Calcium
CLA	ω -3 PUFAs	Tocotrienols		Casein
Lactobacillus acidophilus	Resveratrol	Indole-3-carbonol	Capsaicin	phosphopeptides FOS(fructooligosaccharides)
Sphingolipids	Tannins	α -Tocopherol	Quercetin	
Limonene	β -Sitosterol	Ellagic acid	Curcumin	Inulin
Diallyl sulfide	Saponins	Lycopene		
Ajoene	Guar	Lutein		
α -Tocopherol	Pectin	Glutathione		
Enterolactone		Hydroxytyrosol		
Glycyrrhizin		Luteolin		
Equol		Oleuropein		
Curcumin		Catechins		
Ellagic acid		Gingerol		
Lutein		Chlorogenic acid		
Carnosol		Tannins		
L. bulgaricus				

6. Classifying nutraceutical factors based on chemical nature

Another method of grouping nutraceuticals is based upon their chemical nature. This approach allows nutraceuticals to be categorized under molecular/elemental groups. This preliminary model includes several large groups, which then provide a basis for sub classification or subgroups, and so on. One way to group nutraceuticals grossly is as follows [13, 14]:

- Isoprenoid derivatives
- Phenolic substances
- Fatty acids and structural lipids
- Carbohydrates and derivatives
- Amino acid-based substances
- Microbes
- Minerals

Figure 1. Organizational scheme for nutraceuticals

7. Marketed preparation of nutritional supplements

In world market various nutritional product [15] are present some are given in Table no. 4.

Table 4. Marketed preparation of nutritional supplements

Product	Category	Contents
Coral calcium	Calcium supplements	Calcium and trace minerals
Weight smart	Nutritional supplements	Vitamins and trace elements
Omega women	Immune supplements	Antioxidants, vitamins and phytochemicals (eg. Lycopene)
Appetite Intercept	Appetite suppressents	Caffeine, tyrosine and phenylalanine
Chaser	Hangover supplements	Activated calcium carbonate and vegetable carbon
Rox	Energy drink	Taurine, caffeine and glucuronolactone
Mushroom optimizer	Immune supplement	Mushroom, polysaccharides and folic acid
Biovinca	Neurotonic	Vinpocetine
Proplus	Nutritional supplements	Soy proteins
Snapple-a-day	Meal replacement beverage	Vitamins and minerals
wellife	Amino acids supplements	Granulated-L-glutamine
PNet plus	Neuropathic pain supplements	Vitamins and other natural

Olivenol	Dietary supplements	supplement
Threptin diskettes	Protein supplement	Natural antioxidants
GRD	Nutritional supplements	Protein and vitamin B
Proteinex	Protein supplement	Protein, vitamins, minerals and carbohydrates
Calcitriol D-3	Calcium supplements	Predigested protein, vitamins, minerals and carbohydrates
		Calcium, vitamins

7. Medical foods as nutritional supplements

Medical foods are foods that are specially formulated and intended for the dietary management of a disease that has distinctive nutritional needs that cannot be met by normal diet alone. They were defined in the Food and Drug Administration's 1988 Orphan Drug Act Amendments [6,17] and are subject to the general food and safety labeling requirements of the Federal Food, Drug, and Cosmetic Act.

Medical foods are distinct from the broader category of foods for special dietary use and from traditional foods that bear a health claim. In order to be considered a medical food the product must, at a minimum:

- be a food for oral ingestion or tube feeding (nasogastric tube)
- be labeled for the dietary management of a specific medical disorder, disease or condition for which there are distinctive nutritional requirements, and
- be intended to be used under medical supervision.

Medical foods can be classified into the following categories:

- Nutritionally complete formulas
- Nutritionally incomplete formulas
- Formulas for metabolic disorders
- Oral rehydration products

8. Innovation remains a priority

"Innovation is essential for the business - especially in the sense of improving the handling and application characteristics of existing molecules," says Jager. "We will continue to invest in innovation; it is an unchanged priority for us." BASF is particularly upbeat following the launch of its range of *Universal Formula* products in March. The company has created formulations of all major vitamins and carotenoids - pigments found in plants - that fulfill all regulatory requirements in Asia, Europe or the US. This results in a significantly less complex supply chain and purchasing process for the customer, less risk of mixing up ingredients, and flexibility that allows inventories to be optimized - all important factors in these times. DSM Nutritional Products, meanwhile, is also seeing rising sales for health foods and dietary supplements and decent demand, says Philipp Siebrecht, global business manager. If anything, products promoting health and wellbeing are even more of a priority for money-conscious consumers.

In just over a year since DSM launched its *ResVida* brand in March 2008, the high-purity form of the natural ingredient resveratrol is selling strongly, and Siebrecht is optimistic about growth in the market. The current financial crisis is turning people to drink - but for purely medicinal reasons. Resveratrol - a natural ingredient found in red wine - shows particular promise and has been lauded as having significant health benefits. It has been proven to help minimize the risks

of heart disease, as well as improving locomotor skills - the basis of human movement, and preserving learning abilities and endurance.

Resveratrol occurs naturally in a number of plants, including grapes, mulberries, peanuts, white hellebore and a Chinese plant called giant knotweed. "A lot of people know about the benefits of red wine when drunk in modest quantities," says Siebrecht, referring to a phenomenon known as the French Paradox that suggests that there are fewer cases of obesity and heart disease in France, despite a full-fat diet and a penchant for wine drinking. "DSM managed to extract that molecule, and we now supply it to the functional food industry, which adds it to its dietary supplements or beverages and food products,"

One way to increase life expectancy is to slightly reduce calorie intake, says Siebrecht. Researchers have found that low doses of resveratrol in the diet of mice mimic this effect. DSM has enhanced the qualities of resveratrol and provides a 99% pure form. A dose of 30-200mg a day could have a positive effect on health; just 30mg would be the equivalent of five or six bottles of wine but without the obvious health implications.

Although the nutraceuticals market is a relatively new concept, dating back only a few decades, it has boasted strong, almost unwavering growth in its short lifespan. While other sectors are struggling in the economic gloom, players are still largely upbeat - at least while consumers still have a healthy appetite for functional foods and supplements. [18]

9. Market and demand

Nearly two-thirds of the American population takes at least one type of nutraceutical health product. The US health and wellness industry is approximated to be a \$91 billion dollar market, significantly less than a \$250 billion estimate given by Stephen L. DeFelice. The distinction between which products count as nutraceuticals makes it difficult to accurately quantify the size of the market. Even without specific financial figures, business reports continually suggest that the market is consistently growing.

One possible explanation for the growth of nutraceuticals in the United States is the aging baby-boomer population. As the average age of the citizens continues to rise, the population increases its focus on health and wellness. By halfway through the 21st century, there could be almost 142 million Americans over the age of 50, based on a projected population of nearly 400 million citizens. [19]

Although the price of some nutraceuticals may drop as generic products make their way into the market, people's dependence on these products and their increasing availability suggests that the growth of the market shall remain stable.

10. Effectiveness and safety

Regulation

Unlike pharmaceutical drugs, nutraceutical products are widely available and minimally monitored. Companies are not obligated to back claims about the function and effectiveness of

their product, but many companies attempt to provide scientific backing of their products to increase credibility.

International sources

In the global market, there are significant product quality issues [19] Nutraceuticals from the international market may claim to use organic or exotic ingredients, yet the lack of regulation may compromise the safety and effectiveness of products. Companies looking to create a wide profit margin may create unregulated products overseas with low-quality or ineffective ingredients.

Bioavailability

Bioavailability, which can be thought of as the "absorption rate" of a supplement product, is one of the main challenges in finding effective nutraceutical products. The bioavailability of nutrients is higher in food eaten in its natural state. Even among unprocessed foods, not all foods are broken down and digested as effectively. Nutraceuticals with poor absorption rates results in nutrients being disposed from the body without providing any nutritional or medicinal benefit.

Impact of placebo effect

Part of the effectiveness of nutraceuticals may be attributed to the placebo effect. Consumers using nutraceuticals may inaccurately credit their use of nutraceuticals for healing illness, when the body is often able to recover on its own.

11. Future Prospects

After virtually ignoring nutrition for the past century, even labeling anyone claiming benefits from vitamins or health foods as a food faddist or quack, now scientists and nutritionists are claiming that the connection between nutrition and disease is a new discovery. A new discovery it may be for those scientists who, for the past half century, have been scoffing at the first hand experiences and positive anecdotal reports of millions of consumers around the world, but for the food faddist whose ideas about nutrition have traditionally been much more consistent than those of scientists, there is little that is really new. Natural foods are best. Vitamins and other nutrients protect against disease. Nothing new here for food faddists. Science is however to be congratulated for finally listening to the food faddists.

While current trends in nutrition are a welcome change indeed compared to the negative, simplistic, and biased approach of most nutrition research last century, the fact that food marketers now see functional foods as a way of marketing junk foods is a worrying trend which raises huge doubts about how much has really been learned about nutrition over the past few decades. Functional foods it seems are to many just a marketing gimmick. The challenge here is for public health authorities to demonstrate quite clearly that their allegiance is to public health and not the profits of huge food, chemical, and pharmaceutical companies.

It is interesting to note in this respect that the government is pursuing regulatory changes in the food industry which are not in the best interests of consumers and public health and which increasingly favour political interference.

According to Lawrence [14] , In the current global economic environment, and given the push by multinational companies to add dietary supplements to foods so they can make specific health claims to promote marketing of their foods, the current global campaign to restrict the retail availability of dietary supplements in health food stores is hardly surprising. It is abundantly clear that the functional food industry will not fully succeed if consumers are permitted to make their own choices about the specific dietary supplements and dosages they require. The success of functional foods therefore rests to a considerable degree upon removal of this freedom of choice. Now that the disease preventing potential of nutrients has been discovered by scientists and multinational food and drug companies, the ability of consumers to "medicate" themselves must be prevented and therefore control of dietary supplements must be transferred to doctors, pharmaceutical companies, and food manufacturers. After all, medicine has now finally realized that the dietary supplements freely consumed by nutritionally aware people for decades possess far more potential to prevent or perhaps even cure chronic diseases than all the vast array of prescription drugs they have at their disposal.

Acknowledgements

The authors are thankful to Dr. Suman Ramteke of Dr. H. S. Gour University, Sagar, M.P., for the helping hands.

References

- [1] R.E.C. Wildman, M. Kelley, Handbook of Nutraceuticals and Functional foods; In: Nutraceuticals and Functional Foods, Taylor & Francis, New York, **2007**, 1,9.
- [2] E.K. Kalra, *AAPS Pharm Sci*, **2003**, 5,25.
- [3] <http://www.fimdefelice.org>.
- [4] E.G. Miller, S.A.P. Gonzales, A.M. Couvillon, W.H. Binnie, S. Hasegawa,L.K.T. Lam, *Food Technol.*, **1994**,5, 114.
- [5] C.H. Fong, S.Hasegawa, Z. Herman and P. Ou, *J. Food Sci*, **1990**, 54, 1505.
- [6] <http://www.nibr.novartis.com>
- [7] L. Taiz , E. Zeiger , *Plant Physiology*,**1998**,5,51.
- [8] <http://www.australianreview.net>
- [9] W.R. Madley, *New products*, **2003**, 66, 125.
- [10] J.B. Barham, *J. Nutr.* **2000**,130,1925.
- [11] M.M. Johnson, *J. Nutr.* **1997**, 127,1435.
- [12] V. Brower, *Nat Biotechnol.* **1998**,16,728.
- [13] S.H. Zeisel, *Science*, **1999**, 285,185.
- [14] <http://vm.cfsan.fda.gov>
- [15] N.J. Nelson, *J Natl Cancer Inst.*, **1999**,91, 755.
- [16] M. Whitman, *Clin J Oncol Nurs.*, **2001**, 5, 190.
- [17] D.K. Heyland, *J Nutr.* **2001**, 131(9),2591.
- [18] AC. Elizabeth, *Clin Obstet Gynecol.* **2002**,45(1), 89.
- [19] <http://www.fimdefelice.org/archives/arc.researchact.html>.