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Review

Functional foods and nutraceuticals with special focus on mother and child care

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Abstract

Science has shown that diet affects human health. Therefore, healthy diets promote good health. The suggestion that certain food components and nutrients are associated with the prevention / treatment of chronic diseases such as cancer, coronary heart disease (CHD), and osteoporosis has encouraged consumer's interest in functional foods and natural health products. A nutraceutical is a product, isolated or purified from foods that is generally sold in medicinal forms not usually associated with food. A functional food is similar in appearance to, or may be, a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/ or reduce the risk of chronic disease beyond basic nutritional functions. The creation of nutrigenomics and nutrigenetics, two fields with distinct approaches to elucidate the interaction between diet and genes but with a common ultimate goal to optimize health through the personalization of diet, provide powerful approaches to unravel the complex relationship between nutritional molecules, genetic polymorphisms, and the biological system as a whole. *Ayurveda* as a way of life and habits is the most ideally suited systems to inspire a discovery path to nutraceuticals. *Ayurveda*, enables sub grouping of individuals into three major categories namely: *Vata*, *Pitta* and *Kapha*, based on *Prakriti*. Research with this line will add a newer dimension to functional food science as having great potential for the development of new food science, technology and industry. The emerging disciplines branching from genomics such as transcriptomics, proteomics, metabolomics, RNomics, miRNomics, liponomics, fluxomics, toxigenomics *etc*. will, further facilitate these kinds of research.

Key words : *Ayurveda*, functional foods, nutraceuticals, mother and child care, nutrigenomics, personalised nutrition

1. Introduction

Food and nutrition are indispensable companions of humans since the very beginning of his existence. The early man explored his surroundings to locate materials of natural origin for food and medicine. He continued his search in the plant and animal kingdoms to expand his food basket, to heal his ailments and discomforts. The desire to attain vitality and longevity also prompted the early man to experiment with whatever available in his immediate neighborhood. By a process of trial and error, observation and empirical reasoning and inference, the early man made conscious selections of a variety of biological materials to enhance his health, to alleviate pain or to treat other physical and mental ailments. The knowledge, thus, gathered was passed on to succeeding generations. Creative members of the succeeding generations incrementally improved and even added new knowledge to this body of traditional knowledge system. This traditional wisdom has come down to us from our ancestors and we now term it as traditional knowledge or ethnic knowledge. We find this knowledge system getting perpetuated through folklore, local health traditions, tribal knowledge system, family and community based knowledge systems *etc*. All ancient cultures and civilizations of the world had, thus, evolved their own traditional food, nutrition and medicine from their ambient biological wealth (Pushpangadan *et al.,* 2012).

The relationships between food, physiological function and disease have progressed in recent years, particularly over the past decade. At the start of the 20th century, the main challenge was to provide the population with calories of constant and reliable quality and shelf life (Klaffke, 2007). According to WHO, nutrition is the intake of food, considered in relation to the body's dietary needs. Good nutrition is an adequate, well balanced diet combined with regular physical activity and is a cornerstone of good health. Poor nutrition can lead to reduced immunity, increased susceptibility to disease, impaired physical and mental development, and reduced productivity (WHO, 2014).

2. Importance of ethnic or traditional food and medicine

The new lifestyle adopted by people today has changed the basic food habits of the latter. Consumption of the junk food has increased manifold, leading to a number of diseases, caused due to improper nutrition. "Let food be thy medicine and medicine be thy food",

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quoted by Hippocrates, father of medicine, about 2,500 years ago is certainly the tenet of today (Das *et al*., 2012). Since ancient times, mankind has believed in the role played by the appropriate amount of nutrition in maintaining proper health. In prehistoric ages, people viewed food solely as a means of survival. Early peoples spent most of their time and energy hunting and gathering food. As time passed, people learned to herd and farm. As food resources became more plentiful, people could spend more time in other pursuits. With the development of a more stable food supply came the development of civilization.

Today, throughout the world, 10000 cultures and 6900 languages are involved in thousands of traditional knowledge systems (FAO, 2013). This ethnic or traditional knowledge on food and medicine are mostly location specific and is best suited for the local climate and environment. Such systems of food and practices are deep rooted in the community's social, cultural and religious values. For centuries, these practices of food and medicine helped the people to lead a healthy, holistic life, free from most of the modern day diseases. That is the reason why WHO recognized the intrinsic importance of such traditional food, nutrition and medicine particularly in primary healthcare practices (Pushpangadan and George, 2009; Pushpangadan and Dan, 2011). The general ignorance of the use of nutrient-rich ethnic and traditional food resources has over the years, resulted in these foods being left out of most national strategies put in place to address food security and nutrition problems of the population. This nutrition transition, which has been shown to disproportionately affect indigenous peoples, is believed to be a significant risk factor for the global rise in chronic diseases such as obesity, diabetes, cardiovascular diseases *etc*.

The introduction of modern medicine in 19th century began to exert a negative influence on the traditional healthcare sector. The advances made in biological sciences, chemistry, pharmacology, microbiology, *etc*. contributed to the rapid development of modern medicine in the 19th and 20th centuries. These developments in modern medicine and food processing, caused a rapid decline in ethnic food and medicine. However, by the end of the 20th century, there had been an unprecedented revival of interest in ethnic food and medicine (Pushpangadan and George, 2009; Pushpangadan and Dan, 2011; Pushpangadan *et al.,* 2012).

The revival of interest in plant based drugs and the other herbal products is mainly because of the widespread belief that 'green medicine' is healthier than the synthetic products (Pushpangadan and Govindarajan, 2006). This is mainly due to the increasing evidences of the health hazards, associated with the harmful side effects of many synthetic drugs and the indiscriminate use of modern medicines such as antibiotics, steroids, *etc*. The preference for green food and medicine has resulted in the rapid growth of plant based drugs, pharmaceuticals, functional foods, nutraceuticals and even cosmaceuticals. In 1980s, this led to the rapid spurt of demand for health products like herbal tea, ginseng and products of traditional medicine. The health promotive and disease preventive strategies in treatment, prevalent in oriental systems, especially the Indian (Ayurveda, Siddha, Unani and Amchi) and the Chinese systems of medicine, are finding increasing popularity and acceptance all over the world. Because of this sweeping "green wave" a large number of herbal drugs and plant derived herbal products are sold in the health food shops all over the developed countries. According to some healthcare experts, there will be more dieticians rather than physicians in coming years, as many diseases can be prevented and better health can be maintained if one takes right food containing plant products with specific functional attributes (Pushpangadan, 2006).

3. Functional foods, nutraceuticals and health benefits

At the turn of the 21st century, the industrialized world faces new challenges, *i.e*., an enormous increase in the costs of healthcare, longer life expectancy, improved scientific knowledge, development of new technologies, and major changes in lifestyles. Nutrition scientists want to rise to these new challenges and have embraced the idea of "optimal nutrition", which focuses on optimising the quality of the daily diet in terms of its content of nutrients and non-nutrients as well as other food properties that favour the maintenance of health. This is where the development of functional foods / nutraceuticals comes into play (Ashwell, 2002).

The term functional food was first introduced in Japan in 1980s and refers to processed foods containing ingredients that aid specific bodily functions in addition to being nutritious (Zadik, 2010). The term nutraceutical was first coined by Stephen DeFelice in 1989 from 'nutrition' and 'pharmaceutical'. According to DeFelice, nutraceutical can be defined as, 'a food or part of a food that provides medical or health benefits, including the prevention and/or treatment of a disease' (Zeisel, 1999; Brower, 1998). The Bureau of Nutritional Sciences of the Food Directorate of Health Canada, has proposed the following definitions: A nutraceutical is a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with food. A nutraceutical is demonstrated to have a physiological benefit or provide protection against chronic disease. A functional food is similar in appearance to, or may be, a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease, beyond basic nutritional functions (Health Canada, 2014). The functional foods / nutraceuticals of both plant and animal origin hold exciting opportunities for the food industries to create novel food products in future. The different types of functional foods include: probiotics, cereals and grains, drinks and phytochemicals; while types of nutraceuticals include dietary supplements, food products of particular nutritional use such as infant formulas, diabetic foods *etc*. (Hasler, 2002). Some of the functional components, source and their potential health benefits are described in Table 1.

3.1 Functional foods / nutraceuticals of animal origin

Polyunsaturated fatty acids (PUFAs) are also called "essential fatty acids" as these are crucial to the body's function and are introduced externally through the diet (Escott-Stump and Mahan, 2000). PUFAs have two subdivisions: omega-3- (n-3) fatty acids and omega-6-(n-6) fatty acids. The major omega-3-fatty acids are α-linolenic acid (ALA, C18:3n-3), eicosapentanoic acid (EPA, C20:5n-3), docosahexanoic acid (DHA, C22:6n-3). EPA and DHA are found mainly in fatty fishes such as mackerel, salmon, herring, trout, blue fin tuna and in fish-oils (Kris-Etherton *et al.,* 2000; Institute of Medicine, 2002). The 2000 American Heart Association Dietary Guidelines recommend two servings of fatty fish per week for a healthy heart (Krauss *et al.,* 2000). Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease. FDA evaluated the evidence and determined that, although there is scientific evidence supporting the claim, and concluded that use of (n-3) fatty acid supplements is safe, provided daily intakes of EPA and DHA from supplements do not exceed 2 g/d (FDA, 2000a).

Table 1: Functional components and their health benefits

Functional components	Sources	Potential benefits
PHYTOESTROGENS		
Lignans	Flax, rye, some vegetables	Heart health and immune functions
Isoflavones-daidzein, genistein	Soybeans and soy- based foods	Healthy brain and immune function, bone health, menopausal health
Soy protein	Soybeans and soy - based foods	Reduce risk of coronary heart disease (CHD)
CAROTENOIDS		
Beta-carotene	Citrus, carrots, pumpkin, sweet potato, cantaloupe	Antioxidant defenses
Lutein, zeazanthin	Spinach, corn, eggs, citrus, collards	Vision health
Lycopene	Tomatoes, watermelon, red/pink grapes	Prostrate health
FATTY ACIDS		
Monounsaturated fatty acids	Tree nuts, olive oil, canola oil	Reduce risk of CHD
Conjugated linoleic acid	Beef, lamb, dairy products composition	Immune function and improve body
Omega -3 fatty acids	Fish and fish oils, walnuts, flax	Heart health, mental and visual function
DIETARY FIBER		
Insoluble fiber	Wheat bran, corn bran, fruit skins	Digestive health, cancer prevention
Beta-glucan	Oatmeal, oat bran, barley, rye	Reduce CHD risk
Soluble fiber	Psyllium, peas, beans, apples, citrus fruit	Reduce CHD risk
Whole grains	Whole wheat bread, oatmeal, cereal grains, brown rice	Reduce CHD risk, healthy blood glucose levels
PREBIOTICS		
Inulin, fructo-oligosaccharides, polydextrose	Whole grains, some fruits, garlic, onions, honey, leeks	Gastrointestinal health, improve calcium absorption
PROBIOTICS		
Yeast, lactobacillus, bifidobacteria	Certain yogurts, cultured dairy and non-dairy products	Gastrointestinal health, immune health, menopausal health
SULPHUR COMPOUNDS		
Diallyl sulfide, allyl methyl trisulfide	Onions, leeks, garlic, scallions	Detoxification, immune function heart health
Dithiolethiones	Cruciferous vegetables	Detoxification, immune function
Sulforaphane	Broccoli, cauliflower, kale, cabbage, horseradish	Antioxidant defenses, detoxification
Plant stanols/sterols	Soy, wheat, corn, fortified foods and beverages	Reduce risk of CHD
FLAVONOIDS		
Anthocyanins	Berries, cherries, grapes	Antioxidant defenses, brain function
Flavonols	Tea, cocoa, chocolate, apples, grapes, onions, broccoli	Heart health, antioxidant defenses
Flavanones	Citrus foods	Antioxidant defenses
Proanthocyanidins	Cranberries, cocoa, apples, straw berries, grapes, wine, cinnamon, pea nuts	Heart health, urinary tract health

Source: IFIC, 2014

DHA is an essential component of the phospholipids of cellular membranes, especially in the brain and retina of the eye, and is necessary for their proper functioning. DHA is particularly important for the development of these two organs in infants (Crawford, 2000). Recently, the FDA cleared the use of DHA and arachidonic acid for use in formula for full-term infants (FDA, 2001).

Another class of biologically active animal-derived components that has received increasing attention in recent years is probiotics, defined as viable microorganisms (bacteria, yeast, microalgae) that are beneficial to human health (Salminen *et al.,* 1998; Roberfroid, 2000). Probiotics generally include the following categories of bacteria: 1. Lactobacilli such as *L. acidophilus*, *L. casei*, *L. delbrueckii* subsp. *bulgaricus*, *L. brevis*, *L. cellobiosus*, 2. Gram-positive Cocci such as *Lactococcus lactis*, *Streptococcus salivarius* subsp. *thermophilus*, *Enterococcus faecium* and 3. Bifidobacteria such as *B. bifidun*, *B. adolescentis*, *B. infantis*, *B. longum*, *B. thermophilum*. Specific probiotics are generally used to treat gastrointestinal conditions such as lactose intolerance, acute diarrhoea and antibiotic associated gastrointestinal side effects (Doron *et al.,* 2005). A recent scientific status summary on probiotics from the Institute of Food Technologists summarized the scientific support for the therapeutic and/or preventive use of these functional ingredients for various health concerns including cancer, intestinal tract function, immune function, allergy, stomach health, urogenital health, cholesterol lowering and hypertension (Sanders, 1999).

Prebiotics are short-chain polysaccharides that have unique chemical structures that are not digested by humans. These include short-chain carbohydrates such as fructo-oligosaccharides and inulin, which enter the colon and serve as substrates for the endogenous colonic bacteria. The prebiotic consumption generally promotes the Lactobacillus and Bifidobacterial growth in the gut, thus, helping in metabolism (Hord, 2008; Gibson and Roberfroid, 1995; Gibson, 1999). Vegetables like chicory roots, banana, tomato, alliums are rich in fructo-oligosaccharides. Some other examples of these oligosaccharides are raffinose and stachyose, found in beans and peas. The health benefits of the prebiotics include improved lactose tolerance, antitumor properties, neutralization of toxins, and stimulation of intestinal immune system, reduction of constipation, blood lipids and blood cholesterol levels (Fuller, 1992; Isolauri *et al.,* 1991; Lin *et al.,* 1989; Sanders, 1994). Synbiotics are newer concept which are mixtures of probiotics and prebiotics that beneficially affect the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria, and thus improving host welfare (Gibson and Roberfroid, 1995).

Another animal ingredient that has been the focus of increased research efforts in recent years is conjugated linoleic acid (CLA). CLA is present in almost all foods, but occurs in particularly large quantities in dairy products and foods derived from ruminant animals (Yurawecz *et al.,* 1999). The inhibition of mammary carcinogenesis in animals is the most extensively documented physiologic effect of CLA (Belury, 1995). There is also an emerging evidence that CLA may decrease body fat and increase muscle mass both in rodent models and in humans (Park *et al.,* 1999; Blankson *et al.,* 2000).

3.2 Functional foods / nutraceuticals of plant origin

Numerous plant foods or physiologically active ingredients derived from plants have been investigated for their role in disease prevention and health. Those plant foods currently eligible to bear an FDA-approved health claim include oat soluble (β-glucan) fiber (FDA, 1997), soluble fiber from psyllium seed husk (FDA, 1998), soy protein (FDA, 1999) and sterol- and stanol-ester–fortified margarine (FDA, 2000b). Some plant-based foods or food constituents which currently do not have approved health claims, but have growing clinical research, supporting their potential health benefits are described below:

The soluble components of dietary fibre like β-glucans, pectins, gums, mucilages and hemicelluloses affects the rate of digestion and the uptake of nutrients and creates a feeling of satiety. Soluble fibre has been shown to lower selectively serum LDL cholesterol and to improve glucose tolerance (Glore *et al.,* 1994). The fibre also promotes the growth of bifidobacteria in the gut (especially fructo-oligosaccharides). Persons consuming generous amounts of dietary fibre, compared to those who have minimal fibre intake, are having low risk of CHD (Liu *et al.,* 1999), stroke (Steffen *et al.,* 2003), hypertension (Whelton *et al.*, 2005), diabetes (Montonen *et al.,* 2003), obesity (Lairon *et al*., 2005) and certain gastrointestinal disorders (Petruzziello *et al.,* 2006). Again, increase in the intake of high fibre food improves serum lipoprotein values (Brown *et al.,* 1999b), lowers blood pressure level (Keenan *et al.,* 2002), improves blood glucose control for diabetes (Anderson *et al.,* 2004), aids weight loss (Birketvedt *et al.,* 2005) and promotes regularity (Cummings, 2001). Research reveals that certain soluble fibres enhance the immunity in humans (Watzl *et al.,* 2005).

Alpha-linolenic acid (ALA C18:3 n-3) is popular for preventing and treating diseases of the heart and blood vessels. It is used to prevent heart attacks, lower high blood pressure, lower cholesterol, and for atherosclerosis. Principal sources of ALA are mainly flaxseed, safflower, soybeans, canola, corn, sunflower, some nuts (*e.g.,* walnuts) and red/black currant seeds (Institute of Medicine, 2002). ALA is the precursor of eicosapentanoic acid (EPA) and docosahexanoic acid (DHA). The estimated average ALA intake in the United States and most European countries is 1.3 to 1.7 g/d (Gebauer *et al.,* 2006; Zatónski *et al.,* 2008; Hulshof *et al.,* 1999; Geleijnse *et al.,* 2010).

Cranberries have been recognized since the 1920s for their efficacy in treating urinary tract infections. Research findings confirmed that condensed tannins (proanthocyanidins) in cranberry are the biologically active component and prevent *Escherichia coli* from adhering to the epithelial cells lining the urinary tract (Howell *et al.,* 1998).

Garlic (*Allium sativum*) has been used for thousands of years for a wide variety of medicinal purposes; its effects are likely attributable to the presence of numerous physiologically active organosulfur components (*e.g*., allicin, allylic sulfides) (Block, 1992). Some epidemiologic data suggests an inverse relationship between garlic consumption and certain types of cancer, particularly of the stomach. This may be due in part to garlic's ability to inhibit the activity of *Helicobacter pylori*, the bacterium that causes ulcers (Fleischauer *et al.,* 2000; Takezaki *et al.,* 1999). The best-documented clinical effect of garlic, however, concerns its ability to reduce blood cholesterol. A meta-analysis of 13 placebo-controlled double blind trials indicated that garlic component(s) (10 mg steam

distilled oil or 600-900 mg standardized garlic powder) significantly reduced total cholesterol compared with placebo by 4-6% (Stevinson *et al.,* 2000).

Clinical trials, which have specifically examined the effect of almonds on blood lipids, have found that these tree nuts significantly reduced total cholesterol by 4-12% and LDL cholesterol by 6-15% (Spiller *et al.,* 1992, 1998). More recently, a Life Sciences Research Office review of six clinical intervention trials with walnuts consistently demonstrated decreases in total and LDL cholesterol that should lower the risk of CHD (Feldman, 2002). Chocolate contains flavonoids (procyanidins), which may reduce oxidative stress on LDL cholesterol. In a clinical trial involving 23 subjects, consuming a diet supplemented with chocolate and cocoa powder providing 466 mg procyanidins, time to oxidation of LDL cholesterol was increased by 8% compared with subjects consuming a normal diet (Wan *et al.,* 2001).

There are approximately 8000 different classes of polyphenols, the most important being flavonols, flavones, flavan-3-ols, flavanones and anthocyanins (Das *et al.,* 2012). Dietary polyphenols are of current interest because substantial evidence *in vitro* have suggested that they can affect numerous cellular processes like, gene expression, apoptosis, platelet aggregation, intercellular signaling, that can have anticarcinogenic and antiatherogenic implications (Duthie *et al.*, 2003). A number of studies showed the presence of high concentrations of antioxidant polyphenolics such as resveratrol, a triphenolic stilbene in red grape skins reduce the risk of heart disease in selected populations (Meister *et al.,* 2000). Moderate consumption of red wine (400 ml/day) for 2 weeks significantly increases antioxidant status and decreases oxidative stress in the circulation of humans (Micallef *et al.,* 2007). Consumption of grape juice also has been shown to reduce platelet aggregation (Keevil *et al.,* 2000).

Studies in animals consistently show that consumption of green tea reduces the risk of various types of cancers. Green tea is particularly abundant in specific polyphenolic components known as catechins (Yang *et al.,* 2000; Mukhtar and Ahmad, 1999). The major catechins in green tea are: epicatechin, epicatechin-3-gallate, epigallocatechin, and epigallocatechin-3-gallate (EGCG) (Harbowy and Balentine, 1997).

Vitamin C, vitamin E and carotenoids are collectively known as antioxidant vitamins. These vitamins act both singly as well as synergistically for the prevention of oxidative reactions, leading to several degenerative diseases including cancer, cardiovascular diseases, cataracts *etc*. (Elliot, 1999).

Tomatoes and tomato products are also being investigated for their role in cancer chemoprevention and are unique because they are the most significant dietary source of lycopene, a non-provitamin A carotenoid that is also a potent antioxidant (Clinton, 1998). Epidemiologic studies found an inverse association between tomato intake or plasma lycopene concentration and the risk of cancer. A study found that men with localized prostate adenocarcinoma had significantly reduced prostate DNA oxidative damage after consumption of tomato-sauce based meals containing 30 mg lycopene for 3 week (Giovannucci, 1999; Chen *et al.,* 2001). Another carotenoid that has received recent attention for its role in disease risk reduction is lutein, the main pigment in the macula of the eye. Research is focusing on the role of lutein in eye health due to its ability to neutralize free radicals that can damage the eye and by preventing photo-oxidation. Thus, individuals who have a diet high in lutein may be less likely to develop age related macular degeneration (AMD) or cataracts (Mares-Perlman *et al.,* 2002; Seddon *et al.,* 1994; Brown *et al.,* 1999a; Chasan-Taber *et al.,* 1999). Good sources of lutein include green leafy vegetables such as spinach (7.4 mg/100 g) and cooked cabbage (14.4 mg/100 g).

In vitro and *in vivo* animal studies supports the cancer-preventive benefits of flaxseed lignans, citrus fruit limonoids and various cruciferous vegetable phytochemicals, including isothiocyanates and indoles (Rickard *et al.,* 1999; Crowell, 1997; Jeffery and Jarrell, 2000). Broccoli sprouts are currently being marketed both as a dietary supplement, highlighting the potential cancer-preventive action of one purported physiologically active component, sulforaphane, and as a food containing high levels of sulforaphane (Zhang *et al.,* 1992).

Legumes are consumed worldwide as an alternative source of proteins, since they are rich in amino acids like lysine and tryptophan and they are much cheaper than animal proteins. Of all legumes, soybean has received most attention. Soybean is most significant source of dietary isoflavones (Das *et al.,* 2012). In mice, dietary soybean components inhibited the growth of experimental prostate cancer and altered tumor biomarkers associated with angiogenesis (Zhou *et al.,* 1999). Commonly consumed cowpea, *Vigna unguiculata* (brown) and underutilized legumes, *Cajanus cajan* (brown) and *Sphenostylis sternocarpa* also possess higher antioxidant activity due to their relative higher phenol content. Hence, they can play an active role in combating degenerating diseases along with their traditional role of preventing malnutrition (Das *et al.,* 2012).

Cereals contribute over 60% of the world food production, providing dietary fibre, proteins, energy, minerals, and vitamins required for human health. Possible applications of cereals or cereal constituents in functional food formulations could be used as fermentable substrates for growth of probiotic microorganisms, especially lactobacilli and bifidobacteria or as dietary fibre. It can also serve as a prebiotic due to their content of specific nondigestible carbohydrates or as encapsulation materials for a probiotic in order to enhance their stability (Charalampopoulos *et al.,* 2002). Strong epidemiological evidence has clearly demonstrated that whole-grain cereals protect the body against age-related diseases such as diabetes, cardiovascular diseases and some cancers (Chatenoud *et al.,* 1998, 1999; Venn and Mann, 2004). This may be due to the fibre and micronutrients in the outer layer and germ fractions of the grain acting together to combat oxidative stress, inflammation, hyperglycaemia and carcinogenesis. Whole-grain cereals also contain micronutrients such as vitamin E, folates, phenolic acids, zinc, iron, selenium, copper, manganese, carotenoids, betaine, choline, sulphur amino acids, phytic acid, lignins, lignans, and alkylresorcinols, which all may have potential antioxidant effects (Slavin *et al.*, 1999). Free and esterified phenolic acids in wheat have the greatest potential to be beneficial to health (Baublis *et al.,* 2000).

Barley played an important role in the origin and development of the Neolithic culture. Barley is used as flour, as semolina, and as whole-dehulled grain. A large variety of dishes, including soups,

bread, and couscous are made from barley products (Amri *et al.,* 2005). The major component in barley is β-glucan, which is a major component of soluble fibre implicated in hypercholesterolemia, hypoglycemia, and in reducing incidence of chemically induced colon cancer in experimental animals (Bhatty, 1999). Health benefits associated with regular intake of millet foods, such as the hypocholesterolemic, hypoglycemic and antiulcerative characteristics indicate the scope for its utilization by the non-traditional millet consumer also (McDonough *et al.,* 1986; Ravindran, 1991).

Oats have recently attracted research and commercial attention mainly due to their high content of β-glucan and of compounds with antioxidant activity (Malkki *et al.,* 2004). A daily consumption level of 10 g oat β-glucan results cholesterol reduction, improved gastrointestinal function and glucose metabolism (Malkki and Virtanen, 2001).

Spices, which have long been the basis of traditional medicine in many countries, because of their potential use for improving health. Both *in vitro* and *in vivo* studies have demonstrated how these substances act as antioxidants, digestive stimulants, and hypolipidemics and show antibacterial, anti-inflammatory, antiviral, and anticancerogenic activities. These beneficial physiological effects may also have possible preventative applications in a variety of pathologies (Viuda-Martos *et al.,* 2011). Extensive research over the last 10 years, has indicated that nutraceuticals derived from such spices as turmeric, red pepper, black pepper, licorice, clove, ginger, garlic, coriander, and cinnamon target inflammatory pathways, thereby may prevent neurodegenerative diseases (Kannappan *et al.,* 2011). Aggarwal *et al.* (2009) suggests "adding spice to your life" may serve as a healthy and delicious way to ward off cancer and other chronic diseases.

Selenium (Se) is an essential trace element that is involved in the defense against the toxicity of reactive oxygen species, the regulation of the redox state of cells and in the regulation of thyroid hormone metabolism. Brazil nuts are the richest known source of selenium, one ounce contains approximately 200 mcg. Its deficiency has caused serious health effects in human, such as Keshan's disease, a potentially fatal form of cardiomyopathy (disease of the heart muscle) that affects young women and children (Das *et al.,* 2012). Epidemiological studies have increasingly indicated an inverse relationship between Se status and cancer risks in human populations. A clinical study by Clark and his colleagues revealed that participants who were given 200 μg of yeast-based selenium per day for four and half years, had a 50% decrease in the cancer death rate compared with the placebo group (Clark *et al.,* 1996). Se also plays a significant role in impairment of thyroid immunity involving the action of glutathione peroxidase and thioredoxin reductase, thereby removing ROS and excess H_2O_2 produced by thyrocytes during thyroid hormone synthesis (Tinggi, 2007).

4. Nutrigenomics, nutrigenetics and personalized nutrition

The 21st century will witness a major step forward in nutrition science prompted by characterization of the human genome. The Human Genome Project (HGP) is the largest ever international collaboration in biology. The result has been that the sequence of three billion chemical coding units in human DNA is now known. The next challenge is to identify each of the sequences of codes that are responsible for a specific activity or outcome.

Genes are turned on and off according to metabolic signals that the nucleus receives from internal factors (*e.g*., hormones), and external factors (*e.g*., nutrients), which are among the most influential of environmental stimuli (Harland, 2005). Unbalanced diets alter nutrient gene interactions, thereby increasing the risk of developing chronic diseases. Numerous dietary components can alter genetic events, and thereby influence health. In addition to the essential nutrients, such as carbohydrates, amino acids, fatty acids, calcium, zinc, selenium, folate, and vitamins A, C and E, there is a variety of non-essential bioactive components that seem to significantly influence health (Corthésy-Theulaz *et al.,* 2005; Trujillo *et al.,* 2006).

Nutritional genomics or nutrigenomics, is the study of how food and genes interact and aims to understand the effects of diet on an individual's genes and health. It attempts to study the genome wide influences of nutrition and identify the genes that influence the risk of diet related diseses on a genome wide scale, and to understand the mechanisms that underlie these genetic predispositions (Muller and Kersten, 2003). More practically, nutrigenomics describes the use of functional genomic tools to probe a biological system following a nutritional stimulus that will permit an increased understanding of how nutritional molecules affect metabolic pathways and homeostatic control. Nutrigenetics, on the other hand, aims to understand how the genetic makeup of an individual coordinates their response to diet, and thus considers underlying genetic polymorphisms. It embodies the science of identifying and characterizing gene variants associated with differential responses to nutrients, and relating this variation to disease states. Therefore, both disciplines aim to unravel diet/genome interactions; however, their approaches and immediate goals are distinct. Nutrigenomics will unravel the optimal diet from within a series of nutritional alternatives, whereas nutrigenetics will yield critically important information that will assist clinicians in identifying the optimal diet for a given individual, *i.e.,* personalized nutrition (Mutch *et al*., 2005).

It is already apparent that there are many polymorphisms that influence risk in cardiovascular disease and diabetes. Single Nucleotide Polymorphism (SNP) analysis provides a powerful molecular tool for investigating the role of nutrition in human health and disease, and their consideration in clinical, metabolic and epidemiological studies, can contribute enormously to the definition of optimal diets (Ames, 1999). Despite the extensive data on genetic polymorphisms in humans, its translation into medical practice has been slow because of the time required to accumulate population data on SNP incidence, understand the significance of a given SNP in disease, and develop suitable diagnostic tests. Nutrigenomics revitalized the field by showing that nutrients and botanicals can interact with the genome and modify subsequent gene expression, which has provided a great impetus for nutrigenetic research and nutraceutical development based on nutrigenetics. Polymorphisms in methlyene tetrahydrofolate reductase (MTHFR) (involved in folate metabolism), apolipoprotein E (Apo E) and ApoA1 (in cardiovascular disease), and leptin/leptin receptor (obesity) genes are some good examples for understanding basic nutrigenetics. Developing nutraceuticals to prevent and manage thrombosis risk in women with thrombophilic gene mutations are discussed in the context of the opportunities that exist at the nutrigenetic/ pharmacogenetic interphase leading to personalized nutrition. Further research on individual differences in genetic profiles and

nutrient requirements will help establish nutrigenetics as an essential discipline for nutrition and dietetics practice (Subbiah, 2007, 2008). The emerging disciplines branching from genomics such as transcriptomics, proteomics, metabolomics, RNomics, miRNomics, liponomics, fluxomics, toxigenomics *etc*. will further facilitate nutritional research.

5. Nutraceuticals in Ayurveda and ayurgenomics

The Acharyas of ancient India who codified systems of medicine namely; *Ayurveda* and *Siddha* seemed to have an in depth knowledge and understanding about the delicate relationship between food, nutrition and health. They also had a clear understanding of the delicate cellular mechanisms of the body and the deterioration of the functional capacity of human beings. These ancient medical masters had developed certain dietary and therapeutic measures to arrest/delay ageing and rejuvenating whole functional dynamics of the body system. This revitalization and rejuvenation is known as the 'Rasayana Chikitsa' (rejuvenation therapy) in *Ayurveda*. It is specifically adopted to increase the power of resistance to disease (enhance immunity) and improve the general vitiation and efficiency of the human being. *Rasayana* therapy is done for a particular period of time with strict regimen on diet and conduct. *Rasayana* drugs are very rich in powerful antioxidants, hepatoprotective agents and immunomodulators. *Rasayana* is one of the eight clinical specialities of the Indian classical *Ayurveda*, aimed for the rejuvenation and geriatric care. *Rasayana* is not a drug therapy, but is a specialized procedure practised in the form of rejuvenation recipes, dietary regimen (*Ahara Rasayana*) and special health promoting conduct and behaviour, *i.e*., *Achara rasayana*. *Sushruta* while defining *Rasayana* therapy says that it arrests ageing (*Vayasthapam*), increase life span (*Ayushkaram*), intelligence (*Medha*) and strength (*Bala*) and thereby enable one to prevent disease. There are over 30-35 medicinal plants mentioned in different treatise of *Ayurveda* and *Siddha* having *Rasayana* properties. The important among them are *Acorus calamus* (Vacha), *Aegle marmelos* (Bilva), *Aloe vera* (Kumari), *Andrographis paniculata* (Kalmegh), *Asparagus racemosus* (Shatavari), *Azadirachta indica* (Nimba), *Bacopa monnieri* (Brahmi), *Boerhavia diffusa* (Punarnava), *Centella asiatica* (Mandookaparni), *Convolvulus pluricaulis* (Shankhpushpi), *Desmodium gangeticum* (Shalparni), *Glycyrrhiza glabra* (Yashtimadhu), *Ipomoea digitata* (Vidari), *Phyllanthus emblica* (Amalaki), *Picrorhiza kurroa* (Kutki), *Piper longum* (Pippali), *Piper nigrum* (Maricha), *Premna obtusifolia* (Agnimantha), *Psoralea corylifolia* (Vakuchi), *Semecarpus anacardium* (Bhalatak), *Sida cordata* (Nagabala), *Tinospora cordifolia* (Guduchi), *Terminalia bellirica* (Bibhitaki), *Terminalia chebula* (Haritaki), *Withania somnifera* (Ashwagandha), *Zingiber officinale* (Srungavera) *etc*. (Pushpangadan *et al.,* 2008; Pushpangadan, 2010; Pushpangadan *et al.,* 2012). Some age specific Rasayanas are listed in Table 2.

The roots of the concept of nutraceuticals can be traced to *Ayurveda*. It is clearly stated that food consumed should maintain healthy state and prevent the occurrence of diseases, besides providing nutrition. The classical texts of *Ayurveda* are filled with scattered references of implication of food products in various disease entities. The concept of *Aajasrik Rasayana* (general rejuvenation) deals with food products that can be consumed daily for improving quality of life by offering protection from external and internal stressors. Some commonly used nutraceuticals in *Ayurveda* are: *Chyavanprash* (for general health and prevention of respiratory disorders), *Brahma Rasayana* (for protection from mental stress), *Phala Ghrita* (for reproductive health), *Arjuna Ksheerapaka* (for cardioprotection), *Shatavari Ghrita* (for general health of women during various physiological states), *Rasona Ksheerapaka* (for cardio-protection) *etc*.

Chyavanprash exhibited hepatoprotective (Jose and Kuttan, 2000) and reduced postprandial glycemia and blood cholesterol levels (Manjunatha *et al.,* 2001). *Brahma Rasayana* exhibited antioxidant effect (Bhattacharya *et al.,* 2000; Pawar *et al.,* 2001), increased GABA levels in the brain (Dey and Dutta, 1966) and offered tranquilizing effect (Ganguly and Malhotra, 1967). *Phala Ghrita* is advocated in men and women for reproductive health, nowadays mainly used in females for primary and secondary infertility (Rani and Sharma, 2005).

Table 2: Some age specific rasayanas

Decades of life	Natural biolosses	Suggested rasayanas
0-10	Balya (corpulence)	Ksheera (Milk) Ghrita (*Aloe barbadensis*); Gambhari (*Gmelina arborea*)
11-20	Vriddhi (growth)	Bala (*Sida cordifolia*); Amalaki (*Emblica officinalis*)
21-30	Chhavi (lustre)	Amalaki (*Emblica officinalis*); Haridra (*Curcuma longa*)
31-40	Medha (intellect)	Brahmi (*Bacopa monnieri*); Sankhapushpi (*Convolvulus pluricaulis*)
41-50	Twak (skin quality)	Bhringaraja (*Eclipta prostrata*); Haridra (*Curcuma longa*)
51-60	Drishti (vision)	Thriphala [Amalaki (*Emblica officinalis*); Bibhitaki (*Terminalia bellirica*); Haritaki (*Terminalia chebula*)]; Jyothishmathi(*Celastrus paniculatus*)
61-70	Sukra (virility)	Ashwagandha (*Withania somnifera*); Kapikachhu (*Mucuna pruriens*)
71-80	Vikrama (physical strength)	Amalaki (*Emblica officinalis*); Bala (*Sida cordifolia*)
81-90	Buddhi (thinking)	Brahmi (*Bacopa monnieri*); Sankhapushpi (*Convolvulus pluricaulis*)
91-100	Karmendriyapadavum(sensory perception)	Bala (*Sida cordifolia*); Sahachara (*Nilgirianthus ciliatus*)

The main effect offered by *Arjuna Ksheerapaka* is of cardio-protection (Sumitra *et al.,* 2001). It also exhibited antioxidant activity (Munasinghe *et al.,* 2001), antioxidant and hypocholesterolemic effect in cases of coronary heart disease (Shaila *et al.,* 1998), improved left ventricular ejection fraction (LVEF) in cases of coronary artery disease (Dwivedi and Jauhari, 1997). *Rasona Ksheerapaka* is said to be useful in ailments of *Vata Dosha* (*e.g*., sciatica, arthritis, cardiac disorders), although, use in hyperlipidemia. Various studies showed that it is also effective against atherosclerosis (Mirahadi *et al*., 1991), relaxant effect on aortic rings *in vitro* (Aquel *et al*., 1991), and antiarrhythmic effect in both ventricular and supra ventricular arrhythmias (Martin *et al*., 1992).

The paste of Brahmi (*Bacopa monnieri*) and Vacha (*Acorus calamus*) along with honey is given to the new born to soothe the increased *Kapha Dosha* and to improve the memory of the child. All the *Rasayana* and *Vajikarana* formulations are advocated in the young age while *Chyavanprash* is a *Rasayana* for old aged as well. A unique nutraceutical based on seasonal variations is *Ritu Haritaki i.e*., use of fruit of *Terminalia chebula* as per the season. The fruit should be used along with rock salt (Saindhava) in rainy season, with sugar in autumn, with dried rhizome of ginger (*Zingiber officinale*) in early winters, with fruit powder of long pepper (*Piper longum*) in late winters, with honey in spring and with jaggery in summer season. Another example of use of nutraceuticals as per season is of *Bhallataka Rasayana* (preparation of fruits of *Semecarpus anacardium*), which should not be consumed in summer season. Use of *Satavari Ghrita* (a formulation of *Asparagus racemosus* with clarified butter) is advocated in lactating women to improve lactation. Use of *Dashamoola Ghrita* (*Dashamoola* is a group of ten drugs whose roots are used) after child delivery is advocated to facilitate the involution of uterus to its normal state. *Chyavanprash* is aimed to give strength to the respiratory system. *Pippali Rasayana* (use of fruit of long pepper with honey) is also advocated to confer immunity to the respiratory system. Use of *Triphala* powder (powder of fruits of *Amalaki*, *Bibhitaki* and *Haritaki*) along with honey and clarified butter is advocated for maintaining/improving the eyesight (Rani and Sharma, 2005).

A confection of Indian gooseberry is used in households of India during winter season to prevent rhinitis and respiratory tract infections. A confection of rose petals and sugar is employed as mild laxative for children and as cooling agent, which subdues the vitiation of *Pitta Dosha*. *Ardraka paka* (ginger based confection toffee) is one such preparation, which is made up of ginger, sugar, salt and lemon and is used as an aid to digestion. Confection of bael fruit (*Aegle marmelos*) is used in the household for the problems of gastrointestinal tract. Paste of Mentha leaves (*Mentha arvensis*) is consumed along with meals for preventing abdominal distension. Consumption of grated garlic, fresh ginger and fresh turmeric rhizome mixed with lemon and salt is used as an aid to digestion. Further, certain sugar based confections and herb treated clarified butter (ghee) preparations are also used in India as home-remedial nutraceuticals (Rani and Sharma, 2005).

The ancient Ayurvedic physicians treated every individual as unique. According to them, normally there cannot be two individuals with same constitutional nature. That they referred as *Prakriti* and therefore, the treatment is prescribed only after diagnosing the constitutional nature of the individual. This constitutional nature of the individual is based on the *Tridosha* philosophy. The various permutation combination of the *dosha* in conjunction with '*triguna*'- the qualitative nature could offer countless variation in the constitutional nature of the individual and an experienced physician can very well diagnose it. Interestingly, the modern molecular geneticists also now speak a language similar to this, *i.e.,* genomic composition, *i.e*., DNA finger print is unique to an individual and we are now talking about gene profiling to understand the genetic predisposition and then suggest treatment to correct it, either by proteomic therapy or using other substances that can alleviate the defects or even the genomic therapy- proteomics, metabolomics and genomic methods for correcting disorders or treating diseases and nutrigenomics, genetically designed nutrition or food items. The ancient Ayurvedic masters had advised to consume specific food that suit to the constitutional nature of the individual whom they have categorized into 7 major groups. They have insisted certain dos and don'ts with regard to food and nutrition, according to the *Prakriti*. Modern molecular biology and genetic engineering is offering genetically modified nutrition/food that suit to the constitutional/genomic background of the individual or designer drug suited to the individual, known as nutrigenomics and pharmacogenomics, respectively. With the perfection of technology of mapping the human genome, it is now possible to get the DNA profile of individuals and then develop customized nutrition and treatment regimen (Pushpangadan *et al.,* 2012). Pharmacogenomics is the study of the hereditary basis for differences in response of populations to a drug (Patwardhan *et al.,* 2004). The same view was expressed by the ancient Ayurvedic master *Charaka*, some 4000 years ago. *Charaka* observed that 'every individual is different from another and, hence, should be considered as a different entity; as many variations are there in the Universe, all are seen in the human being' (Shastri, 1995; Valiathan, 2003; Sharma and Clark, 1997).

The Ayurvedic individualized approach in diagnosis and treatment now find acceptance in modern medicine. In 2000, Patwardhan proposed the original hypothesis that the concept of *Prakriti* in *Ayurveda* has strong genetic connotations. A pragmatic review highlighted how the practice of *Ayurveda* is personalized and can form the basis for pharmacogenomics and customized medicine. The term Ayugenomics® was coined and proposed by Patwardhan in 2002. Ayugenomics was planned as a platform to undertake the challenge of developing new strategies of drug discovery by integrating the ancient science and knowledge of *Ayurveda* with modern science, and the technologies of genomics, proteomics and pharmacogenetics (Patwardhan, 2012).

Ayurveda classifies the whole human population in three major constitutions as *Vata, Pitta, Kapha* (VPK) and their possible combinations. Patwardhan *et al*. (2005) hypothesized in a paper published in the Journal of Alternative and Complementary Medicine, there is a genetic connotation to *Prakriti* and as proof of this concept showed a correlation between human leukocyte antigens (HLA) alleles and *Prakriti* type, establishing a rationale and preliminary experimental support for the concept of an association between HLA alleles and the *Ayurvedic tridosha* theory of individual *Prakriti* types. As a pilot study to test the hypothesis, they evaluated 76 subjects both for their *Prakriti* and human leukocyte antigen (HLA) DRB1 types. The genomic DNA was extracted using a standard protocol. Subsequently, HLA DRB1 typing was done by low-resolution polymerase chain reaction sequence specific

primers and oligonucleotide probes and they observed a reasonable correlation between HLA type and *Prakriti* type. The complete absence of the HLA DRB1*02 allele in the *Vata* type and of HLA DRB1*13 in the *Kapha* type are significant, with $X2 = 4.715$ and $p < 0.05$. HLA DRB1*10 had higher allele frequency in the *Kapha* type than in the *Pitta* and *Vata* types. The homologous relation of VPK to human genetic structure needs to be studied for validation.

5.1 Ayurgenomics

Many rare diseases like hemophilia, beta-thallasemia *etc*. are monogenic, caused due to mutations in single genes. Most of the common diseases such as diabetes, asthma, cardiovascular disease *etc*. are multigenic complex disorders involving many genes. It is generally observed that common diseases are a consequence of cumulative effect of a large number of variations in the genome which independently have small effects that are not sufficient to cause the disease. However, it is now being increasingly realized that even those diseases that were considered to be monogenic sometimes exhibit differences in manifestation of disease in different individuals in spite of carrying the same mutations. This is thought to be due to presence of variations in other genes that could modify the effect of the primary mutation. Further, there is a complex interplay of gene and environment involved in the majority of the diseases. Most of these diseases require long term drug administration and there is a high variability in individual response to drug dosage and adverse effects due to mainly variations in the genes responsible for drug transport and drug metabolism within the individual's system. Therefore, design of optimum dosage with least side-effects is difficult to establish.

Tridoshas are not only genetically determined (*Shukra Shonita*) but also influenced by the environment during development, especially maternal diet and lifestyle. *Prakriti* is fixed at the time of birth and remains invariant throughout the individual's lifespan. Ethnicity (*Jatiprasakta*), familial characteristics (*Kulanupatini*), and geoclimatic regions (*Deshanupatini*) are also implicated in influencing phenotypic variability through their effect on *Tridoshas* and *Prakriti*. Thus, most of the factors such as ethnicity, geography, and environment that contribute to inter-individual variability at the genetic or epigenetic levels are embedded in Ayurveda's concept of *Prakriti*. In an individual, the *Tridoshas* work in conjunction and maintain homeostasis throughout the lifetime of the individual (Sethi *et al.,* 2011).

According to *Ayurveda*, a disease is a perturbation of *Vata*, *Pitta*, and *Kapha* in an individual from his or her homeostatic state. Food or medicines including lifestyle factors have been described to enhance or reduce a particular *dosha*, and therefore, an individual specific treatment is provided. Thus, the beauty of *Ayurveda* lies in the fact that an individual, a disease condition, drug, diet as well as environment are described in terms of *doshic* components and appropriate customizations are provided to balance these states (Sethi *et al.,* 2011).

There is no modern methods available to look at inter-individual differences within ethnically matched healthy populations and no studies at the genome-wide scale have, however, been attempted before. Mukherji and her team at the Institute of Genomics and Integrative Biology, have been exploring the concept whether *Ayurveda*, can fill this gap and help in identification of predictive markers for some of these complex diseases (Mukherji and Prasher, 2011).

They conducted a landmark study, the first of its kind in the world, finds links between *Prakriti*, a fundamental principle of personalized medicine of *Ayurveda*, and modern genomics for development of predictive and personalized nutrition/medicine. For their first study, which began in 2002, they took a sample of 96 unrelated healthy individuals, all from north India, with a predominance of either *Vata, Pitta* or *Kapha*. *Ayurveda* describes *Vata* to be the kinetic component, *Kapha* as a structural component and *Pitta* as a metabolic component. They tested the subjects blood samples for various biochemical and genetic markers and observed significant differences in biochemical profiles (otherwise within the normal laboratory range) between the *Prakriti* types that were further validated through bootstrap resampling. For instance, *Pitta* males had higher values for most of hematological parameters such as hemoglobin, packed cell volume, and red blood cell count; *Kapha* males had lower prothrombin time and HDL, higher levels of triglycerides, total cholesterol, VLDL, LDL, LDL/HDL ratio, and serum uric acid. Many of the parameters observed in *Kapha* are independent predictors of cardiovascular mortality and corroborate with disease descriptions associated with *Kapha* (Mukerji and Prasher, 2011).

Transcriptional profiles of pooled RNA from VPK revealed differences in core biological processes between these *Prakriti* groups. Some of these overlapped with the biochemical pathways (*e.g*., hemostasis). This led us to hypothesize that there is indeed an underlying cellular system in each *Prakriti* type that can be assessed through the modern genomics approach. The Ayurvedic abstraction of *Kapha* as being the promoter of anabolic state overlapped with the overall up- regulation of genes involved in cellular biosynthesis including ATP and cofactor biosynthesis and purine salvage pathway. Both male and female individuals of the *Vata* group showed enrichment of differentially expressed genes involved in cellular processes such as cell cycle, DNA repair, and recombination as well as transport functions. *Vata* governing manifestation of shape and cell division and transport has also been described in *Ayurveda* texts (Mukerji and Prasher, 2011).

Interestingly, as might be expected from complex interplay in biology, correlation with other processes/pathways was not so straightforward. For instance, the expression of genes involved in olfactory transduction processes was observed to be significantly low in both male and female individuals of *Pitta Prakriti*. While striking differences with respect to the immune functions were observed, different facets of the immune function seemed to be differentially modulated in deferent *Prakriti* types. *Pitta* had a higher expression of genes involved in innate immunity, where as *Kapha* had a higher expression of genes involved in adaptive immunity. Thus, susceptibility to infections, atopy, and allergic reactions are likely to vary according to the constitution types (Mukerji and Prasher, 2011).

Another study by the same team showed that expression and genetic analysis of healthy individuals phenotyped, using the principles of *Ayurveda* could uncover genetic variations that are associated with adaptation to external environment and susceptibility to diseases. They hypothesized that if the variations in EGLN1 (a key oxygen sensor gene that negatively regulates the activity of hypoxia-inducible factor, HIF-1A) linked to the *Pitta* group are over-represented in natives of high altitude, then the other allele that is linked to the *Kapha* type might be involved in mal-adaptation to

similar altitudes. Analysis of genotype frequencies of EGLN1 in sojourners from Indo-European background who developed high-altitude pulmonary edema (HAPE) revealed a significant over-representation of the genotype linked to *Kapha*. This genotype was also associated with higher expression of EGLN1, which could, thus, be correlated to lower expression of hypoxia-responsive genes. Thus, they speculate that individuals of *Kapha* constitution are likely to mal-adapt to high-altitude conditions. Interestingly, *Ayurveda* assigns *Prakriti* also to environment, *Pitta* constitution being more protected at high altitudes is consistent with the Ayurvedic school of thought that considers mountains mainly as *Kapha-Vata* dominant regions and having more prevalence of *Kapha-Vata* diseases (Sethi *et al.,* 2011). This work further suggests that variations in the hypoxia response pathway are common in most of the world population and could attain different allele frequencies as a consequence of positive selection. Thus, *Ayurveda* assigns *Prakriti* not only to humans but also to environment and food, and it makes specific mention of adaptation as well as dietary and lifestyle recommendations based on one's *Prakriti* for achieving healthy balance (Aggarwal *et al.,* 2010). The findings have been published in internationally reputed Journals, including ACS Chemical Biology and Proceedings of the National Academy of Sciences, USA. The study reveals that it is possible to identify groups within normal individuals of the populations, which could be predisposed to certain kind of diseases, and also might respond differently to drugs. Such integration of the principles of *Ayurveda* with genomics, appropriately termed as *Ayurgenomics* and it holds great potential and promise for future predictive and personalized nutrition/medicine at an affordable cost.

In this regard, the Council of Scientific and Industrial Research (CSIR) in association with Indian Centre for Social Transformation (Indian CST) has started major program called TRISUTRA (Translational Research and Innovative Science Through Ayurgenomics) at the Institute of Genomics and Integrative Biology (IGIB), New Delhi in March, 2009. The European Institute of Systems Biology and Medicine (EISBM) and the Institute of Genomics and Integrative Biology (IGIB) are already planning a research exchange programme in *Ayurgenomics*.

Recently a study by Juyal *et al.* (2012), established that *Pitta* and *Vata Prakriti* groups differ with respect to inflammatory and oxidative stress pathways. The preliminary results of varying disease characteristics in the three specific subgroups as well as different pathway genes being associated in the subgroups, is suggestive that rheumatoid arthritis (RA) in *Vata* subgroup is mediated by inflammatory genes whereas in the *Pitta* subgroup, oxidative stress genes seem to be major determinants. The changing life style of contemporary times including dietary changes and other environmental attributes may then be speculated as a possible reason for observing more RA with *Pitta* and *Kapha Prakriti* compared to the *Vata* subgroup. The results seem to support the common knowledge of varying contribution of genes of minor effect to the complex disease phenotype in different individuals. Further, it supports our hypothesis that conditioning association studies on prior risk will uncover much more variance and potentially open up more predictive health. They may besides supporting personalized drug regimen, also provide useful leads for enhanced understanding of the existence and differential contribution of multiple pathways in the pathogenesis. This finding was also published in Nature India, Science News by Padma in March, 2014.

6. Traditional mother and child healthcare

Child bearing and propagation of culture through the generations are central to any society. In the agrarian society, preparations for this began very early and the birth of a child, particularly the girl, was an important event. Offering prayers to beget a girl was common place, like performing ritual arts like *Theyyam* in Malabar areas of Kerala state. The girl child had many privileges and her attaining puberty was another occasion to celebrate. Family and friends brought choice food items meant to give her the much needed nutrition at that stage. A girl was to take rest during her menstrual periods and eat specific foods which are no longer possible in the fast-paced modern life. Traditional social support systems like the compound families took care of the various needs. Proper pre-marital counseling is a requirement in modern society where plain ignorance leads to far too many complications and diseases. Earlier, elderly women used to advice and counsel. Respect and knowledge empowerment of the girls gave them honor, confidence and courage. The traditional practices continue in many regions and in the Gangetic plains of India, scenes of girls attaining puberty being carried in bullock carts with music and dance could be seen till recently. Of late, this takes place only in remote villages. Majority in the country now consider sexuality and reproduction a private matter, perhaps after the spread of western values when everything related to these are considered sinful and secretive (Pushpangadan and George, 2010).

In traditional societies, the crucial phase of pregnancy-care starts the moment pregnancy is confirmed. The expectant mother is advised to conform to a series of customary behaviours with almost every elder family member or villager monitoring her. The woman receives special care in all day-to-day activities what is now lost in the modern life styles. The treasures of native wisdom on this subject are opened to the new mother-to-be. Certain foods were taboo for pregnant women while some others were mandatory. Do's and don'ts were all part of folk wisdom. Thus, it was mandatory for those in advanced stages of pregnancy to do specific household chores like sweeping the floor, where many others were barred. Such natural exercises enabled easy child birth and are endorsed by modern obstetricians now. Many of the preparations of this tradition remain unwritten, kept alive by being passed on from one generation to the next.

Pregnant women are normally not allowed to stay outside during the night in most villages. They have restrictions in visiting sick people and witnessing traumatic events. In several families, there are also stipulations that these women listen to music, pray and read epics like *Ramayana*. These points to an acute awareness of the latest findings in psycho-somatic linkages, *i.e.*, mind-body connections. It is now known that turbulence in the mother's mind, fear or extreme anxiety, affects the unborn child. The traditional Indian science of Yoga has postures for various stages of pregnancy which makes child birth easy and natural. There are also *asanas* and exercises for post-natal stages which restore the body tone before delivery. Together with this, there are herbal preparations like medicated oils and herbal nutrients.

Breast-feeding is a very important ingredient in baby care in Indian culture. Mother's breast milk is also given as medicine, used as eye drops and used in assorted ways for baby care. Breast milk is considered to have all the nutrients and antibodies what the child needs. It is a sharing of love and the mother child bondage is cemented

at the time. Those receiving long term breast feeding have been shown to be more resistant to various diseases. Many herbs such as *Bacopa monnieri* commonly used by native healers and considered stimulants. There are also specific animal based potions that are given to children at later years. Since the foundation of health is laid in childhood, traditional healing gives great importance to child care (Pushpangadan *et al.,* 2012).

There are significant traditional practices related to antenatal care for managing a range of conditions from early nausea and vomiting symptoms associated with pregnancy to management of worms and anaemia and toning of vaginal muscles before delivery. In postnatal care, the traditional knowledge of women ranges from the healing of vaginal tears to the use of herbs that helps in early uterine contraction and cleaning of the uterus. In Kerala, different methods and medicines are attempted to ease delivery by these birth attendants. This is besides the food and medicines given during the antenatal period. Just before delivery, castor oil with pepper is given as linctus to induce labour. Butter and some special medicinal porridge made from *Sida retusa*, *Cedrus deodara*, *Cuminum cyminum* and *Terminalia chebula* are given to ease pain. Oil is massaged on the abdomen and the vaginal canal is anointed with medicated oil to prevent tears. The birth attendants attend to the cleaning of the orifices and the bathing of the newborns. There are also traditional postnatal healthcare methods, given to the mother soon after delivery. The oil bath for women with *Dhanwantaram* oil is a practice in Kerala. *Ullimarunnu* (garlic is the main ingredient) and *Kurukkumarunnu* are a type of nutraceutical preparations, used for post natal care. These preparations are helpful for rejuvenating the body, healing wounds, reducing pain, increasing breast milk *etc*. (Rajith *et al.,* 2010).

7. Functional food and nutraceutical in mother and child healthcare

Maternal education is acknowledged to be one of the most important criteria for determining good public health. Imbalances in maternal nutrition can adversely affect normal foetal growth and development. Impaired foetal growth is prevalent in developing countries and has been associated with negative short and long term outcomes such as increased perinatal morbidity and mortality, infant mortality and childhood morbidity. Children who experience impaired foetal growth are more likely to show poor cognitive development and neurological impairment. Some chronic adult diseases are hypothesized to originate *in utero:* cardiovascular disease, high blood pressure, obstructive lung disease, diabetes, high cholesterol concentration, renal damage (Barker, 1994). It was, thus, realized that some of the persisting effects of early under nutrition become translated into pathology, and thereby determine chronic diseases in later life (Lucas, 1991).

Energy needs during pregnancy are currently estimated by the sum of total energy expenditure of a non-pregnant women plus the median change in total energy expenditure of 8 Kcal/gestational week plus the energy deposition during pregnancy of 180 Kcal/ day. Because total energy expenditure does not change greatly and weight gain is minimal in the first trimester, additional energy intake is recommended only in the second and third trimester. Approximately, an additional 340 and 450 Kcal/day are recommended during the second and third trimesters, respectively (Institute of Medicine, 2002). The best studied substrate in human pregnancy is glucose and there is a direct relationship between maternal blood glucose, foetal glycaemia and size at birth (Catalano and Kirwan, 2001). Glucose is indeed the major energy source for the foetus comprising around 90% of the energy supply. Therefore, maternal carbohydrate metabolism during pregnancy and the source of carbohydrate may be relevant to the optimal supply for the foetus.

Pregnant women also have high requirements for lipid-soluble vitamins and polyunsaturated fatty acids. During pregnancy, concentration of blood lipids and their constituent fatty acids rise sharply (Al *et al*., 1995). All of the n-6 and n-3 fatty acid structure needed by the foetus must be supplied by the mother and cross the placenta either in the shape of the essential fatty acids linoleic acids (18:2, n-6) or alpha linolenic acid (18:3, n-3) or their long chain polyunsaturated fatty acid derivatives such as arachidonic acid (20: 4, n-6) or docohexaenoic acid (22:6, n-3). An adequate supply of essential fatty acids and of long chain polyunsaturated fatty acids is essential for normal foetal development, particularly high rate during the third trimester. Arachidonic acid is the main precursor of eicosanoids, prostaglandins and leukotrienes and is also essential for neonatal growth, whereas docosahexaenoic acid plays a role in brain development and visual function (Herrera, 2002; Van Aerde *et al.,* 1998). The recommended increment of protein intake over non-pregnancy values is higher than that of energy during pregnancy. In the first trimester of pregnancy, protein synthesis is similar to that of non pregnant women and increases respectively by 15% and 25% in the second and third trimester (Duggleby and Jackson, 2002).

Since mammals cannot synthesize folic acid it must be provided by the diet or by intestinal microorganisms. Compromised maternal folate intake or status is associated with several negative pregnancy outcomes including low birth weight, abnormal placenta, spontaneous abortions, or neural tube defects (Bailey *et al.,* 2003). The recommended supplement is a daily dose of 400-600 μg/day (Institute of Medicine, 1998). There are many other ways in which folate can affect gene function, and so folate is central to nutrigenomics and is a leading contender for panacea of the 21st century.

A low availability of dietary choline during pregnancy alters foetal brain biochemistry and hippocampal development. This induces behavioural changes that persist throughout the life time of the offspring. Humans with choline deficiency but with an otherwise balanced diet develop liver damage due to programmed cell death. Because *de novo* synthesis of choline is not sufficient to compensate this lack of choline (Zeisel, 2000).

There are two approaches with respect to functional foods. One approach makes use of specific foods with a high or low content of a certain component, whereas the other concerns designed foods where ingredients having added or removed. Different types of designed foods are classified as prebiotics, probiotics and synbiotics, vitamins and minerals, bioactive molecules and fatty acids.

Eggs have not traditionally been regarded as a functional food, primarily due to concerns about their adverse effects on serum cholesterol levels. Furthermore, it is now known that there is little if any connection between dietary cholesterol and blood cholesterol levels and consuming up to one or more eggs per day does not adversely affect blood cholesterol levels. Finally, eggs are an excellent dietary source of many essential (*e.g*., protein, choline)

and non-essential (*e.g*., lutein/zeaxanthin) components which may promote optimal health (Hasler, 2000). The presence of high quantities of the essential nutrient choline makes eggs particularly valuable for the foetus and the new born because it benefits cognitive function especially when present during early brain development (Blusztajn, 1998).

Prunes are dried plums, fruits of *Prunus domestica*, cultivated and propagated since ancient times. Prunes have traditionally been consumed for their laxative and antimicrobial effects but their consumption has other beneficial effects on health. Prunes have particularly high content of minerals, vitamins, fiber and phenolics, but contain fewer amino acids. The main amino acids are asparagines, taurine, proline and GABA (Stacewicz-Sapunzakis *et al.,* 2001).

Whole rice is also a functional food due to the presence of rice bran, a rich source of fiber, myoinositol, inositol hexaphosphate and antioxidants. Inositol hexaphosphate, as found for instance in rice bran, is the main dietary supplier of cell membrane, phosphatidyl inositol needed for the maintenance of membrane integrity (Jariwalla, 2001). Rice protein is hypoallergenic and contains good quantity of lysine. Thus, it may act as a suitable ingredient for infant food formulations while adding variety to the restricted diets of children with food allergies (Helm and Burks, 1996; Gurpreet and Sogi, 2007). Amino acid profile of rice protein was better than casein and soy protein, isolate in fulfilling the amino acid requirements for 2-5 years old children (Wang *et al.,* 1999). Anaemia can be overcome by adding vitamin A, riboflavin or folic acid to the iron supplement that is administered to pregnant or lactating women, as well as children (Allen, 2002) or otherwise bioengineered foods like GMOs enriched in vitamin A (*e.g.,* 'golden rice') or iron are used in different parts of the world where nutritional deficiencies of vitamin and mineral intake are common (King, 2002).

Probiotic administration to pregnant and lactating mothers increased immuno-protective potential of breast milk and reduced the incidence of atopic eczema during the first two years of life in their children (Rautava *et al.,* 2002). Probiotics effectively treated diarrhoea and reduced the incidence of respiratory disease in infants (Rio *et al.,* 2002). Prebiotic foods are non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and / or the activity of one or a limited number of bacteria in the colon (Roberfroid, 2000). Prebiotics may be plant and/ or animal polysaccharides or oligosaccharides (Prosky, 2000). Lactulose, xylo and galacto oligosaccharides are the prebiotic oligosaccharides of choice for functional foods aimed at infants (Rastall and Maitin, 2002). Synbiotics are a combination of a probiotic and prebiotic. Synbiotic therapy in the shape of orally administered living being. *Bifidobacterium breve* and *Lactobacillus casei* together with galacto-oligosaccharides was successful in improving the intestinal function of prematurely born baby with laryngo-tracheo-esophagal cleft (Kanamori *et al.,* 2002).

It is particularly important that breastfeeding mothers to eat a well-balanced diet (Azizi and Smyth, 2009). Deficiencies of iron and other minerals have been shown to have immunological and biochemical effects. The complexity of human milk makes it the ideal food source for babies for at least the first 6 months of their life. This early nutrition is an important environmental input that can exert lifelong effects on the metabolism and development of the child. The amount and composition of human milk is probably dependent on the diet of the mother (Shehadeh *et al.,* 2006).

Breast milk provides all the nutrients needed to support adequate growth of the term infant during the first 4-6 months of life. It not only provides the recognized nutrients, but also a number of semi-essential nutrients such as enzymes, hormones, oligosaccharides and growth factors that also intervene in infant growth such as intestinal maturation (Koldovsky and Strbak, 1995). Human milk contains wide variety of proteins that contribute to its unique quality. Some of these proteins are digested and provide the amino acids, needed for rapid growth. Others participate in the digestion and utilization of micro and macro nutrients (Lonnerdal, 2003). As far as infants are concerned, milk oligosaccharides are supposed to be the optimal 'dietary fibre'. The total concentration of these oligosaccharides is of the order of 10 g/L in mid lactation and 25 g/L in colostrums. Colostrum also is rich in various biologically active molecules, which are essential for antioxidant functions. The soluble components of these molecules act in a child's gut without provoking any inflammatory response. The immunoglobulins in milk are also important for importing defence to the host. Approximately 75% of the total immunoglobulin protein milk is I_gG_1. Milk contains 0.6g/L of $I_g G_1$, whereas colostrum has it at a substantially higher level of 48 g/L. Other fractions are I_gG_2, I_gA, I_gM, all of which provide passive immunity.

Besides breast milk, there are anecdotal evidences encouraging the feeding of honey to new born babies by some customs and traditions. It is now an established fact that feeding honey to infants will improve memory and growth, reduce anxiety and enhance the children's performance in later life. In 2009, Chepulis and co-workers gave scientific credence to this beneficial practice in their study in animals. The authors concluded that early introduction of honey diet is beneficial and can improve memory loss and cognitive decline associated with ageing.

During the industrial revolution of the 20th and 21st century, many women left their children during the day to work in cities and artificial feeding became more popular. Many commercial products and formulas were rapidly introduced after the marketing of Liebig's infant food (consisting of cow's milk, wheat and malt flour, and potassium bicarbonate - was considered the perfect infant food) and the invention of evaporated milk (Radbill, 1981). With pasteurization and refrigeration, the very high mortality rate of artificially fed infants declined. In the 2005 Dietary Guidelines, USDA reported that many children do not obtain adequate amounts of calcium, pottassium, fiber, magnesium and vitamins A, C and E. This offers an opportunity for nutraceutical manufacturers to step and fill that void.

The supplementation of infant formula with prebiotic oligosaccharides is still discussed. Most recent findings are linked to the involvement of dietary fibre in occurrence or prevention of obesity. This finding will soon allow appropriate counseling for young mothers at risk of obesity and/or postpartum retention weight, gestational diabetes and preeclampsia (Champ and Hoebler, 2009). Moreover, the use of formula supplemented in oligosaccharides is able to compensate for the lack of some of the complex molecules naturally present in human milk (Champ and Hoebler, 2009).

The Infant Formula Act of 1980 authorized the Food and Drug Administration (FDA) to assure quality control of infant formulas (Fomon, 2001). The FDA requires the following nutrients be present

in all infant formulas: protein; fat; vitamins C, A, D, E, K, B1, B2, B6, and B12; niacin; folic acid; pantothenic acid; calcium; phosphorous; magnesium; iron; zinc; manganese; copper; iodine; sodium; pottassium; and chloride. Although the nutrients in synthetic formulas appear almost identical to the nutrients in breastmilk, manufacturers acknowledge on formula labels that breastmilk is the ideal form of nourishment for infants (Stehlin, 1993). The amount of each formula nutrient varies significantly compared to breastmilk. Moreover, formulas do not change in composition as the infant ages. Thus, formula is not responsive to a growing infant's nutritional needs, which makes the digestive process more difficult (Lawrence, 1994). Some of the name brands for the products included are Nestlé's Food®, Horlick's Malted Milk®, Hill's Malted Biscuit Powder®, Mellin's Food®, Eskay's Food®, Imperial Granum®, and Robinson's Patent Barley® (Radbill, 1981).

The onset of menopause is considered to be one of the most important phases in the life span of a female. Associated with this stage is the fear of various ailments due to progressively diminishing functions of the ovaries. Hormone replacement therapy (HRT) has been considered the traditional mainstay for achieving therapeutic relief of various menopausal symptoms. During the last few years, complimentary products and nutraceuticals have gained immense popularity when compared with HRT (Bajwa *et al.,* 2012).

A clinical study involving 66 post-menopausal women conducted at the University of Illinois (Erdman and Potter, 1997), found that 40 g isolated soy protein (ISP) per day (containing 90 mg total isoflavones) significantly increased (approximately 2%) both bone mineral content and density in the lumbar spine after 6 months. Albertazzi *et al.* (1998), study found that 60 g of ISP daily for 3 months reduced hot flashes by 45% in 104 postmenopausal women. Although these observations are exciting, there is a significant placebo effect in these studies, and it is too premature to suggest that soy may substitute for hormone replacement therapy. In another study of more than 40,000 postmenopausal women, garlic consumption was associated with nearly a 50% reduction in colon cancer risk (Steinmetz *et al.,* 1994). A review of epidemiological studies suggests that allium vegetables, including onions, may confer a protective effect on cancers of the gastrointestinal tract (Ernst, 1997). In contrast, 16-hydroxyestrone is estrogenic and can bind to the estrogen receptor. In humans, Indole-3-carbinol administered at 500 mg daily (equivalent to 350-500 g cabbage/day) for 1 week significantly increased the extent of estradiol 2-hydroxylation in women (Michnovicz and Bradlow, 1991), suggesting that this compound may be a novel approach for reducing the risk of breast cancer.

There has been a great deal of interest in pharmacological effects of tea. The consumption of five or more cups of green tea per day was associated with decreased recurrence of stage I and II breast cancer in Japanese women (Nakachi *et al.,* 1998).

8. Market potential of nutraceutical and its regulations

The desire for food with an added benefit awakened, with the promise not just of health-promoting qualities but also the ability to respond specifically to the needs of individual groups of customers, such as athletes, pregnant women, elderly or stressed people or also consumers with increased risks of contracting certain illnesses (Klaffke, 2007). Functional foods and nutraceutical products possess a high potential to improve the long term health of populations through disease prevention in cooperation with healthcare professionals. Research on functional food and supplements could become an important section of healthcare for its properties and for its high level of acceptance among the general population. Complementary and alternative medicine have been taught for many years in some medical schools and are recognized by many biomedical practitioners as having a sufficient evidence base for recommendation by physicians (*e.g.*, medical herbalism and enzyme therapy). Moreover, increased interest in health questions has drastically changed the factors dictating nutritional behaviour and enhancing the focus on the benefits of nutraceuticals (Giunta *et al.,* 2010). In this context of multiple increasing interests, government regulation of functional foods is needed to provide consumer protection and market support. However, there still exists ambiguity about the regulatory requirements related to nutraceuticals world over. Stringent regulations related to the safety and efficacy of these products is imperative to create a conducive environment for the sustainable growth of the nutraceutical industry (Zeisel, 1999).

According to Rishi (2006) and Hathcock (2001), the nutraceutical industry's three main segments include herbal/ natural products, dietary supplements and functional foods. Among these, the most rapidly growing segments are the herbal / natural products and the dietary supplements. The major ingredients used world wide are vitamins, minerals, PUFAs or specialty lipids, phytochemicals, prebiotics, probiotics, amino acids, peptides, proteins, fibers, carotenoids, polyols and others like CoQ10, glucosamine, chondroitin, lipoic acid, inositol, *etc*. Some of the pharmaceutical and biotech companies, which commit major resources to the discovery of nutraceuticals include Monsanto, American Home Products, Dupont, BioCorrex, Abbott Laboratories, Warner-Lambert, Johnson and Johnson, Novartis, Metabolex, Scio-tech, Genzyme Transgenic, PPL Therapeutics, Unigen, Interneuron *etc*. (Kalra, 2003).

8.1 Market

Globally, the nutraceutical market was estimated to be US$ 140.1 billion in 2010. Of this, USA and Europe formed the largest markets accounting to 36% and 25%, respectively. In 2010, the US nutraceutical market stood at US $ 50.4 billion and was by far the largest nutraceutical market in the world. The total European industry was valued at US $ 35 billion in 2010. Companies in Europe believe that product and ingredient innovation is the way forward for the nutraceutical industry. Germany, Netherlands and Sweden have emerged as the key nutraceutical innovation hubs in Europe, while Great Britain and Spain have emerged as key test markets for new products (Cygnus Report, 2010).

The Indian nutraceutical industry was estimated at US $ 2 billion, 1.5 percent of the global nutraceutical industry. Currently, an Indian nascent market is trying to incorporate traditional herbal ingredients (usually ayurvedic) into the nutraceutical portfolio. Example: *Chyavanprash* supplements (market size US $74.5 million in 2010). Broad segments of Indian nutraceutical industry include dietary supplement (40%) and functional food and beverage market (60%). In India, functional foods and beverages are expected to see increased consumption over the next five years, resulting in this segment garnering greater product share (67%) in the market as opposed to dietary supplements (33%). The total Indian nutraceuticals market in 2015 is expected to be approximately US $ 5 billion (Cygnus Report, 2010). Some of the marketed nutraceuticals are given in Table 3.

Table 3: Some marketed nutraceuticals

Marketed Nutraceutical	Category	Ingredients	Manufacturer
Weight Smart TM	Nutritional supplement	Vitamins and trace elements	Bayer Corporation, Morristown, NL, USA
Omega Women	Immune supplement	Antioxidants, vitamins and phytochemicals (*e.g.*, Lycopene, and resveratrol)	Wassen, UK
Rox	Energy drink	Taurine, caffeine and glucuronolactone	RoxAmerica, Spartanburg, SA, USA
Proteinex	Protein supplement	Predigested proteins, vitamins, minerals and carbohydrates	Pfizer Ltd., India
PNer Plus	Neuropathic pain supplement	Vitamin and other natural supplement	Neuro Help, San Antonio, Texas, USA
Mushroom Optimizer	Immune supplement	Mushrooms, polysaccharides and folic acid	Jarrow Formulas, Los Angeles, CA, USA
Chaser	Hangover supplement	Activated calcium carbonate and vegetable carbon	Living Essentials, Walled Lake, MI, USA
Calcirol D-3	Calcium supplement	Calcium and vitamins	Cadilla Health Care Ltd., India
Appetite Intercept	Appetite suppressant	Caffeine, tyrosine and phenylalanine	Natrol, Chatsworth, CA, USA
Betafactor Capsules	Immune supplement	Beta-glucan	Ameriden international Inc., USA
Tozal Eye Health Formula	Immproved vision	Omega 3 fatty acids, zinc, antioxidants and lutein	AmeriSciences, USA
Snapple-a-day	Meal replacement beverages	Vitamins and minerals	Snapple Beverages, USA
Brain Speed Memory	Brain health	Blend of vitamins and minerals	Natrol, USA
Red Bull	Energy drink	Taurine, caffeine and glucurono lactone, B-group vitamins	Red bull GmbH, Austria
5-Hour Energy	Energy drink	Vitamins, tyrosine, taurine, malic acid,caffeine and glucurono lactone	Living Essentials, USA
WelLife	Amino acid supplement	Granulated-L-glutamine	Daesang America Inc., Hackensach, NJ, USA
Pediasure	Nutritional supplement	Protein, vitamin and other natural supplement	Abbott nutrition Columbus, Ohio
Threptin Diskettes	Protein supplement	Proteins and vitamin B	Raptakos, Brett & Co. Ltd., Mumbai, India
Olivenol	Dietary supplement	Natural antioxidants, hydroxytyrosol	Cre Agri, Hayward, CA, USA
Beneflora Probiotic	Maintain gastro intestinal health	*Lactobacillus acidophilus*, *Bifido bacterium bifidum*	Nupro, USA
Ferradol Food Powder	Nutrition supplement	Carbohydrates, proteins, Niacinamide, calcium, iron, zinc,vitamins	Pfizer Limited, India
Muscle Optimeal	Meal replacement drink mix	Protein, vitamin, dietary fibers, xylitol and trace elements	Jarrow formulas, USA
Revital	Daily health supplement	Ginseng, vitamins and minerals	Ranbaxy, India
Becadexamine	Nutritional supplement	Multivitamins	GlaxoSmithKiln, UK
Glowelle	Beauty drink	Antioxidants, vitamins and botanical and fruit extracts	Nestle, Switzerland

Source: Rajat *et al.,* 2012

Table 4: Regulatory categories and general summary

Category	Scope	Safety	Standard claims
Drug	Product intended to diagnose, prevent, treat, or mitigate disease	New drugs must be demonstrated to be safe and effective	Must be approved by FDA
Conventional Food	Product used primarily for taste, aroma, or nutritive value, and in a conventional food form	Components must present "reasonable certainty of no harm"; must be FDA-cleared unless determined to be generally recognized as safe (GRAS)	Health and nutrient content claims must be FDA - authorized; other claims must not be false or misleading in any particular.
Dietary Supplement	Product intended to supplement the diet; must contain one or more "dietary ingredients" (*e.g.*, vitamins, herbs, substances found in the diet), be intended for ingestion, labeled as a dietary supplement, not represented for use as a conventional food, and not approved as a drug, among other criteria	Must not present a "significant or unreasonable risk of illness or injury"; new ingredients must be notified to FDA	Health and nutrient content claims must be FDA - authorized; structure/function claims must be notified to FDA; other claims must not be false or misleading in any particular
Food for Special Dietary Use	Food intended for supplying particular dietary needs (*e.g.*, those relating to disease, pregnancy, lactation, underweight, or overweight)	See conventional food standard above	Claims of special dietary usefulness (*e.g.*, usefulness in reducing body weight)
Medical Food	Formulated food intended for use under the supervision of a physician for the dietary management of disease with distinct nutritional requirements	See conventional food standard above	Claims for the dietary management of disease

Source: Pew Initiative on Food and Biotechnology, 2007

8.2 Regulations

Globalization of the nutraceutical and functional food industry presents significant challenges to stakeholders, not the least of which is the regulatory variance between countries active in the marketplace. The Federal Food, Drug, and Cosmetic Act (FFDCA; 1), as amended, does not provide a statutory definition of functional foods; thus, the Food and Drug Administration (FDA) has no authority to establish a formal regulatory category for such foods. In marketing such products, manufacturers may come under one of several existing regulatory options. The FDA believes that available regulatory categories of foods provide flexibility and opportunity in regulating the so-called functional foods (Ross, 2000). Accordingly, legislative frameworks are now well developed in countries such as Japan that allows more than 200 functional foods to be marketed under existing FOSHU (Foods for Specialized Health Use) legislation and the United States where the Food and Drug Administration (FDA) permits health claims to be made for about 15 categories of food. An overview of the regulatory categories and claims of drug, conventional food, dietary supplement, food for special dietary uses, and medical food presented in Table 4.

In India, as per the Food Safety Standard Act, 2006 (Chapter 4, Section 22), it has been recommended that food should be classified as follows: novel foods, genetically modified food, irradiated food, organic foods, foods for special dietary use, functional foods, nutraceuticals and health supplements. This makes it very clear that nutraceuticals are a part of the food segment and it should not be considered as a form of pharmaceutical or drug formulation (Smarta, 2010).

Recently, India has implemented the new law FSSA (Food Safety and Standards AOI). The Food Safety and Standard Rules, 2011 have been issued and have become effective from 5th May, 2011. The Food Safety and Standard Authority have also issued regulations with respect to Licensing and Registration of food business, packing and labeling, food products standard and additive *etc*. The Acts, Rules and Regulations are now implemented from 5th August, 2011. Thus, there is now one single legislation and specified authorities to regulate manufacture, distribution and of sale nutraceuticals, functional foods and dietary supplements in India (MOFPI, 2014).

9. Conclusion

There is a strong connection between what we eat and our health. A better understanding of the same would lead to the development of an alternate mode of healthcare through diet regulation. This trend is now fast emerging, particularly in the developed countries. Food and nutritional supplements would be recommended, after studying the constitutional nature of the individual, which would enable him to lead a healthy and agile life. Such a situation will revolutionize the healthcare in the twenty-first century. It will also cut down substantially the expenditure on health sectors, both by the individuals as well as by the governments.

In India, it was a tradition to have specific dietary regimes in different seasons that varied from region to region. The Indian tradition, particularly the traditional system of medicines like *Ayurveda*, gives a detailed account on the type of food to be taken by people in different seasons and in different agroclimatic

conditions. It also recommends various do's and don'ts in the selection and combinations of food articles. We have to learn, thus, a lot from the traditional wisdom of our people and also an urgent need to have fresh look at our traditional dietary habits and revive the use of all those food articles that promote and protect health. Realizing the folly of the fast food culture, the western world are now turning to traditional diets or ethnic foods and converting this knowledge system of the traditional communities to value added forms such as functional foods and nutraceuticals and, thus, making a good market for such products. India with such a diverse traditions in food habits must take best advantage of this situation and strive to become a leader in global market of functional foods and nutraceuticals. In this context, stringent regulation related to the safety and efficacy of these products is imperative to create a conducive environment for the sustainable growth of the nutraceutical industry.

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Conflict of interest

We declare that we have no conflict of interest.

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