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Bioactive substances and functional foods

Kamala Krishnaswamy

Introduction

Throughout the world, including in Asia, consumers are looking for health foods that can not only prevent diseases but can promote health and well-being. New science-based investigations are emerging, which appear to confirm the wisdom inherent in the traditional use of some of these foods, and to support the long history of the use of such foods by humans. Mounting health care costs and the consumer's desire to maintain health and quality of life, have focused the attention of biomedical researchers and public health scientists on diets and disease prevention.

Alternative therapy or complementary therapy with plant-based medicinal foods is rapidly gaining attention, both within the scientific community and among consumers. Foods sculpt the body's needs for nutrients and phytonutrients. They have several physiological and biochemical advantages, and are nowadays particularly being considered for their beneficial effects in the context of chronic ailments. Most of the bioactive constituents appear to modify the aetiopathological processes of atherosclerosis, inflammation, immunopathology, and carcinogenesis. Dr.C. Gopalan has been championing food-based approaches to tackle nutritional disorders and has always preferred dietary approaches. He says, "Look towards Farms and not towards Pharmacies for prevention of nutritional diseases and promotion of health". While identifying active compounds in foods is a scientific approach, the complete foods are more relevant to health and disease, given that the food matrix impacts availability, interactions and responses. The origin of all functional foods is based on the science of analytical epidemiology, and it is essential to understand that there may not be uniformity in responses .

Ancient Hindu religious literature *(Vedas)* says that "Annam is Aham" meaning 'you are what you eat' and Hippocrates declared "Let food be your medicine and medicine be thy food". Current science reinforces these statements and the food markets today, particularly in the Western world, are full of functional/novel foods or nutraceuticals. Technological advances have helped to develop products in concentrated forms, or in forms that can be easily assimilated, or as combinations of foods for greater benefits. It must be stated here that foods are natural sources of nutrients and a diversified diet can be a rich source of all the necessary bioactive substances. It can very effectively impact pathological processes that lead to deficiency and chronic disorders. Nutrition education and food guides can help to promote food-based approaches for all biologically effective molecules. Japan is the first country that explored the boundary between food and medicine. India is a land of herbal products and plant-based vegetarian diets. Countries like China, Korea and Srilanka are also steeped in the medicinal food tradition. Wider acceptance of the medicinal value of foods and their use will cut down the health care costs as well. However, it is important to provide science-based evidence of their biological functions. The health benefits of functional foods should, in fact, extend beyond their macro- and micronutrient composition[1]. A functional food or a medicinal food is any fresh or processed food claiming to have a health-promoting and/or disease-preventing property beyond the basic nutritional function of supplying nutrients, although there is no consensus on the exact definition of these terms.

However, it is important to realise that it is not always possible to ascribe therapeutic benefits to individual components; even if such components are identified, it may not be possible to get the maximum benefits of isolated compounds unless they are given as part of a food-based approach. In other words, the reductionists' approach may not be meaningful; it is the holistic approach that can work. In foods, the bioactive constituents may have synergistic or additive effects. Multiple food components may result in the desired effects, from a particular food matrix. More information on molecular

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and cellular effects of bioactives will be critical in the development of effective and or proactive approaches to reducing the burden of diseases. Strategies for identifying those who will benefit most from dietary intervention are also needed if public health messages are to be effective and have meaningful impact on health and well-being. Current literature accords great importance to the long history of human use of a variety of foods, as they are likely to yield novel drug prototypes for chronic diseases such as cardiovascular (heart attack), cerebrovascular (stroke), and neurodegenerative (Alzheimer's and multiple sclerosis) conditions, as well as in cancer, inflammatory problems such as arthritis, cataract, and toxicity caused by drugs and toxins.

Biological effects

Foods and food ingredients, singly or in combination, have been investigated for their biological effects that could potentially protect against cardiovascular pathology, cancer risk, inflammation, immune suppression, bone problems ,neurological damage, suboptimal performance levels, problems associated with the gastrointestinal tract, and hormone-related problems, besides actively promoting good all-round health and general well-being (Text Box 1)[2].Thus bioactives have a role beyond mere nutrition support. They are substances that are useful in preventing disease and ill-health and also in actively promoting health.

Bioactive compounds

Many bioactive substances have been identified. As on date, more than 500 compounds have been identified and tested for biological functions and mechanisms of action[3]. Some of these are listed in Text Box 2. Some families of fruits and vegetables have characteristic components that may confer a particular health benefit. Cruciferous vegetables are sources of glucosinolates and their products, isothiocyanates and indoles. Allium vegetables contain allicin. Allyl sulphides and allicin in garlic give it its distinctive flavour. Green, leafy vegetables are sources of folate, iron, calcium and carotenoids, while tomatoes contain high levels of lycopene. All these components, as well as other phytochemicals, have potential health benefits.

Text Box 2 Bioactive compounds

Simple phenols	Most vegetables / spices / beverages
Carotenoids	Green / yellow / orange vegetables / fruits
Flavonoids	Vegetables / fruits / tea
Indoles/ Isothiocyantes	Cruciferous / Brassica vegetables
Glucosinolates	Cruciferous vegetables
Organosulfides	Allium vegetables
Polyphenols	Fruits / cruciferous vegetables / nuts / spices
Protease inhibitors	Potatoes / beans / nuts/cereals
Phytoestrogens/isoflavnes	Soya/soy products
Epigallocatechin gallate	Green tea
Lycopene	Tomatoes
Limonene	Citrus fruits
Pre&probiotics	Dairy products

<u>Nutrients</u>

B.complex vitamins	Green leafy vegetables/nuts/pulses
Vitamins E, C	Citrus fruits/cereals/vegetables
N3 fatty acids	Fish / oils / green leafy vegetables / spices/nuts/
Minerals (Ca,Mg,K,Fe)	Several vegetables / milk & dairy products
Fibres	Vegetables/fruits/cereals/legumes
Low energy food	Most vegetables/fruits

Text Box 1 Benefits of functional components

- A general tonic / energy giving / health promoting food.
- A hypolipedemic food/ hypotensive or cardiovascular protectant
- An immune potentiator
- A hormone regulator
- A gastrointestinal function modifier
- 6 .Modifiers of glycemic response
- Memory enhancers
- A bone health modifier
- Promoters of healthy skin
- Reducers of risk of cancer
- Weight reducing agents
- Ageing modifiers

Text Box 3 Mechanisms of action

- Antioxidant activity
- Modulation of activating and deactivating enzymes.
- Anti-inflammatory response and altering immunity
- Alterations of lipid and lipoprotein metabolism and platelet reactivity
- Stabilising endothelial functions and vascularity
- Altering hormone metabolism
- Antibacteriial and antiviral activity
- Cellular division, differentiation, apoptosis and DNA stability and repair.

Mechanisms of action

The bioactives, as present in foods, can be termed as functional foods. When consumed as foods they elicit biological responses.There are several mechanisms by which the bioactives elicit the response. Most of them have strong antioxidant potential while others act by modifying xenobiotic metabolising enzymes, altering lipid metabolism, or altering steroid hormones as shown in Text Box 3.The interaction between the diet and phytonutrients is a complex field, as thousands of dietary components are consumed each day (>25000) through routine diets. Dietary bioactives may modify a multitude of processes in normal cells. A single, bioactive food constituent can modify multiple steps in molecular and cellular events such as nutrigenetics, nutritional epigenomics, nutritional transcriptomics, proteomics and metabolomics. Many of these processes can be influenced by several food components. Further, the dose, timing, duration of exposure, and interactions may alter responses and ultimately the phenotype or manifestations.

Human beings are constantly exposed to genotoxic damage due to activation of foreign compounds, which result in oxidative metabolites. These are further metabolised to watersoluble compounds through the action of deactivating enzymes. This renders them less toxic, and they are eliminated from the body. The biotransformations, pharmacokinetics, pharmacodynamics and toxicokinetics will depend on pharmacogenetic variations of xenoboitic metabolising enzymes that are responsible for inter-individual responses, risk of toxicity, and consequent disease.

Inflammatory reactions are hallmarks of chronic diseases. Several foods can impact inflammatory cytokines, angiogenesis, reactive oxygen and nitrogen species, and eicosanoids. Cellular proliferation, differentiation, and cell death are important events that can respond to various food items. So is the case with DNA stability, damage and repair. Both endogenous substances and exogenous agents (food ingredients) can impact these processes.Thus, a variety of foods, through a variety of mechanisms, either collectively or singly, can exhibit several actions that promote health and well-being and delay the onset of age-related malfunctions and pathogenesis of chronic ailments.

Development of functional foods

The development of functional foods requires a multidimensional approach[4]. In order to meet consumer needs under the existing food regulations, nutritionists, food chemists, food technologists, biochemists, toxicologists and clinicians must work together to produce a product or to claim the appropriate health benefits of existing foods. Epidemiological investigation may provide evidence-based scientific information, whch needs to be studied experimentally for biological responses, using appropriate biomarkers. Further, these will need to be tested in clinical trials for establishing their health benefits or risk-reducing effects. Foods such as cereals, pulses, nuts, vegetables, fruits, beverages and spices have been widely studied. Genetic manipulations to increase the content of active ingredients may also be useful for enhancing bio-potency (for example, omega 3 eggs, golden rice). Technological innovations can improve the product (for example, soy fermented sauces, pre- and probiotics. It is also possible to add a bioactive to a traditional food (for instance guargum, fenugreek powder or bran). In such situations, it is necessary to keep in mind the bioavailability of both the active and other physiologically relevant ingredients. The next few sections encapsulate some effects of functional foods which deserve attention, as they are not only commonly used but can be marketed as functional foods for their potent biological effects.

Dietary fibres

Dietary fibres are cardio-protective, as they decrease cholesterol and triglyceride levels, thereby reducing the risk factors for cardiovascular disorders[5]. The concept of fibre and its physiology has advanced considerably, even though it is still not defined properly. It does encompass a broader range of ingredients than was originally described. Nondigestibility and nonabsorbability in the small intestine are the *sine qua non* characteristic of dietary fibre. It currently includes resistant starch as well as oligosaccharides. Synthetic food fibres have similar properties. As these fibres pass through the gut, they are fermented by the microflora. This process is of physiological importance. Fibres reduce the toxic components in faeces and have prebiotic effects (fructans). Their functions include stool bulking, laxation, fermentation and gut health, hypocholesteremic and triglyceridemic actions, as well as postprandial reduction of glucose and insulin levels. The terms “soluble” and “insoluble” are no longer being used. This is because some insoluble fibres are fermented while not all the soluble fibres affect fat and glucose absorption. They are primarily carbohydrate polymers that are components of plant cell walls, and include cellulose, hemicelluloses, glucans, pectins, gums, mucilages, oligosaccharides and inulin, resistant starch, fructo- and galacto-oligosaccharides, modified celluloses, and lignins. The major sources of food fibre are cereal grains, pulses and legumes, vegetables and fruits. In large epidemiological studies in men in the highest quintile of fibre intake (~ 30g) the death rate due to coronary disease was reduced by 30-40%. Therefore fibre, either in its naturally occurring form in foods or added as a dietary supplement, is encouraged as a method of lowering the incidence of cardiovascular diseases (CVDs).

Fenugreek seeds

Fenugreek (FG) or *trigonella fenum graecum*, a spice introduced into India from South-West Asia and South-East Europe, belongs to the family of leguminose. The dried seed is used as a spice while the leaves are used as vegetables. India is one of the major producers and exporters of fenugreek. The estimate of its nutritive value shows it to be a rich source of protein, fibre and omega 3 fatty acids. Several experiments carried out in animals showed that fenugreek incorporated into the diet at 5, 10 and 20% levels produced a hypolipedemic effect[6]. This functionality was attributed to its fibre content galactomannan. The seeds contain 48% by weight of fibre and 2% omega 3 fatty acids. In a randomised, cross-over design metabolic study of non-insulin dependent diabetes mellitus (NIDDM) cases, fenugreek was administered to subjects (100 g defatted fenugreek powder) for 10 days[7]. There was a significant reduction in blood glucose leading to an improvement in glucose tolerance. Fenugreek seeds, as such or debitterised, exhibited hypochlolesteremic and hypotriglyceredemic effets. In subjects who received FG for a period of 20 days as unleavened bread in a dose of 25g on alternate days, there was a significant reduction in urinary glucose excretion accompanied by reduction in cholesterol and triglycerides[8]. Its hypoglycemic effect has not been fully explained in terms of the fibre present, and therefore intravenous glucose tolerance test (IV GTT) was performed in type 2 diabetic subjects. The results indicated that, even after intravenous administration of glucose, there is a significant reduction in the area under curve (AUC) and half-life, with a significant increase in the clearance as well as red blood cells (RBC) insulin receptors. Obviously there is increased peripheral glucose utilization as well[9] Further studies were done in experimental animals to study the effects of FG on cataract in chemically induced diabetes. The results showed that 10 and 20% levels of FG in the diet led to a significant impact. The biochemical parameters of cataractogenesis were altered and, in the obese animals, there was a significant reduction in glucose, cholesterol and triglycerides when compared with the results following administration of 2.5% of galactomannan isolated from fenugreek. These effects were due to increased bile acid excretion. A peculiar aminoacid, 4-hydroxyisoleucine, extracted from fenugreek seeds, exhibits insulinotropic activity[10]. Thus, fenugreek seeds have great potential as a functional adjunct in the treatment of diabetes. Several recipes have been developed in the Indian context. The gel-forming property of fenugreek fibre reduces gastric emptying, glucose absorption and insulin response. A mild improvement in clinical symptoms such as polydypsia and polyuria was observed in a majority of the patients, with a reduction in anti-diabetic drug doses. Incorporating just around 25 g fenugreek seeds in the daily diet can serve as an effective supportive therapy in the management of diabetes.

Omega 3 fatty acids

Nutritional pharmacology apparently developed as a corollary to medical pharmacology, especially in the management of cardiovascular problems. Based on the epidemiological data in Eskimos, who are fish consumers, it was considered important to study the effects of omega 3 fats. Literature is replete with evidence that omega-3 fats have several biological effects, and the dietary guidelines of all countries suggest the inclusion of fish for the prevention and management of CVD. Omega 3 fats reduce lipids and lipoproteins, bloodpressure, cardiac arrythmias (electrophysiology), vascular reactivity, and endothelial function, and have antiplatelet and anti-inflammatory activity[11]. While docosahexaenoic acid (DHA) affects lipids and lipoproteins, blood glucose, and heart rate, the mixture of eicosapentaenoic acid (EPA) and DHA reduces platelet aggregation. Long-chain n-3 fats reduce triglyceride levels significantly[12]. In a long-term intervention study with fish oil (1g/d) for 3.5 years, the group taking fish oil showed 20% reduction in total mortality, 30% decreased mortality on account of cardiovascular events, and 45% decrease in sudden deaths[13]. Thrombotic and arrhythmic events were much fewer in a group that received alpha linolenic acid (ALNA), though, in this study, other inputs such as fibre and antioxidants were also altered. Although most studies in secondary prevention support the beneficial effects of omega-3 fats, it is not very clear whether these fats will be of use in primary prevention. The results of several studies have suggested that long-chain omega-3 fatty acid intake is associated with a reduced risk of numerous other diseases such as cancers, immune disorders, asthma, and neurologic disorders. In addition to their benefits in the context of CVD and restenosis, they are thought to be useful for therapy of arthritis, psoriasis, and ulcerative colitis .

Other functional foods for CVD prevention

Since single ingredients or fish alone may not be the total answer, combinations of functional foods are currently being investigated. A portfolio diet is being recommended, with functional foods such as soy protein(25g), flavonoids, nuts(1.5 ouncesalmonds), viscous fibre plant sterols (1.3g), and plant stanol esters (4 g), all of which reduce low density lipoprotein (LDL) by 4-7%[14]. The fibre is from vegetables, fruits, and grains that contain soluble fibre. In a clniical trial, this diet was found to be as effective as statins in reducing LDL (30%). It decreased C-reactive protein as well. The Mediterranean diet is a functional diet that is protective against CVD as illustrated by The Lyon Diet heart study[15]. It consists mainly of abundant fruits and vegetables, fish (0.5-1.8g/d of EPA and DHA), nuts, wine and olive oil. There is very little intake of red meat, and the diet in general is low in saturated fats. Similarly, flaxseed, garlic (one fresh clove), black tea, psyllium (1g/d), nuts(phenols, flavonoids, isoflavonoids, phytosterols), cocoa(flavonoids), walnuts (ALNA-1.5 oz/d), red wine (resvertro l8-16oz./d for reducing platelet aggregation) are all functional foods that impact the CVD risk profile[16]. A recent meta-analysis using principal component analysis of several randomised studies dealing with combinations of functional foods and their effects on cardioprotection (lipids), showed significant results. Two principal components were adequate to explain the hypolipidemic results[17]. Phytosterols and fibre had a hypocholesterolemic effect, while n-3 fatty acids lowered triacylglycerol. Thus, mixtures of functional foods or food-based approaches appear to be more attractive than the use of single foods.

Anticarcinogens

Several epidemiological studies reinforce the fact that cancer is a complicated, multifactor, multistage, and multi-manifestation disease with the process of initiation and final manifestation being separated by a long latency period. Hence, it is difficult to establish a cause-and-effect relationship between a particular item of the diet and cancer. Several may be interrelated. One study estimated that almost 35% of all cancers may be attributed to dietary factors[18]. Similar estimates have been made by others as well. Therefore dietary and life-style modifications are of prime importance in prevention of cancers, of various types and at various sites. The medical literature provides mechanistic evidence for the role of several of the dietary substances. Molecular mechanisms further reinforce a role for dietary ingredients through gene-nutrient interactions. Dietary antimutagens and anticarcinogens have a role to play by preventing the damage to macromolecules, particularly deoxy-ribonucliec acid (DNA), through several mechanisms including gene expressions, epigenetic mechanisms and growth inhibition by shutting off proliferative messages, inhibition of cell division, promoting apoptosis, differentiation, telomerase inhibition and angiogenesis inhibition. Research reaching into the fields of genetics, epigenetics, proteomics and metabolomics is required in order to understand the role of diet in the cancer process[19].

Turmeric as a functional cancer-preventing agent

Turmeric, an Asian spice labelled as a “poor man's spice” or as “salt of the Orient” is not only known for its colour, aroma and taste, but is being researched all over the world for its preventive and therapeutic benefits. Derived from the rhizome, the root is routinely used as a spice in Indian cuisine. Ayurveda, an ancient system of medicine originating in India, has eulogized spices as wonder foods. In this connection, turmeric and its active principles curcuminoids have received considerable attention among biomedical scientists, medical professionals, pharmacologists, food scientists and nutritionists all over the world. Literature is replete with mounting evidence that agents such as turmeric and its constituents, curcuminoids, promote health and prevent diseases[20]. Turmeric (along with its active principles, curcuminoids) has pleiotropic effects and has received considerable attention as an anti-inflammatory, antiatherosclerotic and anticancer agent[21]. It exhibits several molecular targets and is similar to many other phenolic compounds found in other spices, in fruits and vegetables, and in beverages such as tea and wine[21]. Traditionally, turmeric has been used as a food preservative, as it protects and preserves foods against spoilage and infestations. It masks off flavour and protects against decomposition and bacterial spoilage. These traditional practices are now supported by new scientific evidence, and apparently the constituents which protect the plant and food also protect several biomolecules of the body, preventing degenerative disorders that result in chronic diseases. The properties and uses of turmeric/curcuminoids are truly kaleidoscopic.

Traditionally, turmeric has been used as a general tonic, as an anti-infective, and also for skin ailments, wound healing, gastrointestinal and respiratory disorders, arthritis, and several viral disorders. To date, we have evidence that it is a potent anti-inflammatory-anti-oxidant with anti-atherosclerotic and anti-cancer effects[20]. Curcumin promotes wound healing and tissue repair. It controls over-reactive inflammatory reactions and improves inflammatory bowel disorder, peptic ulcer and gall stones. Turmeric/curcumin impacts blood lipid and platelet aggregation. The emerging scenario suggests that curcumin, given its multiple effects such as arrest of cell cycle, inhibition of signal transduction cascade and transcription factors (NF-Kappa-B), inhibits growth response gene, growth factors and oncogenes controlling cancer and metastasis[21]. Both curcumin and turmeric are antimutagenic antioxidants, protecting against DNA repair, inducing xenobiotic drug matabolising enzmes (particularly the conjugating systems), promoting apoptosis, preventing angiogenesis and inhibiting telomerase. In keeping with its anticancer effects, it reduces, inhibits or delays tumours in skin, oral cavity, forestomach, duodenum, stomach, colon, breast, prostate, liver, lung and ovary, and also has beneficial effects in blood cancer (leukaemia). Innumerable studies demonstrate its anticancer activity against many cancer cell lines. Thus, curcumin is a potent preventive, and possibly even therapeutic, anticancer chemical agent, as it targets several mechanisms of cancer.

Curcumin has been shown to

- offer protection against
  - ischemic injury to the heart,
  - chronic inflammatory lung diseases,
  - radiation damage,
  - hyaline membrane disease in pre-term infants,
  - pancreatitis,
  - cystic fibrosis,
  - inflammatory bowel disease,
  - multiple sclerosis,
  - Alzheimer's disease,
  - toxicity due to pesticides and aflatoxin,
  - renal injury due to drugs and toxins,
  - scleroderma,
  - hepatotoxicity
  - fibrosis.
- counteract muscle injury and stress responses,
- ameliorate oxidative damage to the lens of the eye,
- reduce diabetes and its complications.

The various effects of curcumin are mainly due to its antioxidant, anti-inflammatory, antiproliferative and antifibrotic effects. It has anti-bacterial, anti-fungal, anti-viral (AIDS & human papillomavirus - HPV) activity as well[20]. However, most of the studies have been either *in vitro* or *in vivo* in animals.Even though curcumin has several biological effects, its pharmacokinetics show a poor bioavailability, and large doses are needed for clinical trials. Oral administration of turmeric and curcumin is well tolerated.

Several trials, albeit not very well designed, have been carried out with positive results[20]. The very first clinical study was in India, and it was aimed at assessing the anti-inflammatory effects of 1200 mg of curcumin in patients with arthritis. The clinical symptoms of arthritis were ameliorated. Similar was the observation with respect to post-operative inflammation and idiopathic orbital tumors. Observations in cancer with turmeric extracts for local applications indicated positive response, in studies carried out in India and in Taiwan[22]. Patients with submucous fibrosis and oral leukoplakia showed clinical improvement and reduced micronuclei in oral cells[23]. Turmeric 1-1.5g/d in reverse smokers reduced pre-cancerous lesions on the palate as well as DNA adducts and micronuclei in oral epithelial cells[20]. In subjects with colon cancer, a dose escalation study did not exhibit any toxicity, and carcinoembryonic antigen (CEA) and cyclo-oxygenase-2 (COX2) levels were reduced[24].

Recent clinical trials have yielded some positive results. Patients with pancreatic cancer who received 8 g/day of curcumin orally for two months were evaluated for response and for toxicity. Four patients had stable disease (2+, 2+, 3+ and 7 months) and one patient had a brief partial remission (73% reduction in tumour size) that lasted one month. No toxicities were observed[25]. Curcumin was well tolerated, and this preliminary clinical trial suggests biologic activity in pancreatic cancer.

In multiple myeloma patients, curcumin in doses of 2-12g/d, was able to downregulate NF-kB, STAT3 and COX2. The authors draw the conclusion that there is a potential therapeutic role for curcumin, that should be further investigated either alone or in combination with other active agents as a modulator of chemo-resistance[26]. Preliminary studies are being undertaken with curcumin in patients with Alzheimers disease and those with cystic fibrosis. In an open trial, turmeric administered in the form of 300 mg capsules was found to cure peptic ulcers. Curcumin is also documented to have antipsoriatic activity in humans[20]. Thus, in the near future, turmeric/cucumin will be recognised as a nutraceutical. Despite its poor bioavailability it can be used in India in higher quantities along with food to help in the prevention of a variety of disorders.

Though there are several substances/ingredients which seem to impact the cancer proceses, as on date we are far from having firm evidence based on science to guide policy decisions. Nonstarchy vegetables probably protect against upper aerodigestive cancers. Foods containing beta carotene and vitamin C probably protect against oesophageal and lung cancers[27]. Similarly, allium vegetables (garlic) and fruits probably protect against stomach cancers. Folate-containing foods probably prevent pancreatic cancers. Foods containing dietary fibre, garlic, milk, and calcium probably protect against colorectal cancers. Foods containing lycopene and selenium, and selenium supplements, probably prevent prostate cancers. In *in vivo* experiments, herbs and spices such as saffron, ginger, pepper and spice mixes are biologically potent as cancer-preventing agents. Only future studies in humans can throw further light.Nevertheless, one can recommend foods containing these to be consumed as dietary supplements[28].

Coccinia indica

Coccinia indica (ivy gourd), belonging to the Cucurbitaceae family, has been widely used in the traditional treatment of diabetes mellitus in India. In a double-blind, randomised placebo-controlled study in newly detected diabetes (type 2) patients, an alcoholic extract of 1g (equivalent to 15g wet weight) of leaves and fruits induced a hypoglycaemic effect within 90 days of treatment. Both fasting and post-prandial blood glucose fell by 16 and 19%, respectively, with lowering of glycosylated Hb. No other alterations in anthropometry or blood lipids were observed[28]. The ingredients present in the extract of *coccinia indica* such as triterpenes, probably act like insulin, correcting the enzymes of the glycolytic pathway and enhancing lipolysis. As a common vegetable in Indian cuisine, it can be an excellent adjunct in diets for persons with diabetes.

Health claims, substantiation and regulations:

A health-related claim can be:

(i) a nutrient function claim,
(ii) a structure/function claim (enhanced function claim), or
(iii) a health claim or disease reduction claim.

However, some countries do not permit a disease reduction claim (eg. Malaysia). “Functional food” was a term that was first proposed by the Japanese scientific academy. Subsequently, it was changed to “Foods for specified health use” (FOSHU), and an attempt was made to pass legislation requiring that its efficacy be described on the label[29]. Appropriate randomised clinical trials need to be carried out in subjects/patients for whom the food is indicated, with necessary markers and statistics. Guidelines have been set for clinical trials.

The “Functional Food Science in Europe” (FUFOSE) project defines a functional food as one that has been demonstrated to affect one or more target functions in the body. On the basis of evidence-based medicine, randomised, placebo-controlled, double-blind trials are to be carried out for recommendations at population level. ILSI Euorope set up a project "Process for the Assessment of Scientific Support for Claims on Foods” (PASSCLAIM) which started with FUFOSE, and built upon the principles defined within the publications arising out of the FUFOSE project[30]. It selects common criteria for how markers should be identified, validated and used in well-designed studies to explore the links between diets and health claims. The development of functional foods should be based on a sound scientific knowledge of the target function in the body and the demonstration of effects relevant to improved health or reduction of disease risk. The project identifies foods based on evidence from human studies using markers relating to biological response or on intermediate endpoint markers of disease, as being capable of providing a sound scientific basis for messages and claims about functional food products. It says that it should examine the existing legislation and dietary guidelines, review the evolving science; and make it comprehensible to consumers. The food or its ingredient should be characterised, and substantiation should be based on well-designed studies in humans comprising the target goup for a sufficiently long duration so as to elicit a respone. When end-points cannot be defined, appropriate biomarker(s) should be identified and used as intermediate endpoints. A relevant biomarker is a well-defined biological, physiological, clinical or epidemiological indicator. Ingestion of the food, food constituent or ingredient should modify the specified biomarker for which there is a relationship between the state of health and the measured parameter. A claim should be scientifically substantiated by taking into account the totality of the available data and after weighing all the evidence.

It is very important to define and implement rigorous, standardized manufacturing stages/procedures, quality assurance and quality control techniques. In the case of dietary supplements, the FDA in the US permits a qualified health claim based on emerging evidence of substance / disease relationships. In India, the recent Food Safety and Standards Act[31], which is yet to be implemented, provides that all functional foods/health foods/nutraceuticals have to be approved by a special panel.

Conclusions

The concept of functional foods has been accepted internationally. While literature is full of reports of the benefits of food ingredients, the strength of evidence ultimately lies in deciphering the role of specific diets or culture-specific patterns with documentation of diseases and risk factors in the groups concerned. Genetic polymormhisms can complicate the issue. In sub-populations, results may vary. Randomised trials, regional differences and cross-country trials may provide the final answers. Well-designed intervention studies can go a long way towards a prescriptive approach. It is also important to realise that effect size may be small and benefits may be seen after long periods of time. Although these foods are known by different names- nutraceuticals, dietary supplements, or functional foods, they hold significant promise in the promotion of human health and disease prevention. However, health professionals, nutritionists, regulatory toxicologists and government regulatory bodies should work together to plan appropriate regulations to provide the ultimate health and therapeutic benefits to Mankind. One should keep in mind a remark attributed to Paracelsus (14931541 AD) : “the dose makes the poison”. The right dose differentiates between the remedy or cure, and toxic/adverse reactions.

The author is Former Director, National institute of Nutrition, Hyderabad

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FOUNDATION NEWS

- NFI is organizing a symposium on "Nutrition and physical performance in school age children" on July 10th 2009.

Nutritional status during childhood is a major determinant of nutritional and health status in adolescence and adult life. As per 2001 census, 7-14 yrs old constitute up to 20% of the total population. This is a critical influencer on the growth and long-term health of the nation. India is currently in the midst of a nutrition transition. Undernutrition continues to be a major public health problem but overnutrition is concurrently emerging as a health concern, especially among urban school going children. The increase in consumption of energy-dense food plays a role in the increasing over-nutrition rates in children.

Iron and other micronutrient deficiencies are widespread both among undernourished and over-nourished children. These micronutrients are key regulators of body metabolism and play an important role in achieving optimal physical performance. Evidence suggests a declining trend in the physical fitness, a key determinant of performance, of all the segments of 'healthy' population including the pediatrics. The steep reduction in the levels of physical activity at home, in school, in transportation and play has been implicated as another major cause. The symposium will review and discuss some of the aspects of nutrition and physical performance in school age children in the Indian context.

Dr C Gopalan will deliver the inaugural address and the following speakers will make presentations in the symposium:

Dr B Sesikeran: Nutritional status of Indian children

Dr Anoop Misra: Health status of Indian children

Dr Luis Moreno: Assessing physical fitness in children methods and considerations

Dr Mario Vaz: Nutritional intervention for optimising physical fitness in children

Dr Anura Kurpad: Framework of physical fitness and role of protein in physical performance

Dr Tarun Gera: Role of micronutrients in physical performance/ fitness

Dr MKC Nair: Need for norms for fitness and performance

Dr D Prabhakaran: Community-based approaches for improving physical activity

- Dr Sarath Gopalan, Deputy Director, NFI attended the Annual Conference of PENSA held in Kaulalampur from 5th 7th June 2009. He also made a presentation on "Feeding the critically ill child a holistic approach".

NUTRITION NEWS

The 41st Annual Conference of the Nutrition Society of India will be held in November 2009 at National Institute of Nutrition, Hyderabad. The details of the conference can be downloaded from the website http://www.nutritionsocietyindia.org.