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BIOACTIVE PHYTOCHEMICALS IN HEALTH PROMOTION AND DISEASE PREVENTION

ABSTRACT:

Other than being a source of nutrients, foods, especially plant foods, are a rich source of bioactive phytochemicals .Studies carried out during the past 2–3 decades have demonstrated that these phytochemicals have an important role in chronic diseases like diabetes, atherosclerosis, obesity, osteoporosis and cardiovascular diseases.

Evidence from a variety of studies strongly points to a positive link between different phytochemicals like carotenoids, various phenolic compounds, organosulphur compounds, dietary fiber and their disease preventing functions and have demonstrated various modes of action. The review emphasizes these health benefits with the importance of consuming fruits, vegetables, soyabean etc for the general condition of wellbeing of the population and points out some technical and scientific opportunities that can be explored in developing countries.

Key words: bioactive phytochemical, chronic diseases, health

INTRODUCTION

For maintaining good health in humans several foods are essential. From 19th century, studies have been conducted on the identification of important nutrients in food and their metabolism and functions. Also Studies have been emphasized on dietary deficiency of these nutrients and their functional and clinical consequences.

Phytochemical Evolution

Studies on some anti-nutritional and toxic factors that are present in various foods were also carried in the 1980s.These non-nutrient components included antitrypsins, which interfere with dietary protein utilization, Phytates and Tannins, which interfere with iron absorption and oxalates, which inhibit dietary calcium absorption. Other non-nutrient components which include ßN oxalyl L αß diamino propionic acid (ODPA) in Lathyrus (Lathyrus sativus) seeds that lead to lathyrism, and goitrogens, such as thiocyanates and isothiocyanates, that interfere with iodine utilisation for the synthesis of thyroid hormones, leading to goitre or iodine deficiency disorders. In 1960s and 1970s, intention was on natural and environmentally-derived toxins such as aflatoxin, pesticide residues and heavy metal contamination. Also on the role of diet in chronic diseases like diabetes, atherosclerosis, cardiovascular diseases, osteoporosis and obesity, due to more intake of nutrients like energy, fat and some fat-soluble nutrients.

Before 4 decades, several group of scientist investigated nutraceutical properties of bioactive substance of plants to identify “Phytochemicals” responsible for such activities. They were successful to identify many chemical compounds involved in modulating immunity through production of enzymes and involved in various heart disease, stroke etc. Phytochemicals occur naturally in plant foods, they promise to create an entirely new philosophy of "functional foods,” eaten not just to sustain minimal basic health but also eaten to prevent disease. They occur naturally protecting plants

from different harmful/damaging agents like insects and microbes, they produce the life saving gas Oxygen and also the UV light they in habitat and convert into the nutrients we need.

'Functional foods' are foods which have potential to prevent many diseases. They also provide health benefits beyond basic nutrition. Functional food science is an interaction of biological responses in response to availability or supply of a specific food ingredient of nutrients.

Several nutrients like dietary fiber, vitamin E (tocopherols), provitamin A (β-carotene), ascorbic acid and selenium also have disease-preventing qualities and have ability to provide good health, like phytochemicals. [1].

BIOACTIVE PHYTOCHEMICALS AS FUNCTIONAL FOODS

Bioactive compounds are used in wide range of applications like: geo-medicine, plant science, modern pharmacology, agrochemicals, nanobioscience, food and cosmetic industry. These areas show great development which results in increase research work, designed to diversify the resources of bioactive compounds and improve their salvage pathways or synthesis [2].

Phytochemicals are the naturally occurring, non-nutrient, bioactive plant metabolite available in vegetable, whole grains and various fruits. It can be classified into various groups like carotenoids, alkaloids, polyphenols, organosulfur compounds, and nitrogen-containing compounds. Though the exact mechanism of immunomodulation is not understood, but many of these groups have a potent effect in disease resistance through several complementary and complicated mechanisms. Surprisingly, many researchers identified a phytochemicals undergone through bacterial modification to produce metabolites which are more active than their parent compounds [3].

ANTIOXIDANTS: THEIR ROLE IN DISEASE PREVENTION

It is well known that Receptive Oxygen Species (ROS) plays an essential part in the etiology of a few noncommunicable diseases. Oxidants and free radicals, for example, singlet molecular oxygen (–O2), superoxide (–O), hydroxyl (OH) peroxide (O-O-H) and lipid peroxides (LOO) are known to damage tissues [4&5].

These radicals include nitrous oxide radicals that are formed in the gastrointestinal tract. When it becomes cumulative, tissue are damaged as free radicals are considered to play an important role in the pathogenesis of several degenerative diseases, like , cancer, cataract, coronary heart disease, dementia, diabetes mellitus, rheumatic arthritis, muscular degeneration, pulmonary dysfunction and radiation sickness.

Other mechanisms wherein the oxygen free radicals and peroxides cause these diseases encompasses of lipid peroxidation of membrane lipids, circulating lipoprotein lipids (including cholesterol), oxidation damage of cellular proteins and DNA, and lens proteins in the retina.

These oxidants and free radical species are generated in cells during utilization of oxygen, which is essential for life's sustainability, and they can also be generated from external sources. Superoxide Dismutase (SOD) can change the O2 radical to hydrogen peroxide, which can be destroyed by catalase, therefore it is necessary for an external source of antioxidants to neutralize the free radical load in the body.

Innumerable antioxidants are present in foods. β-carotene, vitamin C and vitamin E (which are nutrients), a number of carotenoids, phenols and flavonoids also occur naturally in foods and can act as antioxidants. Many plant foods contain phenols and flavonoids. Carotenoids are found in Green leafy vegetables, fruits and yellow vegetables. Vitamin C and vitamin E prevent formation of nitrosamine, which is carcinogenic. Vitamin E is a potent antioxidant agent found in vegetable oils, and

the germ portion of cereal which can act via reducing selenium and protecting polyunsaturated fatty acids (PUFA) in the membrane which ultimately results in protection against oxidative damage.

Other edible oils rich in antioxidants are sesame and rice bran oils. Rice bran oil contains oryzanol, which can act as an antioxidant, and is rich in plant sterols that, along with oryzanol, effectively lower blood cholesterol.

Sesame oil contains sesaminol, which is a powerful antioxidant. Spices which are rich in phenolic compounds have been shown to act as antioxidants. Turmeric (Curcuma domestica), contains a yellow colouring principle, curcumin, which is a powerful antioxidant and can protect against cancer. Vitamin C, is present in Alma (Emblica officinalis) and guava (Psidium guajava), can also be rich and inexpensive sources of antioxidants. Besides being rich in vitamin C, these two fruits also contain phenolic compounds, including flavonoids.

The phenolic compound and flavonoid substance of naturally and routinely developed plants is affected by a few variables, for example, cultivar, seasonal variation , time of harvest, light, atmosphere, maturity stage, degree of readiness, storage conditions, food preparation and processing. Alongside these elements, plant nutrient availability also affects the content of nutrients and secondary plant metabolites in crops. The microorganisms and insect pressure also alters phytochemical synthesis by plants. Absence of pesticides and synthetic manures may put more extended significance on plants and this influences plants to contribute more resources to build up their own chemical defence mechanisms.

COMMON PHYTOCHEMICALS AND HEALTH BENEFITS:

- Carotenoids
- Phenolic compounds
    - Flavanoids
    - Phytoestrogens
    - Phenolic Acids
- Organosulfur Compounds
- Non digestible carbohydrates

CAROTENOIDS

Carotenoids are pigments found ubiquitous in nature with received considerable attention as an antioxidant and provitamin compounds. In more recent years, carotenoids, provitamin A have been credited with other wellbeing advancing impacts: immuno improvement and reducing of the risk of creating degenerative diseases, for example, cancer, cardiovascular diseases (CVD), cataract and macular degeneration [6]. A total of more than 600 different compounds falling in this category have been identified from nature. The physiological activity of these compounds like an antioxidant property is mainly due to quenching of singlet oxygen and interacts with free radicals [7]. The other mechanisms of action against chronic diseases have been progressively referred to; modulation of carcinogen metabolism, regulation of cell growth, retinoid-dependent signalling and filtering of blue light, inhibition of cell differentiation and proliferation and stimulation of cell-to-cell gap junctional communication [6 &8].

PHENOLIC COMPOUNDS

Phenolic compounds are found in every parts of biosphere with more than 8000 structural groups of substances in the plant kingdom. [9].

- **FLAVONOIDS**

It is a group of phenolic compound having antioxidant activity with ability to reduce risk of chronic diseases. Natural harbours almost 4000 distinct flavonoids in their portfolio. More than 4000 dictinct flavonoids are present in nature.
Flavonoids are found in natural produce viz. fruits vegetables, coffee, tea and wine. The flavonoids, quercetin, kaempferol and myricetin are generally distributed in fruits and vegetables. Berries, tomato, potato, broad beans, broccoli, Italian squash, apple, kale and onion are the richest sources of quercetin [10 &11].

The health related properties of phenolic compounds, especially flavonoids, are believed to be based on their antioxidant activity as hydrogen donating free radical scavengers [12]. The primary target of radicals are proteins (including enzymes), lipids (significant to the induction of heart disease), DNA (applicable to the induction of cancer) and RNA. However, the oxidative event that happens most repeatedly inside the body is the oxidation of the unsaturated fatty acid components of cell membranes producing lipid peroxides. Numerous researchers have demonstrated that lipid peroxides and reactive oxygen species have a role to play in causing a variety of diseases, including cancer, atherosclerosis, heart disease, kidney damage, and even accelerated aging. Flavonoids are also metal chelators and have been found to bind metals, such as copper and iron that catalyze lipid oxidation.

Yang et al. [13] reviewed the inhibition of carcinogenesis by dietary Polyphenolic compounds suggesting that polyphenols may inhibit carcinogenesis by influencing the molecular events in the initiation, promotion and progression stages of cancer. Beyond their antioxidative properties, flavonoids may act in a variety of ways, for example, deactivating cancer-causing agents, inhibiting the expression of mutated genes and the activity of enzymes that promote carcinogenesis, promoting detoxification of xenobiotics [14].

- **PHYTOESTROGENS**

The main types of phytoestrogen include the isoflavones (the most powerful), and lignans. Lignans are diphenols affiliated as a minor component with dietary fiber.

Phytoestrogens can compete with steroid hormones for different enzymes and receptors and stimulate production of sex hormone-binding globulin in the liver. Thus, they may change steroid hormone metabolism and may retard the growth and proliferation of hormone-dependent cancer. In parallel with properties of other phenolic compounds; phytoestrogens have antioxidant activity as well as like estrogens, they have impact on lipoprotein metabolism which enhance vascular reactivity Phytoestrogens, in this way, have potential defensive impacts against cardio vascular disease.

Genistein has been found to stimulate the production of osteoprotegerin by human paracrine osteoblasts, providing a further mechanism for the bone-sparing effects of soya isoflavones through suppression of osteoclast activity by inhibition of cytokines, induction of apoptosis, changes in intracellular Ca++, activation of protein tyrosine phosphatase, and membrane depolarization. Presences of estrogen receptors in bone with broad activities of these nonsteroidal dietary estrogens provide a logical basis for thinking that the dietary phytoestrogen can play a role in osteogenic remodeling [15].

As lignans are structurally analogous with estrogen, it has been always assumed that lignans are likely to have a bone-conserving role.Dietary sources of lignans are oilseeds, cereal grains, vegetables, fruits and legumes. Flaxseed and sesame seed have been distinguishedas the richest sources of these compounds [16].Once ingested, plant lignans are changed over by bacteria in the large intestine into enterolactone and enterodiol, which are called mammalian lignans as they have been found only in mammals [17]. Mammalian lignans are associated with a reduced risk of CVD and cancer.

- **PHENOLIC ACIDS**

Phenolic acids such as ferulic, caffeic and ellagic acids are widely distributed in fruits, vegetables, tea and wine; numerous are available in foods as glycosides. Ellagic acid is found in high concentrations in fruits and nuts, strawberry, blackberry, raspberry, pecan and walnut.A major yellow pigments of turmeric i.e. Curcumin consists of 2 ferulic acids linked by methylene in a diketone structure [18]. In raisins, the most rich phenolic acids are caftaric acid, coutaric acid, gallic acid, and clorogenic acid [19, 20].

ORGANOSULFUR COMPOUNDS

Allium compounds are organosulfur compounds (OSCs) found in Allium vegetables such as garlic, onion, scallion, chive, shallot and leek, which account for the distinctive flavor and aroma as well as the many reported medicinal effects of these vegetables.

The OSCs in Allium vegetables have been accounted for to apply different physiological effects, including antimicrobial activity, lipid-lowering effect, hypocholesteremic activity, inhibition of platelet aggregation, hypoglycemic activity, antithrombic effect, and lipoxygenase and tumour inhibition. The glucosinolates are sulphur-containing glucosides prevalent in the cruciferous family of vegetables, especially the Brassicas (e.g. cabbage, broccoli, Brussels sprouts, cauliflower), and are also present at relatively high levels in oilseeds such as mustard seed.

Based on in vitro and in vivo studies many group of researchers recently found that isothiocyanates inhibits carcinogenesis by modulating numerous pathways of cancer development which mainly includes phase I and phase II detoxification pathways; Cell signalling pathways; cell cycle; induction of apoptosis (programmed cell death) and decreasing Helicobacter infections [21, 22 & 23]. Glucosinolates are not bioactive until they have been enzymatically hydrolysed to the related isothiocyanates.

NON DIGESTIBLE CARBOHYDRATES

Dietary fiber

Dietary fibers are polysaccharides and their hydrophilic derivatives, which can't be digested by the human digestive enzymes to absorbable components in the upper alimentary tract. Various non digestible carbohydrates like fructans (e.g. inulin) naturally occurs in various food products and raw materials. fructans occur in edible parts of various plant foods like onion, artichoke, chicory, leek, garlic, banana, rye, barley .Galactosyl sucroses (raffinose and stachyose) are found in soybeans and other leguminous seeds, while xylooligosaccharides occur in bamboo shoots. In some foods NDOs (Write the full name and write NDO in short form in a bracket) are generated during processing. The NDOs have been described as prebiotics [24].

Dietary fibres in foods have been shown to be useful in reducing blood glucose levels in diabetes, in reducing blood cholesterol levels for treatment of cardiovascular disease and also in preventing bowel cancer by various group of researches in their studies [25-26].

Mechanism for the beneficial effects of dietary fiber

Dietary fibre components also bind bile salts, thereby promoting cholesterol excretion from the body and thus reducing blood cholesterol levels, and food toxins in the gut to reduce their toxicity. They can also have some adverse nutritional effects by binding dietary calcium, magnesium, zinc and iron, in this manner lessening their bioavailability.

The second mechanism by which dietary fibre exerts its beneficial effects is through undergoing fermentation in the large intestine (colon) and producing short-chain fatty acids such as acetate, butyrate and propionate. Butyrate helps in the regeneration of colon mucosal cells by serving as a source of energy, thereby reducing the risk of colon cancer and inflammatory bowel disease. The short-chain fatty acids produced are absorbed (especially propionate and acetate) into splenic circulation and transported to the liver where they are known to inhibit cholesterol synthesis by hepatocytes and also glucose release from the liver, thus contributing partly to the hypercholesterolemic and hypoglycaemic effects of dietary fibre. While the soluble fibres are completely fermented, the insoluble fibres are only partially fermented [27 &28].

DIETARY PHYTOCHEMICALS IN PREVENTION OF CARDIOVASCULAR DISEASES (CVD)

There's evidence to recommend that consuming foods rich in phytochemicals may reduce the risk of CVD.Arai and others reported total intake of flavonoids (ficetin, myricetin, luteolin, quercetin and kaempferol) was inversely correlated with the plasma total cholesterol and low-density lipoprotein (LDL) cholesterol concentrations[29]. High fruits and vegetable intake will reduce the risk of CVD by 20-30% [30].Similar observation related to reduced overall mortality and mortality due to CHD has been in people having mediterranean diet which mainly consists of fruits and vegetables, were associated with a 25% reduction in total mortality and a 33% reduction of death due to CHD [31].

Garlic (Allium sativum), widely used in India as a spice, contains sulphur compounds. After a mild processing, garlic has been shown to yield a compound called agoene that can prevent platelet aggregation. This action of garlic may be related to the reported beneficial effect of garlic in heart disease. [32].

Dietary antioxidant prevents atherosclerosis by regulating circulatory level of Low Density Lipoprotein (LDL) in blood. Since oxidized LDL plays a key role in the initiation and progression of atherosclerosis, giving dietary phytochemicals with antioxidant activity capable of preventing LDL oxidation has been an important therapeutic approach [33].Thus, dietary phytochemicals might retard the progression of atherosclerosis. In addition, C-reactive protein, a marker of systemic inflammation, has been accounted for to be a stronger predictor of CVD [34], proposing that inflammation is a critical factor in CVD. Inflammation not only promotes initiation and progression of atherosclerosis, but also causes acute thrombotic complications of atherosclerosis [35]. Moreover, it regulates the prostaglandin synthesis, reduces the blood pressure and also reduces platelet aggregation, it also regulates the synthesis of cholesterol and its absorption.[36].

DIETARY PHYTOCHEMICALS IN THE PREVENTION OF CANCER

All the organisms present on this planet are continuously exposed to a wide variety of oxidizing agents; many of them might be beneficial to life also. These agents are available in air, food, and water, or else they might be delivered by metabolic actions inside cell. A balance between oxidants and antioxidants is an important factor to maintain normal healthy state of the body. Excessive presence of oxidants may results in imbalance which may lead to "Oxidative stress", particularly in chronic type of infections. Oxidative stress can cause oxidative damage to huge biomolecules such as lipids, proteins, and DNA, bringing about an increased risk for cancer and other chronic diseases [37, 38 & 39].

On cogenesis is a heterogeneous disease with poorly defined landscape where "Oxidative Damage" is one among several mechanisms involved in this process. Free radicals induced DNA damage, if remain unrepaired leads to mutation, DNA break, cross-linking and structural chromosomal aberrations [40]. Experimental evidences have been observed by many group of researchers where, dietary antioxidants potentially reduces the risk of cancer and carcinogenesis by inhibiting oxidative damage through various mechanisms which mainly involves regulation of gene expression in cell differentiation & proliferation; suppression of oncogenes; induction of apoptosis; modulating enzyme

activities like oxidation, detoxification, and reduction; cell cycle arrest; stimulation of the immune system; and regulation of hormone metabolism.[41 & 42].

DIETARY PHYTOCHEMICALS IN THE PREVENTION OF OSTEOPOROSIS:

Most of the studies are concentrated towards assaying effect of phytochemicals on bone cells disclose their multiple beneficial role in promoting osteoblast functions, and inhibiting adipocyte and osteoclast functions. Similar observations have been reported for polyphenols in terms of health-promoting properties as it reduces resorption caused by high oxidative stress [43 & 44].There is evidence suggesting that oxidative stress caused by reactive oxygen species (ROS) is associated with its pathogenesis [45].Several in vitro and laboratory animal studies have established that oxidative stress declines the level of bone formation by decreasing the survival and differentiation of osteoblasts.

Besides, it has been accounted for that ROS initiate osteoclasts and thus, improve bone resorption [46]. Antioxidants also palys an important role in preventing postmenopausal osteoporosis. For example, estrogens because of its antioxidant activity protects women from cardiovascular disease, stimulate osteoblastic activity during their reproductive age through receptor mediated action, ultimately favoring osteogenesis [47].Antioxidant deficiency has been found to have adverse effect on bone mass. Antioxidant enzymes are regarded as the markers of antioxidant defense mechanism against bone resorption. There are a few studies to denote the relation between glutathione peroxidase and catalase (CAT) and osteoporosis[48].

DIETARY PHYTOCHEMICALS IN PREVENTION OF DIABETES:

Research recommends that phytochemical-rich foods may specifically diminish the risk of type 2 diabetes, most likely by reducing inflammation and enhancing insulin sensitivity, and indirectly by preventing weight gain, the most important risk factor of the disease.

Constructive outcomes on fasting blood glucose levels and insulin affectability have been discovered particularly with the utilization of polyphenols both in lab and animal studies. Dietary polyphenols may restrain starch processing and glucose ingestion in the digestive system, empower insulin emission from the pancreas, balance glucose release from the liver, initiate insulin receptors and glucose uptake in insulin-delicate tissue, and regulate intracellular flagging pathways and quality expression. Some considers have found that a reduced risk was most grounded with the use of green verdant vegetables, which are rich wellsprings of phytochemicals. [49].

ROLE OF PHYTOCHEMICAL IN MEMORY AND AGING PROCESSES:

Phytochemicals particularly genistein, significantly influences the aging and age-related neuro-degenerative diseases. It protects neuronal cells through activation of estrogen receptors, up regulation of nervous system derived neurotropic factors as well as antioxidant activity [50]. The increased level of choline acetyltransferase expression level in frontal cortex which is ultimately associated with enhancement and protection of cognitive ability in phytoestrogen treated females are worth to note as it's beneficial effect. It also affect the brain calcium-binding protein calbindin (CALB), which is a catalyst in binding intracellular calcium and plays an important role in apoptosis, neurotoxicity and cell proliferation mediation. [51].They are potent antioxidants which reduce the oxidative stress and subsequently relieve many age-related as well as degerative neurological disorders. Oxidative stress affects also several redox-sensitive signaling pathways, mainly NF-kB system, which is almost participant in inflammatory responses associated with aging and age-related disorders like obesity, cancer and diabetes [52].

Interestingly, two major molecular targets of phytochemicals, that is, nuclear factor-erythroid 2-related factor 2 (NRF2) and AMPK signaling pathways, can also inhibit oxidative stress but, in

addition, they can directly repress NF-kB signaling. These signaling effects highlight the role of phytochemicals in the prevention of diseases linked to the activation of NF-kB signaling [53].

CONCLUSION:

Phytochemicals comprises of a large group of non-nutrients compounds derived from variety of foods and chemical originated from plants. A substantial literature narrates the beneficial effect of dietary phytochemicals on overall fitness, health and longevity. Scientific available data strongly suggest that phytochemicals from herbs, vegetables, fruits and spices may exhibit relevant negative immune regulatory, and/or anti-O&NS action in brain aging.

Researchers have found that phytochemicals have an important role to stimulate the overall immunity, prevent toxic substances in the diet from becoming carcinogenic, reduce inflammation, prevent DNA damage, enhances DNA repair, reduce oxidative damage to cells, suppress carcinogenesis, trigger damaged cells to self-destruct before they can proliferate, regulate intracellular signaling of hormones and gene expression. However, even though investigation findings haven't forever interpreted in to a conclusive heath beneficial effect, the anti-inflammatory and antioxidant properties of phytochemicals have been extensively accepted. Many dietary phytochemicals are commercially available as a feed supplements to avert or ameliorate variety of diseases, including aging, cancer etc.

Phytochemicals are rich sources of vitamins, fibers and minerals, whose beneficial effect in maintaining physiology have been already well elucidated. Though it is very difficult, if not impossible to identify whether the beneficial effect is because of individual compound or synergistic effect results as an interaction of many compounds.It will be interesting to explore the possible unique combination of these compounds which may reduce the disease risk and offers health benefits, but that formula hasn't been identified and tested yet.

There is a need to set up an in vivo framework to test the biological potency of a given diet with a particular biological property (antioxidant protection or induction of drug metabolizing enzymes, inhibition of oncogenesis). Future examination in the investigation of nutrition may be profitably directed towards evaluating the potency of dietary phytochemicals and their wellbeing suggestions.

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