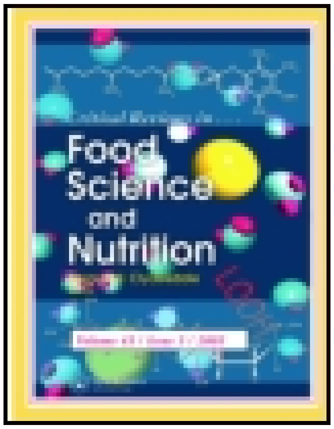

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Status of Bioactive Compounds in Foods, with Focus on Fruits and Vegetables

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Status of Bioactive Compounds in Foods, with Focus on Fruits and Vegetables

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INTRODUCTION

Several epidemiological studies suggest that a high intake of foods rich in natural antioxidants increases the antioxidant capacity of the plasma and reduces the risk of some types of cancers, heart diseases and stroke. These properties are attributed to a variety of constituents, including vitamins, minerals, fibre and numerous phytochemicals, such as flavonoids. Flavonoids are largely distributed in fruits and vegetables and they have been studied mainly because of their potential health benefits as antioxidants, and chemo-preventive agents. However, no recommended daily intake of these compounds has been established mainly because the composition data are incomplete and also because the biological activities are not well determined and especially, the bioavailability and pharmaco-kinetic data are inconclusive. The dietary intake of flavonoids for the Brazilian population was estimated to be 60-106 mg/day, with 70% from oranges, 8.9% from lettuce and 5.8% from onions. This dietary intake could be considered high compared to that of Finland (55mg/day) and Denmark (29mg/day). Intakes of flavonoids for US adults was estimated to be about 190 mg/day, mainly from flavan-3-ols (83.5%), followed by flavanones (7.6%), flavonols (6.8%), anthocyanidins (1.6%), flavones (0.8%) and isoflavones (0.6%). Although these studies

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indicate a reasonable ingestion of these compounds, it is not clear how much of the amount ingested is absorbed and responsible for the biological effects. The International Network of Food Data Systems (INFOODS), created a program with the objective of stimulating and coordinating efforts to improve the quality and availability of food composition data around the world and to ensure that anyone around the globe would be able to obtain adequate and reliable food composition data. Moreover, consumers want more detailed information about the nutritional value of foods and the food manufacturers have responded by seeking new formulations consistent with current health recommendations, which in turn requires information on food and ingredient composition. In this way, beyond the composition of the usual macronutrients and micronutrients, it seems important to also provide information on the composition of bioactive compounds and the antioxidant capacity of foods (Hassimotto et. al., 2009). However, at present there is no conclusive proof that high antioxidant activity is a good indicator of high anticancer activity (Wang et al 2012).

Components of cereals, legumes, pulses, proteins, sea food, milk, carbohydrates and lipids are being evaluated for their influence on human health, as bioactive constituents. However, references dealing with fruits and vegetables exceed any other food group and accordingly, fruits and vegetables are focused first, followed by other food materials.

PROPERTIES AND DIETARY EFFECTS OF SOME PHYTOCHEMICALS

Vitamins

Vitamin C, also known as ascorbate, is a vital micronutrient for humans. A lack of vitamin C hampers the activity of a range of enzymes and may lead to scurvy in humans. Unlike most animals, humans are unable to synthesize their own vitamin C and they must therefore find it in plants, in particular, fruits and vegetables. In addition to its involvement in the production of collagen, ascorbic acid serves as a cofactor in several vital enzymatic reactions, including those involved in the synthesis of catecholamines, carnitine, and cholesterol, and in the regulation of transcription factors controlling the expression of important genes of the metabolism. Ascorbic acid is present in three forms: ascrobate, monodehydroascorbate (MDHA), and dehydroascorbate (DHA), which corresponds to the oxidized form of ascorbate. In most cellular functions, ascorbate scavenges reactive oxygen species (ROS) generated by cellular metabolism. Due to the role of ascorbate in protecting cells against oxidative stress and the involvement of ROS in neurodegenerative disorders (Alzheimer's and Parkinson's diseases) or inflammatory response (arteriosclerosis), it is strongly suggested that vitamin C could prevent heart, chronic inflammatory, and neurodegenerative diseases .Vitamin E (tocopherols and tocotrienols) is present in all cell membranes and plasma lipoproteins, especially in red blood cells of the human body. As the major lipid-soluble chain-breaking antioxidants in humans, vitamin E protects DNA, low-density lipoproteins, and polyunsaturated fatty acids from oxidative damage. It, moreover, plays a role in haemoglobin biosynthesis, modulation of immune response, and stabilization of the structure of membranes. Vitamin K_1 is a liposoluble vitamin, synthesized from phylloquinone by bacteria in the intestinal tract. It plays a positive role in the control of blood clotting, bone formation, and repair. Deficiency of vitamin K_1 may result in hemorrhagic disease in newborn babies, as well as postoperative bleeding, muscle hematomas and intracranial haemorrhages in adults. Vitamin K_1 menadiones were shown to exhibit cytotoxic activity and inhibit growth of tumors in humans (Poiroux-Gonord et.al, 2010).

Phenolics

The specific action of each plant phenolic compound is not easy to assess because only a very small part of it is really absorbed and moreover potentially also may undergo transformations. Enterocyte and epathocyte can cleave glycoside moieties. They are responsible for glucuronidation, methylation, and sulfation of flavonoids. First, they protect some major cellular components from oxidation. Many dietary phenolics are antioxidants capable of quenching ROS and toxic free radicals formed from the peroxidation of lipids and therefore, have anti-inflammatory and antioxidant properties at the body level. Several hydroxycinnamic acid derivatives, for instance, caffeic acid, chlorogenic acid, ferulic acid, p-coumaric acid, and sinapic acid, present strong antioxidant activities by inhibiting lipid oxidation and scavenging ROS . Flavonoids are known to prevent production of free radicals by chelating iron and copper ions to directly scavenge ROS and toxic free radicals and inhibit lipid peroxidation. Production of peroxides and free radicals, which may damage DNA, lipids and proteins, has been linked to aging, atherosclerosis, cancer, inflammation, and neurodegenerative diseases such as Alzheimer's and Parkinson's. Flavonoids were also demonstrated to protect low-density lipoprotein (LDL) cholesterol from being oxidized, thus preventing the formation of atherosclerotic plaques at the level of the arterial wall. Many dietary flavonoids and hydroxycinnamic acids bind to human serum albumin, the main protein involved in lipid transportation within blood. This cotransport provides an efficient antioxidant protection to lipids. Additionally, when tannins form bond with enzymes, they inhibit part of the lipoxygenase and peroxidise activity, therefore exhibiting antioxidant effects. Chlorogenic acid and caffeic acid inhibit N-nitrosation reaction and prevent the formation of mutagenic and carcinogenic N-nitrosocompounds. Without entering into details, it may be said that the range of activities of phenolic compounds encompasses protection against coronary heart diseases, anti-inflammatory effects, and inhibition of the development of cancer cells. Flavonoids modulate signalling pathways. Among signalling roles, isoflavones such as daidzein and genistein have received considerable attention due to their ability to bind to mammalian estrogen receptors (α and β) mimic estrogen and anti-estrogen actions. They modulate the endocrine system and may exert a preventive role against breast cancer and osteoporosis.

Carotenoids

Carotenoids endowed with provitamin A activity are vital components of the human diet. Vitamin A is implicated in hormone synthesis, immune responses, and the regulation of cell growth and differentiation. It can be produced within certain tissues from carotenoids such as β-cryptoxanthin present in Citrus fruits, β-carotene present in carrots, spinach, and sweet potatoes and α-carotene found in carrots, pumpkin, and red and yellow peppers . A carotenoid-deficient diet can lead to night blindness and premature death. Carotenoid-rich diets are correlated with a significant reduction in the risk for certain cancers, coronary heart disease, and several degenerative diseases. Carotenoids have demonstrated anticancer and antimutagenic properties. Underlying mechanisms are not well understood, but the dietary importance of carotenoids is discussed, at least in part, in terms of antioxidant properties. Carotenoids are known for their capacity to efficiently quench $^1O_2$ singlet oxygen by energy transfer. $^1O_2$ is a particularly active ROS, capable of damaging DNA and provoking genetic mutations. Eventually, $^1O_2$ can damage lipids and membranes.

Carotenoids are classified on the basis of three criteria: the dependence on the partial pressure of molecular oxygen, the potential for inhibiting the formation of peroxide, and the potential for quenching of $^1O_2$. Astaxanthin, a xanthophyll produced by some algae, is an excellent antioxidant capable of quenching free radicals in either their standard or excited form. β –Carotene and lycopene are efficient antioxidants, capable of inhibiting strongly the formation of perioxide. They are prone to degradation after ingestion, but their breakdown product seems to have interesting properties that may explain the cancer preventive activity of these carotenoids. ζ–Carotene is a poor antioxidant.When lipophilic antioxidants such as lutein or lycopene are associated with hydrophilic antioxidants such as rutin, a supra-additive protection of low-density lipoprotein occurs. When rutin is associated with ascorbic acid, a synergetic protection also occurs.

Phytosterols

Phytosterols are found in high amounts in broccoli,brussels sprouts, cauliflower, and spinach. They regulate the fluidity and permeability of the phospholipid bilayers of plant membranes. Certain phytosterols are precursors of brassinosteroids, plant hormones involved in cell division, embryonic development, fertility, and plant growth. Some sterols are provitamins upon skin exposure to UV radiation, they may give rise to calciferol, also known as vitamin D_2, which is involved in the absorption of calcium and bone growth. Plant sterols possess, moreover, cholesterol-lowering properties and play a positive role by decreasing the incidence of cardiovascular diseases. Being structurally similar to cholesterol, they can compete with cholesterol, thus limiting its absorption from fat matrices into the intestinal tract. Plant sterols have been hypothesized to have anticancer, antiatherosclerosis, anti-inflammation, and antioxidant activities.

Saponins

Saponins are attritubed with cardioprotective, immunomodulatory, antifatigue, and hepatoprotective physiological and pharmacological properties. Antifungal activity is generally ascribed to the ability of saponins to complex with sterols in fungal membranes, thus causing pore formation and loss of membrane integrity. They also affect membrane fluidity. Dietary saponins have been observed to reduce blood cholesterol, stimulate the immune system, and inhibit the growth of cancer cells. Saponins inhibit active transport by increasing the general permeability of enterocytes. Saponins can also form insoluble complexes with minerals such as zinc and iron.

Glucosinolates

A reduction in the prevalence of certain forms of cancer has been attributed to the anticarcinogenic properties of certain glucosinolates and their breakdown products. Glucosinolates act by activating enzymes involved in the detoxification of carcinogens and by providing protection against oxidative damage. Certain glucosinolates have been observed to inhibit enzymes involved in the metabolism of steroid hormones (Poiroux-Gonord et. al., 2010).

Recent reports provide large number of evidences about the chemo-preventive role of quercetin on various types of cancers such as bladder, prostate, esophagus and in stomach cancers as well as towards other deleterious degenerative diseases (Jan et. al., 2010). Resveratrol has been identified as one of the major active compounds of stilbenes found in grapes, grape products, crane berries, and strawberries. Positive effects of resveratrol on health include the prevention of cell oxidation through resveratrol antioxidant properties , ability to stop pain, stop the growth of bacteria that cause stomach ulcers that can lead to cancer, protect immune cells, protect DNA, protect skin cancer, as well as being cardio-protective, antitumor, estrogenic, anti-platelet and anti-inflammatory actions(Tosun and Inkaya , 2010).Many flavonoids have been studied for their intestinal anti-inflammatory activity; however, their potential therapeutic application in inflammation is not restricted to this organ and extends to other sides, including arthritis, asthma, encephalomyelitis, and atherosclerosis, among others (Gonzalez et. al., 2011).

BIO-FUNCTIONAL ACTIVITIES OF COMPONENTS OF FRUITS AND VEGETABLES

Major natural antioxidants found in fruits and vegetables may be used in promoting cardio-health. Since different food categories possess different bioactive compounds with various antioxidant capacities, specific foods, when consumed together, may produce synergistic antioxidant interactions and in turn have more positive physiological effect on cardio-health than when consumed alone [Table-1](Wang et. al., 2011).

The vital role of fruits, vegetables, and nuts in reducing the risk of cancer and cardiovascular diseases is being studied. In recent years, several meta-analyses strongly suggested that by adding one serving of fruits and vegetables to daily diet, the risk of cardiovascular diseases will be decreased up to 7%.While the consumption of various healthy foods continues, several questions about toxicity, bioavailability, and food-drug interactions of bioactive compounds are yet to be fully understood on the basis of scientific evidence. The multidisciplinary research and educational efforts will address the role of healthy foods to improve eye, brain, and heart health while reducing the risk of cancer (Patil et. al., 2009).Tested clinical trials of bioactive compounds are projected in Tables 2-7.

In the last few years, many important functions of fresh fruits and vegetables have been reported, and they are now recognised as been good sources of natural antioxidants, such as grapes, apples and guavas. The antioxidants can prevent lipid peroxidation and DNA and protein damage. Polyphenols have been acknowledged to have health beneficial effects, owing to derived products such as flavonoids, tannins, coumarins and lignans (Lee et.al, 2010). Local fruits and vegetables consumed in the

Mexican rural diet are rich in polyphenols with antioxidant properties and are important source of bioactive compounds and dietary fibres. Fruit and vegetable intake needs to be promoted and life style and environmental factors enhanced to improve the health status of obese Mexican rural population (Hervert – Hernandez et. al., 2011) Carotenoids and chlorophylls have an important role in the prevention of various diseases associated with oxidative stress, such as cancer, cardiovascular diseases and other chronic diseases with implied importance of leafy vegetables (Znidarcic et.al., 2011).

Natural bioactive compounds in dietary plant products including fruits, vegetables, grains, legumes, tea and wine are claimed to help prevent cancer, degenerative diseases, and chronic and acute inflammation. Modern methods in cell and molecular biology allow us to understand the interaction of different natural bioactive compounds with basic mechanisms of inflammatory response. The molecular path ways of this cancer related inflammation are now unravelled. Natural bioactive compounds exert anti-inflammatory activity by modulating pro-inflammatory gene expressions have shown promising chemo -preventive activity (Pan et. al., 2009). *Ficus religiosa* Linn (Moraceae) was evaluated as a hypolipidemic and antioxidant agent. Ethanol extract of *F.religiosa* exerted hypolipidemic and antioxidant effects (Hamed, 2011).

Work to identify potential sources of bioactive compounds through the determination of flavonoids and ellagic acid contents and the *in vitro* anti oxidant capacity and α-glucocidase and α-amylase inhibitory activities of Brazilian native fruits and commercial frozen pulps is reported (Goncalves et. al., 2010).

Fruits

Lime juice (100 ml) supplies 110-140 kJ (26 kilo cal) of energy, 50 mg of ascorbic acid (Vitamin C), and a trace of dietary fibre. Investigation was conducted to understand the chemoprotective effects of lime juice on pancreatic cancer cells and the possible mechanism for induction of apoptosis using Panc – 28 cells. The chloroform extract of freeze dried lime juice showed the highest (85.4 and 90%) radical – scavenging activity by 1,1-diphenyl-2-picry hydrazyl (DPPH) and 2,2-azinobis-3(3-ethylbenzothiazoline-6-sulfonic acid)ABTS methods at 624 μg /ml, whereas the methanol / water extract showed the lowest (<20%) activity. The active components were identified by high performance liquid chromatography (HPLC), using a C-18 column as rutin, neohesperidin, hesperidin and hesperitin.Further- more, the limonoids identified are limonexic acid, iso-limonexic acid and limonin. All the extracts of lime juice inhibited Panc-28 cancer cell growth. Antioxidant activity is proportionate to the content of flavonoids and proliferation inhibition ability is proportionate to the content of both flavonoids and limonoids (Patil et.al., 2009). Total carotenoid contents of fully ripe papaya ranged from 5414 to 6214 μg per 100 g of fresh weight, while corresponding biosynthetic precursors like phytoene, phytofluene and ς-carotene were only detected in trace amounts. Due to high contents of vitamin-A precursors like β -carotene and β-cryptozanthins, edible parts of the ripe fruit contained 132-166 μg retinol equivalents per 100 g of fresh weight (Schweiggert et. al., 2012).Stage of ripeness significantly influences the contents of bioactive compounds in papaya fruit (Gayosso-Garcia Sancho et .al. 2011). Naringin was the predominant flavanone in pummelo varieties (Zhang et. al., 2011).

Phenolic rich fractions were condensed tannins with structural heterogeneity in monomer units, degree of polymerization and interflavan linkages in mangosteen fruit rind with condensed tannins predominately that contain procyanidins with a significant amount of propelargonidin but much lower signals of prodelphindin (Zhou et. al., 2011). Mangosteen phenolics occupied two binding sites on BSA(bovine serum albumin) molecules located most likely in or near both tryptophan residues in the BSA molecules acting as an intrinsic fluorescence probe(Naczk et. al., 2011).

Avocado *(Persea americana* Mill) is a good source of bioactive compounds such as mono-unsaturated fatty acids and sterols. The main fatty acids identified and quantified in avocado was oleic acid (about 55% of total content), whereas β-sitosterol was found to be the major sterol (about 89% of total content). In general, after refrigerated storage, a significant decrease in fatty acid content was observed. Vacuum/halves and air/slices were the samples that maintained better this content. With regard to phytosterols, there were no significant changes during storage (Plaza et. al., 2009). From Limetto juice, four C-glucosyl flavones, namely vicenin-2, lucenin-2-4’ methyl ether, orientin 4’ –methyl ether and scoparin; the O-glycosyl flavones, rhoifolin; and the O-glycosyl flavanone, eriocitrin are reported. In addition, ABTS+ and DPPH- radical quenching and FRAP assays demonstrate that limetto juice possesses remarkable antioxidant activity (Barreca et. al,, 2011).

The major phenolic compounds in aqueous extracts of straw-berries were ellagic acid, quercetin and chlorogenic acid. Strawberries had high α-glucosidase inhibitory activity. However, α-amylase inhibitory activity was very low in all cultivars. This suggested that strawberries could be considered as a potential dietary source with anti-hyperglycemic potential (Pinto et. al., 2008).

Fruit grown organically had a commercially preferred thinner peel, and the juice was higher in ascorbic acid and sugars, and lower in nitrate and the drug interactive furanocoumarins (Lester, 2007). Fibre rich powder from *Mangifera pajang* peels is a rich source of dietary fibres, antioxidants and other bioactive compounds that can be incorporated with food products to improve the nutraceutical properties of these products (Hassan et. al., 2011).The tested phenolics in *Phyllanthus emblica* fruit showed strong radical scavenging activity, good potency to chelate Fe^{2+} and good inhibition ability of lipid peroxidation. Mallotusinin, mucic acid, and 1,4-lactone 3-*O*-galate were reported for the first time to have antioxidant activity .In addition, *in vitro* anti-proliferative activities of those phenolics against MCF-7 breast cancer cell lines were assessed(Luo et. al., 2011).There are various polyphenos in mango, but mangiferin, is abundant and bioactive. Synergy among various polyphenols and macroelements in mango extracts is responsible for their high bioactivity as compared to pure isolated compounds and explains their use in the management of various degenerative diseases (Masibo and He, 2009).

Diets supplemented with Durian significantly hindered the rise in plasma lipids and the decrease in antioxidant activity. The nutritional values were

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comparably high. In conclusion, it could be suggested that inclusion of studied tropical fruits, especially durian, in known disease-preventing diets could be beneficial (Haruenkit et.al. 2007). FTIR spectra of polyphenols, HPLC profiles of fatty acids, the antioxidants and anti proliferative activities can be used as indicators to characterise different stages of durian ripening. At different stages of ripening, it was found that the total polyphenols, flavonoids, flavanols, ascorbic acid, tannins and the antioxidant activity determined by 4 assays (CUPRAC, DPPH, ABTS and FRAP) differed in immature, mature, ripe and overripe samples. The content of polyphenols and antioxidant activities were the highest in over ripe durian, flavonoids were the highest in ripe durian, and flavanols and anti-proliferative activity were the highest in mature durian (Haruenkit et. al*.,* 2010). The litchi fruit was found to be significantly rich in antioxidant and radio-protective properties, and the antioxidant parameters were found to be well correlated with the phenolics and flavonoid contents. A significant protection to pBr 322 plasmid DNA and *E.coli cells* from radiations induced damage was observed in the presence of litchi juice. Plasmid DNA was well protected even at the dose of 5 kGy, whereas, bacterial cells could be protected up to 0.5kGy (Saxena et. al .,2011).The ascorbic acid content in West Indian Cherry is around 8 mg /1g in ripe fruits, 16mg/g in half ripe fruits and 27mg/g in unripe fruit. In other words, its ascorbic acid content is higher than that of oranges and guava, both of which are well known for their high content of vitamin C (Silva et.al. 2012).

Syzygium cumini, widely known as jamun, is a tropical tree that yields purple ovoid fleshy fruit. Its seed had traditionally been used in India for the treatment of diabetes (Benherlal and Arumughan, 2007). The ethanolic extract of the seed kernel has shown a hypoglycemic effect with a corresponding increase in glucose tolerance and hepatic glycogen levels in STZ-treated rats, and these effects were similar to that of glibenclamide (Ravi *et. al* 2004). The ethanolic extract of the seeds also showed a concurrent improvement of pancreas histopathology. Mandal *et. al* (2008) .Orally administered the ethanolic extract to STZ-treated rats, which showed significant recovery of the pancreatic β-cells. The ethanolic extract of the seed kernels was found to inhibit α-glucosidase enzyme activity, which was the probable mechanism by which these extracts exerted their antidiabetic activity (Shinde et. al 2008). Cherries and in particular sweet cherries are a nutritionally dense food rich in anthocyanins, quercetin, hydroxycinnamates, potassium, fibre, vitamin, carotenoids and melatonin. Cherries exhibit relatively high antioxidant activity, low glycemic response COX1 and COX 2 enzyme inhibition , and other anticarcinogenic effects *in vitro* and in animal experiments(Table 8)(McCune et. al., 2011) .

Obesity–associated inflammation is characterized by recruitment of machrophages (MΦ) into white adipose tissue (WAT) and production of inflammatory cytokines, leading to the development of insulin resistance. The xanthones, α-and √-mangostin (MG), are major bioactive compounds found in mangosteen that are reported to have anti-inflammatory and antioxidant properties. It is to demonstrate that MG attenuates LPS-mediated inflammation of MΦ and insulin resistance in adipocytes, possibly by preventing the activation of MAPK, NF-$_{k}$B, and AP-1, which are central to inflammatory cytokine production in WAT (Bumrungpert et.al, 2009). *Garcinia* *mangostana* Linn is cultivated in the tropical rain forest of some south-east Asian nations like Indonesia, Malaysia, Srilanka, Phillipines and Thailand. People in these countries have used the pericarp (peel, rind, hull) as a traditional medicine for the treatment of abdominal pain, diarrhoea, dysentery, infected wound, suppuration and chronic ulcer (PLedraza-Chaverri et. al., 2008).

The FRP had a high amount of total dietary fibre (TDF; 72.3g/100g FRP) with a balanced SDF/IDF ratio (46.3/53.7%). The FRP had a high glucose retardation index, water holding capacity (WHC), oil holding capacity (OHC), and swelling. The antioxidant capacity of the FRP, as determined by the DPPH assay using an Elisa reader, exhibited a strong potency due to the presence of associated total polyphenols (98.3mg/g FRP). These FRP characteristics indicated that bam-bangan(*Mangifera pajang*) peels are rich source of DF, antioxidants, and other bioactive compounds that can be incorporated into food products to improve the nutraceutical properties of these products. The recommended intake of dietary fibre (DF) is between 25 and 35g/d and DF helps to protect from the risk of cancer and cardiovascular diseases. Moreover, the estimated DF intake is 18 g/d in Western countries. Thus, there is a need to increase DF intake through high consumption of fruits, vegetables, cereals, legumes, or fibre enriched food products (Hassan et. al., 2011).

The pharmacological functions of pomegranate include antioxidation, anti-tumour, anti-hepatotoxicity, anti-lipoperoxidation and anti-bacteria properties. In hematology, pomgranate could reduce the common carotid intima-medium thickness, thus lowering blood pressure and decreasing low-density lipoprotein

(LDL) oxidation and the incidence of heart diseases. The extract from the dried peel of the pomegranate could significantly inhibit NO production. Hence pomegranate contains the antiinflamatory activity components. The pomegranate rich in polylphenols, including mainly ellagitannins, gallotannins (punicalin, punicalagin, pedunculagin, punigluconin, granatin B, and tellimagrandin I) and anthocyanins (delphinidin, cyanidine and pelargonidin). In conclusion, granatin B not only displayed the best NO inhibitory abilities in LPS-induced RAW 264.7, but also had the strongest PGE, inhibitory effects in the *in vitro* and *in vivo* assays. Taken together, granatin B could be used as a standard marker compound to determine the potential anti-inflammatory effect of pomegranate (Lee et. al., 2010).

Kiwi fruit provides a dual protection against oxidative damage, enhancing antioxidant levels and stimulating DNA repair and may be beneficial in cancer. The consumption of two or three kiwi fruits per day for 28 days reduced platelet aggregation in human volunteers. In addition, consumption of kiwi fruit lowered blood triglyceride 4 levels by 15% (Cassano et. al., 2008).

Feijoa sellowiana is a native to Brazil, but is grown in many countries as a food crop, especially Newzealand, where it is valued for its highly aromatic fruit. Proanthocyanidin tannins of the *Feijoa* fruit were in fact the products largely responsible for its antioxidant activity. The phenols are responsible for the immune-stimulating activity, anti-inflammatory activity and probably also the antimicrobial activity of the fruit (Weston, 2010).Besides the colorant property, anthocyanins have been found to exhibit potential therapeutic effect as anti inflammatory, radiation protective, chemo protective, vasoprotective, inhibition of LDL oxidation and also prophylactic action, such as decrease risks of cardiovascular diseases. Acerola (*Malpighia emarginata* DC.) and acai (*Euterpe oleracea* Mart.) belonging, respectively, to the Malpighiaceae and Arecaceae families, are tropical fruits recognised as functional foods. Acerola shows high contents of ascorbic acid and carotenoids, besides the presence of the anthocyanin, cyanidin-3-α-O-rhamnoside and pelargonidin-3-α-O-rhamnoside; acai is considered an energetic fruit, rich in the anthocyanins cyanidin -3-glucoside and cyanidin-3-rutinoside, dietary fibres and iron (Rosso, and Mercadante, 2007).

Mangoes are source of bioactive compounds with potential health promoting activity. Biological activities associated with mango fractions were assessed in cell-based assays to develop effective extraction and fractionation methodologies and to define sources of variability. Two techniques were developed for extraction and fractionation of mango fruit peel and flesh. Many of the extracts were effective in inhibiting the proliferation of human breast cancer cells *in vitro*. This study also suggests that combinations of diverse molecular components may be responsible for cell-level bioactivities from mango fractions (Ashley et. al., 2011). Mango peel extracts protected erythrocytes against oxidative stress and may impart health benefits and it could be used as a valuable food ingredient or nutraceautical product (Ajila and Pradada Rao, 2008). Ripe peels contained higher amount of anthocyanins and carotenoids compared to raw peels while raw mango peel had higher total polylphenol content. The IC_{50} values were found to be in the range of 1.39-5.24 µg of gallic acid equivalents (Ajila et.al, 2007). The mango peel constitute about 15-20% of the fresh

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fruit. The peel contains various bioactive compounds, polyphenols and carotenoids and the peel extract exhibited potential antioxidant properties. Mango peel was incorporated into macaroni at three different levels and found that incorporation up to 5% level into the formulation of macaroni yielded an acceptable product with improved nutraceutical properties (Ajila et.al. 2010). Biscuits incorporated with mango peel improved the nutraceutical and dietary content of biscuits (Ajila et.al. 2008).

Purple *Opuntia* spp., dark purple *Opuntia ficus-indica* and orange *Opuntia megachanta* presented the highest bio-functional compound levels amongst the samples studied. The antioxidant activity of Opuntia fruits was very variable and presented vitamin-C equivalent values between 0.23 and 0.57 mg/g. Purple Opuntia ficus-indica showed the highest antiradical ability (Cora Cayupan et.al., 2011).

Sea buckthorn berries contain many bioactive compounds that have anticancer properties. To investigate whether the antiproliferative effects could be associated with the presence of certain compounds, a sequential extraction was performed. The extraction started with heptane followed by ethyl acetate, ethanol and water. A second protocol using ethanol:water (1:1) was also used. The contents of the extracts were determined and their effects on cell proliferation were investigated on both CaCo-2 and Hep G2 cells. The ethyl acetate fraction was exclusively found to contain high levels of ursolic acid, together with low amounts of phenolics. The ethanol: water extracts contained high levels of phenolic compounds and pro-anthyocianidin, but little ursolic acid. When the antiproliferative effects were examined, the strongest inhibitory was found in the ethyl acetate extract for the CaCo-2 cells and in the ethanol:water extract for the Hep G2 cells. The antiproliferative effects were in both cases dose-dependent and were in the case of the ethyl acetate extract associated with an increase of apoptosis. The results obtained show that the choice of extraction solvent is of considerable importance and that ursolic acid might be more important than the polyphenols in inhibiting the cancer cell proliferation (Grey et.al. 2010). It is possible that watermelon extract may have the potential to induce PDE-5 A-mediated smooth muscle relaxation effect (Jayaprakasha et. al., 2012).

Vegetables

Cooking brassica vegetables as a domestic processing method has a great impact on health promoting bioactive compounds; glucosinolates, flavonoids, hydroxycinnamic acid and vitamin-C. High retentions of individual compounds in steaming and the lowest retentions were obtained in the traditional high pressure cooking. High retention of health promoting compounds in the cooking water should be considered for increasing the intake of properties of *Brassica rapa* (Francisc*o* et.al., 2010*). Glucosinolates (GSs) represent bioactive compounds of* Brassica vegetables whose health promoting effects merely stem from their breakdown products, particularly the isothiocynates (ITCs), released after hydrolysis of GSs by myrosinase. GSs are occasionally discussed as transient S reservoirs, but little is known concerning the interactive effect of S and N supply on ITC concentrations (Gerendas et. al., 2008). Different bioactive compounds are involved in the hypoglycemic effect of the bittergourd. However saponins and lipids seem to be of relevance for the anti-diabetic effects. Therefore, bittergourd varieties with these substances might be most effective in the prevention and treatment of diabetes mellitus and thus should be preferred for cultivation and use (Habicht et. al., 2011).

Broccoli sprouts grown in the light were found to have much higher concentration of vitamin-C (by 83%), glucosinolates (by 33%) and phenolic compounds (by 61%) than those grown in the dark. Therefore, the younger broccoli sprouts are a better source of bioactive compounds for a consumer than the inflorescences (Perez-Balibrea et. al., 2008).

Bio-fortification efforts have increased concentrations of bioactive compounds in carrots. The antioxidant potential and vitamin-A bio-efficacy of 4 bio-fortified carrot varieties (purple/orange, purple/orange/red, orange/red and orange) in Mongolian gerbils (N=73) were measured. Liver antioxidant capacity and vitamin-A stores were higher in gerbils fed coloured carrots than in those fed white carrots. Antioxidant activity is one of several proposed mechanisms by which plant foods, like bio-fortified carrots, may provide additional health benefits beyond maintenance of vitamin-A status (Mills et. al., 2008).

Globe artichoke (*Cynara cardunculus* L. Subsp. Scolymus (L) Hayek, (formerly *Cynara scoly*mus L) represents an important component of the Mediterranean diet, and is a rich source of bioactive phenolic compounds, and also inulin, fibre and minerals. In addition, artichoke leaf extracts have long been used in folk medicine, particularly for liver complaints. These therapeutic properties have been often ascribed to the cynarin (1, 3-O-dicaffeoylquinic acid) content of these extracts (Lattanzio et. al., 2009). Importance of squash as a source of α and β- carotene, lutein, vitamin C, dietary fibre, minerals and phenolics compounds is highlighted (Noelia et. al., 2011) .Banana pseudo stem flour is a potential functional food ingredient for products containing high dietary fibre(Aziz et. al., 2011).

Changes in some health-related compounds (lycopene and vitamin C) and antioxidant capacity of tomato juice treated by high-intensity pulsed electric fields were modelled as a function of the electric field strength and treatment time. The combined effect of treatment time and electric field strength on health-related compounds of tomato juice was successfully predicted through secondary expressions (Odiriozola-Serrano et.al. 2008). Carotenoids constitute an important component of waste originating from tomato processing plant. The optimized conditions for maximum carotenoids yield (37.5 mg/kg. dry waste) were 45% hexane in solvent mixture, solvent mixture to waste ratio of 9.1:1 (v/w) and particle size 0.56 mm (Strati and Orepoulou, 2011). The regular consumption of tomatoes and tomato products has been correlated to a reduction in risk of contracting various types of cancer and cardiovascular diseases. This positive effect is attributed to the antioxidants present in the tomatoes (Borguini and Torres, 2009). Waste obtained from six genotypes of tomato was subjected to evaluation as potential sources of hydrophilic and antioxidants on the basis of content of total .phenolics (11.7-18.6 mg/g), total flavonoids(7.6- 12.1mg/g) and ascorbic acid (0.51 – 1.89 mg/g) and antioxidant activities is dealt (Savatovic et. al., 2012). *Aloe vera* is rich in vitamins (E, C and A) and has a low fat and high fibre content which are responsible for its therapeutic and functional properties and hence its beneficial effects on human (Galvez et.al. 2011).

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Potato isolates and by-products from the potato industry comprise a source of bioactive compounds with ACE-inhibitory potentials of the hydrolysates were high (IC_{50}=0.018-0.086) and antioxidant activities. The bioactivities of protein hydrolysates were most likely related to peptides and / or free amino acids liberated during digestion (Pihlanto et. al., 2008).

The Nepalese herb (*Bergenia ciliate*, Haw.) is one of the traditional remedies used for diabetes since prehistoric times. Isolated compounds demonstrated significant dose dependant enzyme inhibitory activities against rat intestinal alpha glucosidase and porcine pancreatic alpha amylase. IC_{50} value for sucrase, maltase and α- amylase were 560,334 and 739 μM, respectively for [(-)-3-O-galloyl epicatechin] and 297, 150 and 401 μM, respectively for [(-)-3-O-galloyl catechin] (Bhandari et.al. 2008). Bioactive phytonutrients (omega fatty acids, tocopherols, polyphenols), *in vitro* inhibition of nitric oxide production and free radical scavenging activity of non-cultivated Mediterranean vegetables is reported (Conforti et .al. 2011).

The selenium contents of these mushrooms namely *Boletus aestivalis, B.pinophilus, B. edulis, B.aeeus, B fragans* and *B. spretus, Marasmius oreades, Agaricus bisporus* and *Russula cynoxantha* are sufficient to provide nutritionally significant amounts in relation to the total daily intake of selenium(Costa-silva et .al., 2011).Several mushroom species are investigated for their nutraceutical components displaying properties such as liver protective,hypocholesterolemic,antiviral,anticancerous,hypotensive,antiviral,immuno modulatory and so on(Shashirekha and Rajarathnam,2011).Twenty three mushroom

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species grown in different geographic locations of India were studied for phenolics and anti-oxidative index based on several tests conducted(Nethravathi et.al.,2006). An update in the recent truffle research with particular emphasis on the chemical properties (nutritional and aromatic profile) and their potential biological activities such as, antioxidant, antiviral, antimicrobial, hepatoprotective, anti-mutagenic, anti-inflammatory, anti-carcinogenic and anti-tuberculoid is reviewed(Wang & Marcone,2012) .

Pumpkin is widely considered to have active hypoglycemic properties. It contains numerous phyto-constituents, which can be categorized into alkaloids, palmitic, oleic, linoleic acids and flavonoids. In addition, the important medicinal properties are known acting as an antioxidant, an anticarcinogenic, and an anti inflammatory (Adams et. al., 2011).

BIOACTIVE COMPOUNDS FROM OTHER FOODS

Epidemiological and Clinical studies have linked consumption of soy foods with low incidences of a number of chronic diseases, such as cardiovascular diseases, cancer and Osteoporosis. The lower rates of several chronic diseases in Asia, including cardiovascular diseases and certain types of cancer, have been partly attributed to consumption of large quantities of soy foods. Major non-isoflavone phytochemicals in soy as well as their bioavailability and health effects are discussed (Kang et. al., 2010). Anti glycol-oxidative properties are linked to oxidative and advanced glycation end product-related diseases, which suggest that green tea fortification of intermediate moisture apple products could be a valuable means of product innovation, to address consumers' nutritional needs (Lavelli et. al., 2011).

Hot dried peppers at ripe stage had a high content of bioactive compounds that exhibited significant anti-oxidant properties (26-80 micromol trolox equivalents / g of dry matter), such as polyphenols (more than 2000 mg / 100 g of dry matter) and carotenoids (95-437 mg/100 g of dry matter), which were partially bioaccessible. The amount released from the food matrix by the action of digestive enzymes was about 75% for total phenols, up to 49% for both β- carotene and zeaxanthin and up to 41% for β- cryptoxanthin (Hervert-Hernandez et. al., 2010).

Nutrient levels in buckwheats that were maximized in a day 8 sprouts included total phenolics, quercetin and ascorbic acid. Sprouting triggers a variety of nutritional changes in buckwheats. Day 8 sprouts, consisting of high polyphenolic and moderate quercetin contents, are nutriceutically maximized when hypocholesterolemic, hypotriglyceridemic, and antioxidative activities are concerned (Lin et. al., 2008).

The value of proteins as an essential source of amino acids is well documented, but recently it has been recognised that dietary protein exert many other functionalities *in vivo* by means of biologically active peptides. Such peptides are inactive within the sequence of the parent protein and can be released by digestive enzymes during gastrointestinal transit or by fermentation or ripening during food processing. Bioactive peptides have been defined as specific protein fragments that have a positive impact on body functions or conditions and may ultimately influence health. At present, milk proteins are considered the most important source of bioactive peptides. Upon oral administration, bioactive peptides may affect the major body systems – namely the cardiovascular, digestive, endocrine, immune and nervous system. For this reason, the potential of distant dietary peptide sequences to promote human health by reducing the risk of chronic diseases are boosting natural immune protection has aroused increasing scientific and commercial interest over the past decay. The beneficial health effects may be attributed to numerous known peptide sequences exhibiting anti-microbial, anti-oxidative, anti-thrombotic, anti-hypertensive, immune-modulatory and opioid activities among others. The activity of these peptides is based on their inherent amino acid composition and sequence. The size of active sequences may vary from 2-20 amino acid residues, and many peptides are known to reveal multi-functional properties. For above reasons, milk derived bioactive peptides are considered as prominent candidates for various health promoting functional foods targeted at heart, bone and digestive system, health as well as improving immune defence, mood and stress control. Recent studies suggest that bioactive milk peptides may also be beneficial in reducing the risk of obesity and development of type-II diabetes. Milk proteins have received increasing attention as potential ingredients of health promoting functional foods targeted at diet – related chronic disease, such as cardiovascular disease, diabetes type-II and obesity. A great variety of naturally formed bioactive peptide have been found in fermented dairy products, such as yoghurt, sour milk and cheese. Recently, industrial scale technologies suitable for the industrial production of bioactive milk peptides have been developed. In addition, a few commercial food products supplemented with milk protein – derived bioactive peptides have been launched on limited markets. Some of these products carry clinically documented benefits, in particular for reduction of mild hypertension. The multi functional properties of milk peptides appear to offer considerable potential for the development of many similar products in the near future (Korhonen, 2009).

Anti-inflammation – guided fractionation and purification were used to evaluate the bioactivity and components of adlay (*Coix lachrymal-jobi L. Var. Ma-yuen Stapf*) bran. Flavonoids in adlay bran, partially at least, contributed to its anti-inflamatory effect (Chen et. al., 2011).Examples of plant species reported for anti-diabetic effect are presented in Table-9.

Canola is the rapeseed variety which was developed in Canada. Canola proteins have shown interesting and promising functional property and could be potentially used in various food matrices. Some properties of canola proteins were comparable to those of casein and better than those of other proteins, such as soybean, pea and wheat. However, the usefulness of canola protein extract is limited by the presence of some undesirable compounds, such as glucosinolates, phytates and phenols, which are responsible for the toxic, anti-nutritional and undesirable colouration capacity of canola proteins (Aider and Barbana, 2011).

Comprehensive model for the development of meat based functional foods through a presentation of the research achieved in terms of the designed and development of qualitatively and quantitatively modified meat products (through reformulation) in nutrients ,associated with cardiovascular risk (walnut as a source of bioactive substances), their bioavailability and the effect of their consumption on intermediate cardiovascular risk markers in humans are discussed (Jimenez-Colmenero et.al, 2010).

Marine bioactive peptides can be used as antihypertensive, antioxidative, anticoagulant and antimicrobial components in functional foods or nutraceutical and pharmaceutical due to their therapeutic potential in the treatment or prevention of diseases (Kim and Wijesekara, 2010).

INFLUENCE OF PROCESSING CONDITIONS ON BIOACTIVE COMPOUNDS

A great number of factors influence the bioactive components of foods. Conditions of processing have a bearing and accordingly it is most worthwhile to study the stability / transformations of the target compounds in processed products and also during their storage period.

The microwave cooking process presents controversial results in the literature due to the different conditions that are employed (time, power and added water). General decrease is observed in the levels of all the studied compounds except for mineral nutrients which were stable under all cooking conditions. Vitamin C showed the greatest losses mainly because of degradation and leaching, whereas losses for phenolic compounds and glucosinolates were mainly due to leaching into water. The longest microwave cooking time and the higher volume of cooking water should be avoided to minimize losses of nutrients such as glucosinolates, phenolic compounds and vitamin-C (Lopez-Berenguer et. al., 2007). -Ultra high pressure homogenization treatment doesnot disturb the original ascorbic acid and dehydro ascorbic acid content in apple juice (Suarez-Jacobo et al 2011). Recent developments in the chemical investigation of polyphenols emphasizing the extraction, separation and analysis of these compounds by chromatographic and spectral techniques are reviewed (Ignat et.

al., 2011) .*Solanam nigram* polyphenolic extract is a potent agent for hepato cellular carcinoma treatment through targeting G_2/M arrest and apoptosis induction, achieving cell growth inhibition (Vang et. al., 2011).*Citrus aurantium* (bitter orange) juice was characterized by the highest content of total polyphenols(784.67mg GAE/l) and by the greatest inhibition of DPPH (96.10%). *Citrus sinensis* (blood orange) juice was only marked by the high quantity of ascorbic acid (36.90mg/ml) (Tounsi et. al., 2011).

High pressure processing could preserve nutritional value and the delicate sensory properties of fruits and vegetables due to its limited effect on the covalent bonds of low molecular – mass compounds. Small molecules such as volatile flavour compounds and pigments connected with the sensory, eating quality of foods are unaffected by high pressure processing. High pressure treatments at 600 MPa retained more than 90% of ascorbic acid as compared to thermal processing in tomato purees. Heat treatment caused a rapid decrease in ascorbic acid. Phenolic contents were in general unaffected by thermal or high pressure treatments. Colour parameters were significantly affected by thermal and high pressure processing. Antioxidant activity, ascorbic acid and carotenoids after exposure to high pressure treatments (400-600 MPa) were well retained. Redness and colour intensity of purees were better preserved by high pressure processing than conventional thermal treatment. High pressure processed foods could be sold at a premium over their thermally processed counter parts as they will have retained their fresh-like properties (Patras et.al. 2009).

The investigation of berry seed press residues revealed that the total phenols and tocopherols were quantitatively the most important features of this material but there were significant differences between batches and cultures (Helbig et. al., 2008). Drying at 60°C was suggested as an optimum condition to obtain the highest retention of sulforaphane in cabbage dietary fibre powder (Tanongkinkit et. al., 2011) .Betanin/isobetanin pigments measured spectrophotometrically, comprised a major portion of the total betalain content (41%) in Beet root, the highest concentration of betalains reported in industrial products to date (Nemzer et. al., 2011) .

A mixture of concentrated juices of grape (26%), cherry (2%), black berry (0.6%), blackcurrant (0.6%) and raspberry (1%) was tested for their anti-proliferative and cytoprotective activities. The possible role of an iron chelating mechanism, potentially of biological relevance, is proposed as being partially responsible for the health benefits provided by phenolic-rich processed foods (Garcia-Alonso et. al., 2006).

Health related characteristics (carotenoids, flavanones and vitamin C) of minimally processed oranges were retained during refrigerated storage (Plaza et.al. 2011). Dried fruit consumption, in contrast with fresh fruit can provide significant proportions of daily requirements of several micronutrients, particularly folate. Australian industry drying conditions were associated with superior preservation of folate compared with ground based drying methods (Bennett et. al., 2011).

High pressure treatment at room temperature improves the quality of pomegranate juice, increasing the intensity of red colour of the fresh juice and preserving the content of natural anthocyanins (Ferrari et.al. 2010).

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Blending of fruits, under-utilized fruits, vegetables,medicinal plants, and spices in appropriate proportions for preparation of natural fruit and vegetable based nutritive beverages is reported (Bharadwaj and Pandey ,2011).Ultraviolet irradiation constitutes an alternative to thermal treatment that is being studied and developed to obtain a better sensory quality final product, but without neglecting microbial safety (Falguera et. al., 2012) . UV radiation could be employed for enhancing selected antioxidant compounds along with reduction in the microbial load in star fruit juices (Bhat et. al., 2011). Whole mango fruit had a higher content of flavonoids, β-carotene and antioxidant capacity, determined by oxygen radical scavenging capacity, and DPPH assays, than the fresh-cut fruit. Fresh cut mango presented higher amounts of total phenols (Robles-Sanchez et. al., 2012).

CONCLUSION

The economic and cultural and scientific development of our society has given rise to important changes in our food habits and life style. For example, diets in developed countries are highly caloric, rich in saturated fats and sugars, while the consumption of complex carbohydrates and dietic fibre is low. This fact, together with a decrease in physical activity, has given rise to an increase of obesity problems, and along with it, a raise in the incidence of heart disease, diabetes and hypertension in the population. The increase in number of scientific papers published for the last two decades correlating diet and some chronic diseases has shown extraordinary possibilities of foods to support, or even to improve, our health. As a consequence, nowadays, there is a huge interest among consumers and food industries on products that can promote health and well being. These foods have been genetically named functional foods (Plaza et.al. 2008)

Large number of classes and representative examples of compounds from various segments of foods are being investigated for their possible role in human health. Behaviour of compounds on isolation, and *in situ* along with others could differ and this needs detailed study. *In vitro* assessments need to be followed by animal experiments and final confirmation comes out by feeding to human subjects. Accordingly, the series of study is quite long and worth undertaking .Eventually, it is a combination of different classes of compounds related to the food sources, whose consumption should yield to the benefits of health. Thus, it is a synergy of vitamins, minerals, flavonoids, phenolics, pigments, peptides polysaccharides, fibre (soluble and insoluble) and so on, geared towards human health. Influence of processing conditions on the retention, detention, and transformation of the target compounds is worthwhile exploring further. All these available information indicate promising future and evidently confer to the health benefits of components of dietary foods.

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Table 1 Antioxidants and their influence on specific cellular activities related to cardiovascular health.

Cellular activity	**Antioxidants or Antioxidant rich foods**	***in vitro / in vivo* model**	**Observations**	**Reference**
Inhibit lipid oxidation	26 phenolics	Liposomes (0.25 mg phospholipids/ 0.5 ml)	The flavanones eriodictyol and taxifolin, the isoflavone 7,3',4' THIF, & Protocatechuic acid significantly inhibited to'–azo –bis (2, 4–dimethylvaleronitrile) induced lipid oxidation. Flavone quercetin was the most effective at inhibiting 2,2' –axo-bis (2-amidinopropane) (AAPH)-induced lipid oxidation.	Erlejman et. al., 2004
	24 flavonoids	Male balb/c mice	Flavonoids can be divided into 3 categories of antioxidant including good (IC_{50}<45μM) and moderate (45μM-IC_{50} <3000 μM and inactive compounds IC_{50} (>3000 μM) based on measuring their inhibition of both enzymatically (doxorubisin) and non-enzymatically (iron/ascorbate) induced liquid peoxidation.	Van Avker et. al., 1996
Platelet aggregation reduction	Polyphenols extracted from Kiwi fruit	440μL.blood plasma *in vitro*	Platelet aggregation was inhibited by 96% when incubated with kiwi extract in the presence of ADP and collegene	Dattaroy and Jorgensen 2004
	Orange juice, grape juice, or grape fruit juice (450 ml/day) for 1 week.	10 healthy individuals	Whole blood aggregometry showed that drinking two cups /day of grape juice for one week, significantly reduced platelet aggregation by 77% (14Ω at 6 min decrease). Orange and grape fruit juice did not have the same inability effect.	Keevil et .al.,2000
Enzyme induction such	Rutin	Human umbilical vein endothelian	Rutin (50 μM) increased intracellular glutathione (GSH)to 0.48, 1.66 and 2.74	Gong et. al., 2010

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as glutathione (GSH) endothelial NO synthase (gNOS) inducible NOS (iNOS)		cells (HUVECs)	times compared with 200 μM H_2O_2-treated cells by 6h, 12h and 24 h respectively. Rutin (50 μM) reduced NO level to 124.6 μM/L to as compared to 97.6 μM/L of 200 μM H_2O_2 treatment over 6 h.	

Adopted from Wang et. al., (2011)

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Table 2 Tested clinical trials of bio-active compounds.

Phytochemicals	**Health benefits**	**Study design**
Tea phenolics	Antioxidant effects	Study involved ~40 volunteers
Quercetin	Proliferation inhibition ability through, tyrosine kinase	Study resulted in inhibition of tumor through tyrosine kinase inhibition (14 subjects)
β-carotene and lycopene	Prostate cancer prevention	Phase II randomized study (26 newly diagnosed prostate cancer subjects)
Rutin	Antioxidant	Randomized single-blind placebo-controlled trial (18 female subjects)
Isoflavones	Prostate cancer prevention	Phase II randomized, placebo-controlled clinical trial (242 prostate cancer subjects)
Ascorbic acid	Prevention of advanced malignance	Intravenous administration of ascorbic acid (24 subjects)
Epigallocatechin gallate	Anticancer	Protection against mutagenicity and genotoxicity, inhibition of biochemical markers of tumor initiation, inhibition of biochemical markers of tumor promotion, effects on detoxification enzymes, trapping of activated metabolites of carcinogens, and antioxidant and free radical scavenging activity.

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Curcumin	Anti-inflammatory and anticancer	Cox-2 and $NF_{K}B$ inhibition
Ellagic acid (pomegranate juice)	Prostate cancer	Delay in proliferation of prostate specific antigen (PSA)
Fructose and oroanthocyanidin (cranberry)	Urinary tract infections	Acidify urine and prevent adhesion of microbes in urinary tract
Quercetin and apigenin	Cardiovascular risk	Antiaggregators effect
Omega-3 and -6 fatty acids, green tea, licorice, quercetin, shark cartilage, curcumin	Anticancer	Antiangiogenesis
Podophyllotoxin (mayapple)	Breast cancer	Induction of apoptosis

Adopted from Patil et.al.,(2009)

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Table 3 Effect of β - carotene on various cells and cell systems.

Cells	**Activity**
Mammary and mouse	Inhibition of alveolar lesions
Chinese hamster ovary	Reduction of sister chromatid exchange
Human lymphocytes	Inhibits proliferations
Human peripheral blood mononuclear	Prevent decrease in antigen expression
Human polymorphonuclear leukocytes	Inducing secretion of cytotoxic cytokine
Melanoma	Increases differentiation, reduces adenylate cyclase

Adopted from Patil et.al.,*(*2009)

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Table 4 Clinical observations using flavonoids for health benefits

Year published	Trial conducted	Major outcome of the trial
1996	Phase 1 trial on quercetin for *in vivo* tyrosine kinase inhibition activity	Quercetin was safely administered, and inhibition of tyrosine kinase was observed along with antitumor effect
1996	Intake of flavonoids and risk of coronary heart disease (CHD) in male health professionals.	Data do not strongly support the relationship between CHD and flavonoid intake; however, there were some positive responses.
1999	Intake of flavonoids and risk of CHD in postmenopausal women	Broccoli has shown strong benefit in preventing CHD
2000	Micronized flavonoids for control of bleeding from acute internal haemorrhoids	Micronized flavonoids had rapid cessation of bleeding and a reduced risk of relapse
2002	Consumption of dietary antioxidants in association with risk of Alzheimer's disease (flavonoids were one of the treatments).	Vitamins C and E showed significant benefits
2003	Antioxidant effect of tea bioactive compounds (flavonoid is one of the major constituents)	Bioactive compounds protects DNA against oxidative damage
2003	Flavonoid consumption and CHD mortality	Intake of high amount of flavonoid along with tea and red wine are associated with reduced risk of CHD
2005	Flavonoids of *Chrysanthellum indicum* for the treatment of rosacea.	Flavonoids of the plant is well tolerated and help in prevention of moderate rosacea
2008	Flavonoids, flavonoid-rich foods for prevention of cardiovascular risk	Flavonoids of soy and cocoa are helpful in prevention of

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		cardiovascular risk.

Adopted from Patil et.al., (2009)

Table 5 Milestones on carotenoids research

Year	**Development**
1831	Weckenroder coins the term “carotene”
1887	Arnaud described the presence of carotenes in plants
1934	Vitamin A and carotenoids identified in retina
1941	Discovery of carotenoids in human metabolites
1959	Quantitative paper chromatography of carotenoids
1966	Expert Committee on Food Additives from FAO and WHO accepted β-carotene for use in food
1981	Exploit the possible benefits of carotenoids in cancer
2002	β-carotene can help in prevention of ARMD
2005	Lycopene inversely associated with pancreatic cancer

Adopted from Patil et .al., (2009).

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Table 6 Clinical studies on health benefits of ascorbic acid

Year published	Trial conducted	Major outcome of the trial
1974	Ascorbic acid supplementation in the treatment of pressure sores	Ascorbic acid may be accelerate the healing of pressure sores
1975	Effect of ascorbic acid in common cold	No major benefits of ascorbic acid observed in common cold
1990	Effect of ascorbic acid on absorption of iron	Ascorbic acid can help in absorption of iron.
1994	Ascorbic acid as one of the vitamins to prevent colorectal carcinoma	More than vitamins C and E their dietary factors may help in prevention of carcinoma
1995	Randomised clinical trial of ascorbic acid in the treatment of pressure ulcers.	Data did not support benefits of ascorbic acid in peptic ulcer.
1995	Treatment of hypertension with ascorbic acid	Ascorbic acid can help in hypertension.
2001	Ascorbic acid as one of the vitamin for benefits in prevention of atherosclerosis.	More than 74% decrease in incidence of atherosclerosis in vitamin-fed subjects.
2004	Prevention of nephropathy in renal dysfunction undergoing coronary angiography or intervention	Ascorbic acid beneficial in prevention of nephropathy.
2008	Phase I clinical trial of intravenous ascorbic acid in advanced malignancy	High dose of ascorbic acid well tolerated and failed to demonstrate anti-cancer activity when administered to patients with previously treated advanced malignancies.

Adopted from Patil et. al., (2009).

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Table 7 Milestones in the chemistry of limonoid research

Year	Achievement
1841	Identification of limonoids in citrus seeds by Bernay
1938	Isolation of limonin and isolimonin from orange seeds
1940	Identification of limonin in different *Citrus* spp.
1946	Structure of limonin established
1948	Nomilin isolated from orange and lemon seeds; formula established as $C_{26}H_{32}O_8$
1960	Limonin found to contain two lactone rings that can be opened reversibly, a β–substituted furan ring, a ketonic oxygen, and two ethereal oxygen rings
1960	Structure of limonin established using X-ray crystallographic techniques
1960	Application of NMR spectroscopy
1965	Limonin shown to be principal component of grapefruit juice
1975	Development of HLPLC techniques for limonoid quantification
1983	Limonoids possess anticancer activity
1986	Glucosides of limonoids reported from Melia azedarach
1989	Limonoid glucosides were reported from Citrus spp.
2000	Development of liquid chromatography coupled with mass spectroscopy for citrus limonoid analysis
2000	Limonoids inhibit the growth of estrogen receptor – negative and – positive human breast cancer cells.
2000	Limonoids reduce LDL cholesterol levels in a rabbit model and apo-B production in Hep G-2 cells.
2001	Limonin and nomilin inhibits four stomach neoplasia in a mouse model.
2002	Preparative level urification of limonin glucoside
2003	Limonin and nomilin inhibit p-24 antigen activity, protease activity and replication of HIV-1
2006	Improved methods of large-scale limonoid purification
2007	Limonoids inhibit colon cancer, ovarian cancer and human neuroblastoma cells *in vitro*

Adopted from Patil et.al., (2009)

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Table 8 Nutrient composition of fruits within the genus *Prunus* (values /100 g)

Nutrients	**Sweet cherry**	**Tart cherry**	**Apricot**	**Plum**	**Peach**
Energy (kcal)	63	50	48	46	39
Fibre (g)	2.1	1.6	2.0	1.4	1.5
Total sugars (g)	12.82	8.49	9.24	9.92	8.39
Succrose (g)	0.15	0.80	5.87	1.57	4.76
Glucose (g)	6.59	4.18	2.37	5.07	1.95
Fructose (g)	5.37	3.51	0.94	3.07	1.53
Vitamin –A (IU)	64	1283	1926	345	326
Vitamin-C (mg)	7	10	10	9.5	6.6
Vitamin-E (mg)	0.07	0.07	0.89	0.26	0.73
Potassium (mg)	222	173	259	157	190
Anthocyanins (mg)	80.19	NA	NA	12.02	1.61

NA – Not available

Adopted from Mc Cune et. al., (2011)

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Table 9 Plant species reported for their antidiabetic effect

Scientific name	Parts used	Active constituent	Animal model	Mechanism of action	References
Aegle marmelos	Root, bark, leaves	Not known	STZ-rat Alloxan rat	↓ Malate dehydrogenase level, ↑Glycogen	Karunanayake et.al.1984, Das et .al., 1996, Narendhira Kannan et. al., 2006
Aloe vera	Dried sap	Lophenol, cycloartanol, 24-methyl-lowphenol	STZ-rat	↓Blood glucose level	Chalaprawat,1997, Tanaka et.al., 2006
Mangifera indica	Leaves	Mangiferin	STZ-rat	↓Glucose	Aderibigbe et. al., 1999. Muruganandan et. al ., 2005.
Momordica charantia	Seed,& Leaves Fruit	Vicine, memordin Polypeptide – p, charantin	STZ-rat Alloxan-rat STZ-mice	↑ Glucose tolerance ↑Insulin release	Matsuda et.al., 1998 Shane-Mc Whorter, 2001. Virdi ,2003.
Syzygium cumini	Seed, leaves	Flavonoids, gallic acid, ellagic acid, tannins	STZ-rat	↑ Glucose tolerance	Ravi et. al., 2004 Pepato et. al 2005.
Trigonella foenum graecum	Seeds	Soluble dietary fibre, 4-hydroxy isoleucine	DM-human subject. Alloxan –rat	↑Glucose tolerance ↓Blood glucose level	Vats et. al., 2002, 2003, Hannan et. al., 2003, Narender et.al. 2006, Mitra et. al., 2006.

Adopted from Thakur et. al., (2010)

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