MINI-REVIEW

Food as Medicine: Potential Therapeutic Tendencies of Plant Derived Polyphenolic Compounds

Mohd Fahad Ullah*, Md Wasim Khan

Abstract

The last two decades have witnessed a major drift in the interests of the scientific community towards explaining better means to containing the health risks of the human race. The century old chemotherapies against various disorders have never been a success, albeit not a total failure. Such therapies have a major drawback of side effects that give rise to unseen disorders that emerge as a new challenge. In this regard, the concept of foodstuffs as natural medicines is very attractive. Epidemiological studies suggest that the vegeteranian food habit is associated with reduced risk of cancer, cardiovascular and neurodegenerative disorders. Consistent with this hypothesis is the fact that the incidence of these disorders is least in Asian populations where fruits, vegetables and spices are the major elements in the human diet. Recent research has shown that plant-derived polyphenolic compounds are promising nutraceuticals for control of various disorders such as cardiovascular, neurological and neoplastic disease. The richness of the polyphenolic contents of green tea and red wine has made them popular choice for associated anticancer and cardiovascular health benefits. The present article is a brief review of the promises plant polyphenols, bioactive components of our food, hold for the future.

Key Words: Polyphenols - food - French paradox - coronary heart disease; cancer; green tea

Asian Pacific J Cancer Prev, **9**, 187-196

Introduction

Today the world appears to be increasingly interested in the health benefits of foods and have begun to look beyond the basic nutritional benefits of food stuffs to disease prevention and health enhancing ingredients of the same. Traditional systems of medicine owe their significance to the bioactive components that have their origin in plant sources and most of them were associated with routine food habits. Plants have an almost limitless ability to synthesize aromatic substances, most of which are phenols or their oxygen substituted derivatives (Geissman, 1963). Most are secondary metabolites, of which at least 12000 have been isolated, a number estimated to be less than 10% of the total (Schultes,1978).

In many cases these substances serve as plant defense mechanism against predation by microorganisms, insects and herbivores. Polyphenols are widely distributed plant-derived dietary constituents and have been implicated as the active components in a number of herbal and traditional medicines (Wollenweber, 1988). More than 5000 plant polyphenols have been identified and several of them are known to possess a wide spectrum of pharmacological properties (Beretz et al, 1977). Polyphenols exhibit several biological effects such as anti-inflammatory, anti-microbial, anti-carcinogenic, anti-HIV, cardioprotective and neuroprotective influence. In view of their wide range of pharmacological and biological activities they seem to have a great therapeutic potential for cancer.

Chemical Structure

Flavonoids are the major polyphenols present in wide variety of plant sources. The basic structure of flavonoids contains a heterocyclic skeleton of flavan (2-phenylbenzopyrane). The structure is represented by a benzene ring (A), condensed with a heterocyclic six-membered pyran or pyrone ring (C), which in the 2 or 3 position carries a phenyl ring (B) as a substituent (Figure 1). The constituent polyphenolic units are derived from the secondary plant metabolism of the shikimate pathway (Dewick, 1995). Flavonoids are often hydroxylated at positions 3,5,7, 2', 3', 4', 5'. Usually in the plant system, these flavonoids exist in conjugated forms, the most

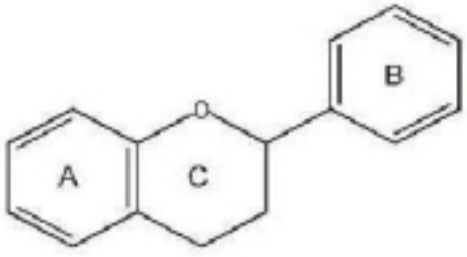
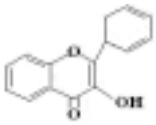
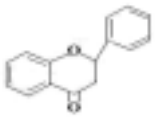
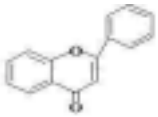
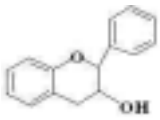
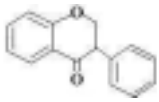
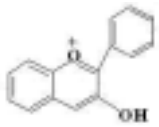


Figure 1. The Basic Structure of Flavonoids

*Department of Biochemistry, Faculty of Life Sciences, Aligarh Muslim University, Aligarh -202002 Uttar Pradesh, India. *For correspondence: Email: f.ullah@rediffmail.com*

Table 1. General Chemical Structures of Different Subclasses of Flavonoids with Important Constituent Members

Subclass	General structure	Bioactive constituents
Flavonols		Quercetin , Rutin
Flavanones		Hesperidin, Naringenin
Flavones		Apigenin, Luteolin
Flavanols		Catechins, Epicatechins, EGCG
Isoflavones		Genistein, Biochanin A
Anthocyanidins		Delphinidin, Malvidin

common being the glycosides. When glycosides are formed, the glycosidic linkage is normally located at position 3 or 7 and the carbohydrate moiety can be L-rhamnose, D-glucose, gluco-rhamnose, galactose or arabinose (Middleson, 1984). Flavonoid is a major class of polyphenols found in plant sources. Table1 illustrates flavonoid subclasses along with their important members that are known to carry pharmacological benefits.

Sources and Bioavailability

For any chemical moiety to exert a biological effect, it should be bioavailable i.e. it must be readily absorbed into the bloodstream and reach concentrations that have the potential to exert effects in vivo. Most of the polyphenols are known to be readily absorbed (Scalbert and Williamson, 2000; Rowland, 2003) but these compounds are prone to be modified into other forms inside biological systems, one such common chemical modification being conjugation (Lambert et al, 2005). Curcumin undergoes metabolic O-conjugation to curcumin glucuronide and curcumin sulfate and bioreduction to tetrahydrocurcumin, hexahydrocurcumin, and hexahydrocurcuminol in rats and mice *in vivo* and in suspensions of human and rat hepatocytes (Ireson et al, 2001). Certain curcumin metabolites, such as tetrahydrocurcumin, possess anti-inflammatory (Mukhopadhyay et al, 1992) and antioxidant activities (Sugiyama et al, 1996) similar to those of their metabolic progenitor. Dietary resveratrol is rapidly absorbed and predominantly present in plasma as glucoronide and sulphate conjugates. When administered in food, such as wine or grape juice, resveratrol metabolism is significantly inhibited by other polyphenols due to competitive reactions with metabolizing phase II enzymes resulting in an increased concentration of the free form (Wenzel and Somoza, 2005).

Isoflavones such as genistein are also known to undergo conjugation with glycosides and is metabolized in human intestine to dihydrogenistein and 6'-hydroxy-O-desmethylangolensin. Concentration of genistein has been shown to be higher in individuals consuming soy rich diet (Adlercreutz et al, 1993) and consequently genistein and its metabolites have been detected in plasma, breast aspirate and prostatic fluid (Mills et al, 1989). Similarly, other polyphenols are also known to be absorbed and metabolized into various end products which may or may not posses the biological effects of the parent compound. Table 2 summarizes the major sources and bioavailable forms of various popular dietary polyphenols.

Therapeutic Potential

Exploring healing powers in plants is an ancient phenomenon. Traditional healers have long used plants to prevent or cure various diseased conditions. An insight into the investigations, both in vitro and in vivo, reveals the properties of plant polyphenols that could form the basis of their use in the prevention and cure of several disorders. Some of the important therapeutic properties of plant-derived polyphenols with strong evidences from the existing literature have been discussed below.

Anti-HIV Properties

Human immunodeficiency virus (HIV), the etiologic agent for acquired immunodeficiency syndrome (AIDS) has been the most successful pathogen to challenge the humans in the last three decades. Globally, about 39.5 million adults are living with the syndrome (UNAIDS, WHO, 2006). In the past few years, several therapies have been tried but as of now, there is no conclusive treatment to eliminate this virus from the body once the infection has taken place. The efforts to develop vaccines against HIV have not been successful so far due to their ever-changing variants (Desrosiers, 2004).

Flavonoids and their derivatives have been reported to inhibit the growth and development of HIV by interrupting at several stages of its life cycle. Derivatives of hesperidin, particularly sulphonated and phosphorylated forms, have been studied by various scientists as hyaluronidase inhibitors and antimicrobial agent (Joyce et al, 1986).Acute HIV-1 infection has been shown to be suppressed by certain flavonoids and evidence for inhibition of HIV-1 protease, integrase and reverse transcriptase by flavonoids also exists (Critchfield et al,1996).Anti-HIV activity of scutellarin has been reported against three strains of human deficiency virus including laboratory-derived virus (HIV-1 IIIB), drug resistant virus (HIV-1 74V) and low passage clinically isolated virus (HIV-1 KM018)(Zhang et al, 2005). Scutellarin was found

Table 2. Major Dietary Polyphenols, their Bioavailable Forms in Plasma and their Major Food Sources

Polyphenols	Major dietary forms	Bioavailable forms in plasma	Common food sources
Anthocyanidins	Cyanidin, Delphinidin Malvidin	glucosides	red, blue and purple berries, red and purple grapes, red wine
Flavanols	Monomers		
	Catechin Epicatechin EGCG	methyl, sulphate or glucuronic acid conjugates. EGCG occurs in the unconjugated form	teas (particularly green), apples, pears, raspberries, chocolate
	Polymers		
	Proanthocyanidins	dimers	apples, red grapes, berries, red wine
Flavonols	Quercetin Rutin	methyl, sulphate or glucuronic acid conjugates	onions, apples, broccoli, tea, berries, Gingko biloba
Isoflavones	Genistein Daidzein Biochanin A	sulphates or glucuronides conjugates. Also occur as glycosides and aglycones	soybeans, soy foods, legumes
Stilbenes	Resveratrol	glucuronides, sulphate conjugates. unconjugated forms also present as products of fermentation	purple grapes, red wine, peanuts, berries

to inhibit several stages of HIV-1 replication with different potencies. It appeared to inhibit HIV-1 reverse transcriptase activity, HIV-1 particle attachment and cell fusion.

In cells harboring proviral HIV-1 DNA, viral transcription represents a potential therapeutic target, if selective inhibitors can be developed (Li et al, 1994). Chrysin, a flavonoid has been characterized as a potent inhibitor of HIV-1 transcription in chronically infected cells (Critchfield et al, 1996). The flavonoid halts the transcription by inhibiting casein kinase-II (CK-II) activity (Critchfield et al, 1997). CK-II may regulate HIV-1 transcription by phosphorylating cellular proteins involved in HIV-1 transactivation. Isoflavones have also been shown to inhibit transcription by repressing HIV-1 promotor activity (Wu et al, 1995).

The multiple steps of the HIV-1 life cycle each lend themselves to potential therapeutic intervention. The interaction between the viral products and the host factors are critical to develop the host-pathogen relationship. HIV-1 cellular entry via binding to CD4 and chemokine receptors well defines the principle of HIV-1 and host factor interaction (Fauci, 1996). Epigallocatechin-3-gallate (EGCG), the major polyphenol in tea has been reported to bind with CD4 receptor of T_H cells, thus interfering with its ability to interact with gp120, an envelope protein of HIV-1 (Kawai et al, 2003). Inhibition of viral adsorption by flavonoids such as epicatechin has been attributed to an irreversible interaction with gp120 (de Clereq, 2003). This protective effect against HIV infection is mediated by inhibiting virions from binding to the target cell surface. Recent studies documented that the beta-chemokine receptors, CCR2b, CCR3 and CCR5, and the alpha-chemokine receptors, CXCR1, CXCR2, and CXCR4 serve as entry coreceptors for HIV-1 (Verma et al, 2007).Grape seed polyphenols, proanthocyanidins, have been shown to down regulate HIV-1 entry coreceptors CCR2b, CCR3 and CCR5 gene expression by normal peripheral blood mononuclear cells (Nair et al, 2002).

These studies have clinical significance since the ability of polyphenols to interfere at multiple target sites of HIV might determine their successful use against ever changing variants.

Antimicrobial Properties

Microbiologists and natural product chemists are exploring the Earth for phytochemicals, which could be developed for the treatment of infectious diseases (Cowan, 1999). Polyphenols particularly, flavonoids are found to be effective antimicrobial agents against a wide array of microorganism. This is probably due to their ability to complex with extracellular and soluble proteins and also with the bacterial cell wall (Tsuchiya et al, 1996). Phenolics present in plants are known to be toxic to microorganisms (Mason and Wasserman, 1987) .

Many plant extracts derived from different parts of the plant have been analyzed for their active constituents possessing antibacterial activities. Antibacterial activity of leaf and stem bark of *Pterocarpus santalinus* was investigated for both gram-positive and gram-negative bacteria (Manjunatha, 2006). The stem bark and leaf extracts showed inhibitory activity against a number of infectious microbial strains including *Enterobacter aerogenes* and *Staphylococcus aureus*. The broad-spectrum antibacterial activity exhibited by *Pterocarpus santalinus* may be attributed to its richness in isoflavone glucosides (Krishnaveni and Rao, 2000) .Flavonoids are known to be synthesized by plants in response to microbial infections (Dixon et al, 1983) and therefore, very obviously they have been found In vitro to be effective antimicrobial substance against a wide range of microorganisms. Catechins, an important group of flavonoids, have been extensively investigated due to their occurrence in oolong green teas. It has been reported in the past, that teas posses antimicrobial activity (Toda et al, 1989) and that they contain a mixture of catechin compounds. These compounds inhibited *Vibrio cholerae*

(Borris, 1996), *Streptococcus mutans* (Batista et al, 1994), *Shigella* (Vijaya et al, 1995) and other bacterial strains in vitro. The catechins have been found to inactivate the cholera toxin from *V. cholerae* (Tsuchiya et al, 1996) and inhibit isolated bacterial glucosyl transferase in *S. mutans* (Nakahara et al, 1993).

Many of the flavonoids are known to be hydroxylated and the site(s) and number of hydroxyl groups associated with the rings are thought to be related to their relative toxicity to microorganisms, with evidence that increased hydroxylation results in increased toxicity (Geissman, 1963). Catechol and pyrogallol both of which are hydroxylated phenols, have been shown to be toxic to microorganisms. Inhibitory interaction between the polyphenols and protein or DNA has also been observed. Quinones are known to complex irreversibly with nucleophilic amino acids in proteins (Stern et al, 1996) often leading to inactivation of the protein via loss of function. This has been attributed for the wide range of quinone anti-microbial effects (Kazmi et al, 1994).

The above references have well established the antimicrobial properties of plant polyphenols supporting their use to combat infective diseases. While 25 to 50% of current pharmaceuticals are derived from plants, none are used as antimicrobials, since our choice had been restricted to bacterial and fungal sources for these activities. However, with the increasing complexities of antibiotic resistance, the use of antibiotic needs to be checked and antimicrobial agents from plant origin be given a favourable insight for their therapeutic use.

Cardioprotective properties

A longstanding tenet of nutrition holds that people with diets rich in fruits and vegetables enjoy better health than those eating few. Consequently, research has sought the components or compounds responsible for this apparent health benefit. Much of current research shows that free radicals are the connecting link between otherwise physiologically distinct diseases. As a result dietary antioxidants hold promise in at least delaying the onset/ progression of these diseases.

The "French Paradox" – the observation that mortality from coronary heart disease is relatively low in France despite relatively high levels of dietary saturated fat led to the idea that regular consumption of red wine (rich source of polyphenols) might provide additional protection from cardiovascular disease (Criqui and Ringel, 1994). In the prevention of cardiovascular disease, many of the observed effects of polyphenols can therefore be attributed to their recognized antioxidant and radical scavenging properties, which may delay the onset of atherogenesis by reducing chemically and enzymatically mediated peroxidative reaction (German and Walzem, 2000).Regular, moderate consumption of red wine is linked to a reduced risk of coronary heart disease (Li et al, 2006). Resveratrol, a component of red wine has been linked to a number of potentially cardioprotective effects (Szewczuk et al, 2004). Anthocyanidins have also been found to have antioxidant potential (Falchi et al., 2006). Studies suggest that EGCG can suppress reactive oxygen species and thereby prevent the development of cardiac hypertrophy (Li et al, 2006). Increase in LDL is taken as a parameter for the occurrence and susceptibility of cardiovascular diseases. Polyphenols such as dicvertin have been reported to produce a 12% decrease in LDL along with a 14% increase in HDL in coronary heart disease patients (Belaia et al., 2006). Lipid-lowering activity has also been reported in tea flavonoids (Li et al., 2006).

Endothelial dysfunction is the pathophysiologic principle involved in the initiation and progression of arteriosclerosis. Some polyphenols have been shown to relax endothelium-denuded arteries. There have been several reports that extracts from grape and wine induce endothelium-dependent relaxation via enhanced and/ or increased biological activity of nitric oxide (NO) which leads to the elevation of cGMP levels (Andriambeloson, 1997). Resveratrol has been found to promote vasodilation by enhancing the production of NO (Wallerath et al, 2002). Genistein, one of the major isoflavones in soy protein, binds to estrogen receptor b with much higher affinity than to ERa (Kuiper et al, 1998) and can elicit endothelium dependant vasorelaxation in vitro (Figtree et al, 2000) and in vivo (Walker et al, 2001). Other isoflavones such as dihydrodaidzeins have also been reported to enhance endothelial function (Shen et al, 2006). Flavonoids have also been found to be good hypochlorite scavenger in vitro and could have favorable effects in diseases such as atherosclerosis in which hypochlorite is known to play a significant role (Firuzi, 2004).

As documented above, it is evident that natural polyphenolic compounds possess antioxidant, vasorelaxant and antihypertensive properties that are beneficial to cardiovascular health.

Neuroprotective properties

Neurodegenerative disorders are a heteregenous group of diseases of the nervous system, including the brain, spinal cord and peripheral nerves, which have different aetiologies. The multifactorial etiology of these diseases suggests that interventions having multiple targets such as polyphenols could have therapeutic potential for them. Moreover, epidemiological studies indicate that dietary habits and antioxidants from diet can influence the incidence of neurodegenerative disorders such as Alzheimer and Parkinson's diseases (Morris et al,, 2002). The nervous system is rich in fatty acids and iron. High levels of iron can lead to oxidative stress via the iron-catalyzed formation of ROS (Bauer and Bauer, 1999). In addition brain regions that are rich in catecholamines are vulnerable to free radical generation. One such region of the brain is the substantia nigra, where a connection has been established between antioxidant depletion and tissue degeneration (Perry et al, 2002).

There is substantial evidence that oxidative stress is a causative or at least an ancillary factor in the pathogenesis of many neurodegenerative diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), Amyotrophic lateral sclerosis (ALS) (Ghadge et al., 1997), Huntington's disease (HD) and Schizophrenia (Philips et al, 1993) Flavonoids exhibit biological effects such as anti-inflammatory, antioxidant and metal chelating

properties, which augment their role in neuroprotection. Reports also suggest that red wine that contains high levels of antioxidant polyphenols reduces the incidence of AD (Wang et al., 2006). Polyphenols such as EGCG, curcumin, extracts of blue berries and Scutellaria are also known to help in AD (Dai et al, 2006). In vitro studies show that green tea extract rich in catechins could protect neurons from the amyloid beta-induced damages in AD (Bastianetto et al, 2006). EGCG is also found to be of use in ALS (Kohstl et al., 2006; Xu et al., 2006) and PD (Ramassamy, 2006). Extract of Scutellaria stem and polyphenols such as curcumin and naringenin also exhibit neuroprotection in PD (Shang et al., 2006). Alzheimer's disease is characterized by chronic inflammation and oxidative damages in the brain. Curcumin posses antioxidative and anti inflammatory properties and has thus been shown to exert a protective effect against oxidative damages initiated by divalent metals or suppress inflammatory damage by preventing metal induction of NF-κB and also inhibits amyloid beta fibril formation (Kim et al., 2005) .

Dietary polyphenols have potential as protective agents against neuronal apoptosis, through selective actions within stress activated cellular responses including protein kinase signaling cascade (Schroeter et al., 2006). Several dietary supplements with blueberries extracts have been reported to reduce some neurological deficits in aged animal models. Blueberries are a rich source of polyphenols such as catechins, epicatechins and anthocyanins. Recent studies investigating the effect of polyphenols in cognitive performance have demonstrated that dietary supplementation with blueberries extracts reversed cognitive deficits in Morris water maze performance test and Y-maze test in aged mice models (Joseph et al., 1999; Joseph et al., 2003).

The studies therefore present a promising class of compound for possible application as health supplements and nutraceuticals for neuroprotection.

Anti-Carcinogenic Properties

Evidence in the literature suggests that the differential regulation (progression and prevention) of several disorders may be characterized through the food habits prevalent in different geopolitical regions of the world. Soybean food comprises a significant portion of Asian diet, providing 10% of the total per capita protein intake in Japan and China where the incidence of breast and prostate cancer is much less than that in the United States (Adlercreutz et al., 2003).Various classes of dietary polyphenols are under investigation for their anticancer properties in order to design novel strategies for chemoprevention (Ullah, 2008).Studies have found that genistein, an isoflavone from soy can inhibit the growth of various cancer cell lines including leukemia, lymphoma, prostate, breast, lung and head and neck cancer cells (Alhasan et al., 1999). Pretreatment with genistein, potentiated cell killing induced by radiation in human PC-3 prostrate cancer cells in vitro (Hillman et al., 2001) and prostate tumor growth in vivo (Hillman et al., 2004). Another isoflavone present in soy, biochanin A has been found to have cytotoxic effect on cell growth in the mammary carcinoma cell line MCF-7 (Hsu et al., 1999), myeloid leukemia (Fung, 1997) and pancreatic tumor cells (Lyn et al., 1999). Biochanin A also induces a dose dependent inhibition of proliferation in LNCaP-cell and [3H] thymidine incorporation that is correlated with increased DNA fragmentation, indicative of apoptosis (Rike et al., 2002).

Protein tyrosine kinases (PTKs) are known to play key roles in carcinogenesis, cell growth and apoptosis (Ulrich and Schlessinger, 1990). Genistein has been identified as a PTK inhibitor (Kyle et al., 1997). Transcription of genes is critical to cell growth and proliferation. Transcription factors interact with enhancer and promoter regions of target genes, which allow the binding of RNA polymerase and initiation of gene transcription process (Papavassiliou, 1995). Investigations have revealed that genistein treatment could inhibit DNA binding activity of a major transcription factor NF-kB in PC3 and LNCaP prostate cancer cells (Davis et al., 1999). Curcumin, a natural phenolic compound found in turmeric have been shown to have antiproliferative action against colon cancer, breast cancer and myeloid leukemia (Tsvetkov et al., 2005; Maheshwari et al., 2006). Antitumor activity of curcumin is believed to be in part due to its ability to block the NF kappa B pathway (Singh et al., 1995). Other studies have shown that curcumin inhibits cell growth and induces apoptosis in MCF-7, a human breast carcinoma cell line through modulation of insulin-like growth factor-1 (IGF-1) system, including IGFs (IGF-1 and IGF-2), IGF-1R (IGF-1 receptor) and IGFBPs (IGF binding proteins), which have been implicated to play a critical role in the development of breast cancer (Xia et al., 2007).

Resveratrol, the phenol antioxidant found in berries and grapes has been reported to posses anticancer properties (Aggarwal et al., 2004) and is able to inhibit the formation of prostate tumors by acting on the regulatory genes such as p53 (Narayanan, 2006). Androgen independent DU145 human prostate cancer cells manifest resistance to radiation-induced apoptotic death (Yacoub et al., 2001). Scarlatti et al have reported that pre-treatment with resveratrol significantly enhances radiation induced cell death in DU145 cells (Scarlatti et al., 2007). Some polyphenols are known to inhibit the cancerous growth by arresting the cell cycle progression rather than inducing apoptosis. Genistein has been demonstrated to induce a G2/M cell cycle arrest in breast cancer cells, gastric adenocarcinoma cells and human melanoma cells (Casagrande and Darbon, 2000). Citrus fruit flavonoids, tangeretin and nobiletin have also been shown to inhibit human breast cancer cell lines MDA-MB-435 and MCF-7 and human colon cancer cell line HT-29 by blocking cell cycle progression at G1 stage of the cell cycle (Morley et al., 2006). Such flavonoids which inhibit the growth and proliferation of cancer cell lines by arresting cell cycle are cytostatic and significantly block the proliferation without apoptosis. Inhibition of proliferation of human cancers without inducing cell death may be advantageous in treating tumors as it would restrict proliferation in a manner less likely to induce cytotoxicity and death in normal, non tumor tissues.

Inhibition of tumor invasion and angiogenesis by

popular flavonoids such as luteolin may also account for the antiproliferative properties of plant polyphenols (Bagli et al., 2004). Another convincing antiproliferative mechanism includes the oxidative DNA breakage by the prooxidant action of plant polyphenols in the presence of transition metals especially copper (Hadi et al., 2000; Azmi et al., 2006; Hadi et al., 2007). Flavonoids are recognized as naturally occurring antioxidants and this property has been implicated for their anticancer activity (Bors et al., 1998). However, evidence in the literature suggests that antioxidant properties of plant polyphenols may not fully account for their anticancer effects (Gali et al., 1992). In the context of copper being an essential constituent of chromatin (Bryan, 1979) and that the copper levels in tissues (Yoshida et al., 1993) and serum (Ebadi and Swanson, 1988) are considerably elevated in various malignancies, the mechanism of oxidative DNA breakage holds significance.

In addition to their potential as anticancer agents, an important role of plant polyphenols as natural modulators of cancer multidrug resistance (MDR) has been realized recently (Ullah, 2008). Resistance of recurrent disease to cytotoxic drugs is the principal factor limiting long-term treatment success against cancer. Flavonoids, a major class of plant polyphenol has been found to inhibit breast cancer resistance protein (BCRP), an ABC transporter, which plays an important role in drug disposition leading to chemoresistance in breast cancer (Shuzhong et al., 2005). Isoflavones such as biochanin A, daidzein (Chung et al., 2005) and green tea polyphenol EGCG (Feng et al, 2005) have also been shown to exhibit anti MDR activities in various drug resistant cancer cell lines such as doxorubicin resistant KB-A1 cells through the inhibition of P glycoprotein transporters. Curcumin has been reported to induce apoptosis in chemoresistant ovarian cancer cell lines SKOV3 and ES-2 (Wahl et al., 2007)

The above findings suggest that the plant polyphenols have indeed emerged as an area of great promise for delineating innovative strategies in cancer chemoprevention.

Conclusions

Hippocrates (460-377B.C), the father of medicine recommended, “Let thy food be thy medicine and thy medicine be thy food”. Such an idea reflected the importance of dietary supplements for their therapeutic and preventive bioactive components due to their elevated margin of safety and desired range of efficacy. The above observation made centuries ago has now gained scientific verifications with epidemiological studies showing that the incidence of cancer and cardiovascular diseases are least in countries like India and China where vegetables, fruits and spices form an essential part of human diet. With regard to the extensive consumption of polyphenols in the diet, the biological activity of these compounds is an important area of scientific investigation. Given the potential therapeutic tendencies of these compounds, one would expect to observe their favourable effects in human population. The investigations, both in vitro and in vivo provide a definite link between the dietary intake of polyphenols and their associated health benefits. However, the issue of bioavailability has to be addressed before any targeted therapy could be designed effectively. On the basis of what is known about the bioavailabilities, it seems likely that the organ sites that are most accessible to dietary polyphenols experience the protective effects of these compounds. Moreover, another way is to explore the biofactors that in combination with dietary polyphenols could stabilize and enhance their effects even under limited bioavailability. Nature has gifted us with numerous natural products, which we consume as food and which are the armamentarium of bioactive substances having diverse activities. Since diseases like cancer are multifactorial phenomenon in which many normal cellular pathways become aberrant, it is highly unlikely that one agent could prove effective against such disorders. In this regard foods, unlike drugs may have the advantage of simultaneously influencing various pathways that go awry in diseases like cancer. Another aspect that needs to be explored is that why the excessive use of fruits and vegetables is not harmful although they are routine part of human diet whereas an isolated compound may show detrimental effects as projected in various studies. Although, it is well understood that dose does determines whether a substance acts as a toxicant or not, it is important to note the significance of synergism among the components that are present together in a particular food. In this respect nutrient-nutrient interactions and synergism are required to be studied to augment their beneficial effects or otherwise reduce the side effects. The concept of food as medicine needs to be propagated to ensure healthy food habits. However, for better and mechanism-based understanding of the potential health benefits of dietary polyphenols further studies are warranted.

Acknowledgements

The authors acknowledge the kind support of Prof. S.M. Hadi and Prof. A.N.K. Yusufi, Department of Biochemistry, Faculty of Life Sciences, Aligarh Muslim University, Aligarh (U.P.) India.

References

Adlercreutz CH, Goldin BR, Gorbach SL, et al (2003). Soybean phytoestrogen intake and cancer risk. *J Nutr*, **125**, 757-70.

Adlercreutz H, Markkanen H, Watanabe S (1993). Plasma concentration of phyto-oestrogen in Japanese men. *Lancet*, 342, 1209-10.

Aggarwal BB, Bhardwaj A, Aggarwal RS, et al (2004). Role of resveratrol in prevention and therapy of cancer: Preclinical and clinical studies. *Anticancer Res*, **24**, 2783-840.

Alhasan S, Pietrasczkiwicz-Alonso MD, Ensley J, Sarkar FH (1999). Genistein induced cell cycle arrest and apoptosis in a head and neck squamous cell carcinoma cell line. *Nutr Cancer*, **34**, 12-9.

Andriambeloson E, Kleschyov AL, Muller B (1997). Nitric oxide production and endothelium-dependent vasorelaxation induced by wine polyphenols in rat arota. *Br J Pharmacol*, **20**, 1053-8.

Azmi AS, Bhat SH, Hanif S, Hadi SM (2006). Plant polyphenols mobilize endogenous copper in human peripheral

lymphocytes leading to oxidative DNA breakage: Implication for a putative mechanism for anticancer properties. *FEBS Lett*, **580**, 533-8.

Bagli E, Stefaniotou M, Morbidelli L (2004). Luteolin inhibits vascular endothelial growth factor induced angiogenesis; inhibition of endothelial cell survival and proliferation by targeting phosphatidylinositol 3'-kinase activity. *Cancer Res*, **64**, 7936-46.

Bastianetto S, Yao ZX, Papadopoulos V, Quirion R (2006). Neuroprotective effects of green and black teas and their catechin gallate esters against betaamyloid- induced toxicity. *Eur J Neurosci*, **23**, 55-64.

Batista O, Doarte A, Nascimento J, Simones MF (1994). Structure and antimicrobial activity of diterpenes from the roots of *Plectranthus hereroensis*. *J Nat Prod*, **57**, 858-86.

Bauer V, Bauer F (1999). Reactive oxygen species as mediators of tissue protection and injury. *Gen Physiol Biophys*, **18**, 7-14.

Belaia OL, Fomina IG, Baider LM, Kuropteva ZV, Tiukavkina NA (2006). The influence of the bioflavonoid dicvertin on the antioxidative system ceruloplasmin-transferrin and lipid peroxidation in patients suffering from stable coronary heart disease with dyslipidemia. *Clin Med*, **84**, 46-50.

Beretz A, Anton R and Stoclet JC (1977). Flavonoid compounds are potent inhibitors of cyclic AMP phosphodiesterase. *Experimentia*, **34**, 1045-55.

Borris RP (1996). Natural products research: perspectives from a major pharmaceutical company. *J Ethnopharmacol*, **51**, 29-38.

Bors W, Heller W, Michael M (1998). Flavonoids as antioxidants: determination of radical scavenging efficiencies. Edited by CA Rice, E Vans and L Packer, Marcel Dekker, New York.

Bryan SE (1979). Metal ions in biological systems. Marcel Dekker, New York.

Casagrande F, Darbon JM (2000). p21CIP1 is dispensable for the G2 arrest caused by genistein in human melanoma cells. *Exp Cell Res*, **258**, 101-8.

Chung SY, Sung MK, Kim NH, et al (2005). Inhibition of P-glycoprotein by natural products in human breast cancer cells. *Arch Pharm Res*, 28. 823-8.

Cowan MM (1999). Plant products as antimicrobial agents. Clin *Microbiol Rev*, **12**, 564-82.

Criqui MH, Ringel BL (1994). Does diet or alcohol explain the French paradox? *Lancet*, **344**, 1719-23.

Critchfield JW, Butsera ST, Folks TM (1996). Inhibition of HIV activation in latently infected cells by flavonoids compounds. *AIDS Res Hum Retroviruses*, **12**, 39-46.

Critchfield JW, Coligan JE, Folks TM, Butera ST (1997). Casein kinase II is a selective target of HIV-1 transcriptional inhibitors. *Proc Natl Acad Sci USA*, **94**, 6110-5.

Dai Q, Borenstein AR, Wu Y, Jackson JC, Larson EB (2006). Fruit and vegetable juices and Alzheimer's disease: the Kame project. *Am J Med*, **119**, 751-9.

Davis JN, Kucuk O, Sarkar FH (1999).Genistein inhibits NF-kappa B activation in prostate cancer cells. *Nutr Cancer*, **35**, 167-74.

de Clereq (2000). Natural products for chemotherapy of human immunodeficiency virus (HIV) infection. *Med Res Rep*, **20**, 323-49.

Desrosiers RC (2004). Prospects for an AIDS vaccine. *Nature Med*, **10**, 221-3.

Dewick PM (1995). The biosynthesis of shikimate metabolites. *Nat Prod Rep*, **12**, 579-607.

Dixon RA, Dey PM, Lamb CJ (1983). Phytoalexins: enzymology and molecular biology. *Adv Enzymol*, **55**, 1-69.

Ebadi M, Swanson S (1988). The status of zinc, copper and metallothionein in cancer patients. *Prog Clin Biol Res*, **259**, 161-75.

Falchi M, Bertelli A, Le Scalzo R, et al (2006). Comparison of cardioprotective abilities between the flesh and skin of grapes. *J Agric Food Chem*, **54**, 6613-22.

Fauci AS (1996). Host factors and the pathogenesis of HIV induced disease. *Nature*, **384**, 529-34.

Feng Q, Dongzhi W, Qiang Z, ShengliY (2005). Modulation of P-glycoprotein function and reversal of multidrug resistance by (–)-epigallocatechin gallate in human cancer cells. *Biomed Pharmacother*, **59**, 64-9.

Figtree GA, Griffiths H, Lu YQ, et al (2000). Plant-derived estrogens relax coronary arteries in vitro by a calcium antagonistic mechanism. *J Am Coll Cardiol*, **35**, 1977-85.

Firuzi (2004). Hypochlorite scavenging activity of flavonoids. *J Pharma Pharmacol*, **56**, 801-7.

Fung MC (1997). Effect of biochanin A on the growth and differentiation of myeloid leukemia. *Life Sci*, **61**, 105-15.

Gali HV Perchellet EM, Klish DS, Johnson JM, Perchellet JP (1992). Hydrolyzable tannins: potent inhibitors of hydroperoxide production and tumor promotion in mouse skin treated with 12-0-tetradecanoyl phorbol-13-acetate *in vivo*. *Int J Cancer*, **51**, 425-32.

Geissman TA (1963). Flavonoid compounds, tannins and related compounds, In: Florkin, M. and Stotz, E.H., (Ed), Pyrrole Pigments, Isoprenoid Compounds and Phenolic Plant Constituents. Elsevier, New York pp 265.

German JB, Walzem R (2000). The health benefits of wine. *Annu Rev Nutr*, **20**, 561-93.

Ghadge GD, Lee JP, Bindokas VP, et al (1997). Mutant superoxide dismutase-1-linked familial amyotrophic lateral sclerosis, molecular mechanisms of neuronal death and protection. *J Neuro Sci*, **17**, 8756-66.

Hadi SM, Asad SF, Singh S, Ahmad A (2000). Putative mechanism for anticancer and apoptosis-inducing properties of plant-derived polyphenolic compounds. *IUBMB Life*, **50**, 1-5.

Hadi SM, Asfar AS, Bhat SH, et al (2007). Oxidative breakage of cellular DNA by plant polyphenols: A putative mechanism for anticancer properties. *Semin Cancer Biol*, **17**, 370-7.

Hillman GG, Forman JD, Kucuk O, et al (2001). Genistein potentiates the radiation effect on prostate carcinoma cells. *Clin Cancer Res*, **7**, 382-90.

Hillman GG, Wang Y, Kucuk O, et al (2004). Genistein potentiates inhibition of tumor growth by radiation in a prostate cancer orthotopic model. *Mol Cancer Ther*, **3**, 1271-9

Hsu JT, Hung HC, Chen CJ, Ying C (1999). Effect of dietary phytoestrogen biochanin A on cell growth in the mammary carcinoma cell line MCF-7. *J Nut BioChem*, **10**, 510-7.

Ireson CR, Orr S, Jones DJL, et al (2001). Characterization of metabolites of the chemopreventive agent curcumin in humans and rat hepatocytes and in rat plasma and evaluation of their ability to inhibit phorbol ester-induced prostaglandin E2 production. *Cancer Res*, **61**, 1058-64.

Joseph JA, Denisova NA, Arendash G, et al (2003). Blueberry supplementation enhances signaling and prevents behavioral deficits in an Alzheimer disease model. *Nutr Neurosci*, **6**, 153-62.

Joseph JA, Shukitt-Hale B, Denisova N, et al (1999). Reversals of age-related declines in neuronal signal transduction, cognitive, and motor behavioral deficits with blueberry, spinach, or strawberry dietary supplementation. *J Neurosci*, **19**, 8114-21.

Joyce CL, Mack SR, Anderson RA, Zaneveld LJD (1986). Effect of hyaluronidase, beta-glucuronidase and beta-N-acetyl glycosamminidase inhibitors on sperm penetration of the mouse oocytes. *Biol Reprod*, **35**, 336-46.

Kawai K, TsunoNH, Kitayama J, et al (2003). Epigallocatechin gallate the main component of tea polyphenol binds to CD4 and interferes with gp120 binding. *J Allergy Clin Immuno*l, **112**, 851-3.

Kazmi MH, Malik A, Hameed S, Akhtar N, Ali SN (1994). An anthraquinone derivative from *Cassia italica*. *Phytochem*, **36**, 761-3.

Kim H, Park BS, Lee KG, et al (2005). Effects of naturally occurring compounds on fibril formation and oxidative stress of beta-amyloid. *J Agric Food Chem*, **53**, 8537-41.

Koh SH, Lee SM, Kim HY, et al (2006). The effect of epigallocatechin gallate on expressing diseases progression of ALS model mice. *Neuro Sci Lett*, **375**, 103-7.

Krishnaveni KS, Rao JVS (2000). A new isoflavone glucoside from Pterocarpus santalinus. *Asian Nat Prod Res*, **2**, 219.

Kuiper GGM, Lemmen JG, Carlsson B, et al (1998). Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor α. *Endocrinology*, **139**, 4252-63.

Kyle E, Neckers L, Takimoto C, Curt G, Bergan R (1997). Genistein-induced apoptosis of prostate cancer cells is preceded by a specific decrease in focal adhesion kinase activity. *Mol Pharmacol*, 5, 193-200.

Lambert DJ, Hong J, Yang G, Lias J, Yand SC (2005). Inhibition of carcinogenesis by polyphenols evidence from laboratory investigations. *AJCN*, **81**, 2845-91

Li CJ, Dezube BJ, Biswas DK, Ahlers CM Pardee AB (1994). Inhibition of HIV-1 Transcription. *Trends Microbiol*, **5**, 164-9.

Li HL, Huang Y, Zhang CN, et al (2006) Epigallocathechin-3 gallate inhibits cardiac hypertrophy through blocking reactive oxidative species-dependent and -independent signal pathways. *Free Radic Biol Med*, **40**, 1756-75.

Lyn Cook BP, Stottman HL, Yan Y, Hamous GJ (1999). The effects of phytoestrogen on human pancreatic tumor cells in vitro. Cancer Lett, 142: 111-119.

Maheshwari RK, Singh AK, Gaddipati J, Srimal RC (2006). Multiple biological activities of curcumin: A short review. *Life Sci*, **78**, 2081-87.

Manjunatha BK (2006). Antibacterial activity of *Pterocarpus santalinus*. *Ind J Pharm Sci*, **68**, 115-6.

Mason TL, Wasserman BP (1987). Inactivation of red beet b-glucan synthetase by native and oxidized phenolic compounds. *Phytochem*, **26**, 2197

Middleson E (1984). The flavonoids. *Trends Pharmacol Sci*, **5**, 335-8.

Mills PK, Beeson WL, Philips RL, Fraser GE (1989). Cohurt study of diet, lifestyle and prostate cancer in Adventist men. *Cancer*, **64**, 598-604

Morley KL, Ferguson PJ, Koropatrick J (2007).Tangeretin and nobiletin induce G1 cell arrest but not apoptosis in human breast and colon cancer cells. *Cancer Lett*, **251**, 168-78

Morris MC, Evans DA, Bienias JL, et al (2002). Dietary intake of antioxidant nutrients and the risk of incident Alzheimer disease in a biracial community study. *JAMA*, **287**, 3230-7.

Mukhopadhyay A, Basu N, Ghatak N, Gujral PK (1982). Anti-inflammatory and irritant activities of curcumin analogues in rats. *Agents Actions*, **12**, 508–15.

Nair MP, Kandaswami C, Mahajan S, et al (2002). Grape seed extract proanthocyanidins down regulate HIV-1 entry coreceptors, CCR2b, CCR3 and CCR5 gene expression by normal peripheral blood mononuclear cells. *Biol Res*, **35**, 421-1.

Nakahara K, Kawabata S, Ono H, et al (1993). Inhibitory effects of oolong tea polyphenols on glucosyltransferases of mutans streptococci. *Appl Environ Microbiol*, **5**9, 968-73.

Narayanan BA (2006). Chemopreventive agents alters global gene expression pattern: Predicting their mode of action and targets. *Curr Cancer Drug Targets*, **6**, 711-27.

Papavassiliou AG (1995). Transcription factors: Structure, function and implication in malignant growth. *Anticancer Res*, **15**, 891-4.

Perry G, Sayre LM, Atwood CS, et al (2002). The role of iron and copper in the aetiology of neurodegenerative disorders: therapeutic implications. *CNS Drugs*, **16**, 339-52.

Philips M, Sabas M, Greenberg J (1993). Increased pentane and carbon disulfide in the breath of patients with schizophrenia. *J Clin Pathol*, **46**, 861-864.

Ramassamy C (2006). Emerging role of polyphenolic compounds in the treatment of neurodegenerative diseases: a review of their intracellular targets. *Eur J Pharmacol*, **545**, 51-64

Rike L, Samedi VG, Medrans TA, Baker HV (2002). Mechanism of the growth inhibitory effect of the isoflavonoid biochanin A on LNCaP cells and xenograft. *The Prostate*, **52**, 201-12.

Rowland I, Faughnan M L, Hoey K, et al (2003). Bioavailability of phyto-oestrogens. *Br J Nutr*, **89**, 838-52.

Scalbert A and Williamson G (2000). Dietary intake and bioavailability of polyphenols. *J Nutr*, **130**, 2073-85.

Scarlatti F, Sala G, Rici C et al (2007). Resveratrol sensitization of DU145 prostate cancer cells to ionizing radiation is associated to ceramide increase. *Cancer Lett*, **253**, 124-30.

Schroeter H, Spencer JP, Evans CR, William RT (2006). Flavonoids protect neuron from toxicologic low-density lipoprotein induced apoptosis. *Biochem J*, **388**, 547-57.

Schultes RE: The kingdom of plants, In: WAR Thomas (Ed), Medicines from the Earth. Mc Graw Hill Book Co, New York 1978 pp 208.

Shang YZ, Qin BW, Cheng JJ, Miao H (2006). Prevention of oxidative injury by flavonoids from stems and leaves of Scutellaria baicalensis georgi in PC12 cells. *Phytother Res*, **20**, 53-7.

Shen J, White M, Husband AJ, Hambly BD, Bao S (2006). Phytoestrogen derivatives differentially inhibit arterial neointimal proliferation in a mouse model. *Eur J Pharmacol*, **548**, 123-8.

Shuzhong Z, Xinning Y, Robert AC, Marilyn EM (2005). Structure activity relationships and quantitative structure activity relationships for the flavonoid-mediated inhibition of breast cancer resistance protein. *Biochem Pharmacol*, **70**, 627-39.

Singh S, Aggarwal BB (1995). Activation of transcription factor NF-kB is suppressed by curcumin (diferulolylmethane). *J Biol Chem*, **270**, 24995-5000.

Stern SL, Hagerman AE, Steinberg PD, Mason PK (1996). Phlorotannin-protein interactions. *J Chem Ecol*, **22**, 1887-90.

Sugiyama Y, Kawakashi S, Osawa, T (1996). Involvement of the beta-diketone moiety in the antioxidant mechanism of tetrahydrocurcumin. *Biochem Pharmacol*, **52**, 519-25.

Szewczuk LM, Forti L, Stivala LA, Penning TM (2004). Resveratrol is a peroxidase-mediated inactivator of COX-1 but not COX-2: a mechanistic approach to the design of COX-1 selective agents. *J Biol Chem*, **279**, 22727-37.

Toda MS, Okubo R, Ohnishi OR, Shimamura T (1989). Antibacterial and bactericidal activities of Japanese green tea. *Jpn J Bacteriol*, **45**, 561-6.

Tsuchiya H, Sato M, Miyazaki T, et al (1996). Comparative study on the antibacterial activity of phytochemical flavanones against methicillin resistant *Staphylococcus aureus*. *J Ethnopharmacol*, **50**, 27-34

Tsvetkov P, Asher G, Reiss V, et al (2005). Inhibition of NAD[P]H: Quinone oxido reductase 1 activity and induction of P53 degradation by natural phenolic compound curcumin. *Proc Natl Acad Sci USA*, **102**, 5535-40.

Ullah MF (2008). Cancer therapeutics: Emerging targets and trends. *Curr Cancer Ther Rev*, **4**, 50-6.

Ullah MF (2008). Cancer multidrug resistance (MDR): A major impediment to effective chemotherapy. *Asian Pac J Chem Prev*, **9**, 1-6

Ulrich A, Schlessinger J (1990). Signal transduction by receptors with tyrosine kinase activity. *Cell*, 61, 203-212.

Verma R, Gupta RB, Singh K, et al (2007). Distribution of CCR5 Delta 32, CCR2-641 and SDF1-3A and plasma levels of SDF-1 in HIV-1 seronegative North Indians. *J Clin Virol*, **38**, 198-203.

Vijaya K, Ananthan S, Nalini R (1995). Antibacterial effect of theaflavin, polyphenol (Camellia sinensis) and Euphorbia hirta on *Shigella* spp. – a cell culture study. *J Ethnopharmacol*, **49**, 115-8.

Wahl H, Tan L, Griffith K, Choi M, Liu RJ (2007). Curcumin enhances Apo2L/TRAIL- induced apoptosis in chemoresistant ovarian cancer cells. *Gynecol Oncol*, **105**, 104-12.

Walker HA, Dean TS, Sanders TA, et al (2001). The phytoestrogen genistein produces acute nitric oxide dependent dilation of human forearm vasculature with similar potency to 17β-estradiol. *Circulation*, **103**, 258-62.

Wallerath T, Deckert G, Ternes T (2002). Resveratrol, a polyphenolic phytoalexin present in red wine, enhances expression and activity of endothelial nitric oxide synthase. *Circulation*, **106**, 1652-8.

Wang J, Ho L, Zhao Z, et al (2006). Moderate consumption of Cabernet Sauvignon attenuates Abeta neuropathology in a mouse model of Alzheimer's disease. *FASEB J*, **20**, 2313-20

Wenzel E, Somoza V (2005). Metabolism and bioavailability of trans-resveratrol. *Mol Nutr Food Res*, **49**, 472-81.

Wollenweber E (1988). Occurrence of flavonoid aglycones in medicinal plants. *Prog Clin Biol Res*, **280**, 45-55.

Wu Baer F, Lane WS, Gaynor RB (1995). The cellular factor TRP-185 regulates RNA polymerase binding to HIV-1 TAR RNA. *EMBO J*, **14**, 5995-6009.

Xia Y, Jin L, Zhang B, et al (2007). The potentiation of curcumin on insulin-like growth factor-1 action in MCF-7 human breast carcinoma cells. *Life Sci*, **80**, 2161-9

Xu Z, Chen S, Li X, Luo G, Li L, Le W (2006). Neuroprotective effects of (-)-epigallocateclun-3-gallate in a transgenic mouse model of amyotrophic lateral sclerosis. *Neurochem Res*, **31**, 1263-9.

Yacoub A, Park JS, Qiao L, Dent P, Hegan MP (2001). MAPK dependence of DNA damage repair: ionizing radiation and the induction of expression of the DNA repair genes XRCC1 and ERCC1 in DU145 human prostate carcinoma cells in MEK K dependent fashion. *Int J Radiat Biol*, **77**, 1067-78.

Yoshida D, Ikada Y, Nakayama S (1993). Quantitative analysis of copper, zinc and copper/zinc ratio in selective human brain tumors. *J Neuro Oncol*, **16**, 109-15.

Zhang GH, Wang Q, Chen JJ, et al (2005). The anti-HIV I effect of scutellarin. *Biochem Biophys Res Commun*, **334**, 812-816.

Food as Medicine: Potential Therapeutic Tendencies of Plant Derived Polyphenolic Compounds.Asian Pacific Journal of Cancer Prevention: Therapeutic Properties of Plant Derived Polyphenolic Compounds. [Online] 2008. Hawkins, Ernest B. and Ehrlich, Steven D. Grape seed. University of Maryland Medical Center Medical Reference: Complementary Medicine. [Online] January 24, 2007. National Center for Complementary and Alternative Medicine. Phenolic compounds originating from edible and non-edible plant parts possess antioxidant activity. They display the capability to inhibit or delay the oxidation of lipids, proteins, and DNA by affecting the initiation or propagation of oxidizing chain reactions. Natural phenolic antioxidants can scavenge reactive oxygen and nitrogen species (RONS), thereby preventing the onset of oxidative diseases in the body (Halliwell and Gutteridge, 1992; Willet, 1994).Â Ullah MF, Khan MW (2008). Food as Medicine: Potential Therapeutic Tendencies of Plant Derived Polyphenolic Compounds. Asian Pacific J. Cancer Prev., 9: 187-196. Ullah MF (2008). Plant phenolic compounds are secondary metabolites ubiquitous in most higher plants and responsible for plant defense against biotic and abiotic stresses (pathogen and insect attack, excess light and ultraviolet radiation, extreme temperature, wounding, and nutrient deficiencies) [21,22]. Furthermore, dietary phenolic compounds in plant-based foods may be beneficial to human health, since such compounds have anti-human immunodeficiency virus (HIV) [21,23], antioxidant [21,24], anticancer [21,25], anti-inflammatory [21,26], anticariogenic [21,27], and cardioprotective [21,28] properties.Â Ullah, M.F.; Khan, M.W. Food as medicine: Potential therapeutic tendencies of plant derived polyphenolic compounds. Asian Pac. J. Cancer Prev.