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Review Article

OXIDATIVE STRESS, BIOMARKERS AND ANTIOXIDANTS RELEVANT TO PROSTATE CANCER AND NEURODEGENERATION: POTENTIAL ROLE OF QUERCETIN

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Abstract
Oxidative stress is a key impairment induced by several conditions including cardiac problems, liver disorders, cancer and neurodegenerative disorders. The cell has numerous protective defense mechanisms against threatening factors. Most cells can tolerate a mild degree of oxidative stress because they have sufficient antioxidant defense mechanisms. Physiological levels of Reactive oxygen species (ROS) are beneficial for cells. Many components of the cell such as mitochondria, endoplasmic reticulum, peroxisomes, membranes and cytosol can be source of ROS. In general, there is a balance between production of ROS and cellular antioxidant agents. If the amount of ROS increases and if these products destroy the apparatus by which antioxidant agents are produced, the cellular defense system is eventually incapacitated. The dietary antioxidants such as ascorbic acid, α-tocopherol, lycopene, and quercetin have protective properties of oxidative stress and damage. This review presents an extensive analysis of key findings from studies on the dietary antioxidants such as ascorbic acid, α-tocopherol, lycopene, quercetin against prostate cancer; neurodegenerative situation in selected brain regions, PCB induced oxidative damage in testicular Leydig and Sertoli cellular, ventral prostatic, epididymal, liver and kidney functions. This research is also leading to identification of novel drug targets.

Key Words: Antioxidants, Neurodegeneration, Oxidative stress, Polychlorinated Biphenyl, Prostate Cancer

1. Oxidative stress
Oxidative stress is implicated in the etiology of many disease however most supplementation trails with antioxidants, micronutrients have shown beneficial effects, and cells are capable of counter balancing the production of reactive oxygen species (ROS) with antioxidants under normal physiological conditions. Endogenous cellular antioxidant defences include superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT). SODs are localized to the cytosol/mitochondria and function to reduce superoxide anion to hydrogen peroxide (H₂O₂) and water. GPx localized in the cytosol and mitochrondria remove the majority of H₂O₂ whereas CAT located in peroxisomes, is responsible for the removal of high levels of H₂O₂ (Klaunig and Kamendulis 2004). ROS produce single or double stranded DNA breaks, purine, pyrimidine or deoxy ribose modifications and DNA cross links. Persistent DNA damage can result in either arrest or induction of transcription, induction of signal transduction pathways, replication errors and genomic instability. Oxidative stress is caused by a cellular excess of ROS and nitrogen species including superoxide (O₂⁻) H₂O₂, hydroxyl radical (·OH) and per oxy nitrite (ONOO⁻). These species have been involved in many processes linked to carcinogenesis such as cell transformation, proliferation, apoptosis resistance,metastasis and angiogenesis. These reactive species have also been found to induce genetic alterations including DNA damage, mutations, epigenetic
changes or genomic instability (Lopez-Lazaro 2007b). It has been shown that the malignant phenotype of cancer cells can be reversed by reducing the cellular levels of O$_2$ and over expression of the O$_2$ detoxifying enzymes SOD can reduce tumor cell growth, metastasis and other malignant features of cancer cells (Zhang et al. 2002).

2. Oxidative stress and cancer
Several studies have demonstrated that H$_2$O$_2$ can induce cell proliferation, apoptosis resistance, increased angiogenesis, invasion and metastasis (Lopez-Lazaro 2007a). It has been reported that an increase in the levels of H$_2$O$_2$ detoxifying enzymes could reduce cell proliferation, promote apoptosis and inhibit invasion, metastasis and angiogenesis. Oxidative stress is generated by a large variety of mechanism, including mitochondrial respiration, ischemia / reperfusion, inflammation and metabolism of foreign compounds. Excessive generation of ROS that overwhelms the antioxidant defense system can oxidize cellular biomolecules. Free radicals generate a large number of oxidative modifications in DNA, including strand breaks and base oxidations.

2.1 Oxidative stress and cancer biology

![Diagram of oxidative stress and cancer biology]

**Fig:1.** Shows the oxidative stress mediated induction of apoptosis leads to the neurodegeneration and oxidative stress mediated cell proliferation and resistance of apoptosis leads to the migration and invasion of cancer

3. Oxidative Stress and Neurodegeneration
Biological tissues require oxygen to meet their energetic demand. However, the consumption of oxygen also results in the generation of free radicals that may have damaging effects on cells. The brain is particularly vulnerable to the effects of ROS due to its high demand for oxygen and its abundance of highly peroxidisable substrates. Oxidative stress is caused by an imbalance in the redox state of the cell, either by overproduction of ROS or by dysfunction of the antioxidant systems. Oxidative stress has been detected in a range of neurodegenerative disease and emerging evidence from in vitro and in vivo disease models suggests that oxidative stress may play a role in disease pathogenesis. Aging has been established as the most important risk factor for the common neurodegenerative diseases, Alzheimer’s Disease (AD) and Parkinson’s Disease (PD).

Alzheimer’s disease is characterized by progressive neuronal loss associated with aggregation of protein as extracellular amyloid (ß A) plaques and intracellular tau tangles. AD brains also show evidence of ROS mediated injury; there is an increase in levels of malondyaldehyde and 4 – hydroxynonenal in brain and cerebrospinal fluid of AD patients compared to controls (Lovell et al. 1995). Protein carbonyl moieties are increased in the frontal and parietal cortices and hippocampus in AD brain, with sparing of the cerebellum where no AD pathology occurs (Hensley et al. 1995).

Parkinson’s disease is the second most common neurodegenerative disease and is characterized by
progressive loss of dopaminergic neurons in the substantia nigra and aggregation of the protein α-synuclein. In PD brain, the concentration of polyunsaturated free fatty acids in the substantia nigra is reduced, while the levels of lipid peroxidation markers are increased. Protein oxidative damage in the form of protein carbonyl is also evident in PD brain compared to control and there is also some evidence to suggest a role for nitrination and nitrosylation of certain proteins due to reactive nitrogen species in PD brain (Brown and Borutaite 2004). In addition to increased levels of 8-hydroxyguanosine in PD brain, it has been reported that there is an increase in the common deletions in mitochondrial DNA in the surviving dopaminergic neurons in PD substantia nigra. Such deletions are believed to be the result of oxidative stress (Bender et al. 2006).

Main ROS producers are monoamine oxidase, complex I and III are major sources within mitochondria. ROS generated in mitochondria target the permeability transition pore (PTP), PARP and mitochondrial DNA. In the cytosol, NADPH oxidase (NOX) and Xanthine oxidase (XO) are the main producers of ROS. The role of NADPH oxidase in neurons of AD disease through β A and presenilins exhibits the direct activation. Genetic models of PD also exhibit increased oxidative stress. NADPH oxidase is activated by high cytosolic calcium concentration, leading to overproduction of superoxide. ROS production from NADPH oxidase inhibits the plasmalemmal glucose transporter resulting in deregulation of mitochondrial metabolism (Gandhi and Abramov 2012). Inhibitor of xanthine oxidase allopurinol significantly suppressed OH generation in rat straiatum of toxic models of Parkinson’s disease induced by parononylphenol and MPP (neurotoxin) (methyl 4 penylpyrodinium MPP, (can block electron transport) suggesting a potential role for XO in the oxidative stress associated with PD.

Certain neuronal groups have high intrinsic levels of oxidative stress and are therefore more vulnerable to additional disease related oxidative stress. Neurons that have long axons and multiple synapses have high bioenergetic requirements for axonal transport or long – term plasticity. Different neuronal groups exhibit different degrees of oxidative stress. For example, in the hippocampus CA1 neurons generate higher levels of expression of both antioxidant and ROS producing genes (Wang et al. 2011). Neurons that are exposed to higher levels of cytosolic dopamine that is dopaminergic neurons are also exposed to additional oxidative stress produced by the metabolism of dopamine by MAO which generates hydrogen peroxide as well as the auto oxidation of dopamine which generates superoxide. Thus, endogenous dopamine, as well as exogenous treatment with levodopa may be a further source of oxidative stress that may worsen pathogenesis (Muller 2011; Muller and Muhlack 2011).

4. Biomarkers
Chemical compounds and reactions capable of generating potential toxic oxygen species can be referred to as pro oxidants. Compounds and reactions disposing of these species scavenging them suppressing their formation, or opposing their actions are antioxidants and include compounds such as NADPH, GSH, ascorbic acid and vitamin E. In a normal cell, there is an appropriate pro-oxidants; antioxidant balance. However, their balance can be shifted toward the pro oxidants when production of oxygen species is increased greatly following ingestion of certain chemicals or drugs or when levels of antioxidants are diminished. Substances that delay, prevent or remove oxidative damages to a target molecule are considered as antioxidants out efforts to develop on effective antioxidant treatment for various diseases have been extensively studied. The various doses of antioxidants alone or in combination of dietary vegetables / fruits on biomarkers of plasma antioxidant status, lipid peroxidation and DNA damage in healthy as well as unhealthy people have been extensively studied on both human and animal models. Environmental toxicants cause the production of ROS by inhibiting complex I of the electron transport chain and decrease the production of ATP. This ROS contributes to a loss in the mitochondrial membrane potential and well as disruption of mitochondrial permeability transition pores and voltage dependent anion channels contributing to apoptosis. ROS also moves to the cytosol where it oxidizes proteins, DNA and lipids (Facecchia et al. 2011).

Lipid peroxidation causes a collapse of plasma and mitochondrial membranes releasing cytochrome c and inducing apoptosis. The brain is most affected by lipid peroxidation because of its high oxidizable lipid and metal content in comparison with other tissue (Gandhi and Abramov 2012). Superoxide radicals and hydrogen peroxide can also create further oxidative stress by metal catalyzed reactions (Lipinski 2011). Up on oxidative stress, superoxide radicals can oxidize iron molecules. The released iron then takes part in the Fenton reaction and generates hydroxyl (Melo et al., 2011). It has been shown that inactivation of mitochondrial aconitase (an enzyme involved in the citric acid cycle) by ROS contributes to the release of free iron and hydrogen peroxide leading to neuronal cell (Facecchia et al. 2011).

As a result of the reaction mentioned above, there are increased levels of oxidized glutathione (GSGLG) with a concomitant decrease in reduced glutathione (GSH), oxidized proteins and increased lipid peroxidation, all of which are commonly used as markers of oxidative stress and the extent of damage caused by it. Direct oxidative stress by H₂O₂ has been shown to induce inflammation by NFκB activation and interleukins and is involved in the stress activated protein kinase pathway (JNK). Recent studies on chronic exposure of neuronal cells to H₂O₂ elicit dynamic responses, including changes in cytoskeletal structure, energy metabolic shifts (aerobic to glycolysis) and transmembrane receptor activity (Melo et al. 2011). In other studies, chronic exposure to H₂O₂ has been shown to have a protective role by inducing the upregulation of antioxidant enzymes such as catalase and SOD (Gomez-Cabrera et al. 2008; Lodovici and Bigagli 2011).

Natural dietary agents such as fruits, vegetables and spices have drawn a great deal of attention from both the scientific community and the general public owing to their putative ability to suppress various diseases. Phytochemicals may provide desirable health benefits beyond basic nutrition to reduce the risk of chronic disease. Epidemiological studies
are available. The rationale behind the protective effects of fruits and vegetables may be the presence of antioxidant molecule which are able to scavenge oxidant species efficiently. ROS include a variety of diverse chemical molecules ranging from extremely unstable moieties such as superoxide anions and hydroxyl radicals to others such as hydrogen peroxide, that is freely diffusible relatively long lived and able to cause DNA damage (Finkel and Holbrook 2000).

Cell signaling kinases such as MAPK, phosphatidylinositol 3 – kinase (PI3K / AKT) and transcription factor NF Kappa β are also important targets for dietary antioxidants. Dietary antioxidants modulate many signal transduction pathways such as NFκβ, MAPKs, PI3K / AKT and β catenin in a manner that favors inhibition of carcinogenesis. They also inhibit DNA modification or could also repair damaged DNA, decrease markers of cell proliferation, metastasis and angiogenesis. They also cause induction of pro apoptotic proteins and suppression of anti-apoptotic proteins.

5. Antioxidants

**Vitamin C:** It protects cell compounds from free radical damage by reducing water soluble radicals, scavenging lipid peroxidation derived radicals or reducing tocopherol radicals to tocopherol (Tappel 1973). It is an essential component in diet of human and other mammals. It has been associated with fertility for many years (Millar 1992). Dawson et al. (1992) indicated that an improvement in sperm viability motility and total mature sperm count in men above the age of 25 years when dietary intake of ascorbic acid is increased. Luck et al., (Luck et al. 1995) reported that ascorbate should be considered as an essential biochemical in the reproductive process and as a potentially significant factor in human fertility. Vitamin C has defined functions in hormone secretion; gamete protection and gonadal tissue remodeling (Sen Gupta et al. 2004a,b). It has protective roles *in vivo* on the cadmium induced overall testisular damage including impaired steroidogenesis and germ cell death possibly through scavenging the reactive oxygen species (ROS) generated by cadmium (Sen Gupta et al. 2004b). The epididymal sperm concentration and plasma testosterone levels significantly increased in the ascorbic acid treated rats (Sonmez et al. 2005).

**Vitamin E:** Vitamin E is the best known lipid soluble antioxidant. Natural vitamin E represents a complex of α tocopherol and tocotrienol isomers of which α-tocopherol is predominant in most species and significantly more potent than any other naturally occurring tocopherol (Rimbach et al. 2002). Vitamin E is considered the prototype of phenolic based chain breaking antioxidant, its primary role consisting in preventing free radical initiated lipid peroxidation damage and thus in protecting the integrity of tissues (Butterfield et al. 2002). Vitamin E is mainly distributed in adipose tissue and in the sub cellular membrane fractions, the intracellular transport and release of α tocopherol into the plasma involves via a Golgi dependent pathway a specific protein, the α tocopherol transfer protein.

Tocopherol, a dietary factor is essential for reproduction in humans and animals. They metabolize either radicals or reactive oxygen intermediates to non – radical products. Cellular antioxidant defense particularly the cellular level of tocopherol and ascorbic acid levels was reduced after exposure to endocrine disruptors (Murugesan et al. 2007a). Tocopherol – OH can transfer a hydrogen atom with a single electron to a free radical thus removing the radical before it can interact with the cell membrane. Ascorbate acts as an antioxidant by being available for energetically favorable. Supplementation of vitamin E reduced ROS production and restored normal testicular function in cadmium exposed rats (Sen Gupta et al. 2004a; Sen Gupta et al. 2004b). The *in vivo* and *in vitro* studies confirmed that vitamin E had significant protective effects on oxidant induced lipid peroxidation in cultured Leydig cells and on the ability of the cells to produce testosterone (Chen et al. 2005). To counteract the damaging effect of ROS, aerobic cells are provided with extensive antioxidant defense mechanisms. These consist mainly of antioxidant enzymes, antioxidant proteins (Thioredoxin and metallothionein) and small molecular antioxidants α tocopherol, ascorbic acid and glutathione.

Vitamin E has been shown to reduce LDL oxidation and to oppose the process in cell cultures and in animal studies (Butterfield et al. 2002). High vitamin E intake correlates with low risk of cardiovascular disease. Vitamin E supplementation has been shown to reduce cognitive impairment in rats probably due to reduced oxidative stress in the cerebral cortex and hippocampus. Combined vitamin E with vitamin C (Liu and Meydani 2002) showed better results because the vitamin C provided a means to neutralize the tocopheroxyl radicals. Vitamin E supplementation in an Alzheimer’s disease mouse model resulted in improved cognition and reduced BA deposition (Conte et al. 2004). Polychlorinated biphenyls (PCBs) are ubiquitous and persistent environmental contaminants that disturb the normal functions including gonadal function in humans and mammals. PCB treatment significantly reduced the serum, LH, FSH, testosterone and estradiol. In addition to this, testicular Leydig cell androgen and estrogen receptors were markedly decreased. Steroidogenic enzymes such as cytochrome P_{450} SCC, 3ß HSD and 17 ß HSD mRNA expressions were decreased significantly after PCB treatment. The simultaneous administration of vitamin C or E in PCB exposed rats result a significant restoration. Thus vitamin C +E have ameliorative role against PCB induced testicular Leydig cells functions (Murugesan et al. 2007a). The role of vitamin E on PCB induced toxicity in ventral prostatic functional parameters has also been studied in our laboratory (Venkataraman et al. 2004).

**Lycopene:** Lycopene, a naturally occurring carotenoid (as tomatoes) has attracted considerable attention as a potential chemo preventive agent. It is highly efficient antioxidant and has a singlet oxygen and free radical scavenging capacity (Cohen 2002). Lycopene has a possible protective role against various toxicants including testicular and prostatic toxicants (Atessahun et al. 2006a, b; Elumalai et al. 2009). Lycopene protects Leydig cellular StAR protein and steroidogenic enzyme expressions and its activity by acting against PCB induced
Lycopene is a highly unsaturated straight chain hydrocarbon containing 11 conjugated and two non-conjugated double bonds. As a polyene it undergoes cis – trans isomerization induced by light, thermal energy or chemical reactions (Zechmeister et al. 1941; Nguyen and Schwartz 1998). Lycopene exists predominantly in trans configuration, the most thermodynamically stable form. In human plasma, Lycopene is an isomeric mixture containing 50% of the total Lycopene as cis – isomers. Stahl and Sies (Stahl and Sies 1992) studied that heat processing of tomatoes and tomato products induces isomerization of lycopene to the cis form which in turn increase its bioavailability. All trans, 5-cis, 9-cis, 13-cis and 15-cis are most commonly identified isomeric forms of lycopene (Clinton et al. 1996). High concentrations of cis isomers were also observed in human serum and prostatic tissue suggesting that tissue isomerases might be involved in in vivo isomerization of lycopene from all trans to cis form.

Lycopene is one of the most potent antioxidants and has been suggested to prevent carcinogenesis and atherogenesis by protecting critical biomolecules including lipid, low density lipo proteins, proteins and DNA (Aagrwal and Rao 1998; Rao and Agarwal 1998). Several studies have indicated that lycopene is an effective antioxidant and free radical scavenger. Lycopene because of its high number of conjugated double bonds, exhibits higher singlet oxygen quenching ability compared to β-carotene or α-tocopherol (Di Mascio et al. 1989). In in vitro systems lycopene was found to inactivate hydrogen peroxide and nitrogen dioxide. Lycopene is highly lipophilic and is most commonly located within cell membranes and other lipid components. In the lipophlic environment lycopene will have maximum ROS scavenging effects. Lycopene provides protections against LDL oxidation. It protects lymphocytes against NO₂ induced membrane damage and cell death twice as efficiently as β carotene. Levy et al., Levy et al. (1995) showed that lycopene inhibited the growth of human endometrial, mammary and lung cancer cells grown in cultures and was more effective than α or β carotene. High intake of tomatoes was consistently associated with reduced risk of digestive tract cancers in a case control study from Italy, where cases were patients with histologically confirmed cancers of oral, pharynx, esophagus, stomach, colon and rectum and controls were patients with unrelated conditions (Franceschi et al. 1994).

Lycopene have been shown to be associated with decreased risk of chronic diseases such as various cancers and cardiovascular diseases (Rao and Agarwal 2000). Modulation of intercellular gap junction communication, hormonal and immune system and metabolic pathways may also be involved after lycopene treatment.

Prostate cancer is the most commonly diagnosed malignancy of men. In our laboratory Lycopene is known inducer of apoptosis in prostate cancer cells. It inhibits the proliferation of prostate cancer cells. Increased secretion of IGF binding proteins 3 and decreased IGF I and IGF II by Lycopene treatment on PC3 and LNCaP cells has been studied in our laboratory (Kanagaraj et al. 2007). Lycopene induces apoptosis through activating intrinsic and extrinsic mediated apoptosis as well as downregulate IGF system and its signaling molecules in both PC3 and LNCaP cells (Kanagaraj et al. 2007).

Lycopene has also been used to protect the testes from PCB induced toxicity and to treat male infertility as an antioxidant. In Sertoli cells also, lycopene protected Sertolic cellular oxidative stress markers, mRNA and protein expressions of androgen; follicle stimulating hormone receptors, transferrin, androgen binding protein, connection 43 in PCB exposed adult male rats ( Krishnamoorthy et al. 2007) in both in vivo and in vitro.

Studies are also available that lycopene has been shown to elevate levels of IGF I and decreased IGF-BP3 in prostate cancer cells (Kanagaraj et al. 2007). In the population, 2481 of 47365 men diagnosed prostate cancer and lycopene consumption through tomatoes was associated with a 23% reduction in prostate cancer risks. It has been reported that there was 20% decreased in PSA levels in patients with benign prostate hyperplasia. Clinical studies are still going on (Peters et al. 2007). Not only prostate cancer, lycopene inhibited proliferation of endometrial, liver mammary, lung, breast human cancer cells (Toledo et al. 2003; Mannisto et al. 2004).

Quercetin: It (3,3′,4′,5,7 – penta hydroxyflavone) is a ubiquitous flavonol in human diets found especially in fruits, vegetables, tea and red wine (Formica and Regelson 1995). It exhibits a wide spectrum of biological activities such as antioxidants, antitumor, antiinflammatory, antimicrobial, antiviral and spasmylocytic effects. In the cardiovascular system quercetin has been shown to prevent atherosclerotic relaxation of cardiovascular smooth muscle. In addition to antioxidant activity, the putative health effects of quercetin have been attributed to bioactivities actions, modulation of the cell cycle and inhibition of angiogenesis and angiotensin converting enzyme II.

It is important to note that the effects of quercetin may be mediated substantially by its metabolites. Quercetin prevents oxidative damage and cell death by several mechanisms inducing scavenging oxygen radicals, protection against lipid peroxidation and chelating metal ions (Salah et al. 1995). Kim and Jang (Kim and Jang 2009) demonstrated that quercetin is able to chelate reactive metal ions that produce ROS react with hydrogen peroxide to reduce ROS and use GSH mediated reduction in order to return ROS to their reduced states. Long term of quercetin may be able to cause cellular damage.

Quercetin is known inducer of apoptosis in multiple cancer cells such as melanoma cells (Thangasamy et al. 2008) lung cancer (Jagtap et al. 2009) gastric cancer (Wang et al. 2011), salivary adenoid cystic carcinoma (Sun et al. 2010) and prostate cancer cells (Vijayababu et al. 2005; 2006; Senthilkumar et al. 2010; 2011.). Quercetin inhibits the proliferation of cancer cells such as breast cancer (Cho et al. 2006), lung carcinoma cells and nasopharyngeal carcinoma cells (Ong et al. 2004). Earlier studies in our laboratory, demonstrated that quercetin induced growth inhibition and cell death in prostate carcinoma cells are associated with increase in P31 and hypo phosphorylated retinoblastoma proteins expression (Vijayababu et al. 2005).

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Insulin like growth factors, IGF I, II modulate a diverse range of biological activities, including mitogenic actions. IGF/BP, and decreased IGF I and IGF II by quercetin treatment have also been observed (Vijayarabbi et al. 2006). Our recent study also demonstrated that quercetin induces apoptosis through activating intrinsic and extrinsic mediated apoptosis as well as down regulate IGF system and its signaling molecules in androgen independent prostate cancer cells (Senthilkumar et al. 2010). The urokinase plasminogen activator system plays a major role in extracellular matrix proteolysis and tumor invasion. Secreted UPA expression was not present in normal prostate cancer but increased UPS expression was found in androgen independent prostate cancer cells (Sankeshan et al. 2003; Senthilkumar et al. 2011) UPA activated the matrix metalloproteinase (MMP2 and MMP 9) during invasion. In our earlier studies also, showed that quercetin down regulates MMP2 and MMP9 protein expressions in PC3 cells (Vijayarabbi et al. 2006). Recent study in our laboratory (Senthilkumar et al. 2010; 2011) demonstrated that quercetin inhibited the phosphorylation of AKT which may consequently inhibit the phosphorylation of GSK–3.

Quercetin is a potent sensitizer by downregulating UPA, UPAR, EGF, EGFR mRNA and NF kappa B, β catenin, Ras, Raf signaling molecules thereby decreasing cell survival, proliferation, migration and invasion of PC3 cells (Senthilkumar et al. 2010; 2011).

Apart from antioxidant property, quercetin acts as a neuroprotectant. Adverse effects of PCBS have been extensively studied as endocrine disruptors (ATSDR 2000; Anbalagan et al. 2003), male reproductive disorders (Murugesan et al. 2005; 2007b; Krishnamoorthy et al. 2007), diabetes (Longnecker and Daniels 2001), thyroid cancer (Bastomsky 1974) and hepatotoxicant (Banudevi et al. 2006). PCBS are neurotoxicants by altering dopaminergic neurotransmission in mammalian forebrain (Tilson et al. 1997) by inhibiting the activity of tyrosine hydroxylase, the rate limiting enzyme in dopamine biosynthesis, produces toxicity by binding to an aryl hydrocarbon (Ab) receptor by accumulating brain following in vivo exposure and decrease dopamine content (Kodavanti 2005).

Quercetin has been shown to have beneficial role in neuroprotection. It has much stronger antioxidant activity. Pu et al. (2007) studied that quercetin increases brain GSH level, OH(‘hydroxyl radical) scavenging capacity and Na+/K+ ATPase activity but decreases brain NOS activity and mitochondrial malondialdehyde content which consequently resulted in the improvement of the spontaneous behavior and cognitive performance and enhancement of brain inherent antioxidant capacity. Quercetin acts against PCBS neurotoxicity in cerebral cortex (Pratheepa Kumari et al. 2011), cerebellum (Bavithra et al. 2012), hippocampus (Selvakumar et al. 2012) by decreasing oxidative stress by scavenging ROS and brought back the mRNA expression of dopaminergic receptors. Our earlier studies also proved that PCB induced neurodegeneration were altered after quercetin supplementation through the restoration of Purkinje of cerebellum, pyramidal cells of cerebral cortex, of adult male rats (Bavithra et al. 2012; Selvakumar et al. 2012).

9. Conclusion

Thus, antioxidants such as Vitamin C, Vitamin E, Lycopene and quercetin show wide spectrum of therapeutic properties as a neuroprotectant, anticancer drug by reducing ROS and use GSH mediated reduction in order to return ROS and use GSH mediated. It is extremely important to consider seriously the issue of bio availability and metabolism of the dietary phytochemicals rich in biological properties of agents depend on their presence at the time of damage. Another issue of concern is whether purified phytochemicals such as ascorbic acid, tocopherol, lycopene and quercetin have the same protective effects as do the whole food/ plant or mixture of foods in which these compounds are present. These antioxidants have protective properties of oxidative stress and damage. The current knowledge base teaches us that they are generally more effective. Prevention is better than cure.

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References


876.

- Senthilkumar K, Arunkumars R, Elumalai P, et al. (2011). Quercetin inhibits invasion, migration and signalling molecules involved in cell survival and
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