REVIEW ON ANTIOXIDANT POTENTIAL OF SOME IMPORTANT MEDICINAL PLANTS

Vaibhav Shinde*, Kamlesh Dhalwal, K. R. Mahadik

Department of Pharmacognosy, Center for Advanced Research in Pharmaceutical Sciences, Poona College of Pharmacy, Bharati Vidyapeeth University, Erandwane, Pune- 38, India.

Summary

Medicinal plants have become extremely popular all over world as an antioxidant supplement. Plethoras of plants are being claimed, as an antioxidant to fight stress and other ailments. At the same time, market is flooded with several herbal formulations. Studies in the United States have reported that roughly 40 to 60 percent of cancer patients who use some form of complementary medicine include the use of herbs, vitamins, antioxidant, or all three. Recent reports have proved association of free radicals and oxidative stress in various diseases like ageing, inflammation, arthritis, diabetes, cancer and also cardiovascular diseases. Since antiquity, many plants, which are commonly used in cooking in order to add flavor, aroma and visual appeal to food. In addition to this, the therapeutic role played by plants, culminated in promotion of their use by many countries. This review summarizes major plants with antioxidant potential along with their mechanism of action to adjudicate their use and to boost further research in this field.

Key words: Antioxidant, Medicinal Plants, Free Radicals.

*****Corresponding author:
Vaibhav Shinde,
E-mail: vaibhavshinde2@rediffmail.com
Telephone No.: +91-20-25437237, +91-20-25389728
Fax: +91-20-25439383

Introduction

Medicinal plants have played a significant role in maintaining human health and improving the quality of human life for thousands of years. Even in the era of combinatorial chemistry and biotechnology, herbal medicines and formulations are in huge demand. Overwhelming influence of modern medicine and tremendous advances in synthetic drugs, still a large segment of the world population prefers antioxidants from plant origin. Different phytochemicals viz., glycosides, alkaloids, phenolics, tannins and flavonoids are free radical scavengers and reported for their therapeutic effects in various diseases.

Oxygen is the molecule of life for aerobic creatures. Oxygen is not only fundamentally essential for energy metabolism and respiration, but it has been implicated in many diseases and degenerative conditions[1]. In mid 1950's, Denham Harman articulated 'free radical theory' of ageing, speculating that the endogenous oxygen radicals were generated in cells and resulted in a pattern of cumulative damage. Regardless of how and where they are generated, a rise in intracellular oxidant level has two potentially important effects: damage to various cell components and triggering of activation of specific signaling pathways. Both of these effects can influence numerous cellular processes linked to ageing and development of various polygenic diseases[2]. Natural products now have received special attention as dietary supplements because of their potent antioxidant activity. Most beneficial health effects are attributed to their capacity to transfer electrons to free radicals, chelate metal catalysts, activate enzyme system, reduce α-tocopherol radicals and have capacity to inhibit LDL oxidation[3]. Ascorbic acid, which is very common in various plants, has ability to act as reducing agent. Vitamin C is effective to some extent in maintaining levels of antioxidant in plasma and liver and reduced glutathione when supplemented to alloxan induced diabetic rats[4]. Free radicals may be involved in the etiology of ageing, inflammation, arthritis, diabetes, cancer and cardiovascular diseases. As correlation of free radicals and various diseases is obvious, demand for herbal antioxidant is on high.

Compounds from natural sources are playing pivotal role in antioxidant activity. The botanical resources provide us with plentiful of all sorts of anti-oxidants as well as incredibly diverse health benefiting nutrition. Many of the phytonutrients produced by plant secondary metabolism are excellent anti-oxidants. Examples are carotenoids as lutein, beta-carotene, lycopene, and zeaxanthin; flavonoids as apigenin, catechin, gentisein, kaempferol, myricetin, quercetin and rutin; phenolic compounds as caffeic acid, ellagic acid, ferulic acid, gallic acid, para-amino benzoic acid; triterpenoid saponins as ginsenosides glycyrrhizin; diterpenes as ginkgolide A, ginkgolide B, and ginkgolide C, and sesquiterpene bilobade.

Plant Containing Flavonoids

Flavonoids are a class of secondary plant phenolics having potential beneficial effects on human health with significant antioxidant and chelating properties in the human diet. Over the years, they have been found to be an important part of the human diet and are considered to be active principles in some medicinal plants. The antioxidant activity of flavonoids is efficient in trapping superoxide anion ($O_2^{\cdot-}$), hydroxyl ($OH^{\cdot}$), peroxyl ($ROO^{\cdot}$) and alcohoxyl ($RO^{\cdot}$) radicals. *Lactuca indica* is an edible wild vegetable used as folk medicine in Asia, possess significant free radical scavenging activity, protecting super coiled DNA against strand cleavage and reducing oxidative stress in human promyelocytic leukemia and inhibited nitric oxide production[5]. Two flavonoids from *Ficus bengalensis*, 5, 7, -dimethyl ether of

leucopelargonidin3-o-α-L rhamnoside and 5, 3'-dimethyl ether of leucopelargonidin 3-o-α-D-galactosyl cellobioside showed significant antioxidant effect in hyperlipidemic rats compared to quercetin[6]. Polyphenols from tea are the group of compounds containing the most powerful antioxidant capacity. Epigallocatechin is 20 times more potent than ascorbic acid[7]. Anthocyanins such as cyanidin responsible for the colors of flowers and fruits have shown antioxidative activity by preventing lipid peroxidation[8]. Chrysoeriol and its glycoside (Chrysoeriol-6-o-acetyl -4'-β-D-glucoside) are the flavonoids isolated from *Coronopus diddymus* that inhibited γ-radiation induced lipid peroxidation and enzymatically produced superoxide anion[9.] Artichoke leaf extract have antioxidative and protective property against hydroperoxide induced oxidative stress in rat liver hepatocytes. It also protects lipoprotein from oxidation induced by hydrogen peroxide.

To build vitality and alertness *Ginkgo biloba* has been used for more than 5,000 years. Terpene-free *Ginkgo biloba* extract contains 33% Ginkgo flavone glycosides; mostly quercetin and kaempferol derivatives have potent antioxidant property[10]. Also other compounds in Ginkogo showed profound antioxidant[11]. Methanolic extract of *Juniperus chinensis* (Cupressaceae) heartwood and its n-BuOH soluble fraction showed the strong antioxidant activity. Quercetin, naringenin, taxifolin, aromadendrin and isoquercitrin were isolated from the n-Butanol fraction[12]. The plant *Moringa oleifera* has radical scavenging effect and peroxyl & superoxyl radical[13]. *Silybum marianum* known as Milk Thistle is an ancient medicinal plant used to purify and protect the liver from as early as 23-79 AD. Silybin part of the chemical structure of silymarin is potent antioxidant[14]. The seed coat extract of *Tamarindus indica*, have antioxidant properties against nitric oxide induced by lipopolysaccharide and interferon gamma[15]. The compound responsible for antioxidative activity were 2-hydroxy-3', 4'-dihydroxy phenyl acetate, 2-hydroxy-3', 4'-dihydroxy acetophenone, Methyl 3', 4'-dihydroxy phenyl acetate, and (-)-epicatechin[16]. *Uncaria tomentosa*[17, 18] and *Cassia fistula* showed highest total phenolic, proanthocyanidin, and flavonoid contents with its good antioxidant potentials[19]. Natural polyphenols include flavonoids; flavanols, flavones, procyanidin and anthocyanins present in grapes, tea, and berries have received special attention as dietary supplements because of their potent antioxidant activity. Thus this class of compounds is playing pivotal role in antioxidant activity and one can expect more research on flavonoids. Liganas, dihydroguayaretic acid, guayacasin and isopregomisin, isolated from *Porlieria chilensis* stems shown powerful antioxidant activities similar to that of the propyl gallate[20]. Procyanidins, in addition to free radical scavenging action, strongly and non-competitively, inhibit xanthine oxidase activity, the enzyme that triggers the oxy radical cascade[21]. Anthocyanidins from fruit extract of *Punica granatum* and Procyanidines from *Vitis vinifera* exhibited antioxidant activity against hydroxyl and superoxide radicals as well as inhibited hydrogen peroxide induced lipid peroxidation[22].

Plant containing phenolics

Phenolics category is very vast and include chemical constituents who have phenolics group in there molecules. There is a striking difference between regular flavonoids and tannins. Tannins are considered superior antioxidants as their eventual oxidation may lead to oligomerization via phenolic coupling and enlargement of the number of reactive sites. This type of reaction has never been observed with the flavonoids themselves[23]. *Ipomoea batatas* methanol extract has markedly strong antioxidative activity. Major phenolic components contained were identified as chlorogenic acid and isochlorogenic acid[24]. The seeds of *Nigella sativa* have been used traditionally for centuries in the Middle East, Northern Africa and

India for the treatment of asthma, cough, and bronchitis. The antioxidant and pro-oxidant effects of thymoquinone, a natural main constituent of the volatile oil of *Nigella sativa* seeds has potent superoxide anion scavenging potentials[25]. Water extract of *Mentha piperita* appears to be good source of antioxidant. It contained high levels of total polyphenols due to high level of eritocin and rosmarinic acid. It also showed protective effect against hydroxyl radical mediated phospholipid degradation[26]. *Vitis vinifera* is the main ingredient of 'Darakchasava' a well-known Indian herbal preparation. HPLC analysis revealed the presence of polyphenols like resveratrol and pterostilbene, which act as antioxidants, chemopreventive agents, and reduce mortality from coronary heart disease by increasing high density lipoproteins like cholesterol and inhibiting platelet aggregation[27]. Resveratrol (trans-3, 5, 4'-trihydroxystilbene) found largely in the skins of red grapes, which is popular antioxidant, an anti-cancer agent, and a phytoestrogen of various researchers[28]. Carnosol, rosmanol, and epirosmanol, which are phenolic diterpenes from *Rosmarinus officinalis*, showed antioxidant activity in inhibiting LDL oxidation[29]. Six phenolic acids - cynarin and caffeic, chlorogenic, ferulic, protocatechuic and rosmarinic acids suppressed cell membrane damage induced by transition metals or tert-butyl hydroperoxide (TBH). Out of six, the most promising activity was given by rosmarinic acid[30]. Out of these isolated compounds hesperidin can be used as a potent antioxidant[31]. *Prunus domestica* (Rosaceae) have been used medicinally in India in combination with other drugs for the treatment of leucorrhoea, irregular menstruation and debility following miscarriage. In recent studies it has been found to lower the plasma LDL in rats[32]. The root of *Polygonum multiflorum* has been used as a tonic and antiaging agent since ancient times. The ethyl fraction obtained from ethanolic extract of roots, exhibited strong antioxidant activity, compounds identified were gallic acid, catechin[33].

Plant containing alkaloids

Increasingly, there is evidence that the basic nitrogenous compounds are potent inhibitors of various oxidative processes. Caffeine, 6-acetonyldihydrochelerythrine, chelerythrine and dihydrochelerythrin, isolated from leaves of *Bocconia arborea* exhibited significant antioxidant activities[34]. In tea and coffee, caffeine along with its catabolic products theobromine and xanthine, is a key component. These compounds are structurally similar to uric acid, a known antioxidant that is present in blood at relatively high concentrations, but also shows prooxidant activity. Caffeine, theobromine and xanthine have a quenching effect on the production of hydroxyl radicals, as well as on oxidative DNA breakage by hydroxyl radicals. The purine alkaloids also show oxidative DNA breakage in the presence of transition metal ions. The alkaloid caffeine and its catabolic products theobromine and xanthine exhibit both antioxidant and prooxidant properties. The results lead to the observation that caffeine and its metabolites may also contribute to the overall antioxidant and chemopreventive properties of caffeine-bearing beverages, such as tea[35]. An alkaloid from *Piper lactum* has shown protective effect on lipid peroxidation and free radical mediated cell injuries[36]. Antioxidant activity of active principle of *Withania somnifera* consisting equimolar concentration of sitoindosides VII-X & withaferin A, showed their effects on rat brain frontal cortical and striatal. Active glycowithanolides, administered once daily for 21 days, induced related increase in SOD, CAT, GPX activity in frontal cortical and striatal, which was statistically significant on days 14 and 21[37].

Plant containing glycoside

Glycosides are complex organic molecules conjugation with sugar having broad use in medicines. *Terminalia arjuna a* novel naphthanol glycoside, arjunaphthanoloside (1), was

isolated from the stem bark of *Terminalia arjuna* and its structure was established as 2,3,6,7,8,9-hexahydroxynaphthalene-2-O-alpha-L (-)-rhamnoside by means of spectroscopic and chemical methods. It showed potent antioxidant activity and inhibited nitric oxide (NO) production in lipopolysaccharide (LPS)-stimulated rat peritoneal macrophages[38]. The administration of asiaticoside, an isolated constituent of *Centella asiatica*, significantly increased the levels of superoxide dismutase, catalase, glutathione peroxidase, vitamin E and ascorbic acid in excision-type cutaneous wounds in rats[39]. A partially purified extract from dry stem of *Tinospora cordifolia* (Menispermiaceae), prevented lipid peroxidation and restored the activity of SOD and catalase. It also prevented oxidative damage caused by peroxynitrite[40]. Tea and bitter tea are popular beverages in China. Bitter tea is brewed from five different species. *Ligustrum pedunculare* is one of them. Bitter tea as a beverage contains effective antioxidant. Crude glycoside fraction of *L. pedunculare* strongly protects human low-density lipoprotein from oxidation. The compound belong to category of phenylethanoid or monoterpene glycosides such as lipedoside A-I, lipedoside A-II, lipedoside B-VI, lipedosideB-V from bitter tea have protecting and scavenging effect[41]. Protective effect of *Picrorhiza kurroa* on mitochondrial glutathione antioxidant system in D-galactosamine-induced hepatitis in rats is also reported[42]. Another important *Rasayana* drug in Ayurveda, *Bacopa monniera* (Scrophulariaceae) is used for memory enhancing, epilepsy, insomnia and as mild sedative. It showed positive response on $FeSO_4$ and cumene hydroperoxide induced lipid peroxidation suggesting potent antioxidant[43]. The alcoholic extract of the bulb of *Scilla indica* is a potent antioxidant in a low dose range with possible mechanism of action through the chelation of transition metals in the body and by breaking the chain reaction of lipid peroxidation by removing the hydroxyl radicals[44]. Rhein and aloe-emodin from *Rheum palmatum* (Polygonaceae) showed the highest inhibitory activity against peroxidation of linoleic acid catalyzed by soybean 15-lipoxygenase. Enthrone, dethrone and rhein enthrone were the most effective radical scavengers of the diphenylpicrylhydrazyl radical[45].

Plant containing tannins

The tannins are considered superior antioxidants as their eventual oxidation may lead to oligomerization via phenolic coupling and enlargement of the number of reactive sites[46]. Fruit of *Emblica officinalis* (Euphorbiaceae) has been used in Ayurveda for treatment of disease of diverse etiology. Active principle of *Emblica officinalis* consists of Emblicanin A (37%), Emblicanin B (33%), Punigluconin (12%) & pedunculagin (14%) all showed good results on SOD, CAT, GPX & lipid peroxidation. The results indicate that the antioxidant activity reside in the tannoid principle which have vitamin C like property. Alcoholic extract was found to show potent bactericidal activity[47]. According to one study Amla is a more potent antioxidant than vitamin C because of other polyphenols, which increases its activity[48, 49]. *Terminalia catappa* is a popular folk medicine for preventing hepatoma and treating hepatitis in Taiwan. The protective effects of *T. catappa* leaf extract and its major tannin component, punicalagin were examined, on bleomycin-induced genotoxicity in cultured Chinese hamster ovary cells. Pre-treatment with extract or punicalagin prevented bleomycin-induced HGPRT gene mutations and DNA strand breaks. Punicalagin suppressed the generation of bleomycin-induced intracellular free radicals, identified as superoxides and hydrogen peroxides[50]. All of the tannin components of *T. catappa* showed potent antioxidant activity. Punicalagin and punicalin were the most abundant components and had the strongest anti-oxidative effects of this group of tannins[51]. Dry fruits of the three medicinal plants, viz. *E. officinalis, Terminalia chebula* and *Terminalia bellerica* in equal amounts in a formulation called *Triphala Churna*, which is rich in phenols/polyphenols. When Triphala was tested for superoxide radical scavenging activity using xanthine and xanthine oxidase assay, it was

observed that in addition to reacting with superoxide radical, it also inhibited uric acid formation, indicative of xanthine oxidase enzyme inhibitory activity[52]. Seeds extract of *Juglans regia* exhibited antioxidant activity against DPPH radical. Three ellagitannins glanrins A-C, along with 13 hydrolysable tannins, had SOD like activity[53]. Leaf extract of *Strobilanthes crispus* contributes antioxidant activity because of presence of high content of water-soluble vitamins. It also contains catechins, alkaloids, caffeine and tannins. Catechins of *S. crispus* leaves showed highest antioxidant activity compare to vitamin E. Leaf extract can be used as an herbal tea to increase nutrients and antioxidants needed in the body to enhance the defense system[54].

Plant containing saponin

Although saponin containing plants are medicinally and commercially important, very few plants are reported as antioxidant. The stem bark of *Kalopanax pictus* is an antirheumatoidal arthritis drug in oriental medicine. Kalopanax saponin-A (KPS-A) significantly reduced malonaldehyde formation and activities of xanthine oxidases and aldehydes of hepatic non-microsomal systems in freund's complete adjuvant (FCA) reagent treated rats. It increased activity levels of superoxide dismutase, catalase and glutathione peroxidase[55]. Two groups of saponins, TS-1 and TS-2, isolated from tea root extract (*Camellia sinensis*) were tested for anti-inflammatory and *in-vitro* antioxidant activity. The antioxidant activity of these compounds was evaluated using the xanthine-xanthine oxidase system. The study indicated that the previously observed antitumour activity might be mediated through scavenging of free radicals by saponins and their anti-inflammatory activity[56].

Plants containing resins

Resins are also complex chemical compounds containing essential oils, oxygenated products of terpene and carboxylic acids. Hot Pepper, *Capsicum annuum* is good source of dietary antioxidant because they have specific constituents such as pungent capsaicinoids (capsaicin, dihydrocapsaicin) the archetypal casaicinoids. These compounds inhibited iron mediated lipid peroxidation and copper dependant oxidation of low-density lipoprotein and prevent formation of lipid hydroperoxides from the auto oxidation of linoleic acid[57]. *Commiphora mukul* and its cholesterol-lowering component, guggulsterone, effectively inhibited LDL oxidation mediated by either catalytic copper ions, free radicals generated with the azo compound 2,2'-azobis-(2-amidinopropane) dihydrochloride (AAPH), soybean lipoxygenase enzymatically, or mouse peritoneal macrophages. The combination of antioxidant and lipid-lowering properties of *C. mukul* and guggulsterone makes them especially beneficial against atherogenesis[58]. Turmeric, *Curcuma longa* has several components with immunomodulatory and antioxidant property. Natural curcuminoids, isolated from turmeric have antioxidant activity. The curcuminoids inhibited lipid peroxidation beside the production of superoxide and hydroxyl radical[59]. Also, diarylheptanoids from ethyl acetate fraction of *C. longa* scavenged peroxynitrite radicals[60].

Plant containing carotenoids

Carotenoids attracted attention because a number of epidemiological studies revealed that an increased consumption of diet rich in carotenoids is correlated to diminish the risk for several degenerative diseases including cancer, cardiovascular or ophthalmologic diseases[61]. The carotenes lycopene and β-carotene are the best antioxidants followed by hydroxy carotenoids,

zeaxanthin and lutein[62]. Lutein and zeaxanthin, pigments responsible for coloration of macula lutea of retina and protects retina against photo-oxidative damage. While β-carotene protects against sunburn (erythema solare)[63]. Administration of lycopene significantly lowered concentration of lipid peroxides and enhanced antioxidant levels[64]. *Lycosporium esculentum* extract contains lycopene and phenolic compounds, which are responsible for its antioxidant activity[65].

Other Miscellaneous

Garcinia indica (Kokum) is also used in Indian as antioxidant and health drink. Recent study showed its antioxidant activity of aqueous and boiled extracts that corroborates its use in cooking and home remedies. The assays employed were ORAC, FRAP, ABTS and the ability to inhibit lipid peroxidation in rat liver mitochondria. Kokam syrup and the two aqueous extracts had significant antioxidant effects in the above assays[66]. Garcinol, a poly-isoprenalyted benzophenone derivative, isolated from *G. indica* fruit rind have antioxidant activity. It exhibited moderate inhibitory activity on lipid peroxidation and superoxide anion scavenging activity[67]. *Allium sativam* and *Allium cepa* commonly known as Garlic are herbs with proclaimed *Rasayana* effect in Ayurveda. Both have been used as medicinal agents for thousands of years. Oils isolated from *A. sativam* and A. *cepa* have very good antioxidant effects on nicotine-induced lipid peroxidation in rat tissues. Lipid peroxidation was significantly increased in the tissues of nicotine-treated rats. Administration of water-soluble protein in alchohol fed rats showed significant increase in the anti-lipid peroxide activity[68]. *Hypericum perforatum* shoot extract have strong antioxidant activity. It also possessed the iron chelating property with more affinity to the ferrous form. It has scavenged both superoxide and hydroxyl radicals[69]. The diterpenes from *Andrographis paniculata* showed significant increase in Ca^{2+}-ATPase and Na^{+}- K^{+} ATPase and lipid peroxidation decrease significantly[70]. Neo andrographolide inhibited NO production both *in-vivo* and *ex-vivo*[71]. *Mucuna pruriens* is the most popular drug in the ayurvedic system of medicine. *In-vitro* study shows that *M. pruriens* possesses dose-dependent protection against superoxide generation, hydroxyl radical production and $FeSO_4$-induced lipid peroxidation[72].

Conclusion

Considerable interest has risen in the idea that oxidative stress is instrumental in the etiology of numerous human diseases. In recent years naturally occurring herbal compounds such as phenolic acids, flavonoids, and high molecular weight polyphenols have gained considerable attention as beneficial protective agents[73]. Overall, examination of the evidence related to potential interactions between ROS and dietary antioxidants and effects on human health indicate that consuming dietary antioxidant supplements has very good results. Overall, current knowledge makes it premature to generalize and make specific recommendations about antioxidant usage for those at high risk for cancer or undergoing treatment[74]. Most of the plants having antioxidant potential have been used in traditional medicine systems from decades for treatment of various illnesses. To date, numerous studies have been carried out in order to understand and evaluate the healing properties of these plants and their formulations. Some of the results obtained from these studies corroborate traditional use of these plants for antioxidant and to fight the stress. We believe that there is considerable scope for further investigation of the potential therapeutic use of plants.

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