

HERBAL ANTIOXIDANTS

In recent times, focus on plant research has increased all over the world. Man is turning to natural products especially those derived from plants for his as well as his animals' health care.

An etiological agent implicated in disease states and ageing is the oxidative stress which is mainly due to generation of prooxidants. The reactive oxygen species (ROS) and reactive nitrogen species (RNS) are major prooxidants and these include excited states, free radicals and other related species derived from oxygen and nitrogen. In a healthy individual, there exists a balance between generation of prooxidants and the antioxidant defence mechanism. During oxidative stress, the balance shifts towards the former. The ROS include singlet oxygen (O_2^1) superoxide hydroxyl radical, peroxy radical and H_2O_2 where as RNS include free radical nitrogen oxide and peroxy nitrite. Singlet oxygen has been implicated in induction of tumour, lung oxidant injury, skin photosensitivity, erythropoietic porphyria and geno toxicity to mammalian cells. Reaction of ROS with lipids lead to a highly damaging reaction, lipid per oxidation which is implicated in haemolysis of erythrocytes, cardiomyocyte damage, cellular membrane function including cell mediate immune reactions involving phagocytic membrane NADPH oxidase. The various antioxidants in the defence of oxidative stress include intracellular Superoxide dismutase, catalase, glutathione peroxidase, glutathione, besides the dietary oral supplements in the form of vitamin C, vitamin E, β -carotene, Zinc, Selenium. Vitamin C, E and β -carotene can inhibit oxidative modification of LDL which could positively influence the atherosclerotic process. The ROS and RNS are directly or indirectly involved in multistage process of carcinogenesis. They damage DNA leading to mutations in tumour suppressor genes and also act as initiator and/ or promoter in carcinogenesis.

Pro oxidant mechanisms.

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O_2 which is essentials for the propagation of all biochemical activities, has the potential to be exceedingly dangerous in the body. The danger occurs when a single electron is acquired by the oxygen molecules to give a superoxide anion, an extremely reactive corrosive chemical agent. Excess neutrophils attracted to irritated joints may lead to superoxide release and contribute to arthritic damage. The superoxide anion attacks and destroys a covalent bond of cellular constituents and generates new free radicals.

Antioxidant Mechanisms

*Basically there are two protective strategies-
Chemical and enzymic.*

i) **Chemical**- The strategy is to dampen or quench the chain reactions, initiated by superoxide by using antioxidants. The quenching agent should itself be attacked by the superoxide anion, but generate a radical insufficiently reactive to perpetuate the chain reaction. The main biological dampening agents are ascorbic acid and α -tocopherol. Some normal metabolites such as uric acid are effective, β -carotene is also an antioxidant. Bilirubin also act as an antioxidant.

(ii) Enzymic:

Probably all animal tissues contain enzyme superoxide dismutase, especially in the cells of mitochondria. It also occur in lysosomes, peroxisomes, extracellular fluids such as lymph, plasma and synovial fluids. H_2O_2 is destroyed by catalase converting it to water

Another enzyme that destroy H_2O_2 is glutathione peroxidase, especially in brain. Glutathione, a thiol tripeptide, found in most cells, functions as reducing agent. Organic peroxides are destroyed by this way. Glutathione peroxidase is subsequently reduced by NADPH, catalysed by glutathione reductase.

The repair enzymes which take care of singlet oxygen induced damage in lipids, proteins and DNA include exonuclease III and endonuclease IV.

Lycopene in tomato and capsorubin in chilies also act as oxygen quenchers. Zinc is a trace element in cytoplasmic Cu-Zn superoxide dismutase and Selenium is a cofactor of glutathione peroxidase. Supplementation with other antioxidants especially from natural sources like medicinal plants will also greatly help in boosting the immune system. (Devasagayam *et al*).

Plants With Proven Antioxidant Potential

A few Indian plants having proven antioxidant property is discussed here. They include *Allium sativum*, *Aloe vera*, *Andrographis paniculata*, *Asparagus racemosus*, *Azadirachta indica*, *Curcuma longa*, *Emblica officinalis*, *Glycyrrhiza glabra*, *Hemidesmus indicus*, *Tinospora cordifolia*, *Withania somnifera*, *Zingiber officinale*.

Aloe vera

This is a plant which is now extensively used in skin care preparations and health products. The low molecular weight constituents of the *Aloe vera* gel was found to inhibit release of ROS by Phorbol Myristic Acid stimulated Polymorpho nuclear cells and its extra cellular effects like lysis of RBC. Extracts of the leaf gel has been found to have glutathione peroxidase activity also.

Allium Sativum (Garlic)

Garlic has been in use as medicinal agent for thousands of years and is shown to have antimicrobial, antiarthritic, antithrombotic, antitumor, hypolipidemic, and hypoglycemic effect. Garlic extract and S-allyl cysteine isolated from garlic were noted to protect pulmonary endothelial cells invitro against H₂O₂ induced oxidative damage. The treatment with S-allyl cysteine sulphoxide reverses the deleterious effect of cholesterol diet significantly and almost completely. S-allyl cysteine (SAC) act via an antioxidant mechanism to inhibit the atherogenic process as SAC exhibited dose dependent inhibition of nuclear factor- κ B (NF Kappa B) activation. The garlic oil supplementation in nicotine treated rats increased resistance to lipid peroxidation and also showed increased activities of anti oxidant enzymes and glutathione. Di allyl sulfide has been showed to decrease thiobarbituric acid reactive substances, a measure of oxidative status. Aged garlic extract and SAC can protect endothelial cells from oxidized LDL induced injury. Borek suggests that since aged garlic extract (AGE) protects DNA against free radical mediated damage, it may have a role in protection against loss of brain function in ageing. Pretreatment with garlic led to a protective effect on heart, liver and pancreas against isoproterenol induced damage. Allicin from

garlic has been found to induce programmed cell death and arrest proliferation of cancer cells.

Asparagus racemosus (Shatavari)

The aqueous extract of the whole plant protects against a variety of biological, physical and chemical stresses. The crude extract as well as purified polysaccharide fraction of *Asparagus racemosus* showed antioxidant effects against membrane damage induced in rat mitochondria and liver by free radicals generated during α -irradiation.

Azadirachta indica (Neem)

Neem has been reported to exert several therapeutic effects. Neem has a very wide spectrum of activity against many infectious and noninfectious diseases. An antioxidant principle was isolated from neem seed using HPLC, with a hydrophobic reverse phase column and was a potent inhibitor of plant lipooxygenases. The water soluble constituents of alcoholic extracts of neem leaves exerted significant anti-inflammatory activity in cotton pellet granuloma assay in rats. The extract also inhibited synthesis of DNA and RNA as well as reduced the levels of lipid peroxide.

Curcuma longa (turmeric)

Turmeric contains several components with antioxidant, medicinal and immunomodulatory activities. The turmeric antioxidant protein from the aqueous extract of turmeric showed a concentration depended inhibitory effect on lipid peroxidation. Natural curcuminoids from turmeric were found to inhibit lipid peroxidation besides the production of superoxide and hydroxyl radical. The activities of SOD, catalase, and glutathione peroxidase was found to be higher in rats fed with turmeric than the controls when both group were injected with iron. The major antioxidant of turmeric- curcumin is found to modulate glutathione, which is important for the detoxification of lipid peroxidation products. Curcumin was also found to provide 80% protection to DNA against peroxidation injury.

Emblica officinalis (Amla)

Fruits of Amla have been used in Ayurveda as a potent Rasayana and also for treatment of diseases of diverse aetiology. Vitamin C is having a potent antioxidant property and the Amla fruit is having a rich source vitamin C. Amla fruits have ascorbic acid conjugated to gallic acid and reducing sugars, forming a tannoid complex.. Bhattacharya *et al*

investigated the antioxidant activity of *Emblica officinalis* (EOT) Emblicanin A, Emblicanin B, punigluconin, pedunculagin, and their effects on rat brain frontal cortex and straital concentration of the oxidative free radical scavenging enzymes superoxide dismutase, catalase, glutathione peroxidase and lipid peroxidation was studied. The results indicated that the antioxidant activity of *Emblica officinalis* may reside in the tannoids which have vitamin C like properties. The extract obtained from *Emblica officinalis* fruits also inhibited lipid peroxidation and reduced serum cholesterol, phospholipids and LDL levels. Bhattacharya found that EOT inhibited acute iron over load hepatic lipid peroxidation and increased serum levels of alanine amino transferase, aspartate amino transferase, and lactate dehydrogenase, which are markers of hepatic dysfunction. The Emblicanin A and Emblicanin B enriched fraction of fresh juice of the *Emblica* fruits produced an antioxidant effect ischemia reperfusion injury (IRI) induced oxidative stress. *Emblica officinalis* can be used as a hepato protective agent in damage. The fruit extract itself was found to increase glutathione, glutathione peroxidase, glutathione reductase and glutathione -S transferase in mice.

***Glycyrrhiza glabra* (Yashtimadhu)**

Glabridin, an isoflavin isolated from *G. glabra* (licorice) root and its derivatives have been found to inhibit the oxidation of LDL induced by copper ions or mediated by macrophages. The antioxidant capacity has been isolated from *G. glabra* which include hispaglabridin, Isoprenylchalone, isoliquintigenin, formononetin. The first 6 are very potent antioxidants, with glabridin being most abundant and potent.

***Hemidesmus indicus*.**

The organic acid isolated and purified from the root extract possessed viper venom inhibiting activity. They also neutralize free radical formation as estimated by TBARS and it also had enhanced the activity of antioxidant enzyme superoxide dismutase.

***Tinospora cordifolia* (Guduchi)**

This is a plant widely used in Ayurveda and is known as amrita, Gulvel, Gulancha, guduchi. The plant has acclaimed importance in treatment of jaundice, skin diseases, diabetes, anemia, emaciation and infections. It also has proven antibacterial, antiphlogistic, analgesic, antipyretic and antioxidant properties. The root extract

administration resulted in a decrease in the level of plasma lipid per oxidation, ceruloplasmin in diabetis and an increase in glutathione and vitamin C. The root extract has also been shown to inhibit superoxide and hydroxyl radical production invitro. Several glycosides with potential antioxidant activity like polyacetates from the *T. cordifolia* stem extract. The extract inhibited ferrous sulphate mediated lipid peroxidation in a dose dependent manner.

***Withania somnifera* (Aswagandha)**

The plant is known to have antistress, immunomodulatory, antinflammatory and anti ageing properties which all depend on the antioxidant property partly or completely. The plant extract gave significant protection against depletion of glutathione peroxidase and glutathione induced by exposure to UV light. The plant has a high content of biologically active steroids of which withaferin A (steroidal lactone) is the major component. The active principles of *Aswagandha* induced a dose related increase in superoxide dismutase, catalase, glutathione peroxidase in frontal cortex and striatum. The glycowithanolides tended to normalize the augmented superoxide and lipid peroxide activities and enhanced the activities of catalase and glutathione peroxidase.

***Zingiber officinale*.**

The plant could significantly lower lipid peroxidation by maintaining the activities of antioxidant enzymes-SOD, catalase, glutathione content.

Other plants that show significant antioxidant activity include *Terminalia arjuna*, *Murraya koenigii* (curry leaves) *Solanum melongena* (Brinjal), *Andrographis paniculata*, *Centella asiatica* etc. *Terminalia arjuna* bark extract contains poly phenols including ellagic acid as its principal antioxidant component. Flavanoids from *Solanum melongena* showed potent antioxidant activity by decreasing the concentrations of malondialdehyde, hydroperoxides and conjugated dienes significantly. Aqueous extract of *Centella asiatica* showed a significant decrease in the brain levels of malondialdehyde (MDA) with simultaneous significant increase in levels of glutathione. 300mg/kg extract showed a significant increase in catalase levels.

