Cardioprotective and Other Beneficial Effects of Some Indian Medicinal Plants

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Summary  The distinguishing feature of the traditional Indian medicinal system, Ayurveda, is its emphasis on the maintenance of positive health. As per Ayurveda, Indian medicinal plants are rich sources of substances that have several therapeutic properties including cardioprotection. Globally, cardiovascular diseases are a leading cause of mortality. Several epidemiological studies suggest a correlation between antioxidant intake and occurrence of various cardiovascular diseases. This review deals with medicinal plants which possess cardiotonic, cardioprotective and antioxidant effects. It also includes our studies on the antioxidant properties of some of these plants such as Terminalia arjuna (arjun), Trigonella foenum-graecum (fenugreek), Curcuma longa (turmeric), Garcinia indica (kokum) and Vitis vinifera (grapes). Among these, Terminalia arjuna possesses the highest antioxidant potential and inhibit whole plasma oxidation in rats besides showing significant intestinal absorption. Other plants studied also exhibit radical scavenging effects as studied using various biochemical assays. These antioxidant effects may possibly be responsible for their known beneficial therapeutic effects including their use in cardioprotection.

Key Words: Cardiovascular diseases, Indian medicinal plants, antioxidant, plant extracts, Terminalia arjuna

Introduction

The World Health Organization (WHO) estimates that 80% of the people of developing countries rely on traditional medicines, mostly plant-derived drugs, for their primary health needs. Medicinal plants are commonly used in treating and preventing specific ailments and are considered to play a significant role in health care. Traditional medicinal systems use plants as indispensable sources of medicinal preparations. Hundreds of species are recognized as having medicinal value. Indeed, ‘phytomedicines’ are beginning to link traditional and modern medicines.

Role of Ayurveda in Human Health

India is well-known for its rich traditional systems of medicine, i.e. Ayurvedic, Siddha, Unani and Amchi (Tibetan) besides a vast reservoir of living traditions of ethnomedicine. Many rural households in India, with limited access to organized health services practice home remedies, the recipes and formulae of which have been handed down from generation to generation. In Indian systems of medicine, generally the medicines of plant origin are preferred over the medicines of animal origin, due to presence of abundant natural flora. The basic concept of disease prevention, has existed in the ancient Vedic scripture and has been practiced in Indian traditional medicine, the Ayurveda, for many centuries. The emphasis on the maintenance of positive health or Swastha Vrutta, is a distinguishing feature of Ayurveda [1]. In Ayurveda, it is clearly mentioned that any
patient can be cured with the help of herbs present in the surroundings. The two main approaches to illness in Ayurveda are preventive and curative. [2]. A harmonious balance between three humors of the bodyviz. ‘Vayu’, ‘Pitta’ and ‘Kafa’ is needed for positive health; imbalance of these may cause disease(s). A significant part of Ayurvedic therapeutics aims to promote positive health. The prescribed procedures include drugs along with daily routine including exercise, diet and nutrition besides mental attitude and discipline. This is achieved by using extracts of various plant materials, the rasayanas. These enhance body’s resistance and by using them, one obtains longevity, regains youth, gets sharp memory and intellect besides curing diseases [3, 4]. Indian medicinal plants are rich sources of substances that have several therapeutic properties like cardioprotective, chemopreventive and other effects.

**Cardiovascular Diseases**

Globally, cardiovascular diseases (CVD) constitute a leading cause of mortality. Developing countries like India are also struggling to manage the impact of CVD along with the growing burden of obesity, Type II diabetes and hypertension [5]. Heart disease in India occurs 10 to 15 years earlier than in the West. One fifth of the deaths in India are from coronary heart disease (CHD). By the year 2020, it will account for one third of the deaths. Current projections suggest that by the year 2020, India will have the largest CVD burden in the world [6]. The prevalence of these diseases is more in urban than in rural areas [7]. Lower vitamin C and selenium in Indians as compared to other ethnic groups, particularly in combination, could play a part in their increased risk of CHD. Lower vitamin C in Indians is probably because of its destruction by prolonged cooking [8]. There are epidemiological correlations between poor plasma levels of essential antioxidants and the risk of coronary heart disease [9].

Epidemiological studies have revealed many important risk factors of environmental and genetic origin that are associated with atherosclerosis. The most important clinical complication is an acute occlusion due to blood clot formation during rupture of the lesion, resulting in myocardial infarction [10]. One of the major initiating event in atherosclerosis is oxidative damage to the cholesterol component of the LDL known as LDL oxidation. Oxidation of LDL contributes to atherogenesis in various ways [11]. An appropriate balance between processes that stimulate or inhibit oxidative stress, LDL oxidation, and additional LDL atherogenic modifications determines the progression of atherogenesis.

LDL oxidation and atherogenesis can be inhibited by antioxidants. Elevation in the activity of nutritional antioxidants over the damaging effects of prooxidants has the potential to attenuate atherosclerosis, which is a leading cause of mortality in several human populations. There are also epidemiological evidences and interventional studies to correlate higher level of antioxidant-rich food uptake with lower incidence of CHD [12, 13]. Contrary to popular belief, CHD is indeed common in the Indian subcontinent. The prevalence of CHD increased from 1% to over 8% in urban population [14]. Indians have among the highest prevalence of CHD and have rather unusual risk factors characterized by high triglycerides, low High Density Lipoproteins (HDL), glucose intolerance, insulin resistance, abdominal obesity and increased lipoprotein (a) levels [15]. Hence there is an urgent need to explore various strategies to combat the increasing risk of CVDs in the Indian subcontinent. Medicinal plants with cardioprotective effects can play a major role in this aspect.

**Oxidative Stress, Antioxidants and CVD**

Evidence for the involvement of free radicals in the etiology of CHD comes from several studies that suggest a correlation between antioxidant intake and various CVDs [16, 17]. Antioxidant defenses also appear to be a distinguishing factor between normal subjects and those with symptomatic CHD. Antioxidants remain higher in normal subjects and keep lipid peroxidation (LP) under control. In symptomatic CHD, antioxidant levels are significantly lowered [18]. Hence, increased intake of antioxidants, especially lipid-soluble and chain-breaking antioxidants that accumulate in lipoproteins, might be expected to have beneficial effects [19]. A large number of studies in experimental animals have shown that hypercholesterolemia, diabetes, hypertension, smoking, ageing and nitrate intolerance are the common risk factors for atherosclerosis. They increase production of free radicals not only by endothelial cells but also by vascular smooth muscle cells and adventitial cells. However, the defense system in terms of exogenous antioxidants, i.e. natural compounds such as curcumin, baicalein and resveratrol prevent atherosclerosis formation by exhibiting radical scavenging effects, as shown in the schematic Figure 1.

**Medicinal Plants with Cardioprotective Properties**

In recent times, there is a lot of interest in ‘phytonutrients’ from plants with potential benefits. While these phytoneutrients are not essential by traditional definitions, they apparently reduce risks of diseases. A large number of epidemiological studies show that diets rich in fruits and vegetables, i.e. foods rich in antioxidants, are associated with lower incidence of CVDs [13]. Apart from these dietary sources, Indian medicinal plants are also known for their cardioprotective properties and are rich sources of antioxi-
Many plants have been used for cardioprotection in the traditional Indian medicinal system. A review of such plants with cardioprotective/antioxidant effects was carried out. Several herbs and herbal products have been recommended to promote a healthy heart. These include garlic, guggulipid, tocotrienols derived from palm oil, soy protein isoflavones, and Chinese red yeast rice. They have been shown to lower cholesterol levels by different mechanisms. Other antioxidant-rich and antiangiogenic herbs such as green tea, black tea, and red wine have the potential to reduce the progression of atherosclerosis.

Indian Medicinal Plants

Ayurveda has identified many plants which possess cardiotoxic and cardioprotective effects. Some of them are Allium sativum (garlic), Allium cepa (onion), Asparagus racemosus (shatavari), Caesalpinia bonduc, Cassia fistula, Curcuma longa (turmeric), Emblica officinalis (Amla), Garcinia indica (kokum), Hemidesmus indicus (anantmul), Ocimum sanctum (tulsi), Phyllanthus amarus, Picrorrhiza kurroa (katuka), Terminalia arjuna (arjun), Trigonella foenum-graecum (fenugreek), Vitis vinifera (grapes), Withania somnifera (ashwagandha) and Zingiber officinalis (ginger). These plants exhibit potent antioxidant effects, which might be the mechanism behind their beneficial therapeutic properties. Details of Indian medicinal plants having cardioprotective, therapeutic and antioxidant properties are given in Table 1.

To elucidate the possible positive correlation between the antioxidant and cardioprotective effects, we studied some medicinal plants in detail. These include Terminalia arjuna (arjun), Trigonella foenum-graecum (fenugreek), Curcuma longa (turmeric), Garcinia indica (kokum) and Vitis vinifera (grapes). A summary of our studies are given below.

Terminalia arjuna (Arjun) is an Indian medicinal plant and very popular cardiac tonic. It improves cardiac muscle function and subsequently enhances pumping activity of the heart. It has been credited with many beneficial therapeutic properties including cardioprotective effects. It is used as a cure for various cardiovascular disorders such as congestive heart failure, coronary artery disease, myocardial necrosis, angina, atherosclerosis and ischemia-reperfusion injury besides having hypolipidaemic activity. Its bark is mainly used in the ayurvedic medicinal preparations. A decoction of the bark and minerals was used in the treatment of heart disease of microbial origin. The other beneficial properties include anti-hemorrhagic, anti-pyretic, anti-al-
Table 1. Indian medicinal plants having antioxidant and cardioprotective effects

<table>
<thead>
<tr>
<th>Indian medicinal plants</th>
<th>Antioxidant effects</th>
<th>Cardioprotective effects</th>
<th>Other therapeutic effects</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Allium sativum</em> (garlic)</td>
<td>Oils isolated from garlic inhibit nicotine-induced lipid peroxidation in rat tissues; Aqueous garlic extract (250 mg/kg) decreases lipid peroxidation, increases GPX, GST and GSH during buccal pouch carcinogenesis in Syrian male hamsters</td>
<td>Cardioprotective, hypolipidaemic, antithrombotic, mild cholesterol lowering effect and reduces blood clotting</td>
<td>Antimicrobial, antiatherosclerotic, antihypertensive, hypoglycaemic effect and cytotoxic to cancer cells</td>
<td>[23, 24]</td>
</tr>
<tr>
<td><em>Allium cepa</em> (onion)</td>
<td>Oils isolated from onion inhibit nicotine-induced lipid peroxidation in rat tissues</td>
<td>Cardioprotective, hypolipidaemic, antithrombotic</td>
<td>Antimicrobial, antiatherosclerotic, hypoglycaemic</td>
<td>[25]</td>
</tr>
<tr>
<td><em>Asparagus racemosus</em> (shatavari)</td>
<td>Purified polysaccharide fraction inhibited γ-radiation-induced lipid peroxidation in rat liver mitochondria</td>
<td>Ayurvedic preparation using this, abana, gives cardioprotection</td>
<td>Immunomodulator, anti-stress agent, antihypertrophic</td>
<td>[25, 26]</td>
</tr>
<tr>
<td><em>Caesalpinia bonducella</em></td>
<td>Leaves decreased lipid peroxidation and increased GSH, SOD, and CAT</td>
<td>Decreases blood glucose levels significantly</td>
<td>Anti-diabetic, anti- pyretic, analgesic, antitumor</td>
<td>[27, 28]</td>
</tr>
<tr>
<td><em>Cassia fistula</em></td>
<td>Aqueous extract of flowers decreased levels of CD, LOOH, TBARS and restored GSH, SOD, CAT, GPX, GR in diabetic rat heart tissues</td>
<td>Used for treatment of cardiovascular diseases</td>
<td>Hepatoprotective, antidiabetic, antitumor</td>
<td>[29]</td>
</tr>
<tr>
<td><em>Curcuma longa</em> (turmeric)</td>
<td>Natural curcuminoids act as antioxidants; turmeric extracts have antioxidant effects, curcumin inhibits O2−-induced DNA damage; inhibits γ-radiation-induced lipid peroxidation in rat liver microsomes</td>
<td>Decreases proliferation of smooth muscles in blood vessels, protects from blockage of arteries</td>
<td>Anticarcinogenic, anti-inflammatory, radioprotective, hepatoprotective and antiallergic</td>
<td>[30–33]</td>
</tr>
<tr>
<td><em>Emblica officinalis</em> (Amla)</td>
<td>Inhibits TBARS formation and increases SOD, CAT, GPX during oxidative stress in rat brain</td>
<td>Hypolipidemic, decreases ischemia-reperfusion-induced oxidative stress in rat heart</td>
<td>Anti-inflammatory, hepatoprotective, antitumoral, anti-atherosclerotic, anti-ergot, anti- pyretic, anti-tumor and analgesic</td>
<td>[34, 35]</td>
</tr>
<tr>
<td><em>Garcinia indica</em> (kokum)</td>
<td>Garcinol is a good antioxidant and inhibits INOS induction in astrocytic cells</td>
<td>Cardiotonic</td>
<td>Neuroprotective, anti-inflammatory, anti-tumor</td>
<td>[36–38]</td>
</tr>
<tr>
<td><em>Hemidesmus indicus</em> (anantnul)</td>
<td>Inhibition of free radical formation, inhibits LP, increases SOD</td>
<td>Caps H2T, a herbal Ayurvedic medicine is antiatherogenic</td>
<td>Anti snake venom activity, anti- pyretic, anti-inflammatory, antitumor</td>
<td>[39, 40]</td>
</tr>
<tr>
<td><em>Ocimum sanctum</em> (tulsi)</td>
<td>Oriental and vicenin inhibited radiation induced lipid peroxidation in vivo; <em>Ocimum</em> seed oil increased SOD, CAT, GST, GSH and decreased lipid peroxidation in mice</td>
<td>Hypoglycaemic in diabetic rats, cardiac protection in isoproteonol induced myocardial infarction in rats</td>
<td>Chemoprotectant, anti-thyroid, radioprotective, neuroprotective, anti-ulcerogenic</td>
<td>[40–42]</td>
</tr>
<tr>
<td><em>Phyllanthus amarus</em></td>
<td>Antioxidant, increases SOD, GST, GPX</td>
<td>Significantly reduces blood glucose</td>
<td>Anti-diabetic, antiinflammatory, anti-mutagenic, anti-diarrhoeal radioprotective</td>
<td>[43, 44]</td>
</tr>
<tr>
<td><em>Picrotoxus buergeri</em> (katuka)</td>
<td>Alcoholic extract prevented lipid peroxidation and increases activities of SOD, CAT during D-galactosamine induced hepatitis in rats</td>
<td>Cardioprotection against isoproteonol-induced myocardial stress in rats, hypolipidaemic</td>
<td>Hepatoprotective, anti-allergic, anti-diabetic, anti-ulcerogenic, antioxidant</td>
<td>[45]</td>
</tr>
<tr>
<td><em>Terminalia arjuna</em> (arjan)</td>
<td>Potent free radical scavenger, inhibits oxidative damage to lipids, proteins and DNA in rats</td>
<td>Cardiotoxic, cardioprotective, hypolipidaemic, anti-angiinal, anti-atherosclerotic</td>
<td>Hepatoprotective, antimutagenic, antioxidantic, antihypertensive, induces union of fractures</td>
<td>[46, 47]</td>
</tr>
<tr>
<td><em>Trigonella foenum-graecum</em> (fenugreek)</td>
<td>Antioxidant in diabetic rats</td>
<td>Decreased blood glucose levels, lowers cholesterol, LDL, VLDL, triglycerides</td>
<td>Antidiabetic activity</td>
<td>[48]</td>
</tr>
<tr>
<td><em>Vitis vinifera</em> (grapes)</td>
<td>Antioxidant activity due to isoflavons</td>
<td>Cardioprotective</td>
<td>Antiinflammatory, chemopreventive; anti-mutagenic</td>
<td>[49–50]</td>
</tr>
<tr>
<td><em>Withania somnifera</em> (ashwagandha)</td>
<td>Sitosterolides VII-X and withaferin A increased SOD, CAT, GPX in rat frontal cortex and striatum</td>
<td>Cardioprotective and anticoagulant</td>
<td>Immunomodulatory, anti-inflammatory, anti-aging, anti-stressor, anticarcinogenic and thyroid stimulatory</td>
<td>[51]</td>
</tr>
<tr>
<td><em>Zingiber officinalis</em> (ginger)</td>
<td>Lowers lipid peroxidation and maintains SOD, CAT, GPX and increased blood GSH levels in rats</td>
<td>Cardiotoxic</td>
<td>Carminative, antibacterial, apheresis, general tonic, blood purifier, anti-inflammatory</td>
<td>[36, 52]</td>
</tr>
</tbody>
</table>

Abbreviations: CAT- catalase; CD- conjugated dienes; DNA- deoxyribose nucleic acid; GPX- glutathione peroxidase; GR- glutathione reductase; GSH- reduced glutathione; GST- glutathione transferase; INOS- inducible nitric oxide synthase; LDL- low density lipoprotein; LOOH- lipid hydroperoxide; LP- lipid peroxidation, O2−- singlet oxygen; SOD- superoxide dismutase; TBARS- thiobarbituric acid reactive substances; VLDL- very low density lipoprotein.
lergic, antimutagenic, antigenotoxic, antitumor, chemopreventive and anti-radical effects [54]. There are several formulations of arjun in Ayurveda/Siddha systems of medicine such as Arjunsal, Arjunaristam, Arjunaghrita and Arjun Siddha Dugdha. Baicalein is a naturally occurring flavonoid (5,6,7-trihydroxy-2-methyl-4H-1-benzopyran-4-one) present in bark of Terminalia arjuna. It is credited with anti-allergic, anti-proliferative, antitumor and other beneficial properties [55, 56].

Trigonella foenum-graecum (Fenugreek, Methi) is an important spice used in India and various other Asian, African and European countries for its health benefits. Its leaves, tender shoots and germinated seeds are being consumed as vegetables. They are also considered as health foods [36]. Fenugreek seeds are mainly used for flavouring pickles and chutneys. The major use of fenugreek is in curry powder. Fenugreek also is credited with many medicinal properties. It has antidiabetic effects and is helpful in digestive disorders as a tonic besides in the treatment for edema of legs, flatulence, dysentery, diarrhea, dyspepsia, chronic cough and enlargement of liver and spleen [57]. In Type 1 diabetic patients, supplementation of fenugreek in the diet lowers lipid peroxidation [48], induces hypocholesterolemia and hypoglycaemia [58]. Germinated fenugreek seeds are used in various food preparations and as a natural remedy for diabetes. They are shown to reduce blood sugar levels and cholesterol in diabetic patients [58]. Fenugreek significantly decreased the blood lipids (total cholesterol and triglycerides) without affecting the HDL and also reduced the blood sugar in patients with coronary artery disease (CAD) [59].

Curcuma longa (turmeric) is a yellow-coloured rhizome known for its use in curries and in different medicinal preparations. It is used for cooking and therapeutic purposes [36]. Turmeric has been used in traditional medicine in India, for more than 2000 years. The characteristic yellow colour of this rhizome is due to the presence of the component ‘curcumin’. Curcumin is a major colouring component of Curcuma longa and exhibits a variety of biological activities including anti-inflammatory, hepatoprotective, antimutagenic and anti-neoplastic properties [32]. The beneficial properties of curcumin include use as deodorizing agent, disinfectant, cold, cough and various types of skin diseases. It is also used in dental diseases, digestive disorders like dyspepsia and acidity, indigestion, flatulence, upper abdominal pain, asthma, gastrica and duodenal ulcers. The rhizome has carminative, diuretic, antimicrobial, antigenotoxic, anti-inflammatory, anticarcinogenic, antiatherogenic and antihelminthic activities [36]. Curcumin was found to protect rat myocardium against ischaemic insult and rat forebrain against ischemia-reperfusion (I/R) insult and the protective effect could be attributed to its antioxidant properties as well as its inhibitory effects on xanthine dehydrogenase/xanthine oxidase (XD/XO) conversion and resultant superoxide anion production [60, 61]. Some of the beneficial activities of turmeric have been linked to the spice’s antioxidant ability in different systems [4, 32]. However, the availability of antioxidant effects of turmeric and its constituents, in relation to the different beneficial properties as is being used in cooking and medicine has not been evaluated earlier.

Garcinia indica (dried rind known as ‘kokam’) is an Indian spice used in many parts of India in making several vegetarian and non-vegetarian ‘curry’ preparations. It is also used in preparing healthy soft drink mixes [36]. Kokam’s refrigerant properties are well documented. It is useful as an infusion, or by direct application, in skin ailments such as rashes caused by allergies. Kokam butter is an emollient being helpful in the treatment of burns, scalds and chaffed skin [62]. Kokam in food preparations is used as an appetizer and good liver tonic. It improves appetite and allevies thirst. It is a cardiotonic and is used in bleeding, piles, dysentery, tumours and heart diseases [36].

Grape juice and red wine are considered to confer certain degree of protection against cardiovascular ailments [63]. Grape is known to have several therapeutic effects. Resveratrol is a natural antioxidant found in grape known to exhibit cardioprotective, chemopreventive/anticarcinogenic and antimutagenic properties. These properties have been linked to its antioxidant activity. The composition and properties of grapes have been extensively investigated. Reports indicate that grapes contain large amounts of phenolic compounds [64], which play an important role in human health, such as lowering of human low density lipoprotein. Grape juice delayed oxidation of LDL in healthy volunteers and CAD patients. It reduced free radical release and DNA damage and increased antioxidant capacity [65]. Grape seed proanthocyanin has also been reported to have potent antioxidant properties [66]. Grape seed oil has the highest antioxidant activity among various other oils. The antioxidant abilities of dominant grape varieties, however, are not examined. We studied antioxidant ability of some grape varieties of the Asian region and Indian subcontinent, mainly Thompson Seedless and its clones (Tas-E-Ganesh, Sonaka and Manikchaman), Sharad Seedless, which are considered the ruling grape varieties.

The mechanisms responsible for the reported therapeutic effects of the above medicinal plants are probably due to their antioxidant and radical scavenging activities. Since antioxidant activities are known to correlate with cardioprotective effects we have examined the antioxidant effects of the extracts from these plants and their pure active ingredients whenever possible, at different levels of antioxidant protection by using various physicochemical and biochemical assays.
Antioxidant Potential of Plant Extracts and Natural Compounds

A number of epidemiological studies show that diets high in fruits and vegetables, the foods rich in antioxidant compounds, are associated with a lower incidence of cardiovascular disease. Observational data in animals and humans suggest that greater intake of antioxidant vitamins are associated with the reduced risk of atherosclerotic vascular disease [67]. Antioxidants may at least in part prevent atherosclerosis and cardiovascular disease [68]. Hence it is pertinent to examine cardioprotective and antioxidant effects of plants used in Indian herbal preparations.

For ease of study, in biological systems, oxidative stress can be generated using various physical/chemical agents. Among them, ionizing radiation such as γ-rays is an important source of reactive oxygen species. The exposure of biological systems to radiation results in radiolytic cleavage of water yielding OH·, H·, eaq, etc. in presence of oxygen even O2·−, H2O2, O2· are produced. Thermal decomposition of an azo-initiator, 2,2'-Azobis (2-amidinopropane) dihydrochloride (AAPH) in presence of oxygen gives rise to a constant source of peroxy radicals. These free radicals especially OH and LOO can initiate lipid peroxidation. Cumene hydroperoxide, ascorbate-Fe2+, and peroxynitrite are some other free radical generators.

Antioxidants exhibit their effects at different levels. These include ability to bind iron that can prevent radical formation, the scavenging of primary and secondary radicals and ability to inhibit free radical induced membrane damage. Among the sub-cellular organelles mitochondria are crucial targets for oxidative damage. In this paper, we have demonstrated that ROS induce significant lipid peroxidation in the model system i.e. rat liver mitochondria as measured by LOOH, an unstable intermediate, which further breaks down to stable aldehydes and react with thiobarbituric acid (TBA) to form TBARS, the final stable end product. Apart from enhancing lipid damage to membranes, oxidative damage leads to protein oxidation resulting in the formation of protein hydroperoxide, protein carbonyls besides inactivation of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPX) and glutathione reductase (GR). To examine the mechanisms underlying the observed protection by the plant extracts and the pure compounds, and to evaluate radical scavenging abilities, we have utilized biochemical assays such as Ferric Reducing Antioxidant Power (FRAP), DPPH (1,1’-diphenyl-2-picrylhydrazyl) and ferrylmyoglobin/ABTS assay. The Oxygen Radical Absorbance Capacity (ORAC) values are used as ‘standard’ measures for comparing antioxidant activity of food materials. We have also used pulse radiolysis to determine the rate constants of the compound with the reactive species, and electron spin resonance (ESR) to study the radical reaction by spin trapping agents. Since flavonoids and polyphenols are major phytochemicals in medicinal plants responsible for antioxidant effects, we have also estimated their content in these extracts.

The methodologies used for determination of antioxidant properties of the compounds have been presented in Table 2. It was clearly established that among the plants examined namely Terminalia arjuna, Trigonella foenum-graecum, Curcuma longa, Garcinia indica and Vitis vinifera, Terminalia arjuna possessed the highest antioxidant potential and inhibit whole plasma oxidation in rats besides showing significant intestinal absorption. In case of primary radical scavenging, as assessed by DPPH method, methanolic extract possesses the highest Trolox Equivalent Antioxidant Capacity (TEAC), among the T arjuna extracts. In ferrylmyoglobin/ABTS assay, TEAC of acidic methanolic extracts was the most significant and in FRAP assay, methanolic extract had the highest reducing activity. Thus methanolic and acidic methanolic extract as well as baicalein showed significant antioxidant capacities as compared to the standard antioxidant, Trolox. We examined the effect of different free radical inducers such as γ-radiation, ascorbate-Fe2+, AAPH and peroxynitrite. When we studied the effect of baicalein on oxidative stress induced lipid peroxidation in rat heart homogenate, we found that it exerts protective effects even at low concentrations such as 10 μM. Baicalein at 100 μM concentration, inhibited radiation-induced single strand breaks in pBR322 plasmid DNA, almost by 96%. Baicalein also possessed fairly high rate constants, in the range of 3.7 × 109, 1.3 × 109 and 8.0 × 109 dm3 mol−1 s−1 for hydroxyl, azidyl and alkylchloroperoxyl radicals, respectively with the biologically relevant radicals as compared to other standard antioxidants, as studied by pulse radiolysis. The IC50 values for baicalein for superoxide and singlet oxygen quenching were 18 and 128 μM, respectively, as determined from ESR. These values are significantly higher than those for catechin, rosmarinic acid etc.

In case of fenugreek seeds, the petroleum ether fraction showed highest peroxy radical scavenging activity with ORAC value of 32.29 μM of Trolox. In case of Soxhlet fractions of fenugreek, petroleum ether fraction showed highest protection of 74.53% followed by Chloroform extract (63.19%), Aqueous extract (59.77%) and then methanolic extract showing 44.32% protection against damage induced by Asc-Fe2+. In another set of experiments, the results obtained showed that the ORAC values of turmeric extract ranging from 10 to 25 μmoles of Trolox equivalent per gm fresh weight, are similar to or higher than the values observed for some fruits and vegetables including those for garlic (19.4), spinach (12.6) and onion (4.5) [69]. Ethanolic preparations of both raw and processed turmeric are effective in giving antioxidant protection at various levels [33].
In case of *G. indica* extracts, in the DPPH assay, fractions from chloroform and methanol-HCl extracts were the most effective while in the ABTS assay, fraction from acetone was the most potent. Studies on ascorbate-Fe$^{2+}$ induced lipid peroxidation showed that chloroform and benzene extracts were very effective. Kokam syrup and the boiled aqueous extract of kokam also had significant antioxidant effects in the above assays. Aqueous and boiled aqueous extracts of kokam besides the commercial kokam syrup have high ORAC values (28.5, 23.8 and 20.4 respectively) comparable to that of other spices.

Our studies also revealed that ethanolic extracts of black and red grapes possess higher levels of antioxidant abilities as compared to the green varieties. This could perhaps be due to high polyphenolics present in the extracts. In the radical scavenging assays, our study indicates that cv. Mango is the most potent followed by cv. Sharad seedless and cv. Flame Seedless. In the lipid peroxidation assay, ethanolic extracts of cv. Sharad seedless and cv. Mango could significantly inhibit peroxidation in rat liver mitochondria by 74% and 70% respectively, as compared to aqueous extracts with 71% and 60% protection respectively.

It has been shown earlier that the antioxidant ability of the plant extracts was possibly responsible for their cardioprotective effects. *T. arjuna* extracts prevented in vivo ischemic-reperfusion injury induced oxidative stress, tissue injury of heart and haemodynamic effects in rabbit hearts [47, 70]. Curcumin was found to protect rat against ischaemia-reperfusion (I/R) insult due to its antioxidant properties as well as its inhibitory effects on xanthine dehydrogenase/xanthine oxidase (XD/XO) conversion and resultant superoxide anion production [60, 61]. Resveratrol from grapes and curcumin from turmeric also appeared to be interesting for atherosclerosis treatment [71]. Resveratrol mediates cardioprotection and neovascularization which may be attributed to its ability to stimulate nitric oxide production and its free radical scavenging activity [72]. Our results also showed that extracts of arjun, turmeric, fenugreek, kokum and grapes possessed significant antioxidant activities. Various extracts of *T. arjuna* as well as baicalin showed significant activities in the different assays used. Other plants studied also exhibit significant radical scavenging effects as studied using various biochemical assays. These observed antioxidant effects may possibly be responsible for their known beneficial therapeutic effects of the above mentioned plants including in cardioprotection.

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**Table 2. Methods used for studying antioxidant actions in relation to health implications of some Indian medicinal plants. Results are given in text.**

<table>
<thead>
<tr>
<th>Antioxidant actions</th>
<th>Methodology used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyl radicals</td>
<td>Scavenging hydroxyl radicals generated by irradiation with γ-ray or Fenton reaction (OH) generated by linear accelerator and detected spectrophotometrically.</td>
</tr>
<tr>
<td>Superoxide anion</td>
<td>Scavenging superoxide anion induced by xanthine-xanthine oxidase as studied by ESR using spin trap, O$_2^{-}$: generated by linear accelerator and detected spectrophotometrically. Protection of iron-containing superoxide dismutase (SOD).</td>
</tr>
<tr>
<td>Peroxyl radicals</td>
<td>Scavenging peroxyl radicals induced by thermolysis of 2,2'-Azobis (2-amidinopropane) dihydrochloride (AAPH) by pulse radiolysis. Scavenging of AAPH induced peroxyl radicals by using Oxygen Radical Absorbance Capacity (ORAC) assay.</td>
</tr>
<tr>
<td>Thiol radicals</td>
<td>Scavenging thiol radicals by pulse radiolysis.</td>
</tr>
<tr>
<td>Singlet oxygen</td>
<td>Scavenging singlet oxygen induced by photosensitization of Rose Bengal by ESR using spin trap, 2,2,6,6-tetramethyl-4-hydroxypiperidine (4-OH TEMP).</td>
</tr>
<tr>
<td>Total ROS</td>
<td>Scavenging of ROS in NIH3T3 cells induced by γ-ray by using DCFDA fluorescence assay.</td>
</tr>
<tr>
<td>Lipid peroxidation</td>
<td>Inhibition of lipid peroxidation in rat liver mitochondria induced by biologically relevant γ-ray, ascorbate-Fe$^{2+}$, peroxynitrite, AAPH, cumene hydroperoxide, photosensitization of Rose Bengal, xanthine-xanthine oxidase systems, <em>in vitro</em> and <em>in vivo</em>.</td>
</tr>
<tr>
<td>Antioxidant enzymes</td>
<td>Protection of Superoxide dismutase (SOD), Glutathione peroxidase (GPx), Glutathione reductase (GR) activities in rat liver mitochondria <em>in vitro</em>.</td>
</tr>
<tr>
<td>DNA damage</td>
<td>Inhibition of γ-radiation induced single strand breaks in pBR322 plasmid DNA.</td>
</tr>
<tr>
<td>Biological applications-Cardioprotection in rats</td>
<td>Inhibition of whole plasma oxidation induced by thermolysis of 2,2'-Azobis (2-amidinopropane) dihydrochloride (AAPH) in blood plasma of rat.</td>
</tr>
</tbody>
</table>
References


