



Contents lists available at ScienceDirect

## Asian Pacific Journal of Tropical Biomedicine

journal homepage: [www.elsevier.com/locate/apjtb](http://www.elsevier.com/locate/apjtb)

Document heading doi:10.1016/S2221-1691(14)60213-6 © 2014 by the Asian Pacific Journal of Tropical Biomedicine. All rights reserved.

## Herbal antioxidant in clinical practice: A review

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## PEER REVIEW

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## Comments

It is a systematic review that clearly focuses on the clinical applications of herbs as antioxidants. Oxidative stress is being reported as the major hallmark in the etiology of chronic diseases such as diabetes, Alzheimer's disease, renal failures, cancer, etc.

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## ABSTRACT

Antioxidant—the word itself is magic. Using the antioxidant concept as a spearhead in proposed mechanisms for staving off so-called "free-radical" reactions, the rush is on to mine claims for the latest and most effective combination of free-radical scavenging compounds. We must acknowledge that such "radicals" have definitively been shown to damage all biochemical components such as DNA/RNA, carbohydrates, unsaturated lipids, proteins, and micronutrients such as carotenoids (alpha and beta carotene, lycopene), vitamins A, B<sub>6</sub>, B<sub>12</sub>, and folate. Defense strategies against such aggressive radical species include enzymes, antioxidants that occur naturally in the body (glutathione, uric acid, ubiquinol-10, and others) and radical scavenging nutrients, such as vitamins A, C, and E, and carotenoids. This paper will present a brief discussion of some well- and little-known herbs that may add to the optimization of antioxidant status and therefore offer added preventive values for overall health. It is important to state at the outset that antioxidants vary widely in their free-radical quenching effects and each may be individually attracted to specific cell sites. Further evidence of the specialized nature of the carotenoids is demonstrated by the appearance of two carotenoids in the macula region of the retina where beta-carotene is totally absent.

## KEYWORDS

Antioxidant, Carotenoid, Free-radical, Herb

## 1. Introduction

Herbs and spices are traditionally defined as any part of a plant that is used in the diet for their aromatic properties with no or low nutritional value<sup>[1]</sup>. However, more recently, herbs and spices have been identified as sources of various phytochemicals, many of which possess powerful antioxidant activity<sup>[2]</sup>. Thus, herbs and spices may have a role in antioxidant defense and redox signaling<sup>[3]</sup>.

### 1.1. How the antioxidants complement rather than compete with one another

As scientific inquiry proceeds we will likely learn of other site-specific attractions and functions of the carotenoids. This will help us understand why we need not reject one class of antioxidant compounds to accept another. They each

may accumulate in specialized cells and tissues, with some overlapping protection, but a variety of them is required to give us the best protection.

Interestingly, just as foods work together so do the antioxidants. Professor Lester Packer of the University of California at Berkeley is one of the world's pre-eminent antioxidant researchers. He and coworkers recently demonstrated how carotenoids interact with vitamins E and C. Beta-carotene, it was shown, can protect low density lipoprotein against oxidative damage even when vitamin E levels are low<sup>[4]</sup>. In this regard, antioxidants act synergistically, offering a rainbow of protection rather than a single band of the spectrum. Moreover, plant antioxidants such as phenols and bioflavonoids may potentiate vitamin antioxidants. For example, rutin, a bioflavonoid, potentiates vitamins C and E when taken in combination, producing a more potent radical scavenging action. That is, adding a third antioxidant (rutin)

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Foundation Project: Supported by Institute of Pharmacy, Bundelkhand University, Jhansi (U.P.), India (Grant number: BU/PHARM/02-13).

Article history:

Received 2 Oct 2013

Received in revised form 18 Oct, 2nd revised form 1 Nov, 3rd revised form 11 Nov 2013

Accepted 20 Dec 2013

Available online 28 Jan 2014

creates a combined effect greater than the sum of the parts[4].

### 1.2. Some major antioxidant herbs

Antioxidant factors found in plants are based upon constituent nutrients with demonstrated radical-scavenging capacities as well as upon non-vitamin or mineral substances. So, in addition to alpha-tocopherol, ascorbate, carotenoids, and zinc, plant-based medicines may contain flavonoids, polyphenols, and flavoproteins. Further, some plants or specific combinations of herbs in formulations may act as antioxidants by exerting superoxide scavenging activity or by increasing superoxide dismutase activity in various tissue sites[5]. These groups of compounds are substances that may exert cell-protective action by more than one biochemical mechanism. In addition to antioxidant properties *per se*, cancer-protective factors are found in many plants including some fruits, vegetables, and commonly used spices and herbs. They can be divided into several different groups based on their chemical structure, *e.g.*, polyphenols, thiols, carotenoids and retinoids, carbohydrates, trace metals, terpenes, tocopherols and degradation products of glucosinolates (isothiocyanates, indoles and dithioliols) and others. These groups of compounds are substances which may exert their cancer-protective action by more than one biochemical mechanism. The biochemical processes of carcinogenesis are still not known in detail and probably vary with the cancer disease in question. Accordingly, the description of the biochemical backgrounds for the actions of cancer-protective factors must be based on a simplified model of the process of carcinogenesis. The model used in this presentation is a generalized initiation-promotion-conversion model, in which initiators are thought to be directly or indirectly genotoxic, promoters are visualized as substances capable of inferring a growth advantage on initiated cells and converters are believed to be genotoxic, *e.g.* mutagens, clastogens, recombinogens *etc.* Experimental evidence for the mechanisms of action of cancer-protective agents in fruits and vegetables that protect against initiation include the scavenging effects of polyphenols on activated mutagens and carcinogens, the quenching of singlet oxygen and radicals by carotenoids, the antioxidant effects of many compounds including ascorbic acid and polyphenols, the inhibition of activating enzymes by some flavonols and tannins, the induction of oxidation and conjugation (protective) enzymes by indoles, isothiocyanates and dithioliols, the shielding of sensitive structures by some polyphenols and the stimulation of DNA-repair exerted by sulphur-containing compounds. Mechanisms at the biochemical level in antipromotion include the antioxidant effects of carotenoids and the membrane stabilizing effects reported with polyphenols, the inhibition of proteases caused by compounds from soybeans, the stimulation of immune responses seen with carotenoids and ascorbic acid, and the inhibition of ornithine decarboxylase by polyphenols and carotenoids. A few inhibitors of conversion have been identified experimentally, and it can be argued on a theoretical basis, that many inhibitors of initiation should also be efficient against conversion. The mechanisms of anticarcinogenic substances in fruits and vegetables are discussed in the light of cancer prevention and inhibition[5].

Plant antioxidants are more than mere supporting players in the battle against cellular damage and disease. As folklore has long instructed, certain plants play specific roles in disease

prevention and treatment. A well known hepatic antioxidant, silymarin, from the milk thistle (*Silybum marianum*), for example, inhibits liver damage by scavenging free radicals among other mechanisms[6]. This powerful antioxidant protects the liver against alcohol and pharmaceutical injury and even poisoning from extremely toxic compounds found in the deathcap mushroom, *Amanita phalloides*. Interestingly, the amanita toxins are not thought to be neutralized via any free-radical scavenging effects. Rather, it is theorized that silymarin competes with the amanita toxins for the identical receptor on cell membranes[6]. Here again, contemporary laboratory science confirms and elucidates the liver-protecting attributes of milk thistle, well known to folk medicine for 2000 years.

## 2. Antioxidant properties in herbs

### 2.1. Ginger

Scientific name: *Zingiber officinale*; Parts used: Rhizome.

Dosage: 1 ounce of rhizome to 1 pint of water. Boil the water separately, then pour over the plant material and steep for 5 to 20 min, depending on the desired effect. Drink hot or warm, 1 to 2 cups per day.

Currently, Ginger has received new attention as an aid to prevent nausea from motion sickness. Ginger tea has long been an American herbal remedy for coughs and asthma, related to allergy or inflammation. The creation of the soft drink ginger ale, is originated from the common folkloric usage of this herb, and remains a popular beverage for the relief of stomach upset. Externally, ginger is a rubefacient, and has been believed to relief headache and toothache.

The mechanism by which ginger produces anti-inflammatory activity is that of the typical non-steroidal anti-inflammatory drug. This common spice is a more biologically active prostaglandin inhibitor (via cyclo-oxygenase inhibition) than onion and garlic. By slowing associated biochemical pathways an inflammatory reaction is curtailed. In one study, Danish women between the ages of 25 to 65 years consumed either 70 g raw onion or 5 g raw ginger daily for a period of one week. The author measured thromboxane production and discovered that ginger, more clearly than onion, reduced thromboxane production by almost 60%. This confirms the Ayurveda "prescription" for this common spice and its anti-aggregator effects.

By reducing blood platelet "clumping," ginger, onion and garlic may reduce our risk of heart attack or stroke. In a series of experiments with rats, scientists from Japan discovered that extracts of ginger inhibited gastric lesions by up to 97%. The authors concluded that the folkloric usage of ginger in stomachic preparations were effective owing to the constituents zingiberene, the main terpenoid and 6-gingerol, the pungent principle.

In an earlier look at how some of the active components of ginger (and onion) act inside our cells, it was found that the oils of these herbs inhibit the fatty acid oxygenases from platelets, thus decreasing the clumping of these blood cell components.

A 1991 double-blind, randomized crossover trial involved thirty women suffering from hyperemesis gravidarum. Ginger was alternated with a placebo. Seventy percent of the women confirmed they subjectively preferred the period in which they took the ginger. More objective assessment verified the

subjective reactions, as significantly greater relief was found after the use of ginger. In a series of experiments with rats, scientists from Japan discovered that extracts of ginger inhibited gastric lesions by up to 97%. The authors concluded that the folkloric usage of ginger in stomachic preparations was effective due to the constituents of zingiberene, the main terpenoid, 6-gingerol and the pungent principle<sup>[7–10]</sup>.

## 2.2. Ginkgo

Scientific name: *Ginkgo biloba* (*G. biloba*); Parts used: leaves.

Dosage: Approximately 0.5 ounce of leaves to 1 pint of water. Boil water separately and pour over the plant material and steep for 5 to 20 min, depending on the desired effect. Drink hot or warm, 1 to 2 cups per day, at bedtime and upon waking.

The free-radical scavenging properties of *G. biloba* extract have been demonstrated as being at least as effective as uric acid, a potent, naturally occurring antioxidant. The plant extract has further capacity to inhibit the formation of radicals which uric acid does not have. Ginkgo research has proceeded in many other areas. The most interesting and important results are related to vascular diseases, brain function, impotency, dopamine synthesis, inflammation, and asthma. An extract from ginkgo leaves is marketed as Tebonin. Clinical research has shown that Tebonin achieves vasodilation and improved blood flow, especially in deeper-seated medium and small arteries. The flow rate in capillary vessels and end arteries is increased. In elderly subjects, Tebonin alleviated dizziness and loss of memory. Ginkgo has proven to be a particularly valuable geriatric drug.

Mild memory loss continues to be one of humankind's tragedies and one of medicine's greatest challenges. Interestingly, ginkgolides and a bilobalide possess a structure that is unique in the vegetable kingdom.

A double-blind, placebo controlled study showed another powerful benefit from this ancient Chinese herbal medicine. Thirty-one patients showing mild to moderate memory impairment were followed for six months while taking a standardized extract of *G. biloba*. All of them were over the age of 50. The extract contained 24% flavonoid glycosides and 6% terpenes. The results show that extract of *G. biloba* "has a beneficial effect on mental efficiency in elderly patients showing mild to moderate memory impairment of organic origin."

Sixty patients suffering from arterial erectile dysfunction received a daily treatment with 60 mg of an extract of *G. biloba*. After 6 months, 50% of the subjects once again were able to achieve penile erections. More than 45% of the remaining subjects showed some improvement. Another study found that *G. biloba* extract might prevent radical mediated human kidney and liver damage caused by cyclosporin A, an immunosuppressive drug used in transplants. This herbal product was found to be as effective as vitamin E and glutathione in protecting against such damage, adding to our understanding of the value of incorporating nutritional and herbal supplements in modern medicine. The protective effects of *G. biloba* extract were diminished in the presence of iron, owing to the limits imposed by this powerful oxidant.

Ginkgo's effect as an anti-allergic, antiasthmatic agent has also been demonstrated. The platelet activating factor has been implicated in pathophysiological states including allergic inflammation, anaphylactic shock, and asthma. One

study concluded that ginkgolide B is the most active platelet activating factor antagonist found in this class of ginkgolides. It appears that ginkgo relieves bronchoconstriction due to its platelet activating factor antagonist activity. A randomized, double-blind, placebo-controlled crossover study in 8 atopic asthmatic patients showed that ginkgo achieved significant inhibition of the bronchial allergen challenge compared to placebo<sup>[11–14]</sup>.

## 2.3. Licorice

Scientific name: *Glycyrrhiza glabra*; Parts used: root.

Dosage: 1 teaspoon of the root or subterranean stem, boiled in a covered container with 0.5 to 1.0 pints of water for about half an hour, at a slow boil. Allow the liquid to cool slowly in the closed container. Drink cold, 1 swallow or 1 tablespoon at a time, 1 to 2 cups per day.

The multitude of pharmacological effects of licorice rhizomes and roots are practically all attributed to the presence of a triterpene saponin called glycyrrhizin, which is about fifty times sweeter than sugar, and has a powerful cortisone-like effect. Several cases have been reported in medical literature in which humans ingesting 6–8 ounces (a very large amount) of licorice candy daily for a period of several weeks are "poisoned" due to the cortisone-like effects of licorice extract in the candy. Proper treatment restores patients to normal. The above amount of this compound is very large compared with the relatively small amount found in supplements. In addition, Licorice rhizomes and roots have high mucilage content. When mixed with water, the resulting preparation has a very pleasant odor and taste, and acts as an effective demulcent on irritated mucous membranes, such as a sore throat. One study found that glycyrrhizin was as effective a cough suppressant as codeine. A experiment in 1991 with mice found that glycyrrhizin protected against skin cancer. The authors speculated that it might be proved useful in protecting against some forms of human cancer as well.

It is not surprising that licorice and glycyrrhizin have such wide applications. It should be noted that this chemical constitutes only 7% to 10% of the total root on a dry weight basis. Glycyrrhetic acid is obtained when acid hydrolysis is applied to the main component of licorice. This compound is extensively used in Europe for its anti-inflammatory properties, especially in Addison's disease and peptic ulcer. Some European researchers concluded that glycyrrhetic acid may be preferred to cortisone because it is safer, especially when prolonged treatment is required.

A study in 1990 demonstrated that glycyrrhetic acid exerts its activity not as a direct effect but by reducing the conversion of cortisol to cortisone, its biologically inactive product. The authors concluded that hydrocortisone, a "weak anti-inflammatory agent," can be greatly potentiated by the addition of 2% glycyrrhetic acid. To lessen the toxic effects of corticosteroids, the authors suggested that patients use hydrocortisone together with glycyrrhetic acid.

Glycyrrhizin has also exhibited anti-viral activity. A study in 1979 demonstrated that glycyrrhizin inhibited Epstein-Barr virus, cytomegalovirus, and hepatitis B virus. In Japan, glycyrrhizin has long been successfully used to treat chronic hepatitis B. This has led to speculation that glycyrrhizin holds promise in the treatment of HIV.

Side effects from the ingestion of large amounts of licorice have been reported. Glycyrrhizin in very large amounts can

promote hypokalemia and hypertension. For these reasons people with heart problems and high blood pressure are advised to avoid consuming large quantities of licorice or its components[15–20].

#### 2.4. *Schizandra*

Scientific name: *Schizandra chinensis*; Parts used: Berry.

Dosage: 1 to 2 g per day in tablet or capsule form.

This interesting plant has many biological activities including anti-bacterial (equivocal results), sympathomimetic (stimulant), resistance stimulation, liver-protective, anti-toxic, anti-allergenic, antidepressant, glycogenesis stimulant, and antioxidant effects. In addition, it is a folkloric “tonic,” this herb protected against the narcotic and sedative effects of alcohol and pentobarbital and exposure to the highly toxic ether in mice. As a result of these data, the authors concluded that schizandra may be a useful clinical agent for reversal of central nervous system depression. They based this antidepressant activity on the reasoning that depression may be due, in part, to adrenergic exhaustion following severe psychogenic stress. It is known that monoamine oxidase inhibitors, as well as other selected compounds that increase noradrenergic neurotransmission within the central nervous system such as imipramine, have proven benefit in depression. This herb is also being promoted for its stimulating effect on the nervous system without being excitatory like amphetamine or caffeine. There are some proponents who claim “the higher the degree of exhaustion, the greater is the stimulating effect.”

A very interesting study on performance in race horses tends to confirm the folkloric claims. Polo horses given the berry extract of this species showed a lower increase in heart rate during exercise, a quicker recovery of respiratory function, a reduction of plasma lactate, and improved performance.

A study in 1990 reported that a lignan component of schizandra fruit suppresses the arachidonic cascade in macrophages. The arachidonic cascade pushes the production of leukotrienes, which may play a role in inflammatory diseases. By inhibiting the arachidonic acid cascade, schizandra both protects the liver and stimulates the immune system—two key roles of an ideal adaptogen.

An interesting non-Western study tested the “tonifying and invigorating yang” powers of schizandra and other herbs in mice. The researchers measured the animal’s body weight, thymus weight, leukocyte count, and other parameters of “yang”. They observed a direct correlation between the amounts of herb ingested (as hot water extracts) and improved immunocompetence. They also noticed a distinct anti-fatigue quality, which was measured by reduced excitability of the parasympathetic nervous system. No toxicity was reported. The antioxidant activity of dibenzo-cyclooctene lignans isolated from species found in the *Schizandra* family was reported in 1992. It appears that this creeping herb from the Far East has valid claims to the title of a “new” anti-fatigue agent which possibly helps to accelerate restorative processes within the human body. Traditional Chinese medicine continues to offer new candidates to the annals of world medicine. As we in the West are slowly learning, “traditional” or “folk” medicine really is the medicine of the people.

While schizandra is a very safe herb with much historical usage one supplier of a standardized extract recommends that this herb be avoided by epileptics who are with high

intracranial pressure or severe hypertension, and those with “high acidity”[21–28].

#### 2.5. *Turmeric*

Scientific name: *Curcuma longa*; Parts used: rhizome

Dosage: 1 to 2 g per day in food or take in capsules/tablets.

Currently, Turmeric is used in India to treat anorexia, liver disorders, cough, diabetic wounds, rheumatism, and sinusitis. In one study turmeric extract was tested for its anticarcinogenic and antimutagenic properties. Laboratory (non-human) experiments found that this ancient spice reduced both the number of tumors in mice and the mutagenicity of benzo(a)pyrene and two other potent mutagens, 4-nitro-o-phenylenediamine and dimethylbenzanthracene.

Preventing cancer now receives the attention it has long deserved. Numerous biochemical and epidemiological studies have demonstrated diet’s role in modulating the development of cancer. Laboratory experiments have established that the active principle of turmeric (curcumin) is a potent antimutagenic agent. For those interested in how curcumin may act to prevent cancer we turn again to the by-now all pervasive theory of free-radical inactivation. The test carcinogens benzo(a)pyrene and dimethylbenzanthracene are metabolically activated to proximate mutagenic/carcinogenic epoxides, which then bind to macromolecules. One study concluded that since curcumin is a potent antioxidant, it may scavenge the epoxides and prevent binding to macromolecules. In other words, this spice’s cell-protective properties are similar to nutrient antioxidants, vitamins C and E, which inhibit free radical reactions.

This type of herb is known as a nonsteroidal anti-inflammatory drug (NSAID). Curcumin inhibits cyclooxygenase and lipoxygenase enzymes. It has three main mechanisms of action: 1) antioxidant activity; 2) lipoxygenase inhibitor; and 3) cyclooxygenase inhibition. By inhibiting the associated biochemical pathways, inflammation is curtailed. Modern science thus confirms what traditional healers have known for centuries. Namely, that the fresh juice from the rhizome will reduce swelling in recent bruises, wounds and insect bites; and that the dried powdered root kills parasites, relieves head colds and arthritic aches. Interestingly, this spice has sometimes been used to adulterate ginger.

A pharmacological review in 1991 confirmed many of turmeric’s folkloric effects, including wound healing, gastric mucosa protection, antispasmodic activity, reduction of intestinal gas formation, protection of liver cells, increasing bile production, diminishing platelet aggregation (*i.e.* blood clumping), lowering serum cholesterol (at very high doses), antibacterial properties, antifungal properties, and potential antitumor activity. While most of the above effects were demonstrated with intravenous extracts in animals, they do parallel folkloric claims in humans and are not to be dismissed as “experimental” or “trivial.” Turmeric’s benefits for arthritis treatment have been demonstrated in human clinical trials. An herbal formula of turmeric, ashwagandha, and boswellin was evaluated in a randomized, double-blind, placebo-controlled study. After a one-month evaluation period 12 patients with osteoarthritis were given the herbal formula or placebo for three months. The patients were evaluated every two weeks. After a wash-out period of 15 d, the treatment was reversed with the placebo patients receiving the drug and vice versa. Again results were evaluated over a three month period. The patients

treated with the herbal formula showed a significant drop in severity of pain and disability score<sup>[29–38]</sup>.

## 2.6. Quercetin

Quercetin is the commonest flavonoid in higher plants. It is usually present as a glycoside such as rutin, isoquercitrin, quercitrin, hyperin, and quercimeritrin, but is also isolated in the free state from the families Compositae, Passiflorae, Rhamnaceae, and Solanaceae, where it mainly occurs on leaf surfaces, in fruits and bud extracts<sup>[39]</sup>.

Quercetin is a powerful antioxidant that decreases the concentration of superoxide anions in enzymic and nonenzymic systems. A recent animal study demonstrated its antiulcer and gastroprotective effects, especially against ethanol injury. The cyto-protective activity was affected through several interacting pathways involving stimulation of prostaglandin and inhibition of leukotriene production and through quercetin's antioxidant

properties. Pretreating experimental animals with 200 mg/kg (a very high dose) 120 min before administering ethanol was found to be the most effective dosage in prevention necrosis<sup>[39]</sup>.

## 2.7. Commonly known antioxidant plants:

Hundreds of plants have been studied and found to possess antioxidant properties. Some antioxidant plants are describe in Table 1.

## 3. Conclusion

As evident from the above discussion, nature is the best combinatorial chemists and has possible answers to all diseases for mankind. Medicinal plants play a vital role in antioxidant properties. The undesirable effect of the modern medicine has already diverted the attention of the people towards herbal

**Table 1**

Some plants with antioxidant property.

Plant/Scientific name/Family	Chemical constituents	Clinical uses
Cumin, <i>Cuminum cyminum</i> , Apiaceae	Γ-terpinene, safranal, p-cymene and β-pinene aromacompounds– Cuminaldehyde, Cuminic alcohol	Seeds are used as a spice for their distinctive flavour and aroma
Plantain, <i>Musa acuminata</i> , Musaceae	Carbohydrates, Sugar, Dietary fibers, Fats, Protien, Vitamins A, B1–B12	Plantain plant have been consumed as human food since prehistory
Leek, <i>Allium cepa</i> , Amaryllidaceae	Glycosides like quercetin 3,4'-diglucoside or quercetin-4'-glucoside	Anti-inflammatory, anticholesterol, anticancer, and antioxidant properties
Turmeric, <i>Curcuma longa</i> , Zingiberaceae	Shallots have the most phenols	Alzheimer's disease, diabetes pancreatitis
Ginseng, <i>Panax ginseng</i> , <i>P. quinquefolius</i> , Araliaceae	Turmeric essential oils, Curcumin, Polyphenol	Respiratory illnesses, Quality of life, Influenza, Central nervous system, Gonadal tissues
Lemongrass, <i>Cymbopogon nardus</i> , Poaceae	Phytoestrogens, Salvianolic acid, Steroids	Citronella, geraniol and citronellol, are antiseptics. Hence They are used in household disinfectants and soaps.
Opium poppy, <i>Papaver somniferum</i> , Papaveraceae	Citronella, Geraniol and Citronellol	Analgesic, CNS stimulant, Sedative
Garlic, <i>Allium sativum</i> , Amaryllidaceae	Morphine, Thebaine, Codeine, Papaverine, Noscapine	Atherosclerosis, High cholesterol, High blood pressure, Cancer. Reduce platelet aggregation, Hyperlipidemia
Beans, <i>Phaseolus Vulgaris</i> , Leguminosae	Diallyl disulfide, Diallyl trisulfide	Respiratory illnesses, Quality of life, influenza or patients
Angelica, <i>Angelica sylvestris</i> , Apiaceae	Starch, Protein, Vitamin A, Vitamin C, Phytohaemagglutinin, Lectin	Make the skin sensitive to light
Celery, <i>Apium Graveolens</i> , Apiaceae	Furocoumarins	Perfume and pharmaceutical industries
Eucalyptus, <i>Eucalyptus obliqua</i> , Myrtaceae	3-n-butylphthalide, Bergapten, Essential oil	Perfume and pharmaceutical industries, Insecticide
Peanut, <i>Arachis hypogaea</i> , Fabaceae	Terpenoids	Antioxidants
Licorice, <i>Glycyrrhiza glabra</i> , Fabaceae	Phytonutrients. P-coumaric acid, Niacin, Folate, Fiber, Vitamin E, Magnesium, Phosphorus	Postural tachycardia syndrome, Mouth ulcers, Peptic ulcers
Allspice, <i>Pimenta dioica</i> , Myrtaceae	Glycyrrhizin, Glycyrrhiza, Glycyrrhizic acid, Isoflavones, 11β-hydroxysteroid dehydrogenase, Aldosterone, Deglycyrrhizinated liquorice	Deodorant, Antimicrobial agent
Bearberry, <i>Arctostaphylos alpine</i> , Bearberriaceae	Essential oil	Nausea, Vomiting, Fever, Chills, Severe Back Pain, Tinnitus.
Ivy, <i>Hedera rhombea</i> , Araliaceae	Arbutin, Ursolic acid, Tannic acid, Gallic acid, Essential Oil, Resin,	It should not be used during pregnancy, breast feeding, or in children or patients with kidney disease
Anise, <i>Pimpinella anisum</i> , Apiaceae	Hydroquinones (Mainly Arbutin, Tannins, Phenolic Glycosides, Flavonoids)	Anticancer, Allergic reaction
Areca nut, <i>Areca catechu</i> , Palmaceae	Triterpenoid, Saponins, Falcarinol	Gastroesophageal reflux disease
Elecampane, <i>Inula helenium</i> , Asteraceae	Anethole	Psychiatric disorders
Betel leaf, <i>Piper betle</i> , Piperaceae	Tannins arecatannin, Gallic acid; a fixed oil gum little terpineol, lignin	Broad spectrum of bacteria
Horseradish, <i>Armoracia rusticana</i> , Brassicaceae	varisaline alkaloids arecoline, arecaidine guvacine	Stimulant, Antiseptic, Breath freshener, Carcinogenic
Nettle, <i>Urtica, Urtica thunbergiana</i> , Urticaceae,	Helenin, Stearoptene	Deodorant, Antimicrobial agent
Black pepper, <i>Piper nigrum</i> , Piperaceae	Alkaloid, Arecoline	Hypertrophy, Diabetes mellitus, Rheumatic disease, Hypertension, Gastrointestinal symptoms
Tarragon, <i>Artemisia dracuncululus</i> , Asteraceae	Sinigrin–glucosinolate allyl isothiocyanate (mustard oil)	Antioxidant properties, Anti-carcinogenic effects
Bay laurel, <i>Laurus nobilis</i> , Lauraceae	Formic acid, Serotonin, Histamine, Oxalic acid, Tartaric acid	Antihyperglycemic activity in streptozotocin-induced rats
Mugwort, <i>Artemisia vulgaris</i> , Asteraceae	Piperine, Sulfur dioxide, Selenium, Vitamin B, Beta-carotene, Curcumin	Astringents, Arthritis, Rheumatism, Aromatherapy
Oak, <i>Quercus robur</i> , Fagaceae	Estragole, Phenylpropanoids such as methyl chavicol (16.2%) and methyl eugenol	Anthelmintic
	Essential oil, Cineole (eucalyptol), Terpenes, Sesquiterpenes,	Gastroenteritis, Depression, Constipation, Diarrhea
	Methyleugenol, α- and β-pinenes, Phellandrene, Linalool, Geraniol, Terpineol	
	Thujone, Flavonoids, Triterpeness, Coumarin	
	Tannin, Tannic acid	

**Table 1, Continued**

Some plants with antioxidant property.

Plant/Scientific name/Family	Chemical constituents	Clinical uses
Oats, <i>Avena sativa</i> , Poaceae	Beta-glucan, Beta-D-glucans, Polysaccharides	Menstrual cycle, Dysmenorrhoea, Osteoporosis, Urinary tract infections
Hoarhound, <i>Leonurus cardiac</i> , Lamiaceae	Alkaloid leonurine, Iridoid glycosides, Diterpenoids, Flavonoids	Uterine tonic, Uterine infection
Blackberry, <i>Rubus ursinus</i> , Rosaceae	Anthocyanins, Salicylic acid, Ellagic acid, Fiber	Antioxidants
Raspberry, <i>Rubus occidentalis</i> , Rosaceae	Anthocyanin pigments, ellagic acid (the polyphenol ellagitannin), Quercetin, Gallic acid, Cyanidins, Pelargonidins, Catechins, Kaempferol, Salicylic acid	Antioxidant, Antiproliferative
Tea, <i>Camellia sinensis</i> , Theaceae	Antioxidant, Flavanols, Flavonoids, Polyphenols, Catechins	Anti-inflammatory, Neuroprotective activities
Mint, <i>Mentha spicata</i> , Lamiaceae	Menthol, Menthone, Pippemint	Antiseptic mouth rinses, Toothpaste, Chewing Gum, Desserts and candies
Pennyroyal, <i>Mentha pulegium</i> , Lamiaceae	Pulegone, a highly toxic volatile organic compound	Self-induced abortion
Schizandra, <i>Schisandra chinensis</i> , Schisandraceae	Lignans schizandrin, Deoxyschizandrin, Gomisins, Pregomisin	Pregnancy, humoral and cell-mediated immune responses
Bell peppers, <i>Capsicum annum</i> , Capasthaceae	Capsicum antioxidant lycopene, Carotene, Like lycopene, Para-coumaric acid, Vitamin C	Mediated immune responses, Antibacterial
Saw palmetto, <i>Serenoa repens</i> , Arecaceae	Fatty acids, Phytosterols	Prostatic hyperplasia, Baldness, Polycystic ovarian syndrome
Sesame, <i>Sesamum indicum</i> , Pedaliaceae	Essential amino acids, Essential fatty acids, Lignans pinorelinol, Lariciresinol	Antioxidant
Nutmeg, <i>Myristica fragrans</i> , Myristicaceae	D-pinene, Limonene, D-borneol, L-terpineol, Geraniol, Safrol, Myristicin	Convulsions, Palpitations, Nausea, Eventual dehydration, Generalized body pain
Spinach, <i>Spinacia oleracea</i> , Amaranthaceae	Vitamin C, Vitamin E, Vitamin K, Magnesium, Manganese, Folate, Betaine, Iron, Vitamin B2, Calcium, Potassium, Vitamin B6, Folic acid, Copper, Protein, Phosphorus, Zinc, Niacin, Selenium, Omega-3 fatty acids, Opioid peptides	Nausea, Vomiting, Fever, Chills, Severe back pain and tinnitus; Should not be used during pregnancy, breast feeding, or in children or patients with kidney disease
Rice, <i>Oryza sativa</i> , Gramineae	Essential amino acids	Antiviral, Antibacterial, Antifungal effects, Arthritis pain or having blood thinning and cholesterol
Ginger, <i>Zingiber officinale</i> , Zingiberaceae	Zingiberacin, Zingiber, Zingiberon	Nausea caused by seasickness, Morning sickness
Oregano, <i>Origanum vulgare</i> , Lamiaceae	Phenolic compounds, Essential oil, Carvacrol, Thymol, Limonene, Pinene, Ocimene, Caryophyllene	High in antioxidant activity
Cranberry, <i>Vaccinium erythrocarpum</i> , Ericaceae	Proanthocyanidins, Flavonols, Quercetin	Antioxidant; fruit are cooked into a compote or jelly, known as cranberry sauce
Coriander, <i>Coriandrum sativum</i> , Apiaceae.	Terpenes linalool, Pinene	Antioxidants, Diuretic, Carminative
Marjoram, <i>Origanum majorana</i> , Lamiaceae	Borneol, Camphor, Pinene	Antiviral, Antibacterial, Antifungal effects
Citrus, <i>Citrus sinensis</i> , Rutaceae	Flavonoids, Limonoids citric acid, Vitamin C, Flavonoids	Kidney stones, Fermentation
Olive, <i>Olea europaea</i> , Oleaceae,	Oleuropein, a bitter glycoside; Phenolic compounds	Antioxidants, Diuretic
Cocoa, <i>Theobroma cacao</i> , Malvaceae	Theobromine, a compound similar to caffeine	Antioxidants

medicines. To increase the acceptability and awareness among the people, there is an urgent need to develop trust and faith towards the safer indigenous system by establishing its validity in treatment for various diseases. Health care systems are going to become more and more expensive, therefore we have to introduce herbal medicine systems in our health care. Let us hope that in future natural products will be competing modern medicines with added advantages of more safety and lower costs.

### Conflict of interest statement

We declare that we have no conflict of interest.

### Acknowledgements

The authors are thankful with our deepest core of heart to Dr. S.K. Jain and Dr. Amita Verma for his valuable guidance.

### Comments

#### Background

The article is mainly focused on the clinical applications of herbal antioxidants. Natural antioxidants are powerful scavengers of excessively generated free radicals in the human

body thereby combating with the devastating consequences of free radicals. So, they are considered to be very useful therapeutic agents in a large variety of human diseases.

#### Research frontiers

The work gives sufficient information for the clinicians as well as the researchers to exploit the naturally available antioxidants as therapeutic drugs for cure of untreated diseases.

#### Related reports

A large number of articles are available which gives the phytopharmacological profile of plant-derived antioxidants. The present work is different from previously published reports in the fact that it gives detailed information of clinical application of each herb covered in the manuscript on the basis of recent research work on such herbs.

#### Innovations and breakthroughs

The authors have tried to present the role of native herbs and the active principles present in many plants that can be explored as therapeutic agents in chronic diseased conditions, where the current conventional treatments are not satisfactory and are full of adverse effects.

#### Applications

The work gives specific information regarding the clinical utility of each herb that is being covered. Also, the herbs covered by the authors are easily available and generally used

in our day to day lives.

### Peer review

It is a systematic review that clearly focuses on the clinical applications of herbs as antioxidants. Oxidative stress is being reported as the major hallmark in the etiology of chronic diseases such as diabetes, Alzheimer's disease, renal failures, cancer, etc.

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