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## POTENTIAL BENEFITS OF INDIAN SPICES ON HUMAN HEALTH: A REVIEW

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### ABSTRACT

apply plant remedy for centuries, but only currently have scientist begun to the study powers of general herbs and spices. In the present set-up, the anti-proliferative, anti-hypercholesterolemia, anti-diabetic, anti-inflammatory effects of spices are dominant importance, as the key health hesitation of mankind. Some disease as like diabetes, cardio-vascular diseases, arthritis and cancer are more prevalence diseases. Spices and their active substances which is used as possible preventive agents for health disorders. Spices are a good sources of antioxidants, and scientific studies suggest that they are also effective inhibitors of tissue damage and inflammation caused by high levels of blood sugar and circulating lipids. Because spices are mostly low calorie providing and are relatively inexpensive also, they are reliable sources of antioxidants and other potential bioactive compounds in diet. In this review, overall the role of few more important spices which are used in the Indian dishes for its flavor and taste their potential uses as a medicine to maintain a health.

**Keywords:** Spices; anti-inflammatory; health disorder; bioactive compounds.

### INTRODUCTION

Spice may be a tropical herbal plant and specific a part of which is valued for providing color and aromatic flavoring alongside stimulating odor to be used in cooking and in condiments, also as in candies, cosmetics, fragrances, and medications. Spices are commonly uses in foods for taste, flavor, and aroma and color. Spices also are some sources of seasoning the food and full of solid healthy reasons to be included in kitchen. There are units several spices we tend to use in our day to day cooking; aside from flavouring, spices also are used as a botanicals, beverages, preservatives, pharmaceutical and other industries. Besides giving the varied flavors to food, all spices also possess some medicinal properties, which keep the physical body during a healthy condition and cure the diseases consistent with the Indian system of drugs called Ayurveda. Since, each of the spices possesses quite one health beneficial property and there's also an opportunity of synergy among them in their action, using spices in diet. Foods make life not only more spicy but also more healthy. These some spices widespread ones like cumin, black pepper, turmeric and coriander seeds. Here's an inventory of some spices, which you ought to start adding to your meals for healthy living. India is that the largest country of spices grown sort of spices thanks to different agro-climatic conditions. Also India is that the largest producer, consumer and exporter of spices within the world. India holds monopoly in export of spice oils and oleoresins. Spices account for six per cent contribution to the agriculture GDP. Among the spices, chilli shares first place in production with the

22.71%, followed by garlic (21.93 %) and turmeric (16.92%) and therefore the lowest share was observed in clove with 0.02% within the country. the world under major spice was 2.13 and 30.75 million ha with the assembly of three .69 and 57.43 million tonnes and productivity was 1.7 and 1.9 t/ha in Karnataka and India respectively. Among the spice producing states in India, Andhra Pradesh stands first with the assembly of 11.88 million tonnes and Karnataka stands fifth position with the assembly of three. 7 million tonnes.

### Black Pepper

Pepper is widely used spice both in Eastern and Western food. it's an efficient antioxidant and antibacterial effect and helps with digestion and weight loss because it stimulates the breakdown of fat cells. Black pepper is taken into account because the king of spices, because it fetches the very best return as judged from the quantity of international trade. Black pepper is a lively principle piperine has been experimentally demonstrated variety of independent investigators to possess diverse physiological effects. Piperine has been demonstrated in in vitro studies to guard against oxidative damage by inhibiting or quenching free radicals and reactive oxygen species. Black pepper are used piperine treatment has also evidenced to lower lipid peroxidation *In vivo* and beneficially influence cellular thiol status, antioxidant molecules and antioxidant enzymes during a number of experimental situations of oxidative stress (Srinivasan *et al.*, 2007). (Wakade *et al.*, 2008) showed that the methanolic extract of long pepper exhibits a considerable safety

against Adriamycin induced cardio toxicity by virtue of its antioxidant and radical scavenging capacity. Black pepper has been reported to influence lipid metabolism predominantly by mobilization of fatty acids. An *In vivo* study on hypolipidemic effect of black pepper (*Piper nigrum* Linn.) in high fat diet fed rats treated with black pepper also as piperine showed remarked decrease within the levels of cholesterol (both the free and ester cholesterol fractions), free fatty acids, phospholipids and triglycerides. Therefore, supplementation of the high fat fed rats with black pepper elevated the concentration of high density lipoprotein-cholesterol (HDL-c) and reduced the concentrations of low density lipoprotein-cholesterol (LDL-c) and very low density lipoprotein-cholesterol (VLDL-c) within the plasma as compared with the amount in unsupplemented high fat fed rats (Shenuarin *et al.*, 2009). Vanadium compounds also promote cardiac function by activating Akt signaling through inhibition of protein tyrosine phosphatases. Black pepper, being rich in containing vanadium in it thus elicits cardiac functional recovery in myocardial infarct and pressure overload-induced hypertrophy (Jayaprakasha *et al.*, 2003).

### Cardamom

Cardamom may be a most vital spices their botanical name is cardamom, and also referred to as elaichi, belongs to the Zingiberaceae family, cardamom found in India, Bhutan, Nepal, and Indonesia that's a tall perennial herb having sub sessile, lanceolate leaves with sheathing base. cardamom is that the world's third most expensive spice. an upscale source of vitamin A and vitamin C, calcium, iron, and zinc, this spice is employed for medicinal purpose prevent some diseases as like heart health, helps in digestion, enhances oral health, helps in diabetes, helps fight depression, fights asthma, prevents blood clots and treats skin infections. Their seeds also are very useful in cases



of bad breath, vomiting, excessive thirst, weakness, pyrexia, and burning sensation. Cineol, terpenene, terpenol, and essential oil are the first active chemical constituents available during this plant, which are cure to anti-inflammatory, antipyretic, carminative, aromatic, and digestive pharmacological properties.

### Cinnamon

*Cinnamon* belongs to genus *Cinnamomum*, family *Lauraceae* which is distributed in India, Egypt, China, Srilanka and Australia. *Cinnamon* leaves and bark are used extensively as spices in food to produce essential oils (Jayaprakasha *et al.*, 2003). Antioxidant and antimicrobial potential (singh *et al.*, 2007) the antidiarrheal activity of Cinnamon is also well predictable. The 'Indian Materia Medica' Nadkarni-1976 and the 'Indian Medicinal Plants – A Compendium of 500 species' classifies cinnamon as a herbal medicine which is very effective for cardiovascular diseases Warriar *et al.*, 1994; Wang *et al.*, 1983. In their study using guinea pig heart showed that a decoction of cinnamon increased coronary blood flow and provoked pituitary induced reduction of blood flow. Also it reduced peripheral vascular resistance, suggesting an undeviating vasodilation of peripheral vessels. Therefore increased cardiac contractile force and beating rate was also exerted by cinnamaldehyde, which is valuable in cinnamon. Circulatory stimulant effects of cinnamon have been reported in several books on medicinal plants and also in Ayurveda (Bhattacharjee 1998). Dietary cinnamon increases biliary secretion of cholesterol and phospholipids without affecting the bile content (Sambaiah and Sreenivasan 1991; Sharma *et al.*, 1996) studied the effect of a 50% alcoholic extract of cinnamon on rats and reported a significant anti-hypercholesterolemic action and reduced serum triglyceride level at a single dose of 250 mg/kg body weight. Suppression of total serum cholesterol, triglycerides, phospholipids and low density lipoprotein levels was observed in another investigation using triton WR-1339-induced hyperlipidaemic rats (Kim *et al.*, 1999). In extension study with 80% methanolic extract and its chloroform fraction of different species of *Cinnamomum* observed that the extracts suppressed the elevated serum total cholesterol and triglyceride levels in corn oil-induced hyperlipidaemic rats.



## Clove

*Syzygium aromaticum* commonly referred to as the spice Lavang belongs to the Myrtaceae family. It's a pyramidal evergreen tree mostly cultivated within the southern parts of India. Their leaves are simple, lanceolate, gland dotted and fragrant while the flowers buds are greenish to pink, clustered at the top of the branches and highly aromatic. Their fruits are fleshy, dark pink drupes with oblong seeds, which are grooved on the one side, an enzyme that catalyses cholesterol biosynthesis. Kamal *et al.*, 2009 during this study describe cinnamon extract improved lipid profile by extensively decreasing total cholesterol, triglycerides and LDL – C levels with increasing serum HDL – C. It also hampers HMG-CoA reductase activity in liver thereby lowering the Cholesterol levels. Cinnamon activates PPAR $\gamma$  leading to improved insulin resistance and reduced fasted LDL-c, thereby managing obesity related hyperlipidemia and also increases NO levels, which may be a potent Vasodilator. Their vital quality may be a demonstrated significant ability to inhibit initiation also as propagation of lipid peroxidation thanks to their polyphenol content, highly reducing power and superoxide radical scavenging activity (Yadav *et al.*, 2007). Cinnamon also are shown direct dose-dependent gas suppressing effect with none effect upon cell viability. Peroxisome proliferator activated receptors (PPARs  $\gamma$  and  $\alpha$ ), one of the transcriptional factors involved within the regulation of insulin resistance and angiogenesis is found to be up-regulated, leading to improved insulin resistance, reduced fasted glucose, FFA, LDL-c, and AST levels in high-caloric diet-induced obesity (DIO) and db/db mice fed with cinnamon water extract (Sheng *et al.*, 2014) their flower buds are traditionally utilized in dental and oral diseases. The active chemical constituents present during this plant include caryophyllene, clove oil, eugenol, salicylic acid, tannin, and B-complex vitamin (Leela *et al.*, 2002) The presence of those active principles, clove has been found to possess local anaesthetic, carminative, stimulant, aromatic, analgesic, antimicrobial, anticonvulsion, and anticarcinogenic pharmacological properties (Deans *et al.*, 1995). Cloves are antibacterial, anti-fungal and antiseptic. This is often a powerhouse of antioxidants and are rich sources of minerals, omega-3 fatty acids, fiber and vitamins and minerals. Their oil may be a richest source of antioxidants which is beneficial in aromatherapy, and an antiseptic and pain reliever especially for toothaches and stomach pain. Therefore typically mixed with different oils to treat numerous disorders. As an example, those that have trouble sleeping can apply some warm oil of cloves along side vegetable oil on the forehead to feel calm and relaxed. The volatile oil from clove exhibited significant antimicrobial activity against a set of 25 different genera of test bacteria and 20 different isolates of *Listeria*

monocytogenes. The oil was also tested against three fungal strains: a plant pathogen, a spoilage type and a mycotoxigenic strain. This resulted in high levels of growth inhibition at both concentrations of 1 and 10 l ml<sup>-1</sup> growth medium. This volatile oil was fed to mice so as to assess the antioxidant capacity, with particular regard to the protection of polyunsaturated fatty acids, within the liver and retina during ageing (Shobana *et al.*, 2000).



## Cumin

*Cuminum cyminum* belongs to the Umbelliferae family and is usually known in India because the spice Jeera. It's a slender, annual, glabrous herb whose leaves are compound and linear. The fruits are cylindrical, with apex and base conical and dorsally compressed seeds. It's mostly cultivated in Punjab and south India. These seeds as medicine, traditionally utilized in colic pain, abdominal discomfort, flatulence, deficient lactation, piles, and worm infestation etc. It's a good source of cumaldehyde, vitamin A, vitamin C, Cuminal, Cuminal alcohol,  $\gamma$ -Terpinene, Safranal, p-Cymene, volatile oils and  $\beta$ -Pinene are a number of the most active chemical constituents present during this plant. (Lahlou *et al.*, 2002) Cumin has been found to possess antioxidant, anticancer, stimulant and carminative pharmacological properties. The anti-diabetic effect of cumin seeds has been found to be remarkably beneficial, as indicated by reduction in hyperglycemia and glucosuria in streptozotocin induced diabetic rats who were placed on an eight-week dietary regimen containing cumin powder (1.25%). Dietary cumin also countered other metabolic alterations as revealed by lowered blood urea level and reduced excretions of urea and creatinine by diabetic animals. This seed contains a bitter taste that's an important part of geographical area cuisines. It's the

pliability to assist digestion, improve immunity and treat skin disorders, insomnia, respiratory disorders, asthma, bronchitis and anemia. For hundreds of years, light gravy flavored with cumin or a glass of zeera water has been utilized in Indian household as a fool-proof remedy for digestive issues (Villatgamuwa *et al.*, 1998).

### Fenugreek

*Trigonella foenum-graecum* is an aromatic, erect annual herb belonging to the Leguminosae family. This spice is commonly known in India as *Methi* and is mostly cultivated in Punjab, Kashmir, and upper Gangetic plains. Its leaves are trifoliate round in shape, flowers are axillary white or yellowish, and fruit pods are having many rectangular yellow colour seeds. Its seeds have been traditionally used in diabetes, body ache, deficient lactation, abdominal pain, and anorexia. The main active chemical constituents present in this plant include volatile oils, calcium, phosphorus, iron, trigonalin, vitexin,  $\beta$ -sitosterol, and tigenine. Fenugreek has been found to possess hypoglycemic, antipyretic, analgesic, hypolipidemic, anti-inflammatory, and antitumor pharmacological properties. The protein content of fenugreek was found to be 28.4%. The crude fibre content was 9.3% and crude fat was 7.1%. The minimum protein solubility was observed at pH 4.5, which was 18.5%, while maximum protein solubility was observed at pH 11, which was 91.3%. Measurement of emulsion and foaming properties of fenugreek protein concentrate showed that they were greatly affected by pH levels and salt (NaCl) concentration (Rohini *et al.*, 2009).

The diuretic activity of the successive extract of fenugreek seeds was investigated in Wistar rat, according to Lipchitz



method. The diuretic response and electrolyte excretion potency from petroleum ether, and benzene extract were remarkable in comparison with the control animals. The extract at 150 and 350 mg/kg body weight showed a dose dependent increase in volume of urine, the naliuretic activity seen by increase in Na<sup>+</sup>/K<sup>+</sup> ions ratio with respect to control.

It improves digestion, is known to increase libido in men, promotes milk flow in mothers, helps those suffering from eating disorders and also reduces inflammation.

### Turmeric

*Curcuma longa* is commonly known as the spice *Haldi* in India and belongs to the Zingiberaceae family. It is a perennial herb with a short stem and erect leaves. The rhizomes are cylindrical, ovoid and branched in shape and yellow-orange in coloured while its leaves are simple, petiolate, and oblong-lanceolate. Its flowers are pale yellow in spikes.

It is cultivated throughout India. This spice is packed with antioxidant, anti-viral, anti-bacterial, anti-fungal, anti-carcinogenic, anti-mutagenic and anti-inflammatory properties. It is good for your brain, relieves arthritis, prevents cancer and has healing properties. Turmeric's anti-inflammatory properties have been instrumental in treating osteoarthritis and rheumatoid arthritis. The inhibitor conjointly destroys the free radicals within the body that harm the cells. The active chemical constituents found in this plant include Curcumin, volatile oils, vitamin A, and proteins. Important pharmacological properties of turmeric include antibacterial, anti-inflammatory, hypocholesteremic, antihistaminic, antihepatotoxic, antifungal, and antiarthritic actions. The essential oils of leaves, flowers, rhizomes and roots of turmeric (*Curcuma longa* L., Zingiberaceae) were analysed by GC-MS. The major constituent of flower oil was *p*-cymene-8-ol (26.0%) while leaf oil was dominated by phellandrene (32.6%) Aggarwal *et al.*, 2007).

The rhizomes and roots contained turmerone (31.0% and 46.8%, respectively) as major constituents. These effects are mediated through the regulation of various transcription factors, growth factors, inflammatory cytokines, protein kinases, and other enzymes. Curcumin exhibits activities similar to recently discovered tumor necrosis factor blockers (e.g., Humira, Remicade, and Enbrel), a vascular endothelial cell growth factor blocker (e.g., Avastin), human epidermal growth factor receptor blockers (e.g., Erbitux, Erlotinib, and Gefitinib), and a HER2 blocker (e.g., Herceptin). Curcumin has been shown in the last two decades to be a potent immunomodulatory agent that can modulate the activation of T cells, B cells, macrophages, neutrophils, natural killer cells, and dendritic cells. Curcumin can also down regulate the expression of various proinflammatory cytokines including TNF, IL-

**Table 1.** Medicinal properties of Indian spices

Sl. No.	Spices	Medicinal properties
1.	Black pepper	Anthelmintic, carminative, alterant, antiperiodic, diuretic, digestive, emmenagogue, rubefacient, stimulant, stomachic, used in fever, asthma, cough, dyspepsia, flatulence, arthritis (Singh 2008).
2.	Cardamom	Stimulant, tonic, diuretic, carminative, digestive, expectorant, cardiogenic & used in several pharmaceutical preparations.
3.	Cinnamon	Astringent, diuretic, carminative, aphrodisiac, deodorant, expectorant, febrifuge, stomachic.
4.	Clove	Refrigerant, ophthalmic, digestive, carminative, stomachic, stimulant, antispasmodic, antibacterial, expectorant, rubefacient,
5.	Cumin	Digestive, carminative, astringent, anti-inflammatory, constipating, diuretic, revulsive, galactagogue, uterine & nerve stimulant.
6.	Fenugreek	Carminative, tonic, aphrodisiac, emollient, antibacterial, used in vomiting, fever, anorexia, colonitis.
7.	Turmeric	Thermogenic, emollient, anodyne, anti-inflammatory, vulnerary, depurative, antiseptic, appetizer, carminative, expectorant, stomachic, anthelmintic, stimulant, ophthalmic, tonic, used in skin diseases, dyspepsia, asthma, cough, bronchitis, inflammations,
8.	Ajowan	Digestive, antispasmodic, stimulant, carminative, expectorant.
9.	Coriander	Carminative, diuretic, tonic, stimulant, stomachic, refrigerant, aphrodisiac, analgesic, anti-inflammatory
10.	Mint	Stimulant, stomachic, carminative, antiseptic, digestive, antispasmodic, contraceptive, used in vomiting, skin diseases (Sokovi <i>et al.</i> , 2006).

1, IL-2, IL-6, IL-8, IL-12, and chemokines, most likely through inactivation of the transcription factor NF-kappa B. Interestingly; however, curcumin at low doses can also enhance antibody responses. This suggests that curcumin reported beneficial effects in arthritis, allergy, asthma, atherosclerosis, heart disease; Alzheimer's disease, diabetes, and cancer might be due in part to its ability to modulate the immune (Jagetia and Aggarwal 2007).



### Ajwain

*Trachyspermum ammi*, usually known by the name of

*Ajwain* in India belongs to the Umbelliferae family. Ajwain is also known as carom seeds. Carom seeds are often chewed for medicinal purposes. Despite a partly bitter style, ajwain or carom seeds give an entire host of health edges. Ajwain promotes digestion, cures abdomen ache and helps relieve tooth pain. These seeds are unit wealthy in metal, proteins and fibre (Thangam *et al.*, 2003). Ajwain has been found to possess antispasmodic, anti-inflammatory, anti-diarrhoeal, stimulant, anticholinergic, antibronchitis, antidyspepsia, and colic pharmacological properties. It is a glabrescent herb having fusi form roots and pinnate, linear leaves. The flowers are white and polygamous and the fruits are ovoid and mucricate. Ajwain is extensively cultivated in the states of Punjab and West Bengal in India. Its fruits have been



traditionally used in flatulence, anorexia, inflammation, and colic pain. The active chemical constituents present in this plant include thimol, carvacrol, thymene, vitamin B, and volatile oils.

### Coriander

*Coriandrum sativum* (Coriander) has been documented as a traditional treatment for cholesterol and diabetes patients. It has a long history as a traditional medicine (Burdock-2009). The seeds of coriander have a remarkable hypolipidemic action. The levels of total cholesterol and triglycerides decreased significantly in the tissues of the animals of the experimental group which received coriander seeds. Significant increases in -hydroxy, -methyl glutaryl CoA reductase and plasma lecithin cholesterol acyl transferase activity were noted in the experimental group. The level of LDL + VLDL cholesterol decreased while that of HDL cholesterol increased in the experimental group compared to the control group. The increased activity of plasma LCAT enhanced hepatic bile acid synthesis and the increased degradation of cholesterol to fecal bile acids and neutral sterols appeared to account for its hypocholesterolemic effect (Chithra *et al*, 1997. Thrombosis, an important event in cardiovascular diseases, can be fatal if platelet aggregation takes place in the narrowed lumen of arteries, causing an impairment of blood flow to the heart. Attempts have been made to study the antiplatelet activity of leaf spice extracts, as these are rich sources of natural antioxidants. Aqueous extracts of coriander leaf and curry leaf were tested on human platelets over a wide range of concentrations. Both these leaf spice extracts inhibited human platelet aggregation (Suneetha-2005). Another *in vivo* study shows that there is a remarkable decrease in the levels of TC, TG, TAG and LDL-c in plasma, also there was a significant increase in the levels of HDL-c observed in the cholesterol-rich (1%) basal diet fed rats treated with coriander seed oil (Chithra *et al*, 1997).



### Mint

*Mentha spicata* is commonly known as *Pudina*, spices

in india. This is belongs to the Labiateae family. Mint is good source of antioxidant, antifungal, and hypotensive pharmacological properties. This is an aromatic herb with suckers having simple, opposite, petioles, ovate, and serrate leaves Kanatt *et al.*, 2007). The flowers are liliacin axillary distant whorls while the fruits are nutlets and silk. There leaves is traditionally used in abdominal discomfort, colic pain, pyrexia, flatulence, and skin disease. Mint is richest of phytochemicals, chemical active and nutrients as like Terpene, ceneol, carvone, vitamin B, vitamin A, calcium, iron, and volatile oils.

Pudina extract was examined for its DNA damage protecting activity and antioxidant potential. *n*- Butanol soluble fraction (PE) derived from methanol extract of *Mentha spicata* at 10 µg/ml exhibited significant protecting activity against DNA strand scission by •OH on p Blue script II SK(-) DNA. IC50 concentration of PE to scavenge DPPH•, ABTS•+ and superoxide radical was 7.47, 4.05, and 57.80 µg/ml, respectively(Telci *et al.*, 2004).



### CONCLUSION

Spices have been traditionally used as an essential ingredient in the preparation of food in many countries, especially in India. They are directly liable for providing the aroma, flavor, color and taste to the food articles. Therefore, they're a neighborhood and parcel of each kitchen. However, most of those Indian spices have also been ascribed with many therapeutic properties and actions within the traditional textbooks of past. The Indian system of medicine called Ayurveda has laid special emphasis on the medicinal and therapeutic actions of these spices and described the same in detail in the various texts of Vedic period Chatterjee 1997, which are several thousand years old. Based on such traditional knowledge base and folklore which has been passed on from generation to generation, many Indian spices have been a part of regular household usage. Many traditional Indian spices are studied rigorously in recent times using modern scientific

methods to know their nature, chemical constituents, and specific pharmacological properties. Such detailed analysis has revealed the presence of specific chemical compounds and constituents in each of those spices. Since many of those chemical compounds are already known to possess specific pharmacological properties and actions, their presence in these spices might be possibly liable for the observed pharmacological actions of these spices. Scientific analysis of the pharmacological and therapeutic actions of these individual spices through experimental and clinical studies has established many of the pharmacological properties of these spices as detailed above. Many of those spices possess crucial therapeutic properties like appetizer, digestive, carminative, analgesic, blood purifier, hepatoprotective, antipyretic, antidiabetic, hypolipidemic, antimicrobial, anti-inflammatory, antioxidant, etc. Spices possess antioxidant activity that can be applied for preservation of lipids and reduce lipid peroxidation in biological systems (Sharma *et al.*, 2001). The potential antioxidant activities of selected spices extracts (water and alcohol 1:1) were investigated on enzymatic lipid peroxidation. Water and alcoholic extract (1:1) of commonly used spices (garlic, ginger, onion, mint, cloves, cinnamon, and pepper) dose-dependently inhibited oxidation of carboxylic acid, linolic acid in presence of soybean lipoxygenase. Among the spices tested, cloves exhibited highest while onion showed least antioxidant activity. The relative antioxidant activities decreased within the order of cloves, cinnamon, pepper, ginger, garlic, mint, and onion. Spice mix namely ginger, onion and garlic; onion and ginger; ginger, and garlic showed cumulative inhibition of lipid peroxidation thus exhibiting their synergistic antioxidant activity. The antioxidant activity of spice extracts were retained even after boiling for 30 min at 100°C, indicating that the spice constituents were immune to thermal denaturation. The antioxidant activity of these dietary spices suggests that in addition to imparting flavor to the food, they possess potential health benefits by inhibiting the lipid peroxidation. As several metabolic diseases and age-related degenerative disorders are closely related to oxidative processes within the body, the utilization of herbs and spices as a source of antioxidants to combat oxidation warrants further attention. Immediate studies should specialise in validating the antioxidant capacity of herbs and spices also as testing their effects on markers of oxidation in parallel with clinical trials that are getting to establish antioxidants as mediators of disease prevention Villatgamuwa *et al.*, 1998).

### CONSENT

it is not applicable.

### ETHICAL APPROVAL

it is not applicable.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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