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Role of Spices Beyond Food Flavoring: Nutraceuticals with Multiple Health Effects

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Spices are esoteric food adjuncts that have been used as flavoring and coloring agents, and as preservatives for thousands of years. Spices have also been recognized to possess medicinal properties and their use in traditional systems of medicine has been on record for a long time. With the advancement in the technology of spices and on knowledge of the chemistry and pharmacology of their active principles, their health benefit effects were investigated more thoroughly in recent decades. Many health benefit attributes of these common food adjuncts have been recognized in the past few decades by pioneering experimental research involving both animal studies and human trials. These studies documented digestive stimulant action, hypolipidemic effect, antidiabetic influence, antilithogenic property, antioxidant potential, anti-inflammatory property, antimutagenic, and anticarcinogenic potential of spices. Among these, the hypocholesterolemic and antioxidant properties of a few specific spices have far-reaching nutraceutical value. These beneficial physiological effects also have the potential of possible therapeutic application in a variety of disease conditions. This review presents an overview of experimental evidence for the nutraceutical potential of spices.

Keywords Spices, Nutraceuticals, Digestive stimulant, Antioxidant, Hypolipidemic, Anti-lithogenic, Antidiabetic, Anti-inflammatory, Antimutagenic, Anticarcinogenic

Introduction

Spices are a group of esoteric food adjuncts that have been in use for thousands of years to enhance the sensory quality of foods, the quantity and variety consumed in tropical countries is particularly extensive. These spice ingredients impart characteristic flavor, aroma, or piquancy and color to foods. Some spices, like fenugreek, can also modify the texture of food. It is a common experience that their distinct aroma stimulates the appetite. Not only are spices used as flavorings and seasonings, but many are also used in perfumery, cosmetics, and toiletries. In addition, several spices have long been recognized to possess medicinal properties such as tonic, carminative, stomachic antispasmodic, and antihelminthic, as listed in Table 1 (Nadkarni and Nadkarni, 1976). Although these observations are largely empirical, these undoubtedly efficacious attributes have earned them pharmacological applications in the indigenous system of medicine not only in India, but in other countries as well.

The spice trade, probably, is the most ancient trade practiced by man. The affluence generated by the spice trade was responsible for several historic voyages and discoveries of new lands. Today, the annual global spice trade is estimated to be in the order of $2000 million involving a quantity of 500,000 tons. India is the largest producer, consumer, and

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Table 1
Medicinal properties of spices recognized for a long time

Spice	Medicinal properties recognized for a long time
Coriander (*Coriandrum sativum*)	Antidyspeptic, flavorant
Cumin (*Cuminum cymminum*)	Antispasmodic, carminative, digestive stimulant
Fenugreek (*Trigonella foenumgraecum*)	Diuretic, emmenagogue, emollient, useful in heart diseases
Garlic (*Allium sativum*)	Antidyspeptic, antiflatulent, for ear infection, duodenal ulcers, as rubefacient in skin diseases
Ginger (*Zingiber officinale*)	Sialogogue, useful in diseases of heart and blood
Onion (*Allium cepa*)	Diuretic, emmenagogue, expectorant, for bleeding piles
Pepper (*Piper nigrum*)	Antipiretic; Rebefacient
Red pepper (*Capsicum annuum*)	Anti-inflammatory, for pain relief (rheumatism/ neuralgia) Useful in indigestion, rubefacient
Turmeric (*Curcuma longa*)	Anti-inflammatory, diuretic, laxative, good for affections of the liver, jaundice, diseases of blood

exporter of spices. India's annual spice exports amount to 2.3 lakh tons and of a value of Rs. 16,000 million. Black pepper, also called "king of spices," is the major spice commodity exported from India followed by red pepper, turmeric, ginger, cardamom, seed spices, curry powders, spice oils, and oleoresins.

Nutrient Makeup of Spices

Spices are not only used individually, but also in the form of spice mixtures, known as "curry powders," to suit different tastes and dishes. Although spices have never been considered to contribute anything to human nutrition, this group of food adjuncts has been used in human diets for centuries as flavor modifiers to make food more palatable. Interestingly, the protein content in spices varies from 4.5% in rosemary leaves to 31.5% in mustard, and the fat level varies from 0.6% in garlic to 42.6% in mustard. The ash content can be anywhere from 2.3% in marjoram to 16.7% in basil leaves reflecting high mineral levels in them. Some spices contain significant levels of vitamins and minerals, which cannot be ignored. A few spices are also rich sources of dietary fiber. Amongst common spices consumed, the dietary fiber is highest in red pepper, as high as 43.3%, although black pepper (27.8%), coriander (36.2%), cumin (23.0%), fennel (28.7%), and fenugreek (33.5%) also are rich sources of dietary fiber, both soluble as well as insoluble. However, due to the low levels of spice consumption, their impact on nutrient make-up may not be as dramatic as that of other food ingredients. The components of spices responsible for the quality attributes have been designated as "active principles," and in many instances, they are also responsible for the beneficial physiological effects of spices.

Safety of Spice Consumption

Extensive animal studies carried out to evaluate the safety aspect of spices have indicated that even at much higher dietary levels (up to 100 times the normal intake), red pepper,

Table 2
Experimentally documented beneficial health effects of spices

Beneficial health effect	Spices observed to exert
Lowering of blood cholesterol	Garlic, Onion, Fenugreek, Turmeric/Curcumin, Red pepper/Capsaicin
Prevention and dissolution of cholesterol gallstones	Curcumin, Capsaicin
Protection of erythrocyte integrity in hypercholesterolemic condition	Curcumin, Capsaicin, Garlic
Hypoglycemic potential	Fenugreek, Garlic, Onion, Turmeric, Cumin
Amelioration of diabetic nephropathy	Curcumin, Onion
Antioxidant effect	Turmeric/Curcumin, Capsaicin, Eugenol
Anti-inflammatory and anti-arthritic	Turmeric/Curcumin, Capsaicin, Eugenol
Antimutagenic/cancer preventive	Turmeric/Curcumin, Garlic, Ginger/Gingerol, Mustard
Digestive stimulant action	Curcumin, Capsaicin, Piperine, Ginger, Cumin, Ajowan, Fennel, Coriander, Onion, Mint
Antimicrobial	Turmeric/Curcumin, Garlic, Asafetida

black pepper and turmeric have no adverse effects on growth, organ weights, Feed Efficiency Ratio, nitrogen balance, and blood constituents. In the past two to three decades, many more beneficial physiological effects of spices have been experimentally documented (Table 2), which suggest that the use of these food adjuncts extend beyond taste and flavor. Among the health problems that affect mankind, diabetes, cardiovascular disease, and inflammatory disorders including arthritis, and cancer have received considerable attention. During recent years, spices and their active principles have been studied as possible ameliorative or preventive agents. The salient features of a variety of health beneficial physiological effects of common spices or their active principles, so far documented, are summarized in this review.

Hypolipidemic/Hypocholesterolemic Effect

Consumption of a high fat diet may lead to an increase in serum cholesterol and plasma fibrinogen levels which in turn may result in decreased fibrinolytic activity and blood coagulation time. These changes would also increase the risk of atherosclerosis and heart diseases. The importance of serum cholesterol levels and of lipoproteins in relation to atherosclerosis and coronary heart disease is well known. In view of this, there has been a continuous search for blood cholesterol lowering agents and dietary adjuncts have been especially screened for this, as it would be most advantageous. Some of the commonly consumed spices were naturally evaluated for a possible hypocholesterolemic action in a variety of experimental situations in both animals and humans. A recent review (Srinivasan et al., 2004) shows the following results. The spices fenugreek, red pepper, turmeric, garlic, onion and ginger were found to be effective as hypocholesterolemic agents under various conditions of experimentally induced hypercholesterolemia/hyperlipemia. Further, fenugreek, onion, and garlic are effective in humans with hyperlipemic condition. Curcumin and capsaicin, the active principles of turmeric and red pepper, respectively, are also efficacious at doses comparable to calculated human daily intake. Turmeric and curcumin showed excellent hypocholesteremic effect in experimental animals. However, endogenous cholesterol synthesis was not affected. Extracts of garlic and onions inhibit platelet aggregation and lower cholesterol levels. The raw form is more effective than the cooked form. About 50 g of onion and garlic corresponding to 5–6 cloves per day may be adequate to bring these beneficial effects.

Other work also documents hypocholesterolemic effects of spices. Fenugreek seeds were hypocholesterolemic in rats with hyperlipidemia induced by either high fat (Singhal et al., 1982) or a high cholesterol diet (Sharma, 1984, 1986). Defatted fenugreek seed was effective in diabetic hypercholesterolemia in dogs (Valette et al., 1984)and in humans (Sharma, 1986). The hypolipidemic effectiveness of turmeric/curcumin (Srimal, 1997), red pepper/capsaicin (Suzuki and Iwai, 1984; Govindarajan and Satyanarayana, 1991; Surh and Lee, 1995; Majid et al., 1997) and of onion and garlic (Fenwick and Hanley, 1985; Carson, 1987; Jain and Apitz Castro, 1994) has been periodically reviewed in recent years by different authors.

Kleijnen et al. (1989) reviewed the clinical research concerning garlic and its preparations. Their main concern is that large amounts of garlic (up to 20 cloves) are needed to prove clinical effectiveness. This is indeed true because large quantities are required to provide relatively very small amounts of active oils or other derivatives. But with the introduction of dehydrated garlic powder containing a standardized level of the parent sulfur compound, alliin, effective clinical work could be undertaken with a relatively low and acceptable daily dosage of 300–900 mg (≡1 clove of garlic). This level produced a consistent 10%–13% reduction in blood cholesterol and triglycerides.

In a recent study, dietary supplementation with aged garlic extract showed better beneficial effects, relative to fresh garlic, on the lipid profile and blood pressure of moderately hypercholesterolemic subjects (Steiner et al., 1996). In another study (Adler and Holub, 1997), garlic supplementation significantly decreased both total and LDL cholesterol in hypercholesterolemic subjects. Co-administration of garlic with fish oil had a better beneficial effect on serum lipid and lipoprotein concentrations by providing a combined lowering of total cholesterol, LDL cholesterol, and triglyceride concentration as well as the ratios of total cholesterol to HDL cholesterol and LDL cholesterol to HDL cholesterol. According to Lin (1994), the anti-platelet aggregation, the antiplatelet adhesion and the antiproliferation properties of aged garlic extracts appear to contribute more to cardiovascular protection than do the hypolipidemic properties. Apart from the hypocholesterolemic effect of capsaicin, its beneficial effect on overall lipid metabolism under different conditions of lipemia has also been reported (Srinivasan and Satyanarayana, 1987, 1988; Sambaiah and Satyanarayana, 1982). In a further study, capsaicin treatment is also shown to enhance energy metabolism in rats (Kawada et al., 1986).

Antilithogenic Effect

The inhibitory effect of a curcuma mixture (Temoe Lawak Singer) on lithogenesis in rabbits has been reported by Beynen et al. (1987). Studies on experimental induction of cholesterol gallstones in mice and hamsters by feeding a lithogenic diet have revealed that the incidence of gallstones is 40%–50% lower when the animals are maintained on 0.5% curcumin or 5 mg% capsaicin-containing diet (Hussain and Chandrasekhara, 1992, 1993). Animal studies have also revealed significant regression of preformed cholesterol gallstones by these spice principles in a 10-week feeding trial (Hussain and Chandrasekhara, 1994). The possibility of such a beneficial prevention and regression of cholesterol gallstones by other known hypocholesterolemic spices remains to be examined. The antilithogenicity of

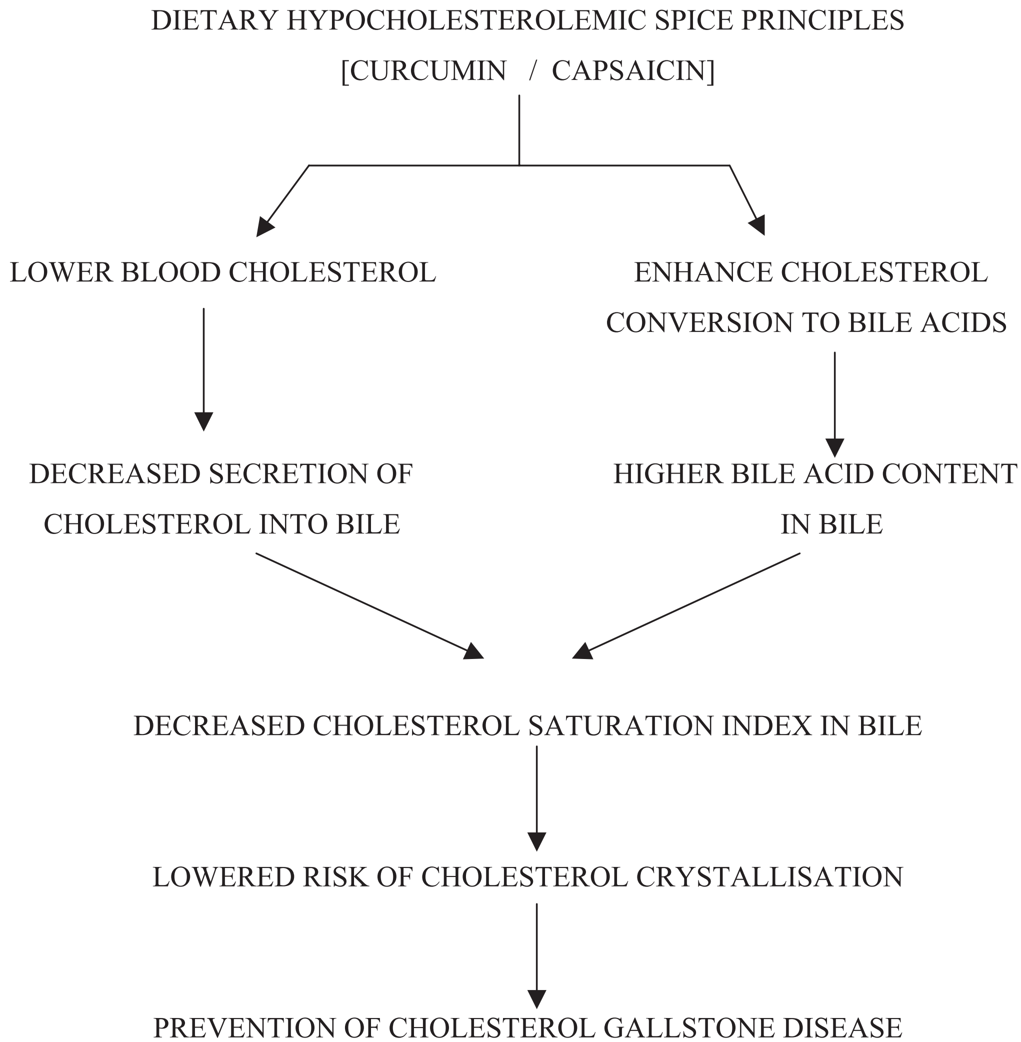

Figure 1. Antilithogenic effect of spices.

curcumin and capsaicin is considered to be due to lowering of cholesterol concentration and enhancing the bile acid concentration, both of which contribute to lowering of the cholesterol saturation index and, hence, reduce crystallization (Fig. 1). In addition to their ability to lower the cholesterol saturation index, the antilithogenecity of these spice principles may also be due to their influence on biliary proteins (Hussain and Chandrasekhara, 1994a).

Antidiabetic Potential

Diet has been recognized as a corner stone in the management of diabetes mellitus. As part of the dietary treatment of diabetes, there has been a continuous search for novel antidiabetic drugs from plant sources. Spices, the natural and common food adjuncts, have also been examined in this direction and their efficacy recently reviewed (Srinivasan, 2004). A considerable number of human experiments have also been carried out on this aspect, in addition to experimentally induced animal diabetic models. Fenugreek, garlic, onion, turmeric, and cumin were studied for their antidiabetic potential, but human trials are limited other than with fenugreek. Fenugreek, turmeric, or its active principle curcumin, onion or its active principle allyl propyl disulfide, garlic, and cumin were observed to improve glycemic status in diabetic animals noninsulin dependent diabetes mellitus (NIDDM) patients.

Studies have unequivocally demonstrated the antidiabetic potential of fenugreek in both type-I and type-II diabetes. Addition of fenugreek seeds to the diets of diabetic patients or animals results in a fall in blood glucose and improvement in glucose tolerance (Sharma, 1986a; Sharma et al., 1996; Khosla et al., 1995). Antidiabetic properties of subfractions of fenugreek seeds have also been studied. The hypoglycemic effect is attributed to the fiber and gum, which constitute as much as 52% of the seeds. The spice probably delays gastric emptying by direct interference with glucose absorption and the gel-forming dietary fiber reduces the release of insulinotropic hormones and gastric inhibitory polypeptides.

Fenugreek is widely used for the treatment of diabetes in Central Anatolia, Turkey (Wetheritt and Pala, 1994). Coumarin and trigonelline are considered to be responsible for the observed hypoglycemic activity of this spice. Recently, Sauvaire et al. (1998) reported that 4-hydroxy isoleucine has insulinotropic activity and might at least partly account for the antidiabetic property of fenugreek seeds.

Garlic and onion are two other spices that have been widely used for their antidiabetic potential. Both these spices were shown to be hypoglycemic in different diabetic animal models and in limited human trials. The hypoglycemic potency of garlic and onion has been attributed to the sulfur compounds, namely di (2-propenyl) disulfide and 2-propenylpropyl disulfide, respectively (Kumudkumari et al., 1995; Augusti and Sheela, 1996). Animal studies indicate that the isolated compounds possess as much as 60%–90% of the hypoglycemic potency of tolbutamide (Jain and Vyas, 1974, 1975). The mechanism of hypoglycemic action probably involves direct or indirect stimulation of secretion of insulin by the pancreas. In addition, it is also suggested that these disulfide compounds have an insulin-sparing effect by protecting –SH inactivation by reacting with endogenous thiol-containing molecules such as cysteine, glutathione, and serum albumins.

Turmeric is another spice claimed to possess beneficial hypoglycemic effect and to improve glucose tolerance in a limited number of studies (Tank et al., 1990). Nephropathy is a common complication in chronic diabetes. High blood cholesterol is an added risk factor that determines the rate of decline of kidney function in diabetics. Hypercholesterolemia is a regular biochemical abnormality in diabetes mellitus and nephropathy is one of the secondary eventualities of this disease. Extensive studies with diabetic rat models were carried out to examine whether with hypolipidemic spices supplementation in the diet would influence renal lesions associated with diabetes by virtue of their possible cholesterol lowering effect. Dietary curcumin (of turmeric) and onion have been found to have a promising ameliorating influence on the severity of renal lesions in streptozotocin diabetic rats (Babu and Srinivasan, 1998, 1999). Hypocholesterolemic effects, and the ability to lower the extent of lipid peroxidation under diabetic condition, are implicated in the amelioration of renal lesions (Fig. 2).

Capsaicin has been shown to be useful in diabetic neuropathy (Capsaicin Study Group, 1992). In an eight-week, double-blind, placebo-controlled study with parallel randomized treatment conducted by 12 independent investigators involving 219 patients, topical application of 0.075% capsaicin cream was effective in pain management. The lisited spices may be used in conjunction with antidiabetic drugs to have better therapeutic potential and to minimize drug dosage. Fenugreek seeds (25–50g), garlic (5–6 cloves)/ onion (50 g), and turmeric powder (1 pinch) incorporated in the daily diet of diabetics

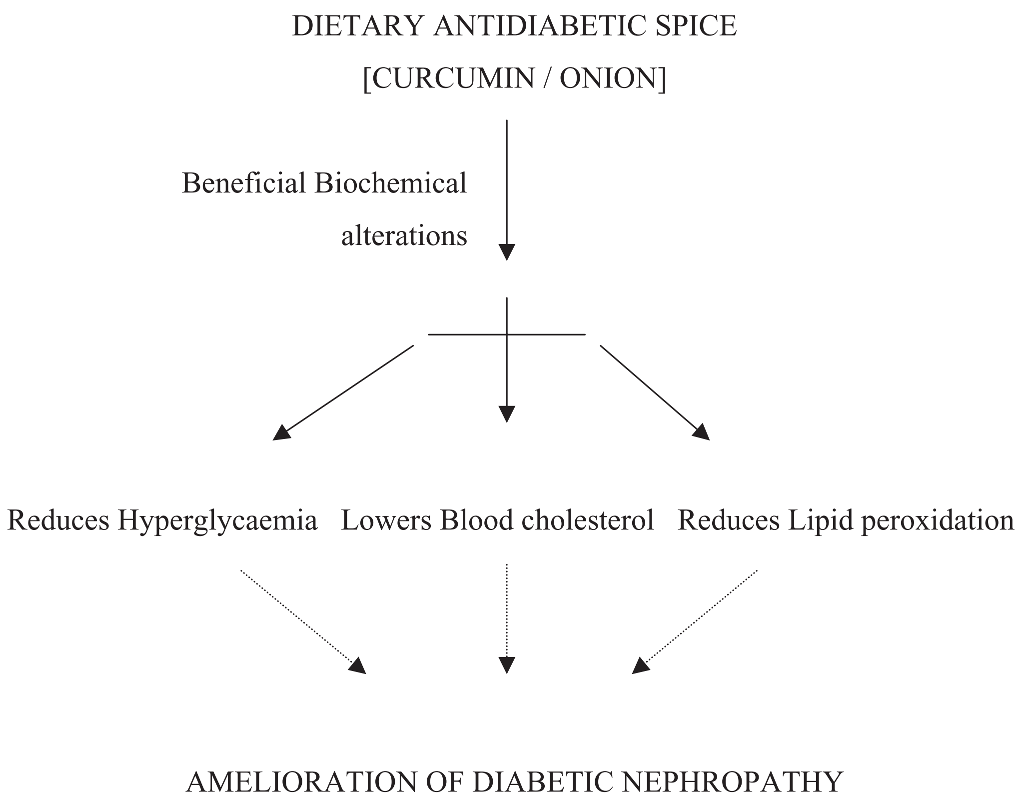

Figure 2. Antidiabetic influence of spices.

could serve as an effective supportive therapy in the prevention and management of long-term complications of diabetes.

Digestive Stimulant Action

Spices are well recognized to stimulate gastric function. They are generally believed to intensify salivary flow and gastric juice secretion and, hence, aid in digestion (Glatzel, 1968). Spices like turmeric are known to reduce the pungency of the food and irritation to stomach. Turmeric has the property of increasing the mucin content of the gastric juice. Spices such as ginger, mint, ajowan, cumin, fennel, coriander, and garlic are used as ingredients of commercial digestive stimulants as well as of home remedies for digestive disorders, like, flatulence, indigestion, and intestinal disorders. Earlier reports on the digestive stimulant action of spices are largely empirical; it is only in recent years that this beneficial attribute of spices has been authenticated in exhaustive animal studies (Platel and Srinivasan, 2004).

Animal studies have revealed that a good number of spices, when consumed through diet, bring about an enhanced secretion of bile with a higher bile acid content, which plays a vital role in fat digestion and absorption (Bhat et al., 1984, 1985; Sambaiah and Srinivasan, 1991; Platel and Srinivasan, 2000). Spices that stimulate bile acid production by the liver and its secretion into bile include curcumin (turmeric), capsaicin (red pepper), ginger, cumin, coriander, ajowan, fenugreek, mustard, onion, and tamarind. Spices such as curcumin, capsaicin, piperine, ginger, and mint have also been shown to stimulate pancreatic digestive enzymes like lipase, amylase, trypsin, and chymotrypsin, which play a crucial

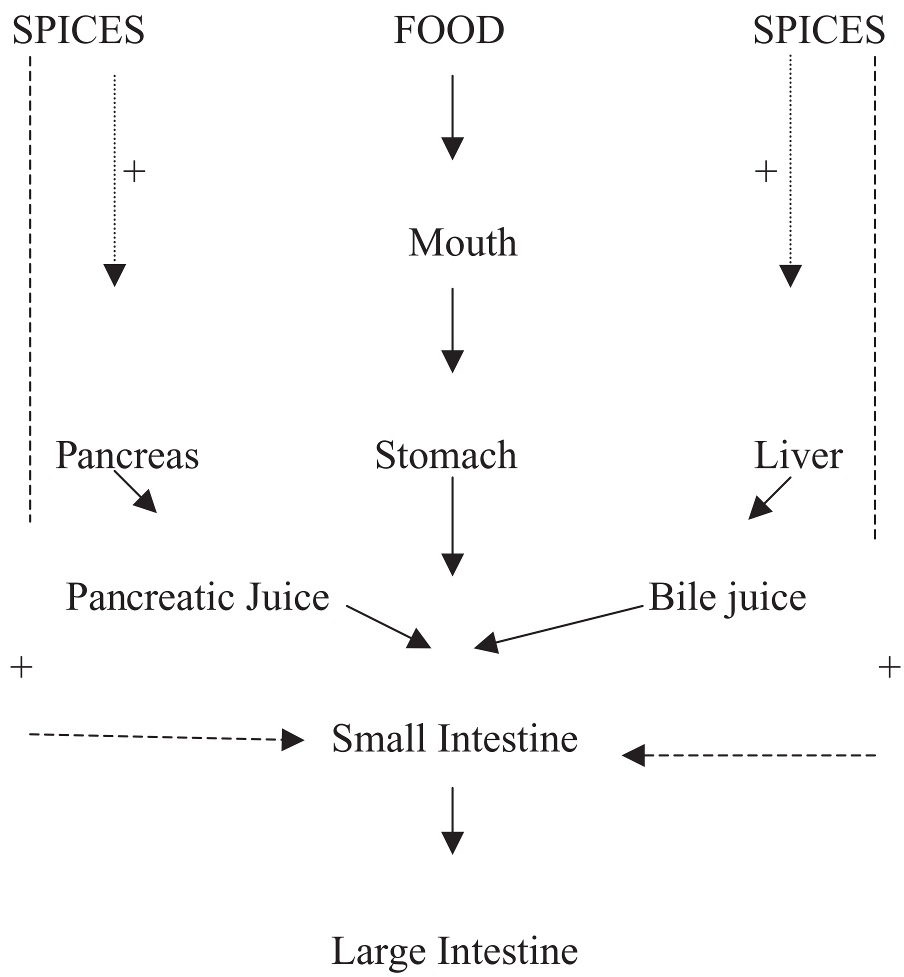

Figure 3. Digestive stimulant action of spices.

role in food digestion (Platel and Srinivasan, 2000a, 2001). A few spices have been shown to have beneficial effect on the terminal digestive enzymes of small intestinal mucosa (Platel and Srinivasan, 1996, 2000a,). Thus, many of the common spices act as digestive stimulants by enhancing biliary secretion of bile acids, which are vital for fat digestion and absorption, and by stimulating the activities of pancreatic and intestinal enzymes involved in digestion (Fig. 3).

Antioxidant Property

Spices have been investigated for their antioxidant potency in food systems for at least 55 years (Ramaswamy and Banerjee, 1948). However, nearly 25 years lapsed before the role of antioxidants in protecting biological systems against oxidative damage came to be appreciated. Oxidative damage at the cellular or subcellular level is now considered to be an important event in disease processes like coronary vascular disease (CVD), inflammatory disease, carcinogenesis, and aging. Reactive oxygen radicals are detrimental to cells at both membrane and genetic levels. They induce lipid peroxidation in cellular membranes, generating lipid peroxides that cause extensive damage to membranes in terms of cross-linking of membrane components, leaks and lysis, and membrane-mediated chromosomal damage.

The antioxidant activity of curcumin and related compounds was reported by Sharma (1976). Lipid peroxidation in human erythrocyte membranes was inhibited by capsaicin and curcumin (Salimath et al., 1986) and by eugenol (Nagashima, 1989). Daily administration of curcuminoids (0.5 g) to healthy human volunteers produced a 33% reduction in blood lipid peroxide levels (Soni and Kuttan, 1992). Besides curcumin, a powerful water-soluble peptide antioxidant, turmerin, has also been reported to be present in turmeric (Srinivas et al., 1992). Sreejayan and Rao (1994) have reported that whereas the different curcuminoids, including curcumin, demethoxy curcumin, bis-demethoxy curcumin and acetyl curcumin, were all more potent than α-tocoferol, among themselves they were almost equally potent as antioxidants.

The antioxidant properties of spice principles, capsaicin, curcumin, and eugenol, were recently documented in animal studies by Reddy and Lokesh (1992, 1994, 1994a, 1994b, 1994c). These compounds inhibited lipid peroxidation by quenching oxygen free radicals and by enhancing the activity of endogenous antioxidant enzymes like superoxide dismutase, catalase, glutathione peroxidase, and glutathione transferase (Fig. 4). At the same time, there was no alteration in a) the fatty acid composition in membrane lipids, b) the levels of endogenous antioxidants like vitamin E, vitamin C, and glutathione, and c) the cytochrome-P_{450}dependent

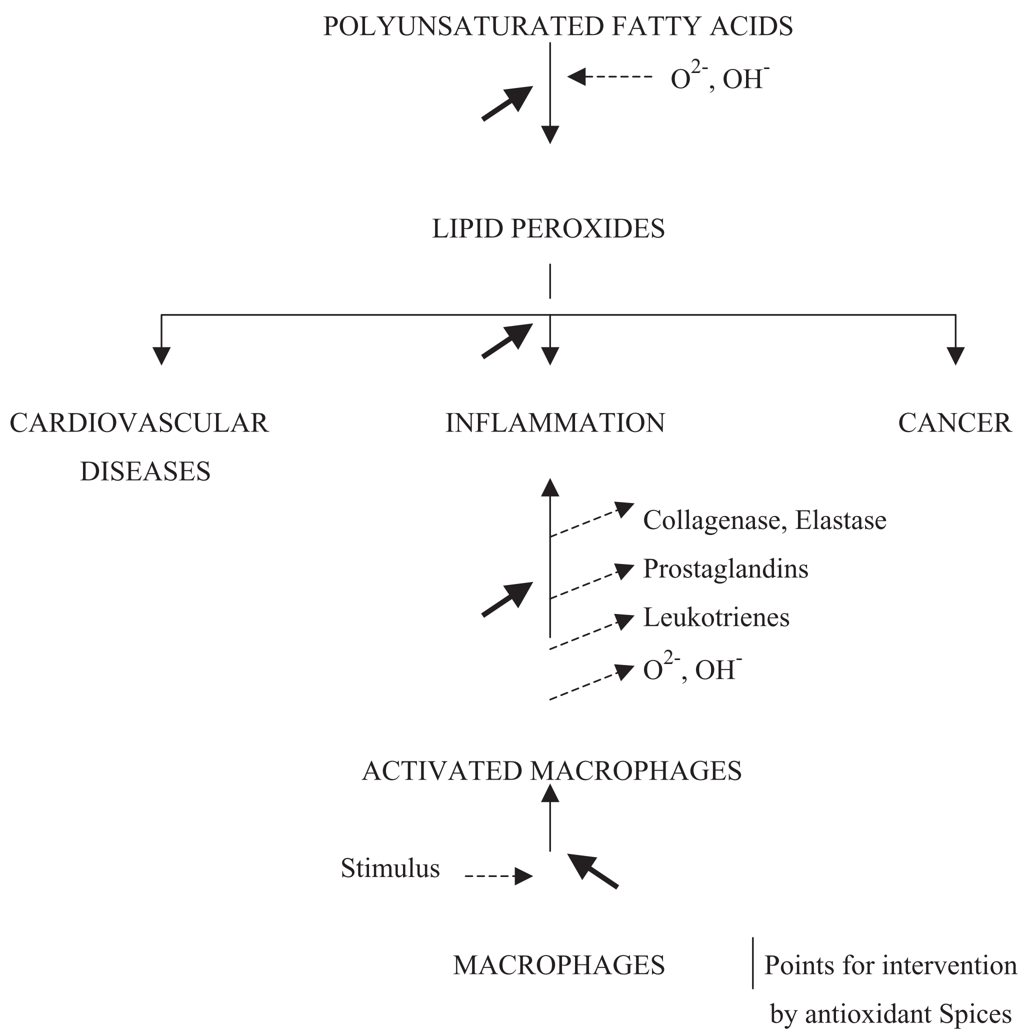

Figure 4. Beneficial intervention by dietary antioxidant spice principles.

mixed function oxygenase system. Curcumin also was found to suppress lipid peroxidation induced in rats by carbon tetrachloride or ^{60}Co radiation (Nishigaki et al., 1992). In view of the limitations of the lipid theory of atherosclerosis and the current suggestion that free radical–mediated oxidation of cholesterol is a key step in atherogenesis (Duthrie and Brown 1994), the antioxidant spices / spice principles have gained more importance for their possible role in the prevention of atherogenesis.

Anti-Inflammatory Property

Lipid peroxides and activated macrophages play a crucial role in arthritis and other inflammatory diseases. Both in vitro and in vivo animal experiments have documented the anti-inflammatory potential of spice principles like curcumin, capsaicin, and eugenol. Animal studies have revealed that curcumin and capsaicin also lower the incidence and severity of arthritis and also delay its onset.

Turmeric happens to be the earliest anti-inflammatory drug known in the indigenous system of medicine in India. Turmeric extract, curcuminoids, and volatile oil of turmeric have been found to be effective in experiments with mice, rats, rabbits, and pigeons. The efficacy of curcuminoids was also established in carrageenan-induced foot paw edema in mice and rats and in cotton pellet granuloma pouch tests in rats; in the latter, curcumin was comparable to phenylbutazone (Srimal, 1997). In carrageenan-induced edema and cotton pellet granuloma models of inflammation in rats, the order of efficacy of analogs of curcumin was sodium curcuminate > tetrahydrocurcumin > curcumin > phenylbutazone (Mukhopadyay et al., 1982; Rao et al., 1982). Curcumin was considered to be advantageous over aspirin because it selectively inhibits the synthesis of the anti-inflammatory prostaglandin T_xA_2 without affecting the synthesis of prostacyclin (PgI_2), which is an important factor preventing vascular thrombosis (Srivastava, 1986). More recently, the anti-inflammatory property of spice principles like capsaicin and curcumin were investigated in rats by Reddy and Lokesh (1994d) and by Joe & Lokesh (1997, 1997a). These compounds reduced the incidence of carrageenan-induced paw edema, reduced the severity of paw inflammation in arthritic rats, and delayed the onset of arthritis. These spice principles also inhibited the formation of arachidonate metabolites (PgE_2, leukotrienes) and the secretion of lysosomal enzymes, such as elastase, collagenase, and hyaluronidase, by macrophages. It is noteworthy that the levels of 6-keto $PgF_{1a,}$ a vasodilator, increased.

The anti-inflammatory effect of curcumin (400 mg) in patients who had undergone surgery for hernia/hydrocele was found comparable to that of phenylbutazone (100 mg) (Satoskar et al., 1986). In another study on rheumatoid arthritis patients, administration of curcumin (1.2 g/day) produced significant improvement similar to phenylbutazone (Deodhar et al., 1980). Recently, capsaicin has received considerable attention as a pain reliever. In two trials with 70 and 21 patients with osteoarthritis and rheumatoid arthritis, topical application of creams containing 0.025% or 0.075% capsaicin was an effective and safe alternative to analgesics employed in systemic medications, which are often associated with potential side effects (Deal, 1991; McCarthy and McCarthy, 1991). Capsaicin has also been suggested for the initial management of neuralgia consequent to herpes infection (Bernstein, 1989).

Antimutagenic and Anticarcinogenic Property

Food mutagens are formed under certain cooking and processing conditions. These harmful products can be modified by the presence of antimutagens in the foods. Spices that have anti-oxidant property can function as antimutagens. Since mutation is one of the mechanisms by which cancer is caused, an antimutagenic substance is likely to prevent carcinogenesis. Among phytochemicals, the antimutagenic effects of curcumin have been studied most widely (Anto et al., 1996; Surh, 1999); and this has been shown to be antimutagenic in several experimental systems. Turmeric and curcumin were effective against benzo(α-)pyrene and DMBA in the Ames' test (Nagabushan and Bhide, 1986). In vivo studies on experimental animals suggest that turmeric and curcumin inhibit the formation of mutagens. Mice and rats maintained on a turmeric- or curcumin-containing diet excreted lower levels of mutagenic metabolites as well as carcinogens than did the controls (Usha, 1994; Polasa et al., 1991). Turmeric and curcumin also inhibited the mutagenicity of cigarette and beedi smoke condensates as well as that of a tobacco-based dentifrice (Nagabushan et al., 1987). Further, curcumin was found to inhibit nitrozation of methylurea in vitro (Nagabushan et al., 1988). Azuine and Bhide (1992) have reported that an aqueous extract of turmeric was protective against mutagenicity.

Studies on smokers revealed that administration of curcumin (1.5 g/day) for 30 days resulted in a significant reduction in the urinary excretion of mutagens (Polasa et al., 1992). Shalini and Srinivas (1987, 1990) observed that turmeric protected DNA against lipid peroxide-induced damage and against fuel smoke condensate-induced damage. Similar to curcumin, the active principle in turmeric, eugenol, found in cloves, and seasamolinol isolated from seasame seed are known to produce antimutagenic effect by protecting the cell from damage to its DNA. Chemically, most of these compounds have a common phenolic structure, which may help in the detoxification of xenobiotics.

Mustard is another spice used for flavoring and as a source of edible oil. Mustard belongs to the cruciferous family whose other members are cabbage, broccoli, and cauliflower. These vegetable extracts have the property of inactivating the mutagenicity of food mutagens like tryptophan pyrolysate. The active principle of mustard, namely dithiolthione, is also used as an antischistosomal drug. From epidemiological studies it has been established that regular consumption of cruciferous vegetables is associated with negative cancer risk. Mustard seeds are rich in sulfur-containing compounds, dithiolthiones, which have protective effect against liver toxicity induced by some chemicals and aflatoxin, a potent toxic compound present in fungal-contaminated peanuts. A concentration of 0.05% of dithiolthiones in the diet was found to stimulate the activity of protective enzymes. The mutagenic effects of mustard seed powder have been assessed in experimental animals treated with potent carcinogens. These experiments suggested that mustard, like turmeric, has excellent antimutagenic properties (NIN Annual Report, 1993–1994).

Although cancer is generally considered to be an incurable disease, research during the past few decades with experimental models, limited human studies, and some epidemiological data have indicated that cancer is preventable by dietary intervention. Extensive reviews have been published in recent years on this aspect (Ho and Huang, 1994; Milner, 1994; Srimal, 1997; Coney et al., 1997; Guhr and LaChance, 1997). Recently, considerable attention has been focused on identifying naturally occurring chemopreventive substances capable of inhibiting, retarding, or reversing the multistage carcinogenesis. A wide array of phenolic substances, particularly those present in dietary and medicinal plants, have been reported to possess substantial anticarcinogenic and antimutagenic activities. The majority of these naturally occurring phenolics possess antioxidative and anti-inflammatory properties, which appear to contribute to their chemopreventive or chemoprotective activity (Surh, 2002).

The anticancer potential of curcumin as evidenced by both preclinical and clinical studies has been exhaustively reviewed (Aggarwal et al., 2003). Several studies indicate that curcumin can suppress both tumor initiation and tumor promotion. Curcumin has been demonstrated to have antitumor effect in animals treated with potent carcinogens. Rats fed different quantities of turmeric/curcumin incorporated in the diet that were then exposed to carcinogens like benz(α-)pyrene, 7,12-dimethylbenzanthracene, 3-methylcholanthrene, 12-O-tetradecanoylphorbol-13-acetate (TPA), and 1,2-dimethylhydrazine, which are ubiquitously present in the environment, showed that turmeric/curcumin can be a potent anticancer agent. Some studies, especially studies of skin tumorigenesis, have also employed topical application of curcumin (Aggarwal et al., 2003). The main observations made with turmeric/curcuminoids with regard to chemopreventive action are summarized in Table 3. Analogs of curcumin have been tested for their ability to inhibit tumor promotion by TPA; curcumin and demethoxy curcumin were equally and most effective, whereas bis-demethoxy curcumin and tetrahydro curcumin were much less effective and bis-dimethyl curcumin (dicatechol) was not at all inhibitory (Coney et al., 1997). It has been shown that the inhibition of arachidonic acid metabolism, modulation of cellular signal transduction pathways, inhibition of hormone, growth factor, and oncogene activity are some of the mechanisms by which curcumin causes tumor suppression (Gescher et al., 1998). Chemopreventive activity of curcumin is observed it is when administered prior to, during, and after carcinogen treatment as well as when it is given only during the promotion/progression phase of colon carcinogenesis in rats (Kawamori et al., 1999). Curcumin is a powerful inhibitor of the proliferation of several tumors cells (Chuang et al., 2000a, 2000b; Dorai et al., 2001). Since many studies have suggested that curcumin can suppress tumor initiation, promotion, and metastasis, and that human clinical trials have indicated absolute safety of curcumin doses administered even up to 10 g per day, curcumin offers enormous potential in the prevention and therapy of cancer (Aggarwal et al., 2003).

Garlic is yet another spice widely studied in recent years for its chemopreventive potential. Epidemiological studies have shown that higher intake of allium products is associated with reduced risk of several types of cancers, especially stomach and colorectal (Fleischauer and Arab, 2001). These epidemiological findings are well correlated with several laboratory investigations. Several mechanisms have been proposed to explain the cancer-preventive effects of garlic and its organosulfur compounds, as recently reviewed (Sengupta et al., 2004). Suggested mechanisms include inhibition of mutagenesis, modulation of enzyme activities that suppress bioactivation of carcinogen molecules, inhibition of carcinogen-DNA adduct formation, free radical scavenging, inhibitory effects on cell proliferation and tumor growth, and induction of apoptosis. Although there is a large body of evidence supporting these mechanisms, they are still speculative, and further research is needed to support causality between such properties and cancer-preventive activity in experimental animals. The important observations on the cancer preventive potential of garlic and its sulfur compounds are summarized in Table 4.

Pungent vanilloids, especially [6]-gingerol, present in the widely used dietary spice, ginger (*Zingiber officinale*), have been found to possess potential chemopreventive activities. Prior topical application of [6]-gingerol or [6]-paradol significantly suppressed the tumor promoter (phorbol ester)-stimulated skin inflammation initiated by 7,12-dimethylbenz [α] anthracene in mice (Surh et al., 1999). Reactive nitrogen species (RNS), such as nitric oxide (NO), have been proposed as being able to influence signal transduction and cause DNA damage, contributing to carcinogenic processes. [6]-gingerol, a pungent phenolic compound present in ginger, is evidenced to be a potent inhibitor of NO synthesis and also an effective protector against peroxynitrite-mediated damage in macrophages (Ippoushi et al., 2003). Dietary ginger constituents, galanals A and B, are potent apoptosis inducers in Human T lymphoma cells(Miyoshi et al., 2003).

Table 3
Cancer prevention by turmeric/curcumin

Model/Cancer	Treatment	Carcinogen	Remarks	Reference
Rat/Colon	Dietary curcumin	Azoxymethane	Inhibition	Samaha et al., 1997; Rao et al., 1995
Rat/Oral	Dietary curcumin	4-Nitroquinoline	Inhibition	Tanaka et al., 1994
Rat/Mammary	Turmeric/Ethanol Extract/ Aqueous extract	DMBA	Strong chemoprevention/Prevention/ Weak chemoprevention	Deshpande et al., 1998
Hamster/Buccal pouch	Turmeric Extract/Turmeric + Betel leaf	Acetoxymethyl nitrosamine	Protection	Azuine and Bhide, 1992
Hamster/Buccal pouch	Dietary turmeric/Curcumin	DMBA	Retardation	Krishnaswamy et al., 1998
Hamster/Oral	Dietary curcumin	DMBA	Inhibition	Li et al., 2002
Mice/Skin	Turmeric extract Topical application	DMBA/Methyl cholanthrene	Prevention	Soudamini and Kuttan, 1989
Mice/Skin	Curcumin Painting	DMBA	Prevention	Nagabushan and Bhide, 1992
Mice/Stomach, Colon	Dietary curcumin		Inhibition of tumorigenesis	Huang et al., 1994
Mice/Skin	Curcumin topical application	UV light + TPA	Inhibition of dermatitis	Lee and Pezzuto, 1999 Huang et al., 1997
Mice/Leukemia Lymphoma	Dietary curcumin	DMBA	Reduced incidence	Huang et al., 1998
Mice/Stomach	Dietary curcumin	Benzpyrene	Inhibition	Azuine and Bhide, 1992a
Humans				
62/Skin	0.5% Curcumin ointment		Reduction in foul smell, pain, itching, and exudate	Kuttan et al., 1987
25/Oral (Reverse smoking)	Turmeric 500 mg Twice a day; 1yr		Complete regression (20%); Partial regression (20%); No change (56%)	NIN Annual Report, 1993–1994

Table 4

Garlic and cancer prevention

Model/Cancer	Treatment	Carcinogen	Remarks	Reference
Rat/Liver, mammary gland	Dietary garlic powder	DMBA, Nitrosamine	in vivo inhibition of DNA adducts	Liu et al., 1992, 1992a; Lin et al., 1992
Rat/Colon, esophagus	Diallylsulfide	N-nitrosomethyl-benzylamine	Prevention	Wargovich et al., 1988
Rat/Mammary	Garlic, S-Allyl cysteine, DADS	Vinylcarbamate	Delayed onset	Schaffer et al., 1996
Rat/Liver	Dietary garlic powder	Diethylnitrosamine	Inhibition	Park et al., 2002
Mice/Colon	Diallylsulfide	Dimethylhydrazine	Prevention	Sumiyoshi and Wargovich, 1990
Mice/Skin	Garlic oil-topical	DMBA	Inhibition	Belman, 1983
Mice/Skin	Diallylsulfide	NDMA	Inhibition	Surh et al., 1995
Mice/Skin	Ajoene		Suppression	Nishikawa et al., 2002
Mice/Skin	Diallylsulfide-topical	DMBA	Inhibition	Arora et al., 2004
Hamster/Buccal pouch	S-Allyl cysteine	DMBA	Inhibition	Balasenthil et al., 2001
Humans				
Normal	Crushed fresh garlic: 5g		Inhibition of nitrosation	Mei et al., 1989
Epidemiological:				
China (Cangshan County)	Garlic: 20g/day		Decreased gastric cancer mortality Decreased NO_2^- in gastric juice	Mei et al., 1985; You et al., 1989
China	Garlic consumption		Decreased incidence of stomach and colo-rectal cancers	Fleischauer and Arab, 2001
China	Garlic consumption		Lesser incidence of prostate cancer	Hsing et al., 2002

The bioactive compounds of spices exert their anticarcinogenic effect by one or more of the following mechanisms: by virtue of their antioxidant property, by deactivating the carcinogens, or by enhancing the tissue levels of protective enzymes in the body. Toxic metabolites of harmful drugs and chemicals are detoxified by the body's defense system. Protective factors in spices like turmeric, mustard, and onion may act in more than one way to confer their beneficial effect. These substances stimulate specifically the levels of glutathione-S-transferase, a group of enzymes that are cellular detoxification enzymes. There is a high correlation between the induction of these enzymes and inhibition of carcinogenesis. There is another class of bioactive substances called phthalides, which have anticarcinogenic potential. They are found in umbelliferous plants like celery, parsley, cumin, dill, fennel, and coriander. The phthalides are known to increase the glutathione-S-transferase level (Wildman, 2000).

Anti-Microbial Activity

The antibacterial property of turmeric is well known. Its active principle, curcumin, is a known bacteriostatic agent, whereas the essential oil of turmeric is bacterial and fungistatic (Govindarajan, 1980). Asafetida, a spice that is actually a gum oleoresin exuded from the rhizome or roots of *Ferula asafoetida*, is used as an antimicrobial agent in traditional medicine. Its uses in treating chronic bronchitis and whooping cough have been documented in ancient literature. Its use in counteracting intestinal flatulence is also well known. Furthermore, antibacterial properties of garlic and onion were described by Louis Pasteur. The sulfur-containing compounds from these plants act against both gram positive and gram negative bacteria (Carson, 1987). The extracts of garlic and onion are known to inhibit growth of many pathogenic fungi belonging to *Aspergillus*, C*andida* and other species (Carson, 1987). Other spices like nutmeg, saffron, cumin, and thyme have antimicrobial potential. The volatile component of these spices is believed to be responsible for this property. These effects have been observed using raw form.

Other Beneficial Physiological Effects

Dietary hypolipidemic spices, like curcumin, capsaicin, and garlic, were found to be beneficial in protecting the structural integrity and fluidity of erythrocytes under conditions of hypercholesterolemia and hypertriglyceridemia (Kempaiah and Srinivasan 2002, 2004b, 2004c). They offer this beneficial effect by correcting the altered cholesterol to phosphorus ratio in the erythrocytes in hypercholesterolemic situation and by restoring antioxidant status of erythrocytes in both hypercholesterolemic and hypertriglyceridemic conditions (Kempaiah and Srinivasan, 2002, 2004, 2004a). Platelets in blood have an active role in hemostasis during damage to blood vessels and thrombosis by forming compact and adhesive aggregates. Compounds that counter platelet aggregation have a protective role against thrombotic disorders. Pretreatment with spices - garlic or onion is evidenced to prevent platelet aggregation by spice principles - cuminaldehyde, eugenol, and zingerone in vitro (Subramoniam and Satyanarayana, 1989). Water extracts of coriander and cumin were also evidenced to have significant inhibitory effect on platelet aggregation.

Conclusions

Many beneficial health attributes of the common food spices have been understood over the past two to three decades. Several of the named physiological attributes of spices have the potential of a possible therapeutic application in a variety of disease conditions. In

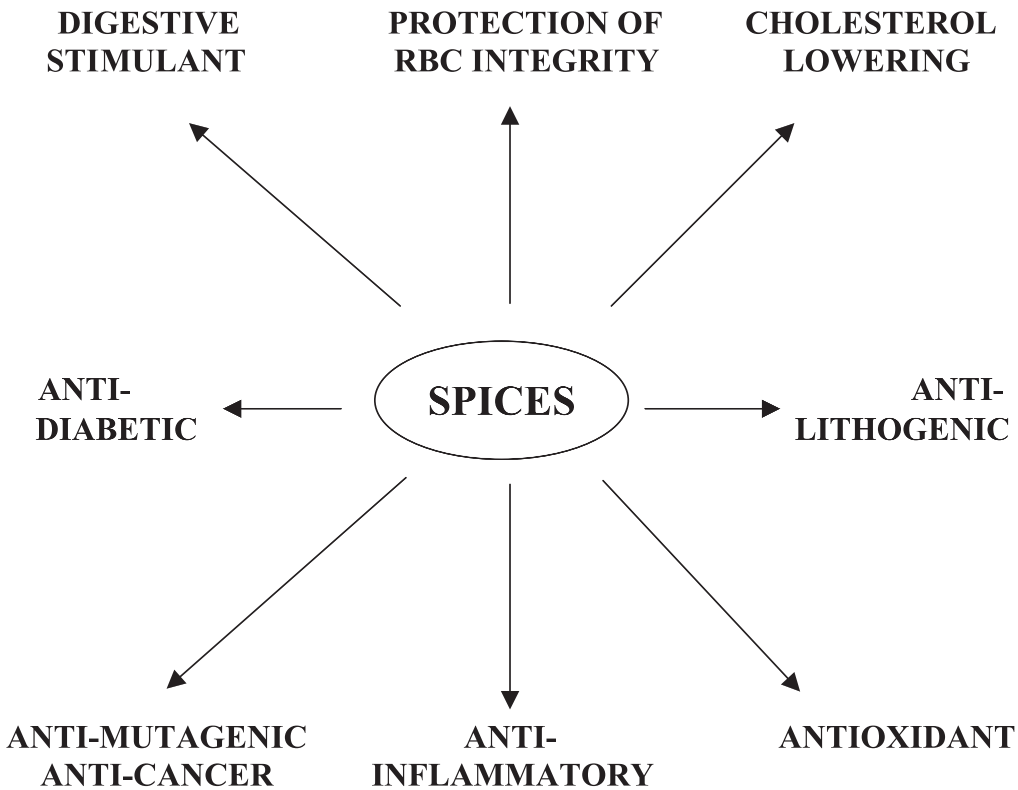

Figure 5. Summary of multibeneficial physiological effects of spices.

view of the many promising beneficial physiological effects spices are understood to exert (Fig. 5), these food adjuncts deserve to be considered as natural and necessary components of our daily nutrition, beyond their role in imparting taste and flavor to our food. Although most of the animal studies that documented the beneficial physiological influence of spices have employed spice concentrations roughly 5–10 times the normal levels found in Indian diets, such higher levels can be comfortably consumed to derive the health benefit. The liberal consumption of spices is not only proved to be safe, but may even offer beneficial effects on the antioxidant status. The effectiveness of lower doses of these spices cannot be ruled out, although it is not experimentally documented. Since each of the spices possesses more than one health beneficial property and there is also a posibility of synergy among them in their action, a spiced diet is likely to make life not only more “spicy” but more healthy also.

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