MINI-REVIEW

Flavoring Agents Used in Indian Cooking and Their Anticarcinogenic Properties

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Abstract

Spices are mainly used for taste and flavor. Mostly all Indian spices are associated with home remedies. They were mainly used for indigestion, chronic diarrhea, common cold, blood pressure, blood sugar. Majority of these spices are rich sources of flavonoids. Some epidemiological and experimental studies suggest that have some protective role against cancer. Further investigation is required to find the role of individual spice .Detailed study of their mechanism of actions is needed to find out at which stage these chemopreventive agents modulate or reverse the process of carcinogenesis. Thus there is a long way to go before scientific validation of the role of flavoring agents of cancer can be achieved.

Key words: Indian spice - flavoring agents - anticarcinogenesis - chemoprevention

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Introduction

Spice and aromatic vegetable products used as flavoring or condiment, normally refers to parts of certain herbs like seeds, leaves, bark, roots etc. They are used mainly for enhancing taste of food. The name spice is derived from the word species, which was applied to groups of exotic foodstuffs in the Middle Age. The earliest literary record in India on spices is the Rig Veda (around 6,000 BC), and the other three Vedas - Yajur, Sama and Atharva. The Rig Veda, one of the ancient Hindu scriptures, lists more than a thousand healing plants. The story of Indian spices thus dates back to 7000 years into the past. Even though with a giant progress in science, spices continue to be used as a rich source of home remedies. Some of the daily used spices have been taken for granted as part of daily food item and are used routinely without a second thought. But in fact they form the basis of remedies of human ailment and have been of much interest in medical research.

Indian Spices and their Medicinal Uses

Indian spices from time immemorial were considered with the philosophic concepts of improving health, since it was understood that they could affect the four humors (blood, phlegm, yellow bile and black bile) and influence the corresponding moods (sanguine, phlegmatic, choleric and melancholic).

Thus, ginger would be used to heat the stomach and improve digestion; clove was believed to comfort the sinus; mace would prevent colic and bloody fluxes or diarrhea; nutmeg would benefit the spleen and relieve any bad cold. Cinnamon, one of the most popular flavors in cooking, was considered to be particularly good for digestion and for sore throats. Hot pungent spices were used more liberally in winter diets or to treat cold diseases accompanied by excess phlegm. It is noteworthy that rheumatism was believed to be caused by abnormal rheum, or phlegm; the appropriate therapy would be pepper just as it is today, with the topical use of capsaicin - a chili pepper extract used to help in a variety of digestive problems. Cardamom helps to soothe indigestion and relieve gas and flatulence. Cumin seeds, which contain high amounts of carotene and iron, were traditionally used to help the digestive processes and be a tonic for the heart and nervous system. On a more practical note, the seeds appear to be useful for chronic diarrhea (probably because they have anathematic properties) and hoarseness of voice (probably because the seeds are mildly antiseptic). *Crocus sativus* L., commonly known as saffron is used in folk medicine for various purposes such as an aphrodisiac, antispasmodic and expectorant (Zargari, 1990). Garlic (*Allium sativum* Linn.), traditionally used as a spice especially in Asian cuisine, is well known for its medicinal properties with varied pharmacological functions (Ross IA, 1999). It may also lower cholesterol, blood pressure, and the risk of cancer. Capsaicin is the major pungent ingredient in red peppers, has a profound antiproliferative effect on prostate cancer cells, inducing the apoptosis of both androgen receptor (AR)-positive (LNCaP) and -negative (PC-3, DU-145) prostate cancer cell lines associated with an increase of p53, p21, and Bax (O'Kelley et al., 2006). Curcumin, turmeric's active constituent, protects against free radical damage because it is a strong antioxidant. It also reduces inflammation by lowering histamine levels and possibly by increasing production of natural cortisone by the adrenal glands. It also protects the liver from a number of toxic compounds. It also has been shown to prevent platelet clumping, which

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in turn improves circulation and helps to protect against atherosclerosis (Aguilera et al., 2002; Schnekenberger et al., 2005). Traditionally, fenugreek tea (*Trigonella foenum-graecum*) was used for relief from bronchitis, sore throats, tuberculosis, as tonic. Poultices made from pulverized fenugreek seeds were used for swollen glands, skin irritations and gout. In the Middle East fenugreek was used to treat diabetes and there is some evidence that seed extracts do lower blood sugar and also significantly reduce cholesterol levels (Misra et al., 1996; Prasanna, 2000).

Flavoring Agents and their Chemopreventive Effects

Cancer continues to represent the largest cause of mortality in the world and claims over 6 million lives each year (Espinosa et al., 2000) An extremely promising strategy for cancer prevention today is chemoprevention, which is defined as the use of synthetic or natural agents (alone or in combination) to block the development of cancer in human beings. Plants, vegetables, herbs, and spices used in folk and traditional medicine have been accepted currently as one of the main sources of cancer chemopreventive drug discovery and development (Abdullaev, 2001). A large and increasing number of patients in the world use medicinal plants and herbs for health purposes. Therefore, scientific scrutiny of their therapeutic potential, biological properties and safety will be useful in making wise decisions about their use.

In Indian cooking varieties of flavoring agents are used for their specific delicious taste. Some of these agents are rich sources of flavonoids which can block carcinogenesis .Among them turmeric is an important one. Curcumin, turmeric's active constituent, protects against free radical damage as an antioxidant and also acts as antiprolifertive agent by down regulating Cox2, iNOS and cyclin D (Song et al., 2003; Singh and Singh, 2009) and undergoing phase I clinical trial (Hsu et al., 2001).

The major components of garlic include allicin, ajoene, various allyl sulfides, S-allylmercaptocysteine, linoleum acid, selenium, quercetin etc (Beecher,1995; Li, 2000; Das et al., 2002). The anticarcinogenic properties of garlic have been indicated in several studies (Wargovich, 1987; Stephens et al., 1988; Wattenberg et al., 1988; Tosk et al., 1990; Das, 2004a; 2004b). Other epidemiological studies suggest regular consumption of garlic is associated with decreased prevalence of adenomatous polyps in the colon and rectum (Bird et al., 1996).

Modern pharmacological studies have demonstrated that saffron extracts have antitumour (Panikkar et al, 1991a; 1991b; Hasegawa, 1995; Das et al, 2004), radical scavenger, hypolipaemic (Abe and Saito, 2000), anticonvulsant effects (Hosseinzadeh and Khosravan, 2002) and improve activity on learning and memory (Polissiou et al., 1995). Chemical studies on *C. sativus* have shown the presence of constituents such as crocin, crocetin, safranal and picrocrocin (Polissiou et al., 1995; Fernandez et al., 1996; Iborra, 2000). Among the constituents of saffron extract, crocetin is mainly responsible for the pharmacological activities (Abe and Saito, 2000).

A traditional remedy for colds is ginger which contains the antioxidants gingerol, shagaol, and zingerone. Zingerone reacts with free radicals that can cause tissue damage and inflammation by inducing apoptosis (Lee and Surh,1998). Bay leaves (*Laurus nobilis*) which is an important ingredient in Indian cooking possess different essential oils (Kamalinejad et al., 1998), sesquiterpine tocopherol (Moteki et al., 2003) and quercetin (Jun et al., 2002). Both water and ethanol extracts show strong antioxidant activity which includes free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, metal chelating acivities (Isidak et al., 2006). Among the essential oils 1,8 cinole is the main component which can inhibit growth in leukemic 4B and HL60 cells by inducing apoptosis (Yayoi et al., 2002). Komiya etal (2004) observed that hot water soluble sesquiterpenes [anhydroperoxycostunolide an 3-oxo-eudesma 1, 4(15), 11(13) triene-12-,6 alphaolide] have strong effect against human promyelotic leukemic cells by induction of chromatin condensation. In a preliminary assay methanolic extract of crude bark of *Lauraus nobilis* inhibit lipid peroxidation (Kovacevic et al., 2003). Matsuda et.al (2000) found sequiterpines (costunolide and dehydrocostus lactone) inhibited inducible nitric oxide synthase (iNOS) induction in accordance with induction of heat shock protein 72 (HSP 72) which thereby prevent nuclear factor-kappaB activation followed by iNOS induction.

Reactive oxygen species (ROS) generated by activated macrophages play an important role in the initiation of inflammation. Ten different spice principles, some of which with known anti-inflammatory properties were tested for their effect on generation of superoxide anions, hydrogen peroxide and nitrite radical generation by activated rat peritoneal macrophages. Preincubation of macrophages with 10 microM capsaicin (from red pepper) or 10 microM curcumin (from turmeric) completely inhibited the production *in vitro* by macrophages. Higher concentrations (500 μM) of eugenol (from clove) and piperine (from pepper) were required to completely inhibit superoxide anion A. and hydrogen peroxide release by macrophages (Joe and Lokesh, 1994). Piperine was found to promote DNA damage and cytotoxicity induced by benzo[a]pyrene (B[a]P) in cultured V-79 lung fibroblast cells (Wang et al.,1994). Ethyl acetate extract of greater cardamom (*Amomum subulatum*) gives four fractions with high radical scavenging activity. Compounds 1 and 3 showed stronger activity than such natural antioxidants as alpha-tocopherol and L-ascorbic acid. Compounds 2 and 4 were comparable to alpha-tocopherol and L-ascorbic acid (Nakatani et al., 2001). Essential oils from common spices such as nutmeg, ginger, cardamom, celery, xanth,,oxylum, black pepper, cumin, and coriander were tested for their ability to suppress the formation of DNA adducts by aflatoxin B1 in vitro in a microsomal enzyme-mediated reaction. All oils were found to inhibit very significantly and ose-dependently. Adduct formation appeared to be modulated through the action on microsomal enzymes, because an effective inhibition on the formation of activated metabolite was observed with each oil (Dhuley,1993; Rao et al.,1994).

Cinnamon is an important spice and aromatic crop

having wide applications in flavoring, perfumery, beverages, and medicines. *Cinnamomum cassia*, a predominant species in Southeast Asia, can induce apoptosis via the mitochondrial route the apoptosis-conducting mechanism acted through a cascade involving caspase-3 (Yoshioka et al., 1993). Both aqueous and ethanol extracts shows antioxidant activity (Ng et al., 2003; Cheng et al., 2003). In a recent work Cinnamomin, a new ribosme inactivating protein, displays cytotoxicity to carcinoma cells and insect larvae by modifying their ribosomal RNA (He and Liu, 2003). An active compound isolated from bark of cinnamon, is a potent inducer of apoptosis and it transduces the apoptotic signal via ROS generation, thereby inducing mitochondrial permeability transition (MPT) and cytochrome c release to the cytosol (Jung et al., 2003).

Another important flavoring agent clove has five active known compounds: beta-caryophyllene [1], beta-caryophyllene oxide [2], alpha-humulene [3], alpha-humulene epoxide I [4], and eugenol [5] These compounds showed significant activity as inducers of the detoxifying enzyme glutathione S-transferase in the mouse liver and small intestine. The ability of natural anticarcinogens to induce detoxifying enzymes has been found to correlate with their activity in the inhibition of chemical carcinogenesis (Lam et al., 1992). Eugenol, the active principle of clove, was shown to offer protection against CCl_4 induced hepatotoxicity in rats. It also showed anti-peroxidative activity in addition to decrease in O_2 formation (Krishnaswamy, 1998). Clove was also reported to be a potential chemopreventive agent for lung cancer (Das et al., 2006).

Curry leaves used in Indian dishes for aroma and preservation, were shown to reduce DMH induced micronuclei formation. A 50% reduction was seen in the micronuclei induced by DMH and a 30% reduction in the activity of gamma-glutamyl transpeptidase when the rats were fed a curry leaf-supplemented diet (Sudarshana Krishna et al., 2000). It is well known that oxidative stress play a key role in the complications of diabetes. Fenugreek can enhance the antioxidant enzymes like catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPX) (Baquer NZ). Five flavonoid compounds were isolated from fenugreek seeds and identified as vitexin, tricin, naringenin, quercetin and tricin-7-O-beta-D-glucopyranoside (Baquer et al., 2002). Dimethylhydrazine (DMH)-induced colon carcinogenesis in male Wistar rats resulted in increased lipid peroxidase (LPO) and decreased antioxidant enzyme(Han et al.,1998) . Inclusion of fenugreek in the diet significantly decreased with simultaneous enhancement of circulating antioxidants (Devasena and Menon, 2002). Surhs group (2001) reported alcoholic extract of Fenugreek can inhibit tumor growth in EAC tumor carrying mice by 70. Protodioscin, isolated from Fenugreek is a strong growth inhibitor in HL-60 cells through apoptosis.

Interest in Indian spices and flavoring agents worldwide as health promoters is rather recent. Evidence from experimental and epidemiological studies suggest that most of the flavoring agents used in Indian cooking also have some protective role against cancer. But these works are done to some extent in a scattered way. Some have found beneficial result using the spice while some used the active component. Some of the studies were done in an in vitro system others have selected an in vivo model. Therefore more focused research on specific experimental model and an understanding the mechanism of action is necessary. Further investigations are required to define the protective role of different spices and herbs when used as food components as well as when used pharmacologically using specific compounds. It is also important to find out at which stage these chemopreventive agents modulate carcinogenesis by cell cycle analysis and in situ proliferation. Detailed study on their mechanism of action is also desirable. Thus there is a long way to go before scientific validation of the role of flavoring agents of cancer can be achieved.

References

Abdullaev FI (2001). Plant-derived agents against cancer. In ' Pharmacology and Therapeutics in the New Millennium' Ed Gupta SK. Narosa Publishing House, New Delhi pp345-354.

Abdullaev FI, Rivera LR, Roitenburd BV, et al (2000). Pattern of childhood cancer mortality in Mexico. Arch Med Res, 31,526–531.

Abe K, Saito H (2000). Effects of saffron extract and its constituent crocin on learning behavior and long-term potentiation. *Phytother Res*, **14**, 149-52.

Beecher C (1995). Potential chemopreventive compounds in the diet. In 'Chemoprevention of Cancer' Ed. Nixon, D.W., CRC Press, London pp21-62.

Banerjee S,Panda CK and Das S (2006). Clove (Syzgium aromaticum) a potential chemopreventive agent for lung cancer. *Carcinogenesis*, **27**, 1645-54.

Chu CY, Chang JP, Wang CJ (1994). Modulatory effect of piperine on benzo [a] pyrene cytotoxicity and DNA adduct formation in V-79 lung fibroblast cells. *Food Chem Toxicol*, **32**, 373-7.

Chun KS, Keum YS, Han SS, et al (2003). Curcumin inhibits phorbol ester-induced expression of cyclooxygenase-2 in mouse skin through suppression of extracellular signal-regulated kinase activity and NF-kappaB activation. *Carcinogenesis*, **24**, 1515-24.

Cheng AL, Hsu CH, Lin JK, et al (2001). Phase I clinical trial of curcumin, a chemopreventive agentin patients with high risk or premalignant lesion. *Anticancer Res*, **21**, 2895-900.

Dhuley JN (1999). Anti-oxidant effects of cinnamon (Cinnamomum verum) bark and greater cardamom (Amomum subulatum) seeds in rats fed high fat diet. J Exp Biol, 37,238-42.

Duvolx A, Blasius R, Delhalle S, et al (2005). Chemopreventive and therapeutic effects of curcumin. *Cancer Lett*, **223**,181-90.

Das S (2002). Garlic - a neutral source of cancer preventive compounds. *Asian Pac J Cancer Prev*, **3**, 305-11.

Das I, Chakraborty RN, Das S (2004). Saffron can prevent chemically induced skin carcinogenesis in swiss albino mice. *Asian Pac J Cancer Prev*, **5**,70-6.

Devasena T, Menon VP (2002). Enhancement of circulatory antioxidants by fenugreek during 1, 2-dimethyhydrazine-induced rat colon carcinogenesis. *J Biochem Mol Biol Biophys*, **6**, 289-92.

Elmastas M, Gulcin I, Isidak O, et al (2006). Radical scavenging activity and antioxidant capacity of Bay leaf. *J Iranian Chem Soc*, **13**, 258-66.

Escribano J, Alonso GL, Coca-Prados M, and Fernandez JA (1996). Crocin, safranal and picrocrocin from saffron (*Crocus sativus* L.) inhibit the growth of human cancer cells in vitro. *Cancer Lett*, **100**,23-30.

Genet S, Kale RK, Baquer NZ (2002). Alterations in antioxidant enzymes and oxidative damage in experimental diabetic rat tissues: effect of vanadate and fenugreek (*Trigonellafoenum graecum*). *Cell Biochem*, **236**, 7-12.

Hosseinzadeh H, Khosravan V (2002). Anticonvulsant effect of *Crocus sativus* L. stigmas aqueous and ethanolic extracts in mice. *Arch Irn Med*, **5**, 44-7.

Hibasami H, Yamada Y, Moteki H, et al (2003). Sesquiterpenes (costunolide and zaluzanin D) isolated from laurel (*Laurus nobilis* L.) induce cell death and morphological change indicative of apoptotic chromatin condensation in leukemia HL-60 cells. *Int J Mol Med*, **12**,147-51.

Hiroyuki M, Hiroshige H, Yayoi Y et al (2002). Specific induction of apoptosis by 1,8- cinole in two human leukemia cell line, but not in a stomach cancer cell line. *Oncol Reports*, **9**,757-60.

Hibasami H, Moteki H, Ishikawa K et al (2003). Protodioscin isolated from fenugreek (*Trigonella foenumgraecum* L.) induces cell death and morphological change indicative of apoptosis in leukemic cell line H-60, but not in gastric cancer cell line KATO III. *Int J Mol Med*, **11**, 23-6.

Hashim S, Aboobaker VS, Madhubala R, et al (1994). Modulatory effects of essential oils from spices on the formation of DNA adduct by aflatoxin B1 *in vitro*. *Nutr Cancer*, **21**, 169-75.

Hou WC, Lin RD, Cheng KT, et al (2003). Free radical-scavenging activity of Taiwanese native plants. *Phytomedicine*, **10**,170-5.

He WJ, Liu WY (2003). Cinnamomin: a multifunctional type II ribosome-inactivating protein. *Int J Biochem Cell Biol*, **35**,1021-7.

Joe B, Lokesh BR (1994). Role of capsaicin, curcumin and dietary n-3 fatty acids in lowering the generation of reactive oxygen species in rat peritoneal macrophages. *Biochim Biophys Acta*, **1224**, 255-63.

Krishnaswamy K, Raghuramulu N (1998). Bioactive phytochemicals with emphasis on dietary practices. *Indian J Med Res*, **108**, 167-81.

Kang HW, Yu KW, Jun W et al (2002) Isolation and characterization of alkyl peroxy radical scavenging compound from leaves of *Laurus nobilis*. *Pharm Bull*, **25**, 102-8.

Komiya T, Yamada Y, Moteki H, et al (2004). Hot water soluble sesquiterpines[anhydroperoxy- costunolide and 3-oxoeudesma 1-4(15),11(13) triene-12 6alpha olide] isolated from Laurel(*Laurus nobilis* L) induce cell death and morphological change indicative of morphological apoptotic chromatin condensation in leukemic cells. *Oncol Rep*, **11**, 85-8.

Kikuzaki H, Kawai Y, Nakatani N (2001). 1,1-Diphenyl-2-picrylhydrazyl radical-scavenging active compounds from greater cardamom (*Amomum subulatum* Roxb.). *Nutr Sci Vitaminol*, 47, 167-71.

Khanum F, Anilakumar KR, Sudarshana Krishna KR, et al (2000). Anticarcinogenic effects of curry leaves in dimethylhydrazine-treated rats. *J Plant Foods Hum Nutr*, **55**, 347-55.

Lozano P, Delgado D, Gomez D, Rubio M, Iborra JL (2000).A non-destructive method to determine the safranal content of saffron (*Crocus sativus* L.) by supercritical carbon dioxide extraction combined with high-performance liquid chromatography and gas chromatography. *J Biochem Biophys Methods*, **43**, 367-78.

Lee A, Surh YJ (1998). Induction of apoptosis in HL 60 cells by pungent vanilloids [6]-gingerol and [6] paradol. *Cancer Lett*, **1134**, 163-8.

Li, TSC (2000). In Medicinal Plants. Pennsylvania: Techonomic Publ. Co,pp 4-11

Mori A, Lehmann S, O'Kelley, et al (2006). Capsaicin, a component of red peppers, inhibits the growth of androgen-independent, p53 mutant prostate cancer cells. *Cancer Rev*, **66**, 3222-9.

Nair SC, Pannikar B, Panikkar KR(1991). Antitumour activity of saffron (*Crocus sativus*). *Cancer Lett*, **57**, 109-14.

Nair SC, Kurumboor SK, Hasegawa JH (1995). Saffron chemoprevention in biology and medicine: a review. *Cancer Biother*, **10**, 257-64.

Nishida S, Kikuichi S, Yoshioka S, et al (2003). Induction of apoptosis in HL-60 cells treated with medicinal herbs. *Chin Med*, **31**, 551-62.

Prasanna M (2000). Hypolipidemic effects of Fenugreek – a clinical study. *Ind J Pharmacol*, **32**, 34-6.

Quiles JL, Musa MD, Tortosa CL, et al (2002). *Curcuma longa* extract supplementation reduces oxidative stress and attenuates aortic stroke developments in rabbits. *Arterosclero Thromb Vasc Biol*, **22**, 1225- 31.

Ross IA (1999). In Medicinal plants of the World.Vol1, 2nd edition, Humana Press, Totowa, New Jersey pp 65-70.

Sharma RD, Sarkar A, Hazra DK, et al (1996). Hypolipidaemc effect of Fenugreek Seeds: a chronic study in Non-insulin dependent Diabetic patients. *Phytother Res*, 10, 332-334.

Singh M, Singh N (2009). Molecular mechanism of curcumin induced cytotoxicity in human cervical cells. *Molec Cell Biochem*, **325**, 107-19.

Sengupta S, Ghosh S, Das S (2004). Indian food ingredients and cancer prevention-an experimental evaluation of anticarcinogenic effects of garlic in rat colon. *Asian Pac J Cancer Prev*, **5**, 126-32.

Sengupta S, Ghosh S, Das S(2004). Modulatory influence of garlic and tomato on cycloxygenase 2 activity,cell proliferation and apoptosis during azoxymethane induced colon carcinogenesis in rat. *Cancer Lett*, **208**, 127-36.

SparninsVL, Barany G, Wattenberg LW (1988). Effects of organosulfur compounds from garlic and onions on benzo [a] pyrene induced neoplasia and glutathione S-transferase activity in the mouse. *Carcinogenesis*, **9**, 131-4.

Salomi MJ, Nair SC, Panikkar KR (1991). Inhibitory effects of Nigella sativa and saffron (*Crocus sativus*) on chemical carcinogenesis in mice. *Nutr Cancer*, **16**, 67-72.

Sayyah M, Saroukhani G, Peirovi A, Kamalinejad M (2003). Analgesic and anti-inflammatory activity of the leaf essential oil of *Laurus nobilis* Linn. *Phytother Res*, **17**, 733-6.

Simic M, Kundakovic T, Kovacevic N (2003). Preliminary assay on the antioxidative activity of *Laurus nobilis* extracts. *Fitoterapia*, **74**, 613-6.

Wargovich MJ (1987). Diallyl sulfide, a flavor component of garlic (Allium sativum), inhibits dimethylhydrazine-induced colon cancer. *Carcinogenesis*, 8, 487-9.

Wargovich MJ, WoodsC, Eng VWS, et al (1988). Chemoprevention of N-nitrosomethylbenzylamine-induced esophageal cancer in rats by the naturally occurring thioether, diallyl sufide. *Cancer Res*, **48**, 6872-5.

Witte JS, Longnecker MP, Bird CL et al (1996). Relation of vegetables, fruits and garlic consumption to colorectal adematous polyps. *Am J Epidemiol*, **144**, 1017-25.

Zheng GQ, Kenney PM, Lam LK (1992). Sesquiterpenes from clove (*Eugenia caryophyllata*) as potential anticarcinogenic agents. *J Nat Prod*, **55**, 999-1003.

Zargari A (1990). In Medicinal Plants. Vol 4, Tehran University Publications, Tehran, pp574-8.