

REVIEW ARTICLE

**INDIAN FOOD AND SPICES AS A
CANCER REMEDIES**

Thakar Bhaumik^{1*}, Dr. Agarwal Alka², Dr. Rawa Rakesh M³

1. PhD Scholar- Pacific Academy of Higher Education and Research University, Udaipur, Rajasthan, India
2. Principal – U.S. Ostwal Institute of Pharmacy, Mangalwad, Chittorgarh, Rajasthan, India
3. Professor – Department of Life science, Gujarat University, Ahmedabad, Gujarat, India

ABSTRACT

Due to the widespread esteem and deliberate supremacy of modern medicine in today's swift society, till date natural medicine has been criticized for being backwards and unreliable. But the truth is that in name of ease, our swift society has gifted us many life threatening diseases like cancer. Apart from the western medicines, use of natural remedies is making its own way now days just because of its less side effect and prominent pharmacological properties. Even though many research works is done for traditional Indian spice and foods, we need to emphasize this field with systemic approach of research. In this article a small effort is made to catalog the Indian spices and food as cancer remedies. However it is not possible to wrap all the Indian spices in one single pack of article, we have selected a few of them and indexed theirs till days research work on their anti-cancer chattels.

Correspondence

Bhaumik Thakar,
Pacific Academy of Higher
Education and Research
University, Pacific Hills,
Pratapnagar, Debari, Udaipur,
Rajasthan, India
dr.bhaumikthakar@gmail.com

Keywords

Indian Spices, Anti-Cancer,
Natural Remedies, Indian
Food, Modern Medicines

Received

21 November 2017

Reviewed

24 November 2017

Accepted

26 November 2017

INTRODUCTION

The medicinal effects of Indian foods and spices have been recognized since many centuries. It is well known that the Indian spice's need and requirement persuade the European people to find out the new travelling path towards India, which was later conveyed the discovery of United States of America. However it's strange that the obvious nutrition has become overlooked in the modern lifestyle, and how in the name of ease our swift society has gifted fast foods, junk food, quick fix medicines, and eating on the dash approach. [1]

It has always being center of debates around worlds that urbanization being curse or blessing for the humanity, howsoever apart from the convenience offered by the technology, many life threatening diseases like cancer may worsen due to our blind adaptation of urbanization and swift life style. Fortunately, there is an emerging focus in the important role that nutrition plays for maintenance of wellness and prosperity of peoples. As per Ayurveda the India's ancient science of life, health and longevity, the Indian foods are always playing a prominent role in buoying up health and are therefore considered as a medicine.

So far cancer is concerned, it is accounted that dietary factors has been the primary cause for about 30% of cancers in Western countries, and it's making diet as a second most preventable cause after tobacco.^[2] However the contribution of dietary factor to cancer risk in developing countries is being lower, perhaps around 20%.^[3] This statistics pointing us towards believe that use of healthy and traditional diet might decrease epidemiology of cancer like life threatening diseases. Due to this reason, less epidemiology of breast cancer in rural area is observed as compare to urban area. As per research in urban areas, 1 in 22 women develops breast cancer during her lifetime as compared to rural areas where 1 in 60 women develops breast cancer in her lifetime. ^[4]

Unscrambling the effects of Indian food and spices on minimizing cancer risk is always being a great point of interest for researchers. Researches to date have uncovered many denoted property but any how they left annoyingly large areas of uncertainty. Howsoever to fill the gap of uncertainty the current review article has been prepared. However abridgment of all the Indian food and spices with anticancer property is the gigantic errand and can't be direct in bounded words.

In this review, we have summarized our view of the current state of knowledge on Indian food and spices towards their curing mysterious properties for the cancer. So far numerous reviews had been published in correlation between diets and cancer, but on our review we are scrupulously summarizing cancer related pharmacological activity, this review is based on either the results of large prospective studies or the few randomized controlled trials.

CAPSAICIN

Capsaicin and several related compounds which are called as capsaicinoids are produced as a secondary metabolites of chili peppers. And it had been linked with suppression of tumorigenesis. Capsaicin has exhibited its anticancer assets on animal models by suppressing carcinogenesis of the skin (5), colon (6), lung (7), tongue (8), and prostate (9, 10). In culture, capsaicin has also suppressed the growth of various human tumor cells (11, 12), including leukemic (13–15), gastric (16), hepatic (17), glioma (18), and prostate cells (9).

The mechanism of action of capsaicin is not fully understood, but it have been implicated due the roles of NADH oxidase activity (11), proteasome (9), cyclooxygenases (19), c-Jun NH2-terminal kinase (20), nuclear factor- κ B (21), peroxisome proliferator-

activated receptor γ (22, 23), peroxynitrite (18), and mitochondrial respiration (24). Its immunosuppressive effects had also been linked to its ability to suppress nuclear factor- κ B activation (25).

CURCUMIN

Curcumin (diferuloylmethane) is a polyphenol originated from the plant *Curcuma longa*, commonly known as turmeric. Its anti-cancer effect had been seen in a few clinical trials, mainly as a native chemoprevention agent in colon and pancreatic cancer, cervical neoplasia and Barrets metaplasia. Curcumin has a low systemic bioavailability after oral consumption which limits its therapeutic concentrations in tissues outside the gastrointestinal tract. Nevertheless, many pre-clinical studies had shown anti-carcinogenic effects in different tumor cell-lines and animal models.

For example, Labbozzetta et al. lay bared a multidrug-resistant (MDR) variant of the MCF-7 breast cancer cell line (MCF-7R) and found substantial anti-tumor activity of curcumin was on both cell lines. It has been thought anti-tumor effects of curcumin in breast cancer is may be either ER-dependent or ER-independent mechanisms; or it act as a drug transporter-mediated MDR reversal agent. [26]

The efficacy of curcumin as an anti-cancer agent was also shown in bladder cancer cell lines [27] and in prostate cancer [28, 32]. Moreover, the *in vivo* study revealed that curcumin induced apoptosis *in situ*, which inhibits the development of bladder carcinoma.

To demonstrate chemo-resistance reversal and enhance the activity of thalidomide and bortezomib used to treat patients with multiple myeloma was investigated along with curcumin by *in vitro* and in a xenograft model in nude mice [29, 30]. The results showed that curcumin inhibited the proliferation of human multiple myeloma cells regardless of their sensitivity to dexamethasone, doxorubicin, or melphalan.

In a separate study of human mammary epithelial carcinoma cells, prostate cancer cells and B-lymphoma cells grown *in vitro*, curcumin was found to induce apoptosis selectively in the malignant cell lines by increasing p53 expression at the G2 phase of the cell cycle and by releasing cytochrome c from mitochondria [31]. An interesting finding in this study was that curcumin appeared to be sparing of the normal epithelial cells by arresting them at the G0 phase of the cell cycle by down regulation of cyclin D1 and its related protein kinases

(Cdk4/Cdk6) or upregulation of the inhibitory protein p21Waf-1.

The mechanisms of curcumin-induced apoptosis have been tested from different aspects. One interesting finding in a recent publication shows that it activates the caspase enzymes as a trigger for apoptosis. [33]

ALLICIN

Alliin is an organo-sulfur compound obtained from garlic, a species in the family Alliaceae. When fresh garlic is chopped or crushed, the enzyme alliinase converts alliin into allicin, which is responsible for the aroma of fresh garlic.[34] The allicin generated is unstable and quickly changes into a series of other sulfur-containing compounds such as diallyl disulfide. [35]

Alliin induced activation of extracellular signal-regulated kinases 1 and 2 (ERK1/2) in human peripheral mononuclear cells which later leads to cell-mediated cytotoxicity in human peripheral mononuclear cells. [36]

Alliin has repressed the invasion and metastasis of human colon carcinoma cells *in vitro* at non-cytotoxic concentration through down-regulating the expression of vascular endothelial growth factor (VEGF), urokinase receptor (uPAR) and heparanase mRNA. [37] Alliin can inhibit telomerase

activity and induce apoptosis of gastric cancer SGC-7901 cells. [38]

Allicin had reduced the development of mammary cancer in animals and suppressed the growth of human breast cancer cells in culture. [39] Artesunate and allicin in combination exert synergistic effects on osteosarcoma cell proliferation and apoptosis. [40]

ANETHOLE

Anethole (anise camphor) is an organic compound that is extensively used as a flavoring substance. It is a derivative of phenylpropene, a type of aromatic compound that transpire widely in nature, in essential oils. It contributes a large component of the odor and flavor of anise and fennel (both in the botanical family Apiaceae), anise myrtle (Myrtaceae), liquorice (Fabaceae), camphor, magnolia blossoms, and star anise (Illiciaceae). [41]

Anethole has shown antibacterial activity against selected food-borne pathogens by making firstly a break through the permeability of cell membrane associated with generalized the integrality of membrane-disrupting effects, leading to the leakage of electrolytes as well as losses of proteins, and reducing sugars. These changes resulted in cell decomposition and

death eventually, and this corresponded to a simultaneous reduction in the number of viable bacteria. [42]

Anethole and its derivative anethole dithiolethione (ADT) have been shown to increase intracellular levels of glutathione and glutathioneS-transferase [43-45]. These two compounds and two other derivatives (eugenol and isoeugenol) can also act as antioxidants [46] with the ability to suppress tumour necrosis factor (TNF)-induced lipid peroxidation and generation of reactive oxygen species (ROS), and to reduce oxidative stress by acting as scavengers of hydroxyl radicals [43, 47].

Anethole has also been shown to block both inflammation and carcinogenesis. It suppresses activation of the activator protein 1 (AP-1) and nuclear factor-kappa B (NF- κ B) [48, 49], TNF-induced activation of c-JUN N-terminal kinase and mitogen-activated protein kinases (MAPK) [50, 51]. It is also a potent inhibitor of kappaB-alpha ($\text{I}\kappa\text{B}\alpha$) phosphorylation and degradation, and of expression of NF- κ B reporter gene. There is one report on the anticancer effect of anethole in vivo in a murine carcinoma model. [52].

CROCETIN

Crocetin is a natural apocarotenoid dicarboxylic acid that is obtained in the crocus

flower and *Gardenia jasminoides* (Saffron) [53] (fruits). It forms brick red crystals with a melting point of 285 °C.

Crocin and crocetin may provide neuroprotection in rats by reducing the production of various neurotoxic molecules, based on an in-vitro cell study.[54] Crocin and Diglucosylcrocetin inhibited early tumor antigen expression of adenovirus infected cells. [55].

Saffron inhibited the DEN-mediated elevations in numbers of cells positive for Ki-67, cyclooxygenase 2, inducible nitric oxide synthase, nuclear factor-kappa B p-65, and phosphorylated tumor necrosis factor receptor. [56] Crocetin proves to scavenge free radical and plays an important role in cellular function. Tumor incidence and histopathological studies proves crocetin is a potent antitumour agent. [57, 58]

Gingerol

Gingerol or [6]-gingerol, is the active constituent of fresh ginger rhizome (*Zingiber officinale* - Zingiberaceae). The [6]-gingerol, a major pungent ingredient of ginger is having a potent antiangiogenic activity in vitro and in vivo. [6]-gingerol may inhibit tumor growth and metastasis via its anti-angiogenic activity [59]. Topical application of [6]-gingerol inhibited COX-2

(cyclooxygenase-2) expression along with suppressed NF- κ B DNA binding activity in mouse skin. [59]

The proposed mechanisms of action of gingerol involved in anticancer and chemopreventive properties via multiple pathways that includes the inhibition of cyclooxygenase -2 (COX-2) expression by inhibiting p38 MAPK–NF- κ B [59],(mitogen activated protein kinase – necrosis factor kappa B) signaling pathway[60], Ovarian cancer Inhibitor NF- κ B [61].

Ginger extract has shown significant action on Liver cancer by reducing the elevated expression of TNF- α and NF- κ B rats. [62] It has also inhibited cell adhesion invasion motility in vitro in Breast cancer cell lines. [63]

Gingerol has also exhibited significant anti-cancer property against Skin cancer by enhancing apoptosis in Mouse [64] and against colon cancer by inhibition of leukotriene activity in mice mice. [65] It has also revealed noteworthy property against human liver tumor cell (lines) in vitro. [66]

CONCLUSION

Indian spice products have been proved a prime source for the treatment of cancers from a long era, many of them are consumed daily with the diet. They provide significant

protection against various cancers and many other diseases. The antioxidant medicinal plants and their products prevent us from the cancer and other diseases by protecting cells damage. Thus, consuming a rich diet of Indian spices will provide unquestionably health-shielding to us.

All the spices discussed in this review exhibit anticancer activities. Indian spices offer a great opportunity to us for discovery of not only totally new chemical classes of anticancer agents, but also a novel and potentially active remedies with relevant mechanisms of action. Since we can't cover all the Indian spices with anti-cancer property it recommend us to intensify our research towards anticancer properties of Indian spices. We may need also to formulate some novel formulation with this potent ingredient of Indian spices to build a healthy human society.

References:

1. Shanthy A, Bowman, Bryan T. Vinyard, 2004. Fast Food Consumption of U.S. Adults: Impact on Energy and Nutrient Intakes and Overweight Status. Journal of the American College of Nutrition Volume 23, Issue 2.

2. Doll R, Peto R., 1981. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. Journal of the National Cancer Institute; 66: 1191–308.
3. Miller AB., 2001. Diet in cancer prevention. http://www.who.int/ncd/cancer/publications/abstracts/abs_9810.05.
4. Vikas Chaurasia, Saurabh Pal, 2014. A Novel Approach for Breast Cancer Detection using Data Mining Techniques. International Journal of Innovative Research in Computer and Communication Engineering .Vol. 2, Issue 1.
5. Park KK, SurhYJ, 1997. Effects of capsaicin on chemically induced two-stage mouse skin carcinogenesis. Cancer Lett; 114:183-4.
6. Yoshitani SI, TanakaT, Kohno H, Takashima S, 2001. Chemo prevention of azoxymethane induced rat colon carcinogenesis by dietary capsaicin and rotenone. Int J Oncol, 19 :929-39.
7. JangJJ, KimSH, YunTK, 1989. Inhibitory effect of capsaicin on

- mouse lung tumor development. *In Vivo*, 3: 49-53.
8. Tanaka T, Kohno H, Sakata K, 2002. Modifying effects of dietary capsaicin and rotenone on 4-nitroquinoline 1-oxide-induced rat tongue carcinogenesis; 23:1361-7.
 9. Mori A, Lehmann S, O'Kelly J, 2006. Capsaicin, a component of red peppers, inhibits the growth of androgen-independent, p53 mutant prostate cancer cells. *Cancer Res*; 66:3222-9.
 10. Sanchez AM, Sanchez MG, Malagarie Cazenave S, Olea N, Diaz Laviada I, 2006. Induction of apoptosis in prostate tumor PC-3 cells and inhibition of xenograft prostate tumor growth by the vanilloid capsaicin. *Apoptosis*; 11:89-99.
 11. Morre DJ, Chueh PJ, Morre DM, 1995. Capsaicin inhibits preferentially the NAD Hoxidase and growth of transformed cell sinculture. *Proc Natl Acad Sci USA*; 92:1831-34.
 12. Morre DJ, Sun E, Geilen C, 1996. Capsaicin inhibits plasma membrane NADH oxidase and growth of human and mouse melanoma lines. *Eur J Cancer*; 32A:1995-2003.
 13. Kang SN, Chung SW, Kim TS, 2001. Capsaicin potentiates 1, 25-dihydroxyvitamin D3- and all-trans retinoic acid induced differentiation of human promyelocytic leukemia HL-60 cells. *Eur J Pharmacol* 420:83-90.
 14. Zhang J, Nagasaki M, Tanaka Y, Morikawa S., 2003. Capsaicin inhibits growth of adult T-cell leukemia cells. *Leuk Res*; 27:275-83.
 15. Ito K, Nakazato T, Yamato K, 2004. Induction of apoptosis in leukemic cells by homovanillic acid derivative, capsaicin, through oxidative stress: implication of phosphorylation of p53 at Ser-15 residue by reactive oxygenspecies. *Cancer Res*; 64:1071-8.
 16. Kim JD, Kim JM, Pyo JO, 1997. Capsaicin can alter the expression of tumor forming-related genes which might be followed by induction of apoptosis of a Korean stomach cancer cell line, SNU-1. *Cancer Let*; 120:235-41.
 17. Jung MY, Kang HJ, Moon A., 2001. Capsaicin induced apoptosis in

- SKHep-1hepatocarcinoma cells involves Bcl-2 down regulation and caspase-3 activation. *Cancer Lett*; 165:139-45.
18. Qiao S, Li W, Tsubouchi R, Haneda M, Murakami K, Yoshino M., 2005. Involvement of peroxy nitrite in capsaicin induced apoptosis of C6 glioma cells. *Neuro sci Res*; 51:175-83.
 19. Lee YS, Kwon EJ, Jin DQ, 2002. Redox status-dependent regulation of cyclooxygenases mediates the capsaicin-induced apoptosis in human neuro blastoma cells. *J Environ Pathol Toxicol Onco* 1; 21:113-20.
 20. Kang HJ, Soh Y, Kim MS, 2003. Roles of JNK-1 and p38 in selective induction of apoptosis by capsaicin in has transformed human breast epithelial cells. *Int J Cancer*; 103:475-82.
 21. Singh S, Natarajan K, Aggarwal BB. , 1996. Capsaicin (8 methyl-N-vanillyl-6-nonenamide) is a potent inhibitor of nuclear transcription factor-kappa B activation by diverse agents. *J Immunol*; 157:4412-20.
 22. Kim CS, Park WH, Park JY, 2004. Capsaicin, a spicy component of hot pepper, induces apoptosis by activation of the peroxisome proliferator-activated receptor gamma in HT-29 human colon cancer cells. *J Med Food*; 7:267-73.
 23. Parkb JY, Kawadab T, Han IS, 2004. Capsaicin inhibits the production of tumor necrosis factor alpha by LPS-stimulated murine macrophages, RAW 264.7: a PPAR gamma ligand-like action as a novel mechanism. *FEBSLett*; 572:266^70.
 24. HailN, Jr., Lotan R., 2002. Examining the role of mitochondrial respiration in vanilloid induced apoptosis. *J Natl Cancer Inst*; 94:1281^92.
 25. Sancho R, Lucena C, Macho A, 2002. Immunosuppressive activity of capsaicinoids: capsiate derived from sweet peppers inhibits NF-kappa B activation and is a potent anti-inflammatory compound in vivo. *EurJImmunol*; 32:1753^63.
 26. Labbozzetta, M, Notarbartolo M, Poma P, Maurici A, Inguglia L, Marchetti P, Rizzi M, Baruchello R, Simoni D, D'Alessandro N, 2009.

- Curcumin as a possible lead compound against hormone-independent, multidrug-resistant breast cancer. *Ann. N.Y. Acad. Sci.*, 1155, 278-83.
27. Tian B, Wang Z, Zhao Y, Wang D, Li Y, Ma L, Li X, Li J, Xiao N, Tian J, Rodriguez R, 2008. Effects of curcumin on bladder cancer cells and development of urothelial tumors in a rat bladder carcinogenesis model. *Cancer Lett*, 264, 299-308.
 28. Aggarwal BB, 2008. Prostate cancer and curcumin: add spice to your life. *Cancer Biol. Ther*, 7, 1427-35.
 29. Mendonça LM, Dos Santos G C, Antonucci G A, Dos Santos AC, Bianchi M L, Antunes L M, 2009. Evaluation of the cytotoxicity and genotoxicity of curcumin in PC12 cells. *Mutat. Res.*, 675, 29-34.
 30. Park J, Ayyappan V, Bae EK, Lee C, Kim BS, Kim BK, Lee YY, Ahn KS, Yoon SS, 2008. Curcumin in combination with bortezomib synergistically induced apoptosis in human multiple myeloma U266 cells. *Mol. Oncol.*, 2, 317-26.
 31. Piwocka K, Bielak Mijewska A, Sikora E, 2002. Curcumin induces caspase-3-independent apoptosis in human multidrug resistant cells. *Ann. N.Y. Acad. Sci.*, 973, 250-4.
 32. Dorai T, Cao YC, Dorai B, Buttyan R, Katz AE, 2001. Therapeutic potential of curcumin in human prostate cancer. III. Curcumin inhibits proliferation, induces apoptosis, and inhibits angiogenesis of LNCaP prostate cancer cells in vivo. *Prostate*, 47, 293-303.
 33. Lin YT, Wang LF, Hsu YC, 2009. Curcuminoids suppress the growth of pharynx and nasopharyngeal carcinoma cells through induced apoptosis. *J. Agric. Food Chem.*, 57, 3765-70.
 34. Kourounakis PN, Rekkas EA, 1991. "Effect on active oxygen species of alliin and *Allium sativum* (garlic) powder". *Res Commun Chem Pathol Pharmacol*. 74 (2): 249–252.
 35. Ilic, Dusica, Nikolic, Vesna, Nikolic, Ljubisa, Stankovic, Mihajlo, Stanojevic, Ljiljana, Cakic, Milorad 2011. "Allicin and related compounds: Biosynthesis, synthesis and pharmacological activity". *Facta Universitatis*. 9 (1): 9–20.

36. Miriam Patya, Miriam Patya, A Novogrodsky, M Feldmann, Muayad A, Zahalka, Muayad A, Zahalka, Alexey Vanichkin , Alexey Vanichkin, Aharon Rabinkov, Aharon Rabinkov, Talia Miron, Talia Miron, David Mirelman, David Mirelman, Meir Wilchek, Meir Wilchek, Harry M, Lander , Harry M, Lander, Abraham Novogrodsky, Abraham Novogrodsky, 2004. Allicin stimulates lymphocytes and elicits an antitumor effect a possible role of p21ras. *Int Immunol* 16 (2): 275-281.
37. Zhonghua Yi, Xue Za Zhi, 2009. Effects of allicin on invasion and metastasis of colon cancer LoVo cell line in vitro. 26; 89(20):1382-6.
38. Li Sun, Xu Wang, World J, 2003. Effects of allicin on both telomerase activity and apoptosis in gastric cancer SGC-7901 cells; 9 (9):1930-1934.
39. Sharma D, Mishra A, Yagnik S, Ganuly G, 2011. Independent of estrogen receptor status. *Jour. of med pharm. allied science.* 19(8-9): 563-567.
40. Drukarch B, Schepens E, Stoof JC, Langeveld CH, 1997. Anethole dithiolethione prevents oxidative damage in glutathione depleted astrocytes. *Eur Pharmacol* 329 (2/3): 259-262.
41. Bouthillier L, Charbonneau M, Brodeur J, 1996. Assessment of the role of glutathione conjugation in the protection afforded by anethol dithiolthione against hexachloro-1, 3-butadiene-induced nephrotoxicity. *Toxicol Appl Pharmacol* 139(1): 177-185.
42. V Bondet W, Brand Williams Bersetf C, 1997. Kinetics and Mechanisms of Antioxidant Activity using the DPPH Free Radical Method. *LWT - Food Science and Technology* Volume 30, Issue 6, Pages 609-615.
43. Rajakumar DV, Rao D, 1993. Dehydro zingerone and isoeugenol as inhibitors of lipid peroxidation and as free radical scavengers. *Biochem Pharmacol* 46(11): 2067-2072.
44. Chainy GBN, Manna SK, Chaturvedi MM, Aggarwal BB, 2000. Anethole blocks both early and late cellular

- responses transduced by tumor necrosis factor: effect on NFB, AP-1, JNK, MAPKK and apoptosis. *Oncogene* 19(25): 2943-2950.
45. Aggarwal BB, Shishodia S, 2006. Molecular targets of dietary agents for prevention and therapy of cancer. *Biochem Pharmacol* 71(10): 1397-1421.
46. Baeurle PA, Baichwal VR, 1997. NF- κ B as a frequent target for immunosuppressive and anti-inflammatory molecules. *Adv Immunol* 65: 111-137.
47. Karin M, 1996. The regulation of AP-1 activity by mitogen-activated protein kinases. *Phil Trans Royal Soci London, Biol Sci* 351(1336): 127-134.
48. Eferl R, Wagner EF. 2003. AP-1: A double edged sword in tumorigenesis. *Nat Rev Cancer* 3(11): 859-868.
49. Al M M, Al Harbi, S Qureshi, M Raza, M M Ahmed, A B Giangreco A H Shah, 1995. Influence of anethole treatment on the tumour induced by Ehrlich ascites carcinoma cells in paw of Swiss albino mice. *Eur. J. Cancer Prev.*, 4, 307–318.
50. Umigai N, Murakami K, Ulit MV, 2011. "The pharmacokinetic profile of crocetin in healthy adult human volunteers after a single oral administration". *Phytomedicine*. 18 (7): 575–8.
51. Nam KN, Park YM, Jung HJ, Lee JY, Min BD, Park SU, Jung WS, Cho KH, Park JH, Kang I, Hong JW, Lee EH, 2010. "Anti-inflammatory effects of crocin and crocetin in rat brain microglial cells. *European Journal of Pharmacology*. 648 (1–3): 110–6.
52. Molnár J, Szabó D, Pusztai R, Mucsi I, Berek L, Ocsosvzki I, Kawata E, Shoyama Y, 2000. Membrane associated antitumor effects of crocine-, ginsenoside- and cannabinoid derivates. *Anticancer Research*, 20(2A):861-867.
53. Amr Amin, Alaaeldin A. Hamza, Khuloud Bajbouj, Salman Ashraf, Sayel Daoud. Saffron, 2011. A potential candidate for a novel anticancer drug against hepatocellular carcinoma. *Hepatology* Volume 54, Issue 3, 2, Pages 857–867.

54. Venkatraman Magesh, Jayapal Prince Vijaya Singh, Karupaya Selvendiran, Ganapathy Ekambaram, Dhanapal Sakthisekaran, 2006. Antitumour activity of crocetin in accordance to tumor incidence, antioxidant status, drug metabolizing enzymes and histo pathological studies. *Molecular and Cellular Biochemistry*, Volume 287, Issue 1–2, pp 127–135.
55. Sue Ok Kim, Joydeb Kumar Kundu, Young Kee Shin, Jin Hong Park, Myung Haing Cho, Tae Yoon Kim & YoungJoon Surh, 2005. [6]-Gingerol inhibits COX-2 expression by blocking the activation of p38 MAP kinase and NF- κ B in phorbol ester-stimulated mouse skin. *Oncogene* 24, 2558–2567.
56. Yogeshwer Shukla, Madhulika Singh. 2007. Cancer preventive properties of ginger A brief review. *Food and Chemical Toxicology* Volume 45, Issue 5, Pages 683-690.
57. Jennifer Rhode, Sarah Fogoros, Suzanna Zick, Heather Wahl, Kent A Griffith, Jennifer Huang, J Rebecca Liu, 2007. Ginger inhibits cell growth and modulates angiogenic factors in ovarian cancer cells. *BMC Complementary and Alternative Medicine*, Volume 7, Number 1, Page 1
58. Shafina Hanim, Mohd Habib, Suzana Makpol, Noor Aini Abdul Hamid, Srijit Das, Wan Zurinah Wan Ngah, Yasmin Anum Mohd Yusof. 2008. Ginger extract (*Zingiber officinale*) has anti-cancer and anti-inflammatory effects on ethionine-induced hepatoma rats. *Clinics* vol.63 no.6 São Paulo.
59. Hyun Sook Lee, Eun Young Seo, Nam E Kang, Woo Kyung Kim. 2008. [6]-Gingerol inhibits metastasis of MDA-MB-231 human breast cancer cells. *The Journal of Nutritional Biochemistry* Volume 19, Issue 5, Pages 313-319.
60. Nidhi Nigam, Kulpreet Bhui, Sahdeo Prasad, Jasmine George, Shukla Yogeshwer, 2009. [6]-Gingerol induces reactive oxygen species regulated mitochondrial cell death pathway in human epidermoid carcinoma A431 cells. *Chemico-Biological Interactions*. Volume 181, Issue 1, Pages 77-84.

61. Chul Ho Jeong, Ann M Bode, Angelo Pugliese, Yong Yeon Cho, Hong Gyum Kim, Jung-Hyun Shim, Young Jin Jeon, Honglin Li, Hualiang Jiang and Zigang Dong, 2009. [6] Gingerol Suppresses Colon Cancer Growth by Targeting Leukotriene A4 Hydrolase. Cancer Research.
62. Fang Peng, Qiaofeng Tao, Xiumei Wu, Hui Dou, Shawn Spencer, Chaoyong Mang, Lu Xu, Lianli Sun, Yu Zhao, Haibo Li, Su Zeng, Guangming Liu, Xiaojiang Hao, 2012. Cytotoxic, cytoprotective and antioxidant effects of isolated phenolic compounds from fresh ginger. *Fitoterapia* Volume 83, Issue 3, Pages 568-585.