



Review Article

ANTI CANCER POTENTIALS OF INDIAN SPICES - A SCIENTIFIC APPRAISAL

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ABSTRACT

Cancer is the leading cause of death in economically developed countries and second leading cause of death in developing countries. It accounts for 7.4 million deaths (around 13 % of all deaths) in 2004 according to WHO. Recently great emphasis has been given towards the researches on Complementary and Alternative medicine that deal with cancer management. The present day need for new ideal drugs has prompted various researches evaluating possible anticancer agents in fruits, vegetables, herbs and spices. Thus in the present paper an attempt has been made to systematically reviews the anticancer potentials of very common Indian herbs mentioned in *Ayurveda* that are widely used in almost every kitchen in India as ingredients of Indian traditional dishes. India is known as 'the home of spices and has been a hub of spice cultivation and processing from ancient times. Evidence-based resources include both databases and compendiums of clinical trials, systematic reviews, meta-analyses and specialty journals devoted to disseminating evidence-based information revealed that the Indian spices like *Crocus sativus*, *Curcuma longa*, *Syzygium aromaticum*, *Piper nigrum*, *Piper longum*, *Allium Sativum*, *Zingiber officinale*, *Nigella sativa*, *Trigonella foenum*, *Myristica fragrans* possess anticancer activity. These findings from scientific studies marks a significant contribution as prevention of cancer as these spices are readily available and can be used as a condiments to any cooking procedure. It is recommended that families of every household should include spices in preparation of food for their family members to have cancer prevention.

INTRODUCTION

Cancer is the leading cause of death in economically developed countries and second leading cause of death in developing countries¹. The World Health Organisation (WHO) has stated that Cancer is the major fatal challenge to be met in the 21st century (Roopesh et al., 2010). It is the major cause of death or morbidity in human population². It accounts for 7.4 million deaths (around 13 % of all deaths) in 2004 according to WHO. Unfortunately, more than 70% of all cancer deaths occur in low and middle income countries. There has been significant increase in the incidence of cancer in recent times, this is mainly attributed to urbanization, industrialization, lifestyle changes, increased population and life span (increased elderly population).³ Cancer is the second leading cause of death in the united states.⁴

Cancer is the disease of various aetiology and involves a wide variety of clinical syndromes. The basic underlying pathological event is disorganized excessive uncontrolled division of cells leading to impairment of function of the relevant organs ultimately leading to

mortality. The human body is made up of different cells. Cells divide and multiply according to the need of body system. However when balance between Protoncogenes and tumor suppressor gene is disturbed due to various factors, these cells continue to divide needlessly resulting in ever – growth, it is known as a tumour.⁵

The theory of neoplastic diseases is available since Vedic period. The first reference is traced from *Atharva Veda* where the neoplasia have been described under the heading of *Apache* or *Apachit*. Later on during the *Samhita* period our ancient scientists of *Ayurveda* like *Charak*, *Sushrut* and *Vagbhat* were well aware of malignant disorders under the heading of *Arbuda*, *Asadhya Vrana* etc and their management along with prognosis. According to *Ayurveda* characteristics of *Arbuda* are described as a deep rooted, immovable circular growth which is ever growing and everlasting in nature. It is associated with mild pain, but it is devoid of any inflammatory changes.

Nowadays Multidisciplinary scientific investigations are doing their best efforts to combat this disease, and several chemotherapeutic, cytotoxic and immuno - enhancing agents along with radio therapy are available for the treatment of cancer but the sure- shot perfect cure is yet to be brought into world of medicine. Recently great emphasis has been given towards the researches on Complementary and Alternative medicine that deal with cancer management. Several studies have been conducted on herbs under the multitude of ethano botanical grounds. For example Hartwell has collected data on about 3000 plants; those of which possesses anti cancer properties and have subsequently been used as potent anti cancer drugs. Thus the emphasis is made over the natural products and a number of common herbs that are screened for their anti tumor and anti leukemic properties. Extensive research during the last thirty years has revealed much about the biology of cancer. Drugs used to treat most cancers are those that can block cell signalling, including growth factor signalling (e.g., COX2); inflammation (e.g., inflammatory cytokines: NF-kappa B, TNF, iL-1,IL-6 Chemokines); drug resistance gene products (e.g, multi drug resistance); cell cycle proteins (e.g., cyclin D1 and Cyclin E); angiogenesis(e.g., vascular endothelial growth factor); invasion (e.g., matrix metalloproteinases); antiapoptosis (e.g., bcl-2, bcl -X (L), XIAP, surviving, FLIP); and cellular proliferation (e.g., C-myc, AP-1 growth factors). Numerous reports have suggested that *Ayurvedic* plants and their components mediate their effect by modulating several of these recently identified therapeutic targets⁶ and Plants have long been used in the treatment of cancer.⁷

In the US, the National Cancer Institute collected about 35,000 plant samples from 20 countries and has screened around 114,000 extracts for anticancer activity of the 92 anti cancer drugs, commercially available prior to 1983⁸ and also it has been observed that among approved anti cancer drugs between 1983 and 1994, 60 % are of natural origin.⁹ Among 121 prescription drugs in use today for cancer treatment, 90 are derived from plants, almost 74 % of these, including Taxol were discovered by investigating a folklore claim¹⁰

The present day need for new ideal drugs has prompted various researches evaluating possible anti-cancer agents in fruits, vegetables, herbs and spices. Thus in the present paper an attempt has been made to systematically reviews the Anti Cancer potentials of very common Indian herbs mentioned in *Ayurveda* that are widely used in almost every kitchen in India as ingredients of Indian traditional dishes.

India is world renowned for its biodiversity and its deep rooted cultural heritage & traditions. India is known as 'the home of spices' and has been a hub of spice cultivation and processing from ancient times, therefore Indian food items are in more demand due to high spice content in them as a result Indian food is

making its presence felt on a global stage. In fact, the most remarkable aspect being: Indian spices not only add to the taste, aroma, flavour, but consumption of spices provides infinite health benefits. These spices prove to be the perfect remedy against a range of diseases like common cold, cough to cancerous tumours. Almost all Indian spices are associated with some unique quality.

METHODS

Evidence-based resources include both 1) databases and compendiums of clinical trials, systematic reviews, meta-analyses and 2) specialty journals devoted to disseminating evidence-based information. Various databases like MEDLINE, PUBMED, are systematically searched for peer-reviewed published research studies. In vitro analysis, as well as experimental trials was included in the present review.

RESULTS & DISCUSSION:

Systematic search from evidence based resources revealed that the following Indian spices possess Anti Cancer activity.

1. *Kesar* (*Crocus sativus*)
2. *Haridra* (*Curcuma longa*)
3. *Lavang* (*Syzygium aromaticum*)
4. *Kali marich* (*Piper nigrum*)
5. *Pipalli* (*Piper longum*)
6. *Lashuna* (*Allium Sativum*)
7. *Shunthi* (*Zingiber officinale*)
8. *Kaulinji* (*Nigella sativa*)
9. *Medhika* (*Trigonella foenum*)
10. *Jatiphala* (*Myristica fragrans*)

The important studies for the individual above mentioned herbs are summarized as below:

1. ***Kesar (Crocus sativus)***
Common Name: Saffron



The anti tumour activity of Saffron extract was conducted against intraperitoneally transplanted carcinoma-180 (S-180), Ehrlich Ascites Carcinoma (EAC) and Dalton's lymphoma Ascites (DLA) tumours in mice. Oral administration of 200mg/kg body wt. of the extract increased the life span of S-180, EAC, DLA Tumour bearing mice to 111.0%, 83.5% & 112.5% respectively. The same extract was found to be cytotoxic to P38B,S-180 EAC & DLA Tumour Cells in vitro. The haematological and biochemical parameters were found

within the normal range during toxicological studies. Hence these results indicate the potential use of saffron as an anticancer agent.¹¹

Crocetin, an important carotenoid constituent of saffron, has also shown significant potential as an anti-tumor agent in animal models and cell culture systems. Crocetin affects the growth of cancer cells by inhibiting nucleic acid synthesis, enhancing anti-oxidative system, inducing apoptosis and hindering growth factor signaling pathways.¹²

Likewise Bakshi et al (2010) reported that crocin induces apoptosis and G1 -phase cell cycle arrest of BxPC- 3 cells (human pancreatic cancer cell line), at the same time, decreasing cell viability in dose dependent and time dependent manners. Cells treated with 10µg/L crocin exhibited apoptotic morphology and reduction of volume. During DNA analysis typical ladders were observed as early as 12 hrs after treatment that is indicative of apoptosis. These results suggest its potential as a supplementary chemotherapeutic agent.¹³

2. *Haridra (Curcuma longa)*

Common Name: Turmeric



Curcumin (1,7-bis-hydroxy-3-methoxyphenyl)-1E,6E-hepatadiene-3,5-dione or diferuloyl methane) is a poly phenol derived from the *Curcuma longa* plant, commonly name as turmeric. This substance has been used extensively in Ayurvedic formulations for centuries for its anti oxidant, Analgesic, Anti inflammatory, and Anti septic activity. More recently curcumin has been found to possess anti cancer properties linked to its pro-apoptotic and anti proliferative actions. Despite increasing evidence indicating that different cation channels can be a molecular target for curcumin, very little is known about the effect of curcumin on chloride channels since (i) the molecular structure of curcumin indicates that the substance could potentially interact with chloride channels (ii) Chloride channels play a role during a apoptotic process and regulation of the cell volume and (iii) apoptosis is well known effect of curcumin after the proper investigations it was confirmed that curcumin could (i) exert a modulatory effect on the swelling activated chloride current ICI (swell) in human cell system, therefore affect cell volume regulation and ultimately modulate cell survival.¹⁴ Curcumin (diferuloyl methane) has been found to possess anti cancer activities via its effects on variety of biological pathways involved in mutagenesis and metastasis.¹⁵

Extensive research over the last half century has revealed several important function of curcumin. It binds to a variety of proteins and inhibits the activity of various kinases. By modulating the activation of various transcription factors, curcumin regulates the expression of inflammatory enzymes, cytokines, adhesion molecules and cell survival proteins. Curcumin also downregulates cyclin D1, cyclin E, and MDM2; and upregulates p21,p27 and p53. xApoptosis is well known effect of curcumin after the proper investigations it was confirmed that curcumin could (i) exert a modulatory effect on the swelling activated chloride current ICI (swell) in human cell system, therefore affect cell volume regulation and ultimately modulate cell survival.

Structure of curcumin enables it to inhibit multiple kinases. Kinases pathways are like phone lines which carry messages to cancer cells. kinase inhibitors can cut these lines and stop the growth of some types of cancer cells. Curcumin effectively blocks some of these lines. Nuclear growth factor KB is blocked by curcumin.¹⁶

3. *Lavang (Syzygium aromaticum)*

Common Name: Clove



Eugenol, the major constituent of *Syzygium aromaticum*, is a phenylpropene, an allyl chain-substituted guaiacol. Eugenol is a member of the phenylpropanoids class of chemical compounds has been widely used for its anaesthetic and analgesic action in dentistry. Eugenol exhibits pharmacological effects on almost all systems. Since most of the drugs used in the cancer are apoptotic inducers, the apoptotic effect and anticancer mechanism of eugenol were investigated against colon cancer cells. Antiproliferative effect was estimated using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay]. MTT assay signified the antiproliferative nature of eugenol against the tested colon cancer cells. PI staining indicated increasing accumulation of cells at sub-G1-phase. Eugenol treatment resulted in reduction of intracellular non-protein thiols and increase in the earlier lipid layer break. In this study the result showed the molecular mechanism of eugenol-induced apoptosis in human colon cancer cells and this research will further enhance eugenol as a potential chemo preventive agent against colon cancer. (<http://www.ncbi.nlm.nih.gov/pubmed/21044050>)

Similarly In other study, it was known that Eugenol increases the chemotherapeutic potential of gemcitabine and exhibit anticarcinogenic and anti inflammatory activity in human cervical cancer cells.¹⁷

4. Kali marich (*Piper nigrum*)

Common Name: Black pepper



In a recent study, in vivo effect of piperine on serum and tissue glycoproteins level in benzo(a) pyrene- induced lung carcinogenesis in swiss albino mice was studied. It was observed that piperine was found to suppress benzo(a) pyrene(B(a)p)- induced lung cancer in swiss albino mice. In lung cancer bearing mice altered level of total proteins and protein bound carbohydrate components (hexose, hexosamine, sialic acid) were observed in serum, lung and liver tissues.¹⁸

In an another study the alkaloid Piperidine was purified by refluxion method to check the anti tumour activity which shows 51.38% of inhibition at 5µg/ml concentration that confirms the compound piperidine to be used as anticancer drug for further mechanistic works.¹⁹

Similarly a study comprising of evaluation of anti oxidant, anti inflammatory and Anti cancer activities of extracts and compounds from Black pepper concluded that the extracts of Black pepper at 200 µg/mL and its compound at 25µg/mL inhibited Lipid Peroxidation (LPO) by 45-85%, Cox enzymes by 31 – 80 % and cancer cell proliferation by 3.5 to 86.8%. Overall these results suggest that Black pepper and its constituents exhibit anti inflammatory, Antioxidant and Anticancer activities.²⁰

5. Pipalli (*Piper longum*)

Common Name: Long Pipalli



A study was conducted on alcoholic extract of the fruits of the *Piper longum* and its major component piperine for their immunomodulatory and anti tumour activity. Alcoholic extract of the fruit of *piper longum* was 100 % toxic at a concentration of 500µg/ml to

Dalton's lymphoma Ascites (DLA) cells and 250 µg/ml to Ehrlich Ascites Carcinoma (EAC) cells.

Piperine was found to be cytotoxic towards DLA and EAC cells at a concentration of 250 µg/ml. Alcoholic extract and Piperine was also found to produce cytotoxicity towards L929 cells in culture at a concentration of 100 and 50 µg/ml, respectively.

Administration of Alcoholic extract of *Piper longum* (10 mg/dose/animal) as well as piperine (1.14mg/dose/animal) could inhibit the solid tumour development in mice induced with DLA cells and increase the life span of mice bearing Ehrlich Ascites Carcinoma tumour to 37.3 and 58.8 % respectively.²¹

Other studies also prove that piperine possess an anti oxidative property in vitro and in vivo conditions.²²

6. Lashuna (*Allium Sativum*)

Common Name: Garlic



Researches over the past 15 years has revealed that Garlic derived Organo sulphur compounds (OSC) can not only inhibit chemically induced cancers but can suppress growth of cancer cells in culture and in vivo. It is a well known epidemiologic evidence that high garlic intake decreases the incidence of prostate cancer, and compounds isolated from garlic have been shown to have cancer-preventive and tumor-suppressive effects. Recent in vitro study titled "Garlic-derived S-allylmercaptocysteine is a novel in vivo antimetastatic agent for androgen-independent prostate cancer" by Howard EW and his team have shown that garlic-derived organosulfur compound S-allylmercaptocysteine suppresses invasion and cell motility of androgen-independent prostate cancer cells via the up-regulation of cell-adhesion molecule E-cadherin. S-allylmercaptocysteine is therefore a potential antimetastatic drug.

Oral administration of Aged Garlic extract (AGE) can significantly reduce tumour growth and animal mortality in the MBT2 murine bladder cancer model. The result suggests that *Allium sativum* is potentially an effective therapy for bladder cancer.²³

A major constituent of Garlic, Diallyl trisulphide (DATS) was studied on growth of PC-3 human prostate cancer xenograft in vivo by Xiao et al (2006). DATS was administered orally (6 micromol, thrice in a week) to male athymic mice s.c. implanted with PC-3 cells. It was observed that DATS administration inhibits growth of PC-3 xenografts in

association with induction of proapoptotic proteins Bax and Bak.²⁴

7. *Shunthi (Zingiber officinale)*

Common Name: Zinger



A study shows that in the choline- deficient diet supplemented with ginger in male wistar rats, the expression of NFkB (Nuclear Factor-Kappa B) was observed to be significantly reduced. A significant correlation was demonstrated between NFkB and TNF- α (tumour necrosis factor α) in the choline deficient diet group but not in the choline deficient diet treated with ginger extract group. Ginger extract significantly reduced the elevated expression of NFkB and TNF- α in rats with liver cancer.²⁵

In other study Ethyl acetate fraction of ginger extract can inhibit the expression of the two important molecular targets of cancer, the human telomerase reverse transcriptase (h TERT) and c-Myc, in A 549 lung cancer cells in a time- and concentration - dependent manner. Telomerase inhibition and Myc inhibition are considered cancer- specific targets for cancer therapy and thus this can be used as a supplementary therapeutic agent.²⁶

Whole ginger extract exerts significant growth inhibitory and death inhibitory effects in a spectrum of prostate cancer cells. Comprehensive studies have confirmed that whole ginger extract perturbed cell - cycle progression, impaired reproductive capacity, modulated cell cycle and apoptosis regulatory molecule and induced a caspase - driven mitochondrial mediated apoptosis in human prostate cancer cells. Tumour tissue from whole ginger extract treated mice showed reduced proliferation index and apoptosis compared with controls²⁷.

8. *Kaulinji (Nigella sativa)*

Common Name: Black Fennel



Recently in 2012 an article titled 'Thymoquinone as an anticancer agent: evidence from

inhibition of cancer cells viability and invasion in vitro and tumour growth *in vivo*' by Samir Attoub and his team was published in journal of fundamental and clinical Pharmacology. The purpose of this study was to investigate the potential impact of thymoquinone (TQ), the major constituent of *Nigella sativa* on survival, invasion of cancer cells in vitro, and tumour growth *in vivo*. Exposure of cells derived from lung (LNM35), liver (HepG2), colon (HT29), melanoma (MDA-MB-435), and breast (MDA-MB-231 and MCF-7) tumors to increasing TQ concentrations resulted in a significant inhibition of viability through the inhibition of Akt phosphorylation leading to DNA damage and activation of the mitochondrial-signaling proapoptotic pathway.

In view of the available experimental findings, it was observed that thymoquinone and/or its analogues may have clinical potential as an anticancer agent alone or in combination with chemotherapeutic drugs such as cisplatin.

Similarly in an another experimental study, thymoquinone exhibited strong anti proliferative effect in breast cancer cells and when combined with doxorubicin and 5- fluorouracil, increased cytotoxicity. Moreover it was observed that anti tumor effect of thymoquinone may also be mediated through modulation of the Peroxisome proliferator-activated receptor (PPAR) - γ activation pathway.²⁸

9. *Medhika (Trigonella foenum)*

Common Name: Fenugreek



Seeds of the plant *Trigonella foenum* commonly called fenugreek are cytotoxic in vitro to a cancer cells but not to normal cells. There was a growth inhibitory to breast, pancreatic and prostate cancer cell line (PCa) after treatment with 10-15 micro gram/ml of seed extract for 72 hrs.²⁹

Similarly the results from the in vitro experiments, indicated that diosgenin a major steroidal saponin constituent of Fenugreek inhibits cell growth and induces apoptosis in the HT-29 human colon cancer cell line in a dose dependent manner.³⁰

10. *Jatiphala (Myristica fragrans)***Common Name: Nutmeg**

Methanol extract of *Myristica fragrans* was used to study the effect on jurkat human leukemia T cells line and at the concentration of 50 and 100 µg/mL, the methanol extract of *Myristica fragrans* significantly inhibited jurkat cell proliferation and induced apoptosis as detected by annexin V staining.³¹

CONCLUSION AND RECOMMENDATION

These findings from above mentioned scientific studies marks a significant contribution as prevention of cancer as these above mentioned spices are readily available and can be used as a condiments to any cooking procedure.

In the light of this conclusion it is recommended that families of every household should include spices in preparation of food for their family members to have cancer prevention.

Furthermore, substantial researches have to be done on these Indian medicinal spices to find a novel agent to treat and prevent cancer.

Thus lastly it can be understood that *Ayurvedic* sciences has broad scope to derive the ideal Anti cancer agent from medicinal plants, which need a series of systematic research and investigations.

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