



Therapeutic plants of Siddha Medicine having Anticancer effects : A Review

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Abstract

Cancer is a well know dreadful diseases all over the world. Several research data possessing that, southern part of India has reported more cancer cases in the last decades. Siddha system of medicine has its unique way of treating very rare and life threatening diseases, In that way this system have its own way of clinical aspects, diagnosis, treatment and management of complications for almost all 4448 diseases mentioned in its literature.

In siddha cancer is mentioned by various names (synonyms) such as *putru*, *kazhzhalai*, *sathai valarchi*, *vipuruthi* etc. Apart from the literatures has mentioned anatomical part based indication for specific drugs such as *Kanna Putru* (Oral cancer), *Linga Putru* (Male Genital cancer), *Sthana Putru* (Breast cancer) etc. In this work, reviewed the indications for several herbs exclusive for cancer and their recent research on cancer were recorded. The data suggesting that, the selected herbs showing potent anticancer activity in invitro and animal model of research. Furthermore intention to raise awareness among public to promote siddha medicine for the management of various types of cancers.

Keywords

Siddha, Cancer disease, chronic diseases. Cancer care, herbs.

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INTRODUCTION

Cancer, group of more than 100 distinct diseases characterized by uncontrolled growth of abnormal cells in the body, tumors or neoplasms are abnormal growth of cells arising from malfunctions in the regulatory mechanism that oversee the cell growth and development. However, only some types of tumors threaten health and life, the most threatening tumors are those invade and destroy healthy tissues in the body's major organ systems by gaining access to the circulatory or lymphatic, tumors that grow and spread aggressively in this manner are designated as malignant or cancer.

Nowadays various sophisticated treatments are available for cancer such as surgery, radiation therapy, chemotherapy, immunotherapy, targeted therapy, hormone therapy, stem cell transplant, precision medicine, biomarker testing for cancer treatment, though all this treatment measures are not affordable to all population and it has notable ill effects.

Due to severe ill effect, patients are moving towards Indian traditional system of medicines like Siddha, Ayurveda, Unani etc for better management and to prevent the treatment burden (complications) of the population.

Siddha system is one among these Indian traditional system of medicine found by the siddhars, represented the spiritual thinking, detailed observation and various treatment measures to cure the life threatening condition like cancer called as *puttru*, *vipuruthi*, *kazhalai*, *megakatti*, *kandamalai*, *kiranthinoigal*, *pilavai* etc, but all the thoughts of the siddhars are given as verses scattered in various siddha literatures. In this review anti-cancer plants as indicated for cancer in siddha text have been highlighted and revisited.

Plants with anticancer activity

1. Alangium salviifolium

In siddha texts *Therayar yamaga venba* the seeds of this plant is used as a rejuvenating drug along with pepper and other ingredients, since it is a rejuvenating drug it is used as a karpam to prevent aging and against many life threatening diseases.

The phytoconstituents like sterols, glycosides, saponins, carbohydrates, alkaloids, flavonoids, tannins, proteins and triterpenoids are identified in the ethanolic, chloroform, alcohol and distilled water extract of *Alangium salviifolium* (AS) [Cornaceae (Alangiaceae)] seeds, flowers, roots and leaves showed significant antitumor activity against Ehrlich Ascites Carcinoma (EAC) in mice at the doses of 10 mg/kg body weight intraperitoneally. The anticancer activities of chloroform extract of *A. salviifolium* are probably due to the presence of alkaloid, phenolic compounds, flavonoids as well as terpenoids. Flavanoids such as quercetin, kaemferol and their glycosides showed anticancer activity¹. They also alter signal transduction in pathways leading to tumor growth and stimulate apoptosis in tumor cell lines.

2. Acorus calamus

Several essential oils bioactive compounds like β -asarone (46.78%), linalool (0.41), farnesol (11.09%), methyleugenol (6.10%), α - and β -pinene (both 0.06%), [E]-caryophyllene (0.11%), β -elemene (0.39%), ocimene (0.7%), aromadendrene (0.26%), camphor (0.03%), from *Acorus calamus* (Araceae) were identified for the antitumor activity².

The plant possesses anti-tumor properties at the dose of 30 μ g/ml. Sesquiterpenes, phenylpropanoid etc. are isolated from of the ethanolic extract of *A. calamus* rhizomes and were evaluated for anticancer activity. The ethanolic extract of *A. calamus* dried aerial part showed antiproliferative activity at dose of 250-500 mg/kg.

3. Centella asiatica

In siddha text Aathmaratcha amirthamennum vaithiya sara sangeraham vallarai nei prepared from its leaves is used to cure Yoni putru (vaginal cancer). The aqueous extract (AE) of *Centella asiatica* leaves had a promising activity against mouse melanoma, human breast cancer and rat glioma cell lines, with IC50 values of 698.0, 648.0 and 1000.0 μ g/mL, respectively. The ability of methanolic extract of *C. asiatica* to induce apoptosis in different cancer cell lines, Triterpenes, phenolic and flavanoids constituents are responsible for the antiproliferative activity³.

4. Crocus sativus

Crocetin, crocetin, picrocrocetin and safranal are isolated from 80% ethanolic extracts of the whole plant of *Crocus sativus* (Iridaceae) have been reported to inhibit cell growth of human tumor cells. Saffron can prevent chemically induced skin carcinogenesis in Swiss Albino Mice. Crocin inhibits proliferation, nucleic acid synthesis and induces apoptosis in the human tongue squamous cell Carcinoma⁴.

5. Allium sativum

In siddha texts *allium sativum* is used externally to treat small growth or lumps. The compound allicin, methyl allyl trisulfide, and diallyl trisulfide have antibacterial, antithrombotic, and anticancer activities respectively. It is a remarkable plant, which has multiple beneficial health effects such as hypolipidemic, antiarthritic, antimicrobial, antithrombotic, hypoglycemic and antitumor activities. Different garlic preparations including fresh garlic extract, aged garlic, garlic oil and a number of organo sulfur compounds derived from garlic shown to have chemopreventive activity. The chemopreventive activity has been attributed to the presence of organo sulfur compounds in garlic⁵. The two major compounds in aged garlic, S-allylcysteine and S-allylmercapto-L-cysteine possess the highest radical scavenging activity. In addition, S-allylcysteine has been found to reduce the growth of chemically induced and transplantable tumors in animal models. Therefore, the use of garlic may provide some kind of protection from cancer development.

6. Boerhavia diffusa

Boerhavia diffusa (Linn.) (Syn. *B. repens* L.; *B. procumbens* Roxb) commonly known as "Punarnava" in indian system of medicine is a perennial creeping herb belong to family Nyctaginaceae. Its ethanolic extract showed cytotoxic effect against Hela cell lines⁶ and inhibit the S-phase of the cell cycle. It also inhibits the growth of cancer cells in DMBA- induced cancer carcinogenesis in mice through free radical scavenging mechanism (Bharali et al., 2003).

7. Vitis vinifera

Proanthocyanidins (PAs), also known as condensed tannins, are naturally occurring oligomers and polymers of flavan-3-ol monomer units widely found Grape seeds (*Vitis vinifera* L.) which have been used as nutritional supplements and, as antioxidants, to prevent atherosclerosis and cardiovascular diseases. Proanthocyanidins shows the antimutagenic activity. Antitumor and antioxidant activity of ethanolic extract of *Vitis vinifera* L. leaves were evaluated against Ehrlich ascites carcinoma (EAC) induced in Swiss albino mice. The results suggest that ethanolic extract of *Vitis vinifera* exhibited significant antitumor, antioxidant response in EAC tumor bearing mice.

8. Ricinus communis

Ricin A is a newly isolated lectin from *Ricinus communis* which has a strong inhibitory effect on the growth of tumor cells⁷. By using cell cultures, it was found that the tumor cells were more sensitive to lectin than non-transformed cells, and that this could be due to higher binding affinity of lectin to tumor cells than to non-transformed cells (Lin et al., 1986).

9. Curcuma zedoaria

Curcuma zedoaria belonging to the family Zingiberaceae has been used in the traditional system of medicine in treating many human ailments and is found to possess many biological activities. Isocurcumenol was characterized as the active compound of *C. zedoaria* and was found to inhibit the proliferation of cancer cells without inducing significant toxicity to the normal cells

10. Catharanthus roseus

It is an important medicinal plant and belongs to the Apocynaceae family. It is commonly known as Madagascar periwinkle. It contains actinoplastidemic, vinblastin, vincristine, vindesine, vindeline, tabersonine etc. *Catharanthus* is native to Madagascar but now-a-days it is being cultivated in Tanzania, Kenya, and many other countries. This plant is used for the treatment of cancer, diabetes, fever and hypertension. It contains many bioactive compounds which include vinblastine, vincristine, ajmalicine and serpentine. Vinblastine and vincristin are commonly used for the treatment of leukemia and lymphoma.

11. Wedelia chinensis

Wedelia chinensis, indigenous to India, South-East Asia, and China, is one of the important anticancer plants belonging to family Asteraceae which is rich in many important secondary metabolites like phenol, flavonoids, and tannin. The essential oils of *W. chinensis* give a positive effect on lung cancer during the in vitro study. The GC-MS analysis recorded the presence of two important compounds carvacrol and trans-caryophyllene. High anti-scavenging activities were found at different levels of dose.

12. Garcinia indica

Garcinia indica, commonly known as kokum, is also an important medicinal plant that belongs to the *Garcinia* genus. The garcinol of *G. indica* shows positive activities in the experimental HT-29 and HCT-116 colon cancer cells along with normal immortalized intestinal cells (IEC-6 and INT-407). In another study, the fruit extract of *G. indica* was used for the isolation of garcinol. The garcinol at IC₅₀ values (3.2–21.4 μM) for 72 h treatment shows strong inhibitory properties in all intestinal cells. The anticancer properties were higher in the cancer cells as compared to normal immortalized cells

13. Phyllanthus amarus

Phyllanthus amarus is found in tropical Asia, especially in warmer parts of India and is known as bhunyamalaki in Sanskrit, jaramla in Hindi and stone breaker in English. The whole plant, leaves, roots and shoots are reportedly used for their medicinal values. *P. amarus* contains various lignans, flavanoids and tannins, and evidence suggests that *P. amarus* extract may exert antitumor effects.

Oral administration of *P. amarus* extract significantly increased the life span and reduced tumor size in mice bearing Dalton's lymphoma ascites (DLA) and Erlich ascites carcinoma (EAC). The chemoprotective properties of this plant may be related to its ability to inhibit metabolic activation of carcinogenic compounds, induce cell cycle arrest and interfere with DNA repair.

14. Andrographis paniculata

Andrographis paniculata, commonly known as bhunimba and kalmegha in Sanskrit, kiryat in Hindi and the king of bitters and chiretta in English, is found in India and Sri Lanka. The parts of the plant generally used for medicinal purposes are the roots and the leaves. *A. paniculata* extract contains diterpenes, flavonoids and stigmaterols. The primary medicinal component of *Andrographis* is the diterpene andrographolide (chemical structure shown below). Andrographolide, described as a "diterpene lactone" due to its ring like structure, has a very bitter taste and has a colorless crystalline appearance. *Andrographis* leaves contain the highest concentration of andrographolide (~ 2.25%), while the seeds contain the lowest. *A. paniculata* is used in the treatment of wide variety of conditions such as jaundice, cholestasis and as an antidote for hepatotoxins. Its anti-HIV activity has also been reported. Studies conducted on mice have shown that *A. paniculata* is a potent stimulator of the immune system and that it activates both the antigen-specific and non-specific immune responses. Due to its ability to activate both types of immune response, *A. paniculata* is a potent chemoprotective agent and is effective against a variety of infectious and oncogenic agents. Andrographolide shows cytotoxic activity against a variety of cancer cells.

15. Ficus carica

Ficus is one of the largest genus of medicinal plants with around 750 species of woody plants, trees, and shrubs found in subtropical and tropical regions throughout the world. *F. carica* Linn, commonly called "Tin" in Indonesia and globally known as *F. carica*, has previously been studied for health-promoting properties. These effects were mediated through phenolic acids, chlorogenic acids, flavones, and flavonols present in *F. carica*. Quercetin compounds are the main phenolic compounds found in *F. carica*. Quercetin has the ability to stimulate the apoptosis of Caco-2 and HT-29 colon cancer and HL-60 leukemia cancer cells by stimulating the release of cytochrome c from mitochondria.¹⁰ This compound also showed a synergistic effect with cisplatin (chemotherapeutic drug) in vitro and in vivo through the inhibition of protein kinase C (PKC).¹⁰ *F. carica* also contains fiber, vitamin A, vitamin C, calcium, magnesium, and potassium which are needed by the body. Other bioactive compounds of *F. carica* are arabinose, β-amirin, β-carotene, glycosides, β-sitosterol, and xanthol, which are antioxidant compounds.

16. Curcuma longa

Curcumin (Di-feruloyl-methane) and curcuminoids isolated from *Curcuma longa* suppress cancer at every step, i.e. initiation, growth and metastasis. Curcumin arrests the cancer cells proliferation in G₂/S phase and induces apoptosis (programmed cell death). It inhibits angiogenesis, a crucial step in the growth and metastasis of cancer. Curcumin and Genistein (isolated from *Glycine max*) act synergistically to inhibit growth & spread of oestrogen-positive breast cancer. Curcumin works even in multidrug-resistant breast cancers. Curcumin suppresses adhesion of cancer cells, thus preventing metastasis. Curcumin inhibits growth & spread of various cancers including that of breast, lung, oesophagus, liver, colon, prostate, head & neck and skin. Curcumin is particularly effective in radiotherapy-resistant prostate cancer. Curcumin is effective even in advanced stages of cancer. Curcumin also protects from stomach cancer and colon cancer. *Curcuma longa* also possesses antimutagenic, antioxidant, immunostimulant, antiinflammatory, hepatoprotective and radioprotective properties.

17. *Azadirachta indica*

Azadirachta indica contains about 40 different active principles, known as liminoids, which exhibit immunoenhancing, anti-inflammatory, antiulcer, antifungal, antiviral, antioxidant, hepatoprotective, antimutagenic, anticancer and antimetastatic properties. Liminoids regress growth & spread of various cancers such as cancers of breast, lung, stomach, prostate and skin. Nimbolide, a natural triterpenoid, isolated from *Azadirachta indica* leaves and flowers inhibits growth & spread of various cancers including colon cancer, malignant lymphoma, malignant melanoma and leukaemia by inducing apoptosis (programmed cell death), a process that directs the body's immune cells to identify and destroy cancer cells. Nimbolide also prevents metastasis of cancer. Ethanolic extract of *Azadirachta indica* inhibits growth & spread of prostate cancer by inducing apoptosis and its antiandrogenic effect. *Azadirachta indica* reduces side effects of chemotherapy & radiotherapy

18. *Zingiber officinale* /Ginger

Some pungent substances present in ginger rhizome have antioxidant and anti-inflammatory activities. The anticancer properties of ginger are attributed to phenolic substances such as 6-gingerol and 6-paradol and other constituents such as shogaols and zingerone. A study published in the journal *Biochemical and Biophysical Research Communications* reported that . can reduce viability of gastric cancer cells and limit the spread of cancer. Gingerols isolated from *Zingiber officinale* inhibit growth & spread of various cancers including that of the ovary, cervix, colon, rectum, liver, urinary bladder, oral cavity, neuroblastoma and leukaemia by inducing apoptosis. The most active individual component, 6-shogaol, isolated from *Zingiber officinale*, inhibit growth & spread of many cancers particularly the ovarian cancer by blocking formation of new blood vessels and by inducing apoptosis & autophagy. It is effective even in chemotherapy resistant ovarian cancer. *Zingiber officinale* also possesses antioxidant, antimutagenic and anti-inflammatory properties and reduces side effects of chemotherapy & radiotherapy.

19. *Nigella sativa*

Thymoquinone and dithymoquinone isolated from *Nigella sativa* have strong anticancer activity against various cancers including cancers of the colon, prostate, pancreas, uterus, malignant ascites, malignant lymphoma, malignant melanoma, sarcomas and leukaemia. Thymoquinone is effective in both hormone-sensitive and hormonerefractory prostate cancer. *Nigella sativa* kills cancer cells by binding to the asialofectin (lectin) on the surface of cancerous cells, causing their aggregation and clumping. *Nigella sativa* also possesses immunoenhancing and anti-inflammatory properties. It protects against liver cancer. *Nigella sativa* enhances immune function of the body and reduces side effects of chemotherapy & radiotherapy.

20. *Plumbago zeylanica*

In siddha medicines prepared from plumbago root is used to cure ranakiranthi, yoniputtru, kannapilavai, linga puttru etc. Plumbagin isolated from *Plumbago zeylanica* inhibits growth & spread of breast cancer, liver cancer, fibrosarcoma, malignant ascites and leukaemia by inhibiting cancer cell proliferation. *Plumbago zeylanica* also possesses strong antioxidant, hepatoprotective, neuroprotective and immunoenhancing properties

21. *Psoralea corylifolia*

In siddha seeds are used to treat kiranthi and many skin diseases. Bavachinin, corylfolinin and psoralen isolated from *Psoralea corylifolia*, possess strong anticancer activity against lung cancer, liver cancer, osteosarcoma, fibrosarcoma, malignant ascites and leukaemia. Psoralen enhances immunity of the body by stimulating natural killer cell activity. Psoralidin isolated from *Psoralea corylifolia* inhibits growth & spread of stomach and prostate cancers by inhibiting G2/M phase of cell cycle. Psoralidin induces apoptosis in both androgen-responsive and androgen refractory prostate cancers. *Psoralea corylifolia* also possesses strong antioxidant, immunoenhancing and hepatoprotective properties.

CONCLUSION

This review article had identified few cancer drugs in siddha medicine, there are numerous literature are available and it contains various concepts of siddhas for different types of cancer. In this work, reviewed the indications for several herbs exclusive for cancer and their recent research on cancer were recorded. The data suggesting that, the selected herbs showing potent anticancer activity in invitro and animal model of research. Furthermore intention to raise awareness among public to promote siddha medicine for the management of various types of cancers.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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