

## **Diagnosis and Treatment of Cancer – Siddha Perspective**

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### **ABSTRACT**

**Background:** Cancer is one of the leading causes of mortality worldwide and the burden is increasing day by day. This dreadful disease existed in our society from time immemorial and the way of management including therapeutic aspects has been widely described in classical siddha texts. The rationale of this paper is to highlight the clinical features, pathology, diagnosis and therapeutic management of various types of Cancers mentioned in siddha literature. **Methods:** The literature review on the aetiology, pathology, clinical features and therapeutic aspects of 'Cancer like illnesses' mentioned in Siddha system in the form of condensed poems is expressed in this Manuscript. The descriptive aspects of Cancer have resemblance with the clinical entities of *Vippuruthinoipadalam* (Carcinoma like illness), *Mega Katti*, *Kandamaalai Rogapadalam* (Lymphoma like illness), *Kiranthinoigal*, *Pilavai* and *Putrunoi* (tumour) revealed in Siddha Literatures. This paper explicates the review of literature on herbal drugs indicated for cancer related ailments and the pre-clinical study review of Siddha formulations. **Results:** The formulations in Siddha system are deemed to work on multiple biochemical pathways and are capable of influencing several organ systems simultaneously; most of the Siddha medicines provide nutrition and reduce the side effects of conventional cancer therapy due to effective antioxidant activity. **Conclusion:** This review manuscript strongly emphasize that the ancient literatures are scientifically driven one and not simply unconventional.

### **KEY WORDS**

Cancer, *Kandamaalai*, *Mega katti*, *Pilavai*, *Putru*, *Vippuruthi*

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### **1. Introduction**

Cancer is one of the major Non Communicable Disease (NCD) of developing and developed countries of the world. It is one of the leading causes of mortality worldwide and the burden is increasing day by day. The urbanization, life style modality changes, highly polluted environment are the triggering factors for cancer disease.<sup>[1]</sup> The incidence of cancer in India is high in recent days. Early detection of cancer is good essential to overcome cancer easily.

The term cancer denotes a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. The clinical features include lump which grows or ulcerates, abnormal bleeding, unexplained weight loss, change in bowel movements, etc. There are more than 100 types of cancer. Types of cancer are usually named for the organs or tissues where the cancers form, but they also may be described by the type of cell that formed them.

Cancer has existed in the ancient civilization, the written records of Egyptian

Edwin smith papyrus in 1600 BC describes about breast cancer.<sup>[2]</sup> Hippocrates 460 BC to 370 BC describes several kinds of cancer referring to them with Greek word *Karkinos* (Crab or Cray fish)<sup>[2]</sup>. This name comes from the appearance of the cut surface of solid malignant tumor with the veins stretched on all sides as the animal crab.<sup>[2]</sup>

Siddhars – the great scientists who exposed the reality of nature through their spiritual knowledge, continued experience and keen observation threw light on the illness of new growths or lumps, explained in various chapters their aetiology, pathology, clinical features and therapeutic aspects in the form of condensed poems.

## 2. Aetiology

The 90-95% of cancers are due to environmental factors, remaining may be due to inherited genetics. Common environmental factors that contribute to cancer includes tobacco, excessive alcohol, certain infections such as hepatitis B, C, HPV, radiation, UV rays, stress, obesity, lack of physical exercise, poor diet and pollution.<sup>[1]</sup>

The most obvious chapter in Siddha text that correlates with cancer is *Vippuruthinoipadalam* (carcinoma like illness). This is the Tamil verse denoting the aetiology of *Vippuruthi* (Carcinoma like illness) in Siddha literature.<sup>[3]</sup>

“வாளப்பா மெல்ல முப்புரைப்பு  
மிகுதி யாலும்  
வகைவகையாய்  
கிழங்குவகை அருந்த லாலும்  
தாளப்பாமெல்லன்  
சதைத்துன்னி ரத்த மீறி  
தறித்துமா மிசங்கள்  
துன்னித் தாக்க லாலும்  
காளப்பா மெல்லங்க்  
காரசாரங்கள் மிஞ்சில்  
கணக்குமிஞ் சிப்பெண்  
ணோடே கருத லாலும்  
ஆளப்பா மெல்லா மாறினதோ  
றன்னந் தன்னை

அருந்தலால் விப்புருதி  
யணுகுந் தானே”

-யுகி வைத்திய சிந்தாமணி<sup>[3]</sup>

Siddha literary review explains the aetiology of *Vippuruthi* (carcinoma like illness) in *Tamil Verses* as excessive intake of salty, pungent diet and tubers, over indulgence in sex, effects of people's karma, intake of contaminated food items, indulgence in prohibited activities and consumption of food containing incompatible and adulterated food articles.<sup>[3]</sup> The change in people's life styles from that of nature to the modern machine life paves the way for the occurrence of Cancer like illness.

## 3. Molecular Basis of Cancer

Even though the genetic origins of cancer have been building up over several decades, a full accounting of the extent of these genetic aberrations is only now coming to light.

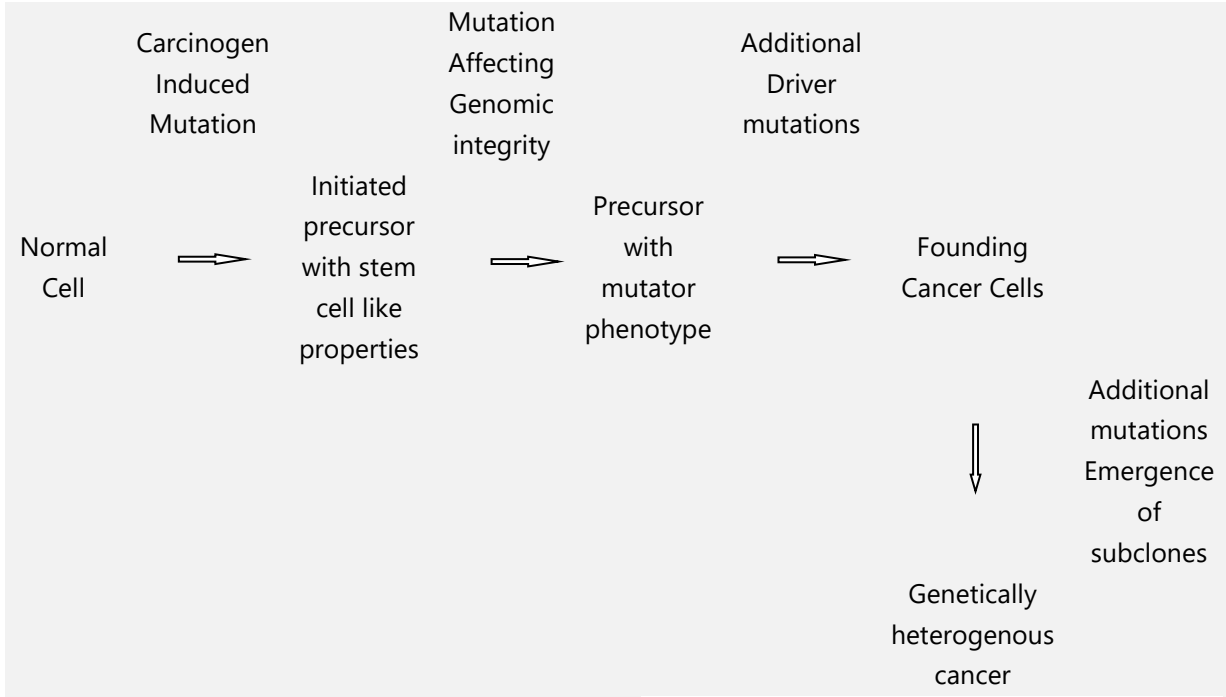
Non-lethal genetic damage lies at the heart of carcinogenesis. The initial damage may be caused by environmental exposures, may be inherited in the germ-line or may be spontaneous.

A tumour is formed by the clonal expansion of a single precursor cell that has incurred genetic damage. Alterations in DNA are heritable, passed to daughter cells and thus all cells within an individual tumour share the same set of mutations.

Four classes of normal regulatory genes – the growth promoting proto-oncogenes, growth inhibiting tumour suppressor genes, genes that regulate programmed cell death or apoptosis, and genes involved in DNA repair are the principal targets of cancer-causing mutations.

- Mutations that activate proto oncogenes cause a “gain of function” and an excessive increase in the normal functions of encoded gene product.
- Mutations of tumour suppressor genes cause a “loss of function” and releases brakes on cell proliferation and survival.

- Mutations in apoptosis regulating genes result in less cell death and therefore enhanced survival of cells.
- Mutations affecting DNA repair genes contribute to carcinogenesis by impairing the ability of the cells to recognise and repair nonlethal genetic damage in other genes.
- Carcinogenesis results from the accumulation of complementary mutations in a stepwise fashion over time.<sup>[4]</sup>



#### 4. Disorders in Siddha system that resembles Cancer

The condensed poems in classical Siddha literature give ample indication that cancer was known to ancient Siddha physicians. This review is to explore the descriptions of cancer in the classical texts.

Siddha Literatures reveals the clinical features of cancer in certain chapters namely *Vippuruthinoipadalam* (Carcinoma like illness), *Mega Katti*, *KandamaalaiRogapadalam* (Lymphoma like illness), *Kiranthinoigal*, *Pilavai* and *Putrunoi* (tumour like illness) in various organ systems. Some disease of male and female genitalia also explains the clinical outcome of cancer.

According to the classical Siddha text, *Vippuruthinoi* (carcinoma like illness) is being classified into seven types based on the pathogenicity, site of lesion, stages and severity of lesion.<sup>[3]</sup> This is the Tamil verse illuminating the types of *Vippuruthinoi* (carcinoma like illness).

“ஆண்மையாம் விப்புருதி ஏழு  
மாகும்  
அதினுடைய னாமத்தைய  
றையக் கேளாய்  
கேண்மையாங் கெர்ப்பவிப்பு  
ருதி யொடு  
குவளைவிப் புருதியாம்பித்  
தவிப்பு ருதி  
தாண்மையாண்ச் சந்து விப்பு  
ருதியாகும்  
தரித்தோடும்  
விப்புருதிச்சேட்பவிப்பு ருதி

வாண்மையாம் வாதவிப்பு ருதி  
யோடு

வகையாக ஏழுவித

வளப்பந் தானே”

-யூகி வைத்திய சிந்தாமணி<sup>[3]</sup>

According to the site of lesion *Vippuruthi*(Carcinoma like illness) is classified into *Kuvalaivippuruthi* (genitalia), *Karppavippuruthi* (uterine) and *Chanthuvippuruthi* (abdomen). As per the pathogenesis of disease it's being divided into *Vathavippuruthi*, *Pithavippuruthi* and *Chethmavippuruthi* (3 humour based), *Oduvippuruthi* (metastatic) denotes the stage and severity of lesion. Moreover, the literature explains about the curable and incurable types of *Vippuruthinoi*.<sup>[3]</sup>

1. *Karppavippuruthi* (Carcinoma in lower abdomen / uterine) depicts the lump below the umbilicus, rupture and discharge of blood and pus from the lesion.
2. *Kuvalaivippuruthi* (Carcinoma in genitalia) expressed as swelling in scrotum, pain and pricking sensation in genitalia.
3. *Chanthuvippuruthi* is being characterised by lump in the side of abdomen, severe pain and burning sensation, gradual redness and hardness of lump.
4. *Vathavippuruthi* explains tongue shaped lumps, hepatomegaly, fever, vomiting, diarrhoea, pain and delirium; mentioned as incurable.
5. *Pithavippuruthi* is a disease with the features of blood vomiting, pallor, itching in the body, delirium and abdominal pain.
6. *Chethmavippuruthi* is characterised by fever, generalised oedema and green coloured stools; mentioned as incurable.
7. *Oduvippuruthi* (Metastatic carcinoma) is characterised by Red and white rashes,

lump in the body, pain in the bone, ulceration in the body.<sup>[3]</sup>

Apart from that, there are six types of *Vippuruthi* in ears namely *ChathaiVippuruthi*, *Odu Vippuruthi*, *Madu Vippuruthi*, *Enbu Vippuruthi*, *Rana Vippuruthi* and *Puttru Vippuruthi*.<sup>[5]</sup>

The *Megarogapadalam* in literature reveals the group of disorders characterised by pallor, increased sweating, weight loss, dry mouth, tiredness, syncope, loss of nails, pain and numbness of both limbs, discharge of blemished foul smelled urine from urethra, etc. This includes *Mega putru*, *Yoni putru* (tumour in Vagina & genitalia) and *Nithambasoolai* (pain) i.e, cancer in female genitalia.<sup>[5]</sup> As a consequence of 21 types of *Mega rogam*, Ten types of *Mega Kattikal* (lumps) may be expressed in the body, that are explained in literature according to the location and size of lump.<sup>[6]</sup>

The *Kandamaalairogapadalam* (lymphoma like illness) explains the diseases due to chronic *Mega noigal* with the clinical features of lymphadenopathy, lump with pain, rupture, ulcer and suppuration around the neck region, weight loss, etc. Herein the derangement in *Vali*, *Azhal* and *Iyya* humour affecting the *Udalthathu* (body constitution) – *Kozhuppu* (fat) and *Oon* (muscle) gradually results in lump in neck, eyes and axilla, rupture of them and ulceration.<sup>[6]</sup>

The clinical features of five types of *Chevi Pilavai* and ten types of *Kabala Pilavai* also denote the resemblance with cancer of ears and skull. As per the pathological concept in Siddha system the three humours *Vali*, *Azhal* and *Iyyam* gets affected which damages the body constituents like blood, muscles and fat gradually and produce lumps in groin and genital region and express as *Ariyappunoi* (Inguinal pubo).<sup>[6]</sup>

Certain Siddha literatures explains *Kiranthinoigal* as capsular lesions characterised by burning sensation, red coloured rashes on the skin, mass, rupture and ulceration in chronic

stage leading to *Arpudha Kiranthi*. Some of the literatures reveals pathogenicity of *Kiranthi* as the aggravation of *Iyya* humour that combines with *Vali* humour and then gradually affecting the body humours namely *Saaram* (body fluid), *Chenneer* (blood), *Oon* (muscle) and *Kozhuppu* (fat); express the nodular lesions in the body.<sup>[5]</sup>

*Kiranthi* is being classified into nine types according to the affected humours—*ValiKiranthi*, *Azhalkiranthi*, *IyyaKiranthi*, *ChathaiKiranthi*, *Kozhuppu Kiranthi*, *Kuruthi Kiranthi*, *Enbu Kiranthi*, *Narambu Kiranthi* and *Pun Kiranthi*. The *Kiranthinoi* in chronic stage has been called as *Arpudha Kiranthi*.<sup>[6]</sup>

In certain Siddha literatures Cancer is being explained as *Kazhalai*, *Putru*, *Thunmangisam*, *Vanmeegarogam* etc. The chapter *Peruvayirunoi* (ascites) in Siddha literature also describes certain clinical features of Cancer. Chapters such as *Chathaiperuvayiru*, *Nazhuvaiperuvayiru*, *Veppupaavaiperuvayiru*, *Kulaimuttiperuvayiru*, *Keezhkavisai*, *Maelkavisaiperuvayiru*, *Vallaiperuvayiru* explains abdominal distension due to several encroachments.<sup>[7]</sup>

According to Tamil – English Dictionary of medicine malignant tumours are very harmful because all the three major humours lose their mutual coordination and thus cannot prevent tissue proliferation resulting in deadly morbid conditions.

Some of the Siddha literature like *Agasthiyar Ranavaithyam*, *Nagamuni Nayanavithi*, *Agasthiyar Nayanavithi* describes cancers as *Putrunoikal* viz., *Naakkuputru*, *Seviputru*, *Vaiputru*, *Kanputru* which are cancer of tongue, ear, mouth and eyes respectively. *Danvandhirivaidhyam*, *Pararasasegaram* and *SiddharAruvaimaruthuvam* are some other books that deal with different cancers.

## 5. Laboratory Diagnosis of Cancer

Every year the approach to laboratory diagnosis of cancer becomes more complex, more sophisticated and more specialized.

### 5.1. Histologic and Cytological methods

The specimen made available for examination must be adequate, representative and properly preserved. Different sampling approaches available are excision/biopsy, needle aspiration and cytological smears.<sup>[4]</sup>

Fine needle aspiration – Involves aspirating cells and attendant fluid with a small bore needle, followed by cytologic examination of the stained smear.<sup>[4]</sup>

Cytologic Smears – Used to screen for cancer of cervix at an in-situ stage and to evaluate suspected malignancy in which tumour cells are shed.<sup>[4]</sup>

5.2. Immunohistochemistry – Specific antibodies facilitate identification of cell products or surface markers.

It helps in the categorization of undifferentiated malignant tumours and determination of site of origin of metastatic tumours.<sup>[4]</sup>

5.3. Flow Cytometry – Identify cellular antigens expressed by tumour cells and thus rapidly and quantitatively measure individual cell characteristics.<sup>[4]</sup>

The main advantage of flow cytometry is that multiple antigens can be assessed simultaneously an individual cells using specific antibodies linked to different fluorescent dyes.<sup>[4]</sup>

### 5.4. Molecular and Cytogenetic diagnosis

- PCR based evaluation for distinction between monoclonal (neoplastic) and polyclonal (reactive) proliferations
- FISH – for detection of trans locations in different types of blood born malignancies
- DNA microarrays – cover the entire genome wide mapping.<sup>[4]</sup>

## 6. Therapeutic approach

The Cancer patients are acquiring resistance to current chemotherapeutic agents and hence it is necessary to search for new novel compounds that provide suitable specific anti-cancerous effects. Though we have a number of anticancer agents now, adequate control of cancer is still lacking. Hence there is a persistent demand to develop newer and more effective anticancer drugs which can help tackle this problem.

The therapeutic aspect in Siddha system is based on the body constitution of the subjects and pathogenesis of the disease. The treatment is usually initiated with the diagnosis of imbalance in humours and its maintenance with cleansing therapies and life style approach. Then the drugs to balance the deranged humours, to improve the physical condition and quality of life of subjects is to be used with dietary restriction schedule.

The rate of success depends on the regularity in intake of medicines and care taken by the patient in observance of diet regimen. Even patients with secondary metastasis in lymph nodes also have significant response and disappearance of mass by using Siddha medicines. Being gentle in their healing effects they work by assisting nature in its own healing powers. Regular intake of medicines improves metabolism, reduces the chances of recurrence; the patient's quality of life improves, adding years and peace to his life.

The proposed cure as an alternative to the modern treatment that focuses on killing the cancer cells is to restart normal metabolism which allows the cells to revert back to being normal cells again. If the cells are held in a normal state of metabolism, with time they will go through the normal process of usual cell death and the cancer cells are permanently eliminated.

As per the classical, in certain types of Cancer the Bloodletting, Leech therapy, Cauterisation and other surgical procedures

were performed along with herbal and mineral medicines in order to destroy the metabolically deranged and dead cells in the body. According to Siddha literature, *Nakkaranai*, *putru*, *pilavai*, *kiranthi* and *pun* (tumours and ulcer) can be treated with the Cauterisation procedure by using equipments like *Aazhisootukaruvi* and *Pottusootukaruvi*, etc.<sup>[6]</sup>

### 6.1. Significance of Herbs in Cancer Therapy

Natural Products have long been a fertile source for the treatment of non - communicable diseases like cancer. The harsh side effects of cancer treatments are one motivating factor to find new alternative methods. The Plant derived phytochemicals possessing anticancer activities have received considerable attention in recent years. Ongoing research is being done throughout the world to seek out effective treatments for cancer, including the use of plants to relieve and treat cancer patients. This treatment makes use of the compounds naturally present in plants that are known to inhibit or kill carcinogenic cells. Specially, plants growing at high altitude in Himalayan pastures are time-honoured sources of health and general well-being of local inhabitants.<sup>[8]</sup>

Plants growing at higher altitudes are subjected to an assault of diverse testing situations including higher doses of mutagenic UV-radiation, physiological drought, desiccation and strong winds.<sup>[8]</sup> Plants interact with stressful environments by physiological adaptation and altering the biochemical profile of plant tissues and producing a spectrum of secondary metabolites. Secondary metabolites are of special interest to scientists because of their unique pharmacophores and medicinal properties. Secondary metabolites like polyphenols, terpenes and alkaloids have been reported to possess antimutagenic and anticancer properties in many studies.<sup>[8]</sup>

The major groups of anticancer drugs such as Vinca alkaloids, taxanes, camptothecins

and epipodophyllotoxins which are currently a part of many standard anticancer regimens are derived from plants.<sup>[9]</sup>

## 6.2. Herbs of proved Anti-Cancerous activity

### 6.2. 1. *Mimosa pudica* – *Thottarchurunki*

The verse in Siddha literature *Gunavaagam* denotes the anticancerous activity of *Thottarchurunki* (*Mimosa pudica*) herb.

*Meganeeraithadukku* .....

.....

*Agasthiar Gunavaagam*

According to the literature, leaf of *Mimosa pudica* is indicated for *Meganeer*, *Oduvaayu* with *Kazhalai*, *katti* (lumps) in the body,<sup>[10]</sup> which can be correlated with the Metastatic tumours in the body.

The review of Journals reports the presence of alkaloid, glycoside, flavonoids and tannins in *Mimosa pudica*; It has antimicrobial, anti-convulsant, hyperglycemic, anti-oxidant, anti-venom, diuretic, anticancer, antidiabetic, anti-fertility and anti-histaminic activities. Cytotoxic study suggested that flavonoid from *Mimosa pudica* has the maximum cytotoxic effect against MCF-7 and Human breast cancer cell line.<sup>[11]</sup>

### 6.2. 2. *Asparagus racemosus* - *Thannirvittan*

*Thannirvittanis* indicated for *Somano*, *Elumpurukki*,<sup>[10]</sup> etc the clinical features of which can be correlated with leukaemia.

*Neerizhvaippokkaum*.....

.....

*Agasthiar Gunavaagam*

*Asparagus* extract administered in AOM-injected rats exerted various anti-carcinogenic and protective effects on the colonic mucosa at early post-initiation stages. At the molecular level, the *asparagus* extract exhibited multi-targeted effects on the pre-neoplastic colonic mucosa including the inhibition of cellular pro-inflammatory

mediators such as IL1 $\beta$ , TNF- $\alpha$ , MMP-7 and MMP-9, in association with an increased expression of the host-defence mediators  $\alpha$ -defensin-5 and lipocalin. In the colonic mucosa of AOM-injected rats receiving the *asparagus* extract confirmed the pro-apoptotic effects observed *in vitro* involving the activation of the TRAIL death receptor signalling pathway.<sup>[12]</sup>

### 6.2. 3. *Plumbagoindica* – *Kodiveli*

As per Siddha literature all varieties of *Plumbago* is having anticancerous activity. The Verse in Siddha literature denotes the indication of *Kodiveli* for *Katti*, *Viranam*, *Kiranthi*, *Araiappu*, etc.<sup>[10]</sup>

*Kattiviranankiranthikaalkalaaraiyappuk*

*Katti*.....

*Agasthiar Gunavaagam*

*Plumbagin* isolated from *Plumbago zeylanica* inhibits growth and 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 immune enhancing properties.<sup>[9]</sup>

The cytotoxic effect of *plumbagin* and ETPR on human lymphocytes was evaluated by MTT assay. Cell lines were sensitive to *plumbagin* when compared to ETPR, indicating that *plumbagin* could well induce cytotoxicity to the lymphocyte cell lines.

*Plumbago rosea* is studied for antiproliferative effect on SK MEL 28 melanoma cell line showed growth inhibition in a dose-dependent manner. *Plumbagin* a phytochemical in all varieties has anticancerous potential but the side effects limits its use. In combination with other ingredients (root of the plant as such) it shows significant synergy leading to a stronger anticancer effect with less toxicity.<sup>[13]</sup>

*Plumbago zeylanica* derived 1,4-naphthoquinone significantly inhibited the growth and metastasis of PC-3M-luciferase cells

in this pre-clinical mouse model. It concludes that PL may be a potential anti-metastatic agent for the treatment of human metastatic Prostatic Ca.<sup>[14]</sup>

**6.2. 4. Semecarpus anacardium – Cherankottai**

*Cherankottai* seeds are useful in the treatment for group of *Kiranthinoigal, Kaya noigal*, etc.

*Kuttankayarogank*.....

.....

*Agasthiar Gunavaagadam*

The phytochemicals isolated from *Semecarpusanacardium* is studied for acutemyeloblastic leukaemia, chronic myelogenic leukaemia, breast adeno carcinoma, cervical epithelial carcinoma and colon carcinoma cancer by using cell lines with MTT assay. The milk extract of *Semecarpus anacardium* produces regression of hepatocarcinoma by stimulating host immune system and normalizing tumour markers including alpha-fetoprotein levels.<sup>[15]</sup>

**6.2. 5. Taxusbuccata - Thalishabathari**

In addition to Respiratory ailments, *Thalishabathari* is indicated for *kandamaalai, mega noigaletc.*<sup>[10]</sup>

Taxanes extracted from *Taxus buccata* exhibit unique cytotoxic activity by stabilizing microtubules rather than destabilizing them as vinca alkaloids do. In particular they promote the assembly of microtubules and prevent their depolymerization, thus interfering with a number of normal cellular functions that depend on the physiological balance between tubulin and microtubules.<sup>[16]</sup>

Paclitaxel and docetaxel have very high activity in a spectrum of solid tumours (ovarian, breast, lung, head and neck, gastro-oesophageal, bladder, testis, endometrium neoplasms) and in some haematological and

paediatric malignancies. Both drugs are active as single agents and in combination chemotherapy.<sup>[16]</sup>

**6.2. 6. Vitex negundo – Nochi**

*Nochi Kudineer* is indicated for Hepatomegaly; the leaf of *Nochi* is being used for external application in Splenomegaly; the leaf is effective for *Muppininoigal* also.<sup>[10]</sup> The therapeutic applications of *Nochi* may be correlated with Immunomodulatory and anti-cancerous activity of *Vitex negundo*.

The leaf extract of *Vitex negundo* (EVN)increase the life span of DAL treated mice and restore the hematological parameters as compared with the DAL bearing mice in dose dependant manner. The study revealed that the EVN showed significant antitumour activity in tested animal models. The EVN was found to be cytotoxic to mouse lung fibroblast (L-929) cells in long term chemosensitive cytotoxic assay.<sup>[17]</sup>The extracts of *Vitex trifolia* leaves which showed a strong inhibition against the MCF-7 cell lines and weak inhibition against the Vero cell lines.<sup>[18]</sup>

**6.2. 7. Glycyrrhiza glabra- Athimathuram**

The root of *Athimathuram* is being used for several diseases, the indication includes *Enpurukkinoi, Muppini, Kaamaalai*, etc.<sup>[10]</sup>

*Katthiyarimuppiniyaalvarupunthaagank*

.....

*Pitthamelumpurukkikiricharam*.....

.....

*Theran Gunavaagadam*

The chloroform extract of *Glycyrrhiza glabra* reveals higher percentage of 18β-glycyrrhetic acid which could be considered as a potential source of natural anticancer component. The in-vitro cytotoxic screening of standard 18 β-glycyrrhetic acid and also for natural anticancer drug *G. glabra* using three different extracts (chloroform, methanol and water) of the drug through MTT method disclose that chloroform extract inhibited



abnormal cell proliferation more effectively, shows good cytotoxicity against cancerous MCF7 cells (Human Breast cancer) than the other two extracts of *G. glabra*.<sup>[19]</sup>

#### **6.2. 8. *Allium sativum* and *Allium cepa***

There is evidence that onion – shallot and garlic which are indicated for lumps in Siddha Literature can protect humans against Cancer.<sup>[10]</sup>

A number of studies have demonstrated the chemopreventive activity of Garlic by using a number of organosulfur compounds derived from garlic. Moreover *Allium* contains Selenium, which control genes involved in carcinogenesis.<sup>[20]</sup>

#### **6.2. 9. *Punica granatum* - *Mathalai***

The study on chemopreventive effect of Pomegranate fruit extract (PFE) employing human prostate cancer cells revealed significant inhibition in tumour growth concomitant with a significant decrease in serum prostate-specific antigen levels. Hence Pomegranate juice may have cancer-chemopreventive as well as cancer-chemotherapeutic effects against prostate cancer in humans.<sup>[21]</sup> As per Siddha text Pomegranate fruit is effective for *Muppinoinigal*.<sup>[10]</sup>

#### **6.2. 10. *Alstonia scholaris* - *Ezhilaipaalai***

*In-vitro* and *in-vivo* evaluation of Anticancer activity of the alkaloid fraction of *Alstonia scholaris* in cultured human neoplastic cell lines (HeLa, HepG(2), HL60, KB and MCF-7) and in Ehrlich ascites carcinoma bearing mice reveals time dependent increase in the antineoplastic activity and the greatest activity was observed when the cells were exposed to ASERS for 24 hour.<sup>[22]</sup> In Siddha Literature *Ezhilaipaalai* or Saphthaparni is indicated *Muppinoinigal*.<sup>[10]</sup>

#### **6.2. 11. *Ocimum gratissimum* - *Rama Thulasi/ African Basil***

In Siddha literature *Rama Thulasi* and *Kalthulasi* is indicated for lumps especially *Vippuruthi*.<sup>[10]</sup> Aqueous Extract of *Ocimum gratissimum* induces apoptotic signalling in Lung adenocarcinoma Cell A549. OGE treatments significantly alter viability of lung adenocarcinoma A549 cells through a synergy of induction of apoptotic signalling and suppression of antiapoptotic signalling. OGE treatments significantly alter viability of lung adenocarcinoma A549 cells through a synergy of induction of apoptotic signalling and suppression of anti-apoptotic signalling.<sup>[23]</sup>

#### **6.2. 12. *Withania somnifera* - *Ammukura***

*Ammukura* in Siddha literature is indicated for lumps; is being practically used for external and internal application. Antitumor and radiosensitizing effects of alcoholic root extract of *W. somnifera* and their modification by heat were studied in vivo on Sarcoma-180 grown on the dorsum of adult BALB/c mouse. *Ashwagandha* increased the effect of radiation on tumor regression as well as growth delay and gave a better tumor cure. It is concluded that *Ashwagandha*, in addition to having a tumor inhibitory effect, also acts as a radiosensitizer and heat enhances these effects.<sup>[24]</sup>

#### **6.2. 13. *Aegle marmelos* - *Vilvam***

Pulp and seeds of *Aegle marmelos* fruit contain Lupeol, showing strong positive action against breast cancer, thyroid cancer and other form of malignancies. Lupeol affects the gene expression of MDA-MB-231 breast cancer cell-line and inhibits cell proliferation. Adverse effects of both radiotherapy and chemotherapy get diminished by antioxidant property of *Aegle marmelos*.<sup>[25]</sup>

Some other plants with anti-cancerous activity are *Curcuma zedoaria*, *Albezia lebbek*, *Vitis vinefera*, *Rubia cordifolia*, *Catharanthus roseus*, *Smilax china*, *Helianthus annuus*,

*Andrographis paniculata*, *Embllica officinalis*, *Boerhaavia diffusa*, *Tinospora cordifolia*, *Morinda charantia*, *Crocus sativus*, *Rhus succedanea*, *Bacopa monnieri*, *Picrorrhiza kurroa*, *Linum usitatissimum*, *Aloe vera*, *Zingiber officinale* and others.

In parallel, there is increasing evidence for the potential of plant-derived compounds as inhibitors of various stages of tumorigenesis, associated inflammatory processes, and oxidant scavenging. The plant based drugs administered orally as mentioned in the literature are safe and more effective than synthetic formulations.

### 6.3. Pre-clinical study review of Siddha formulations

The Siddha formulation *Surulpattai chooranam* is evaluated for anti-proliferative activity by employing MTT assay using SK-Mel-28 cell lines; the study shown significant anti-proliferative activity in skin melanoma.<sup>[26]</sup> The drug was clinically reported as safe on oral administration at the prescribed dose.

The Comparative in vitro Anticancer Activity of *Neeradi Muthu Vallathymezugu* (NMV) and *Thamira Kattu Chendooram* (TKC) reveals anti-cancer potential of these two formulations. NMV showed good cytotoxic effect even at low dose when compared with TKC. In this study, Human hepatic cancer cells responded well even at very low dose, when compared to other cancer cells. These drugs have been clinically reported to be safe and effective when given orally.<sup>[27]</sup>

In vitro evaluation of anti-cancerous activity of *Gowri Chinthamani Chendhooram* (GCC) on *HeLa* cell lines by using MTT assay reveals potent anti-cancerous activity on human cancer cells.<sup>[28]</sup> *Gowri Chinthamani Chendhooram* was evaluated for acute and Chronic toxicity studies; the toxicity findings were dose specific, tissue damages at higher dosages only.<sup>[29]</sup>

The anticancer property of the *Guru Pathangam* in swiss albino mice against Dalton ascites lymphoma (DAL) evaluated with the

assessment of mean survival time, increase in life span, cell count and hematological parameters. *Guru Pathangam* treatment decreases the volume of solid tumor as well as ascites volume, viable cancer cell count and increased the life span. An acute toxicity study was also carried out in *Guru Pathangam* using mice, toxic signs were observed at the higher dose levels. Hence 1/10th of toxic dose (5 mg/kg) was considered as therapeutic dose for this study. It may be concluded that *Guru Pathangam* decreases the nutritional fluid volume and thereby arrest the tumor growth and increase the life span. The *Guru Pathangam* was found to be good anticancer drug in Siddha system.<sup>[30]</sup>

Publications reveal the possible potential of *Rasaganthi Mezhugu* (RGM) as alternative medicine for prostatic cancer and also a sensitizing agent in the context of radiation therapy for prostate cancer. In the acute and chronic toxicity studies, the *Rasaganthi Mezhugu* did not produce any significant organ or hematologic toxicity or mortality in rats. Another study brings up scientific evidence for the efficacy of RGM against the HPV-mediated cervical cancer cells and RGM would be a suitable candidate as evidence-based complementary and alternative medicine for HPV-positive cervical cancers.<sup>[31]</sup>

The classical Siddha herbomineral preparation *Siva Guru Kuligai* (SGK) which is being indicated for *Kiranthi* (syphilis), *Algulputru* (uterine cancer), *Algulranam* (uterine ulcer) etc is subjected to *in vitro* evaluation of anticancerous activity. The test drug SGK significantly inhibited the proliferation of human cervical cancer HeLa cells evaluated in MTT assay.<sup>[32]</sup>

The evaluation of *in vitro* Anti-cancer efficacy of a Polyherbal Siddha formulation against A549 – Human Lung Carcinoma cells through MTT Assay Method followed by Cytotoxicity profile provides encouraging results even at the lower concentration level. At the concentration of 6.25µg/ml the test drug kills nearly about 40% of cancer cells. From the study

results, it is evident that Traditional Siddha medicine can be useful in the management of Cancer, besides being safe, cost-effective and non-invasive.<sup>[33]</sup>

The formulations consisting of multiple herbs, metals or minerals each possessing tremendous potential for a cancer cure are being used in Siddha System. These formulations are deemed to work on multiple biochemical pathways and are capable of influencing several organ systems simultaneously.

## 7. Conclusion

As per the review above results, it is evident that traditional Siddha medicine can be useful in the management of cancer, besides being safe, cost-effective, and non-invasive. Most of the Siddha medicines provide nutrition and reduce the side effects of conventional cancer therapy due to effective antioxidant activity. The compound formulations or single drugs in Siddha literature shall be subjected to retrospective analysis for the exploration of scientific background behind the therapeutic aspects. More researches could be taken up the concept to explore and evaluate them scientifically for the betterment of cancer population.

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## References

1. Preetha A, Ajaikumar BK, Chitra S, Kuzhuvilil BH, Sheeja TT, Oiki SL, Bokyung S, Bharat BA. Cancer is a Preventable Disease that Requires Major Lifestyle Changes. *Pharm Res* 2008;25(9):2097-116.
2. Guy BF. A brief history of cancer: Age-old milestones underlying our current knowledge database. *Int J Cancer* 2015;136(9):2022-36.
3. Thiyagarajan R, editor (2<sup>nd</sup>ed). *Yugimunivar Vaithya Chinthamani (Perunool 800)*: Chapter 30. Chennai: Directorate of Indian Medicine and Homeopathy Publications, 1976; p.442-49.
4. Robbins and Cotran, editor, (9<sup>th</sup>ed). *Pathologic basis of disease*, Vol-1, Chapter7, Elsevier India Pvt. Ltd, 2014; p.280,332-34.
5. Kanthasamy Mudhaliar, editor (1<sup>st</sup>ed). *Pathinensiddhararulicheytha Aathma Ratshamirtham Ennum Vaidhya Saara Sangiragam*: Rathnanayakkar and Sons Publications; 1993; p.356,382,387,418-21.
6. Utthamarayan KS, editor (2<sup>nd</sup>ed). *Iddhar Aruvai Maruthuvam*. Chennai: Directorate of Indian medicine and Homeopathy, 1984; p.80-82,87,91,108,136,159.
7. Kuppusamy Mudhaliar KN, editor (2<sup>nd</sup>ed). *Siddha Maruthuvam (Pothu)*. Chennai: Directorate of Indian medicine and Homeopathy, 1987; p.356-66.
8. Umadevi M, Sampath Kumar KP, Debjit B, Duraivel S. Traditionally Used Anticancer Herbs in India. *J Med Plants Stud* 2013;1(3):56-74.
9. Ansari JA, Khan HJ. Anticancerous Medicinal plants: A Review. *International Journal of Advanced Pharmaceutical Research* 2013;1(4):1706-22.
10. Murugesu Mudhaliar KS, editor (5<sup>th</sup>ed). *Gunapaadam (Porutpanpu Nool)*, First Part, Mooligaivaguppu. Chennai: Directorate of Indian medicine and Homeopathy, 1998; p.13,29,161,170,381-6,488,499, 510,531,552,627,749,820,846.
11. Joby J, Sudheesh S, Sumesh Kumar TM, Sony J, Jayadevi V. A Comparative evaluation of Anticancer activities of flavonoids isolated from *Mimosa pudica*, *Aloe vera* and *Phyllanthus niruri* against human Breast Carcinoma cell line (mcf-7) using MTT assay. *Int J Pharm PharmSci* 2014;6(2):319-22.
12. Souad Bousserouel, Julie Le Grandois, Francine Gossé, Dalal Werner, Stephan w. Barth, Eric Marchioni, Jacques Marescaux, Francis Raul. Methanolic extract of white Asparagus shoots activates TRAIL apoptotic death pathway in human cancer cells and inhibits colon carcinogenesis in a preclinical model. *International Journal of Oncology* 2013;43(2):394-404.
13. Alexander Ronaldo Anuf, Rajesh Ramachandran, Rajaram Krishnasamy, Sudhakar Gandhi PS, Sureshkumar Periyasamy. Antiproliferative effects of *Plumbago rosea* and its purified constituent plumbagin on SK-MEL 28 melanoma cell lines. *Pharmacognosy Res* 2014;6(4):312-9.
14. Bilal Bin Hafeez, Weixiong Zhong, Joseph W Fischer, Ala Mustafa, Xudong Daniel Shi, Louise Meske, Hao Hong, WeiboCai, Thomas Havighurst, KyungMann Kim, Ajit K Verma. Plumbagina Medicinal plant (*Plumbago zeylanica*) - derived 1,4-naphthoquinone, inhibits growth and metastasis of human prostate cancer PC-3M-luciferase cells in an Orthotopicxenograft mouse model. *Molecular Oncology* 2013;7(3):428-39.
15. Premalatha B, Muthulakshmi V, Sachdanandam P. Anticancer potency of the milk extract of *Semecarpus anacardium* Linn. Nuts against Aflatoxin B1 mediated hepatocellular carcinoma bearing Wistar rats with reference to tumour marker enzymes. *Phytotherapeutic Research* 1999;13:183-7.
16. Stefania Nobili, Donatella Lippi, Ewa Witort, Martino Donnini, Letizia Bausi, Enrico Mini, Sergio Capaccioli. Natural compounds for cancer treatment and prevention. *Pharmacol Res* 2009;59(6):365-78.
17. Chitra V, Shrinivas Sharma, Nandu Kayande. Evaluation of Anticancer Activity of *Vitex negundo* in Experimental Animals: An *In Vitro* & *In Vivo* Study.

- International Journal of PharmTech Research 2009;1(4): 1485-9.
18. Mohammed I Garbi, Elbadri E Osman, Ahmed S Kabbashi, Mahmmoud S Saleh, Yuosof S Yuosof, Sara A Mahmoud, Hamza AA Salam. Cytotoxicity of *Vitex trifolia* leaf extracts on MCF-7 and Vero cell lines. Journal of Scientific and Innovative Research 2015;4(2):89-93.
  19. Rathi SG, Suthar M, Patel P, Bhaskar VH, Rajgor NB. *In-vitro* Cytotoxic Screening of *Glycyrrhiza glabra* L. (Fabaceae): A Natural Anticancer Drug. J Young Pharm 2009;1(3):239-43.
  20. Ana L, Colín-González RA, Santana CA, Silva-Isla ME, Chánez-Cárdenas AS, Perla DM. The Antioxidant Mechanisms Underlying the Aged Garlic Extract- and S-Allylcysteine- Induced Protection. Oxid Med Cel Longev 2012;2012:907162.
  21. Malik A, Afaq F, Sarfaraz S, Adhami VM, Syed DN, Mukhtar H. Pomegranate fruit juice for chemoprevention and chemotherapy of prostate cancer; Proc Natl Acad Sci USA 2005;102(41):14813-8.
  22. Jagetia GC, Baliga MS. Evaluation of anticancer activity of the alkaloid fraction of *Alstonia scholaris* (Sapthaparna) *in vitro* and *in vivo*. Phytother Res 2006;20(2):103-9.
  23. Han-Min Chen, Mu-Jang Lee, Cheng-Yi Kuo, Pei-Lin Tsai, Jer-Yuh Liu, Shao-Hsuan Kao. *Ocimum gratissimum* Aqueous Extract Induces Apoptotic Signalling in Lung Adenocarcinoma Cell A549. Evidence-Based Complementary and Alternative Medicine 2011, Article ID 739093, 7 pages. Available from <https://www.hindawi.com/journals/ecam/2011/739093/>
  24. Devi PU, Sharada AC, Solomon FE. Antitumor and radiosensitizing effects of *Withania somnifera* (Ashwagandha) on a transplantable mouse tumor, Sarcoma-180. Indian J Exp Biol 1993;31(7):607-11.
  25. Shaktiprasad Pradhan, Ranjit Mohapatra, Debasish Pradhan. Ethnomedicinal plants of Odisha used against Breast Cancer - A Review. Int J Chem Pharm Rev Res 2015;1(2):38-42.
  26. Ravichandran M, Mubarak H, Elangovan S. An *in vitro* study of Anti-cancer activity of a Siddha drug *Surul Pattai Chooranam* (SKT) using SK-MEL28 cell line model. Proceedings of International Conference on Radiation Biology and Clinical Applications. Mangalore: 2013.
  27. Vasudha Devi, Arul Amuthan K, Narayana K, Venkata Rao J. Comparative *in vitro* Anticancer Activity of Two Siddha Formulations: *Neeradi Muthu Vallathymezugu* and *Thamira Kattu Chendooram*. World Academy of Science, Engineering and Technology International Journal of Pharmacological and Pharmaceutical Sciences 2014; 1(12). Available from [waset.org/pdf/books/?id=1451&pageNumber=1](http://waset.org/pdf/books/?id=1451&pageNumber=1)
  28. Mantela D, Velpandian V, Ramalingam S, Dhanalakshmi G, Pitchiahkumar M, Banumathi V. *In Vitro* Evaluation of Anticancer Activity of *Gowri Chinthamani Chendhooram*, Siddha Medicine Against *HeLa* Cells. British Journal of Medical and Health Research 2015;2(11):1-7
  29. Shanmugapriya P, Thamodharan S, Ramamurthy M, Jiji Mol VC, Nijavizhi M. Toxicological Screening of *Gowri Chinthamani Chendooram* – A Siddha metallic preparation. Pharma Tutor 2014;2 (9):119-122.
  30. Babu P, Anbu J, Ashwinianjana, Velpandian V. Anti tumour activity of Guru Pathangam against Dalton ascites Lymphoma (dal) in Mice. International Journal of Pharma and Bio Sciences 2012;3(3):281-9.
  31. Shyamala Rajkumar V, Vijaya Kumar C, Ponmuthu Rani, Gopakumar K, Ramaswamy RS. Management of Fibroid Uterus with a Traditional *Siddha* Formulation – A Review. International Journal of Multidisciplinary Health Sciences 2014;1(1):1-14
  32. Karthik Raja SR, Rajagopal N, Tamizhinian M, Ravichandran V, Arihara Sivakumar G. Evaluation of Anticancer Activity of Classical Siddha herbomineral preparation Siva Guru Kuligai by *in vitro* assay. Proceedings of the International Conference Asian Journal of Pharmaceutical and Clinical Research 2017;10 (2):37-9.
  33. Thomas M Walter, Merish S. Anticancer efficacy of a Polyherbal Siddha formulation against a 549-human lung carcinoma cells. Asian Journal of Pharmaceutical and Clinical Research 2017;10(2):34-5.