Antimetastatic Plants in Siddha System of Medicine

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Abstract: Siddha system of medicine is a traditional system practiced in South India. The plant based formulations as well as plant derived phytochemicals possessing therapeutic potential have drawn considerable attention in recent years. Cancer is one of the major Non-Communicable Disease and remains one of the leading causes of morbidity and mortality. As a number of undesired side effects occur during chemotherapy, natural therapies involving the plant derived products are used in cancer treatment, may reduce adverse side effects. A plethora of many plant products that has shown very promising anticancer activity in vitro, but have yet to be evaluated in clinical trials. Prominently using anticancer plants in Siddha medicine include *Plumbago indica, Taxus baccata, Asparagus racemosa, Glycyrriza glaba* and *Ocimum gratissimum*. 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.

Keywords: Anticancer, natural sources, chemical constituents, Siddha medicine

For many years herbal medicines have been used and are still used in developing countries as the primary source of medicines to treat various ailments. Plants have been used in medicine for their natural therapeutic properties. In line with this, the research has developed into investigating the potential properties and uses of terrestrial as well as marine plant extracts for the preparation of potential nanomaterial based drugs for various dreadful diseases including cancer (Kuppuswamy et al., 2016; Siddique & Chow, 2020). Many plant species are already being used to treat or prevent development of cancer. Multiple researchers have identified species of plants that have demonstrated anticancer properties with a lot of focus on those that have been used in herbal medicine in developing countries. The National Cancer Institute (NCI) has screened approximately 35,000 plant species for potential anticancer activities. Among them, about 3,000 plant species have demonstrated reproducible anticancer activity. The untapped structural diversity of natural compounds is having major importance in drug discovery.

Cancer is a dreadful as well as a high profile disease in developing countries. The alarming and frightening rise in the number of people dying from various types of cancer has prompted researchers to search for alternative anticancer drugs with fewer side effects to

battle the illness in an effective manner (Cai et al., 2006; Ochwangi et al., 2014). The great potential of plant based compounds for the treatment and prevention of cancer is attributed to their safety, low cost and oral bioavailability; while a few plant based compounds induce some side effects. The side effects can be overcome by dose dependent administration and usage of plant extracts (Raina et al., 2014). The already available expensive conventional therapies for cancer like chemotherapy and radiotherapy have a number of side effects such as myelo-suppression and neurological, cardiac, pulmonary and renal toxicity, which pose

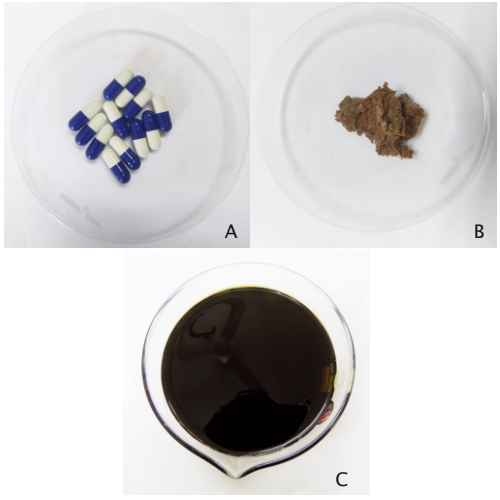

Fig.1. A. Rasagandhi Mezhugu Capsules, B. Gandhaka, C. Rasayanam Megathennai

serious harm to the quality of life (Alonso-Castro et al., 2011). Siddha system of medicine is a traditional system of medicine practised by saint from ancient period. It is getting more attention nowadays due to its less toxicity rendered by plant based drugs. According to Siddha system, Vippuruthinoi (carcinoma like illness) is being classified into seven types based on the pathogenicity and site, stages and severity of lesions developed on a particular part of body (Lekha et al., 2018). The therapeutic aspect in Siddha system is based on the body constitution of the subjects and pathogenesis of the disease.

1. Plant derived anticancer agents

1.1. *Clerodendron inerme* (L.) Gaertn.

The species belongs to family Verbenaceae with a lot of ethnomedicinal properties. The plant contains some important phytoconstituents viz. pentadecanoic acid–β-D-glicoside, stigmasterol, 4α-methyl-24βethyl-5α-cholesta-14, 25-dien-3β-ol, 24β-ethylcholesta-5, 9(11), 22-trien-3β-ol and betulinic acid. Anticancer potential of *C. inerme* has been proved on lung cancer, Burkitt's lymphoma cancer and human colon cancer cell line (Chouhan et al., 2018; Kumar et al., 2018; Trieu, 2019).

1.2. *Plumbago indica* L.

It is a well-known medicinal plant belongs to the family Plumbaginaceae. The potential phytoconstituent, Plumbagin, is known to exert various bioactivities. The plant extract exhibits selective cytotoxic and anti-proliferative effects in human skin cancer SK MEL-28 cells (Anuf et al., 2014). A significant synergy of cytotoxicity towards cancer cells demonstrated in the use of *P. rosea* extract due to interactions among plumbagin and other components present in the herb. In addition to plumbagin, several other potential bioactive components such as sitosterol, stigmasterol, campesterol, napthaquinone, 5, 6-dihydroxy-2-methyl-1,4-naphthoquinone (6-hydroxyplumba-

gin) α-amyrin and β-sitosterol are present in plant (Checker et al., 2010; Hafeez et al., 2012).

1.3. *Smilax chinensis* L.

It is a climbing plant species belonging to Smilacaceae. The ethanol extract of *S. chinensis* proved to be effective in arresting the proliferation and migration of MDA-MB-231 human breast cancer cells (Nho et al., 2015). A flavonoid, glycoside that isolated from *S. chinensis* rhizome effects against human cancer cell lines (HeLA) (Li et al., 2007).

1.4. *Morinda tinctoria* Roxb.

It is an evergreen shrub or small tree in the family Rubiaceae commonly known as Indian mulberry. GC-MS analysis shows the presence of compounds like scopolamine, a secondary metabolite and Malvidin-3, 5-diglucoside, an anthocyanin and a glycoside, as main constituents (Arunachalam et al., 2015). Significant anticancer and cytotoxic effect found in the methanolic extract against EAC and human cancer cell lines (Kumar et al., 2017).

1.5. *Trapa natans* L.

The small free-floating plant grows mainly in shallow water or swampy regions and belongs to family Trapaceae. The plant contains carbohydrates, minerals, calcium, phosphate, iron, copper, manganese, magnesium, sodium and potassium. The kernels contain some vitamins like thiamine, riboflavin, nicotinic acid, vitamin C, vitamin A, D-amylase and considerable amount of phosphorylases. Even though not many studies and formulations of *T. natans* are documented, the plant has been indicated for cancer (Bharthi et al., 2015).

1.6. *Taxus baccata* L.

The tree species belongs to the family Taxaceae, has both toxic and medicinal properties. Identifying the chemical components of different parts of the tree can be useful in the better understanding of toxicity and medicinal effects. A large number of chemical constituents have been reported from the Himalayan yew, *T. baccata* or *T. wallichiana* in which the main constituents are taxoids and phenolics. Taxol and paclitaxel are important anticancer constituents using to prepare the anticancer drugs (Das & Anjani, 1998). These alkaloids interrupt mitosis by promoting and stabilizing microtubule formation. Methanolic extract of *T. baccata* displays significant anticancer activity on MDA-MB-231 and HCT-116 cell lines (Milutinovic et al., 2015).

1.7. *Allium sativum* L.

It is a bulbous perennial plant coming under the family Alliaceae, which is characterized by its peculiar aroma and pungent taste. The species is rich in sulphur containing compounds such as allicin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, alliin, S-allylcysteine and S-allylmercaptocysteine that impact various stages of carcinogenesis. The anticancer actions by these garlic derived phytochemicals include altering the mitochondrial permeability, inhibiting angiogenesis, enhancing antioxidative and proapoptotic properties and regulating cell proliferation. The effects of various garlic-derived products, the phytoconstituents and nanoformulations has negative impact on skin, prostate, ovarian, breast, gastric, colorectal, oral, liver and pancreatic cancers. The constituents inhibit different stages of cancer including initiation, promotion and progression. Besides, these bioactive metabolites alter the lipid peroxidation, activity of nitric oxide synth-

etase, nuclear factor-κB and protein kinase C, cell cycle and survival signalling (Greef et al., 2021; Mondal et al., 2022).

1.8. *Erythrina variegata* L.

It is a showy, spreading, deciduous tree legume that can reach a height of 18-25 m and involving in Fabaceae. The plant is a rich source of alkaloids like 3- Demethoxyerythratidinone, erythraline, erythramine, erythrinine, erythratidinone, erysonine and erysotine. Species acts as a potential source of anticancer agent by MTT assay, nucleoprotein assay and cell morphology studies on MDA-MB-231 cells (Rai et al., 2017).

2. Outlook

The poly herbal formulations or formulations consisting of metals or minerals possessing a 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. Siddha medicine can be useful in the management of cancer, besides being safe, non-toxic, cost effective and non-invasive. Owing to the high antioxidative potential, most

1. Plants used in Siddha system of medicine as anticancer agents

Plant species	Mode of administration	Formulation
Clerodendron inerme (L.) Gaertn.	The leaves are indicated for cancerous lesions. The intake of leaf/ root juice twice a day is beneficial in treatment of tumours in neck region. The leaves roasted in castor oil can also be used for the external application in cancerous legion.	Vippuruthi ennai
Plumbago indica L.	*Plumbago* root barks are generally indicated for tumours.	Kodiveli ennai, Kodiveli tailam, Megathennai Chitramoola kuligai
Smilax chinensis L.	Root tuber of *S. chinensis* is indicated for cancerous growths.	Parangipattai rasayananm
Morinda tinctoria Roxb .	The root bark of *M. tinctoria* is indicated for tumours, ulcers and cancer.	Nunappattai thylam
Trapa natans L.	The tender leaves and stem of *T. natans* can be grinded and applied externally for the treatment of cancers.	-
Taxus baccata L.	The leaves of *Taxus buccata* grinded in vinegar can be applied externally for cancerous lesions.	Nanti Mezhuku, Rasaganthi melugu, Kantaki Rasayanam
Allium sativum L.	Garlic paste is being used externally for the treatment of tumours.	Megathennai
Erythrina variegata L .	The leaves of *E . variegata* can be applied externally for cancerous lesions	-

(Ref.: Classical Siddha Literature, Gunapadam)

of the Siddha medicines confer nutrition and reduce the side effects imposed by conventional cancer therapy. The compound formulations or single drugs in Siddha literature shall be subjected to retrospective analysis for the scientific validation behind the therapeutic aspects.

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