Cancer Preventive Potential of Musaceae Members

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Abstract: The genera of Musaceae are well known due to the secondary metabolite induced medicinal properties. Anticancer potential of *Musa* and *Ensete* species are better remedy to suppress the cancer initiation, proliferation and metastasis related apoptosis in different human cell lines without interfering the healthy cells.

Keywords: *Musa, Ensete,* antiproliferative, cytotoxicity, secondary metabolites

The monocotyledonous family, Musaceae, consists rhizhomatous plants that growing commonly in humid areas. The members are distributed in South East Asia and African countries. The plants may be perennial or monocarpic rhizomatous herbs with terminal large inflorescence on huge pseudostem. This ancient family consists of three genera viz. *Musa* L., *Ensete* Horan. and *Musella* (Franch.) H.W.Li; while Indian wild Musaceae represented by two genera, *Ensete* and *Musa*. Both genera are economically important due to the presence of a number of medicinal, nutritious and aesthetic values. The wild genus, *Ensete*, can easily identify from *Musa* by the presence of non stoloniferous pseudostem with seeded fruits which consists a number of phytochemical compounds (Sabu et al., 2013).

The fruits of cultivated or wild genus, *Musa*, are rich with starch, sugar, potassium, calcium, sodium and magnesium (Doymaz, 2010). Moreover, it shows the antioxidant, antibacterial, antifungal, antidiarrheal and antiulcer properties due to the presence of phytochemical compounds. Presence of secondary metabolites in *Musa* sp. includes alkaloids, flavonoids, terpenoids, coumarins, phenols, tannins, steroids, glycosides and saponins which in turn improve the medicinal properties. Various parts of the plant including leaves, flowers, pseudostem and fruit and fruit peel are using in various industries nowadays that makes the edible members as one of the major cultivated crops in India. Applications in bio fuelproduction, biosorbents, pulp and paper, cosmetics, organic fertilizer, environmental clean-up etc. are very popular from the ancient time onwards.

In recent decades, advanced medicines have replaced by traditional medicines for treating human illnesses. Extensive phytoch-

emical studies in plants promise the anticancer properties which interfere the cancer initiation and proliferation by modulating various pathways in cells. Cancer is a hyper proliferative disorder and the second most frequent cause of morality. According to the Global Observatory Report, the number of newly diagnosed cancer cases is projected to increase to 29.5 million per year and projected cancer related deaths are expected to increase to 16.4 million per year by 2040. Currently, many of the anticancer medications destroy both cancer and healthy cells. In addition, the cancer therapy causes non specific targeting and induction of drug resistance. To overcome the present obstacles, the more effective anticancer medications with improved safety profiles are urgent to defeat the dangerous disease. Because of this reason, the use of medicinal plants for health promotion and disease prevention has increased now. In Musaceae members, the phytochemicals are being extensively investigated and demonstrated that promising anticarcinogenic properties by interfering with cancer modulating pathways.

1. Anticancer plants in Musaceae

1.1. *Musa* L.

The genus *Musa* comprises of 65 species including both wild and cultivated taxa. At present, the different cultivars of the species, *Musa paradisiaca*, cultivated around the world and the significant producers of fruits are India, China, Philippines and Brazil. But *M. acuminata* has been discovered from the native habitats of India historically. The species are perennial herb with large fruit bearing pseudostem that emerges from the rhizome. The stem is a compact assembly of wrapping with spirally arranged leaf sheaths. The leaf arising from the centre of pseudostem by elongating the distal end of the leaf sheath in to a petiole, in turn split the lamina in to two equal halves. Inflorescence is a spike which turning downward towards the soil and consists both male and female flowers. The fruits are normally parthenocarpic fleshy berry without seeds. In each cultivar, the fruits vary in their arrangement, position, number per hand, size, shape, colour, nature etc.

Anticancer activities: The phytochemical analysis of *Musa* spp. reveals the presence of numerous secondary metabolites including polyphenols, terpenoids, alkaloids, steroids, anthocyanins, tannins etc. The plant extract with the phytochemical compound is better strategy to prevent cancer cell proliferation in human beings. The aqueous methanol extract of *Nendran* banana peel exhibits significant antitumour activity against MCF-7 breast cancer cell line (Durgadevi et al., 2019). Through induction of apoptosis, the anthocyanin from methanol extract of *M. acuminata* bract and *M. cavendish* green peel hydroalcoholic extract suppresses the proliferation of MCF-7cells (Jenshi & Aravindhan, 2011; Barroso et al., 2019). The hexane extract of *M. sapientum* peel and pulp blocks the proliferation of MCF-7 cells (Dahham et al., 2015); meanwhile, the acetone extract of *M. acuminata* leaves exhibits prominent activity against breast tumour cell lines (Salama et al., 2020). *M. paradisiaca* floral extracts has shown the potent antitumourigenic activity in MCF-7 and MDA-MB-231 breast cancer cell lines (Lavudi et al., 2022).

By the increased activity of caspase enzyme, the ethanol extract of *M. paradisiaca*

flower exhibits anticancer activity against HeLa cervical cancer cell line (Nadumane & Timsina, 2014). Due to the effect of eugenol and phytol, ethyl acetate extract shows anticervical carcinoma in HeLa cell lines (Deep et al., 2020). By enhancing DNA fragmentation, ferulic acid isolated from banana peel using *Staphylococcus aureus* induces antiproliferative and cytotoxic activities against HeLa cervical cancer cells (Srinivasan et al., 2017). The methanol extract of *M. acuminata* flower reveals antiproliferative and cytotoxic potential against HeLa cells (Das et al., 2020). An ethyl acetate fraction of *M. x paradisiaca* leaves also indicates strong cytotoxic and anticancer activity against HeLa and A375 cervical cancer cell lines. At a concentration of 100 µg/mL, *M. cavendish* green peel hydroalcoholic extract demonstrates antiproliferative and cytotoxic activity against A-375 human malignant melanoma cells (Barroso et al., 2019). Due to the presence of eugenol and phytol, ethyl acetate extract of *M. paradisiaca* leaves prevents malignant melanoma (Deep et al., 2020).

By arresting cell growth, the hexane fraction of *M. sapientum* peel and pulp exhibits in vitro anticancer activity against HCT-116 colon carcinoma cell line (Dahham et al., 2015). *M. cavendish* green peel hydroalcoholic extract suppresses the proliferation of Caco-2 human colorectal adenocarcinoma cells (Barroso et al., 2019). Protocatechualdehyde (PCA, 3,4-dihydroxybenzaldehyde) from green cavendish bananas promises antiproliferative activity by triggering apoptosis in human colorectal carcinoma cells, HCT116 and SW480, through histone deacetylase 2 (HDAC2) initiated cyclin D1 suppression. The compound, 2-pentanone present in banana ameliorates antiproliferative action by inhibiting the prostaglandin (PGE2) production and cyclooxygenase 2 (COX-2) protein expression in colon cancer cells, HT29 (Pettersson et al., 2008).

By decreasing the level of mitochondrial membrane potential (MMP) and increasing the reactive oxygen species (ROS) level, *M. cavendish* green peel hydroalcoholic extract exhibits antiproliferative activity against HepG2 human hepatocellular carcinoma cell lines (Barroso et al., 2019). Various extracts of banana (*Musa* AAB var. Nanjanagudu Rasabale) pseudostem and rhizome demonstrates cytotoxicity against HepG2 cell lines. Crude chloroform and acetone extracts of the banana pseudostem and rhizome express substantial cytotoxicity against the cell lines (Kandasamy et al., 2016). The isolated bioactive compounds, 4-epicyclomusalenone, cycloeucalenol acetate and chlorogenic acid, from banana rhizome exhibit potent cytotoxicity against HepG2 cell lines. Acetone extract of *M. acuminata* leaves possesses a high content of phenolics, flavonoids and tannins of which vanillic and ferulic acids are more intensive in turn shows vigorous activity against liver hepatocellular tumour cell lines (Salama et al., 2020).

Ethyl acetate subfraction of the ethanol extract of *M. paradisiaca* soft piths exhibits potent cytotoxic and antiproliferative activity against the human oral squamous cell carcinoma cell line (HSC-4) (Ghafar et al., 2019). Aqueous banana flower extract shows anticancer activity against benign prostatic hyperplasia in vitro. The extract at a concentration of 2 mg/mL normally reduces the viability of BPH-1 cells through cell cycle

arrest at the G_1 phase (Liu et al., 2018). By inhibiting 5α-reductase activity, the methanol fraction of the banana peel inhibits testosterone induced cell growth in the androgen responsive LNCaP human prostate carcinoma cell line (Akamine et al., 2009). In MG-63 cell lines, the hexane extract of *M. acuminata* promotes the anticancer activity (Agustine et al., 2020).

1.2. *Ensete* Bruce ex Horan.

The genus *Ensete* (False Banana) was first named by Horaninow (1862) and later 25 species of *Ensete* were included by Cheesman (1947). Later, the number of species under the genus has shrunken and recorded as seven species viz. *Ensete gilletii, E. homblei, E. perrieri, E. ventricosum, E. glaucum, E. lasiocarpum* and *E. superbum.* Among the species, *E. superbum* and *E. glaucum* are commonly distributed in North-East and Whestern Ghats of India.

E. superbum is commonly known as Wild Banana. It is monocarpic and non stoloniferous perennial shrub found in Dindigul and Anaimalai Hills, Western Ghats and some parts of peninsular India. The species is well documented for the medicinal and nutritional purposes for the local peoples in India and Ethiopia. It is well recorded in different regions of the world for ailments such as dog bite, semen production, abortion, leucorrhoea, stomachache, immune response, diabetes, psychosomatic, contraceptive, umbilical cord care, pneumonia, cholera, labor and delivery pain, dehydration, appendicitis, chickenpox, measles, urinary problems, food poisoning, snake bites, diarrhoea, dysentery, jaundice, bone fracture, fever, asthma and leucoderma. Plant is the source of many phytochemical compounds like triterpenoid esters, proanthocyanidin, propelargonidin glucosides, pelargonidin, anigorufone, hydroxyanigorufone, β-carboline alkaloids etc. Pharmacologically, *E. superbum* possesses antiurolithiatic, antidiabetic, antifertility, antiestrogenic, antiviral, cardiovascular and antiinflammatory activities (Sethiya et al., 2019).

Naturally, *Ensete glaucum* is distributed in Burma, Thailand, China, Laos, Viet Nam, Philippine, Papua New Guinea and Solomon Islands up to Java; and its probable existence in North-East India was reported by Simonds (1960). The species is monocarpic nonstoloniferous herb with pseudostem, persistant bracts, hermaphrodite flowers and large seeds. Seeds are black, smooth and asymmetrically subglobose to irregular due to the pressure in packed fruit. Long dormancy period of seed make it unique habitat and limited distribution (Majumdar et al., 2013).

The fruits have been used in folk medicine to treat kidney stones, diabetes, perforated edema, stomach ulcers and skin allergies. The seeds contain flavonoids, saponins and tannins; meanwhile, the presence of amino acids, flavonoids and terpenoids in peel and flavonoids, tannins, saponins and amino acids in pulp is also confirmed. The total content of polyphenols and flavonoids is higher in the seeds than in peel and pulp (Ly et al., 2022). Presence of secondary metabolites induces the antioxidant and antimicrobial properties of the species (Tuan, 2021).

Anticancer activities: The ripe peel aqueous extract of *E. superbum* exhibits higher cytotoxic, antiinflammatory and antimutagenic activities compared to the aqueous extracts of

seed, flower and bract. The active compounds like quercetin-3-*O*-rutinoside, 3,5-dimethoxy-4-hydroxybenzoic acid and 4',5,7-trihydroxyflavone present in the species possesses the antiproliferative potential in colorectal cell lines (Mathew et al., 2021).

2. Outlook

Two genera in Musaceae, *Musa* and *Ensete*, are naturally distributed in India which show nutritious, medicinal, aesthetic and religious values. The parthenocarpic fruits of wild and cultivated species of *Musa* play significant role in diet. In addition, the plant parts viz. leaf, pseudostem, flower, corm etc. prevent a number of human diseases due to the properties including antimicrobial, antioxidant, anticancer etc. The wild genus, *Ensete*, is nonstoloniferous herb with seeded fruits rich with secondary metabolites in turn improves medicinal values. Nowadays, the production of natural medicines from plants becomes very relevant and safe strategy to prevent cancer initiation and proliferation. The identified Musaceae members are better source of anticancer compounds. Hence, it will be helpful in production of natural anticarcinogenic medicines in present decades without causing any side effects in human beings.

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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

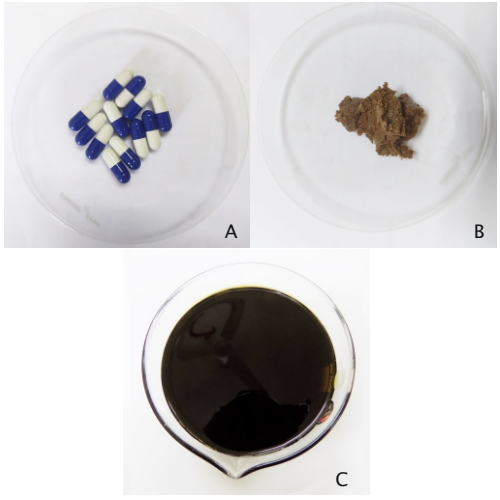

Fig.1. A. Rasagandhi Mezhugu Capsules, B. Gandhaka, C. Rasayanam Megathennai

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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