Exploration of Lamiaceae Members in Cancer Treatment

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Abstract: The members of Lamiaceae are aromatic with a number of phytochemical compounds having anticancer properties against different human cancer cells. The major compounds in plants include menthol, geraniol, eucalyptol, camphor and thymol in turn consider as a source of anticancer drugs. The reduction of tumours and inhibition of metastasis by arresting cell cycle are due to the antiproliferative bioactivities of phytocompounds.

Keywords: Anticarcinogenic, Lamiaceae, cytotoxicity, chemoresistance, cell proliferation

Cancer is a worldwide public health problem, which involves uncontrolled growth of cells and the main reason for cancer today is life style. The cells lose their interaction with each other, invade neighboring tissues and finally spread to distant tissues of the body. It is one of the leading causes of death in both developed and developing countries. It has been reported that in India there will be 19 to 20 lakhs death in 2022 due to cancer. The anticancer properties of plants have been recognized many years ago. The natural compounds in plants and microbes fight against cancer. Recent researches in the field of plant based natural compounds have move towards advanced and molecular level understandings, leading to the development of potent anticancer agents and also plants have been accepted as abundant and rich sources for the development of novel therapeutic agents for the management and prevention of different cancer types.

The Lamiaceae is a family of flowering plants commonly known as the mint, deadnettle or sage family. Many of the members of the family are aromatic due to the presence of secondary metabolites. Many members have demonstrated considerable efficiency in inhibiting cancer cell growth through synergistic effects. Lamiaceae is among the largest families of flowering plants with about 250 genera and over 7,000 species distributed around the world. It is considered as the important source of essential oils such as menthol, geraniol, eucalyptol, camphor and thymol; therefore, it is widely used in various medicines. In addition to proven biological activities, essential oils have recently been evaluated for anticancer activities and considered as a source of anticancer drugs. The present chapter helps to assess the anticancer properties of essential oils obtained from different members of Lamiaceae and also we can understand which plants are used as anticancer agents.

1. Anticancer plants in Lamiaceae

1.1. *Anisochilus* Wall. ex Benth.

The genus, *Anisochilus* is commonly known as 'Kapuri'. The native place of the genus is China, the Indian Subcontinent and Indochina. The plants are herbs or under-shrubs with opposite or whorled leaves. Flowers are usually small in whorled spike inflorescence. The calyx is 2-lipped or 5-lobed with 2-lipped corolla tube of slender below and inflated above. Stamens are four in number and didynamous with free filaments. The ovary is 4-partite and style bifid at apex. Fruit are 4 ovoid dry nutlets. The plant has healing qualities that help with dermal problems and address conditions like stomach ulcers. Additionally, it contains active ingredients such as apigenin, leutiolin and camphor (Bhagat, 2014). Moreover, the secondary metabolites like alkaloids, flavonoids, saponins, glucosides, tannins, lignin, pectin, starch, cellulose and carbohydrates are abundant in the plant (Reshi, 2015).

Anticancer activities: *A. carnosus* extracts play a significant role in lowering of tumour volume, tumour weight and cell viability in EAC induced organisms. It helps in considerable prolongation of host life span and restoration of hematological parameters to almost normal levels. The ethanol extracts and fractions of the plant include luteolin along with phytosterols, terpenoids and flavonoids that induce anti-tumour potential in the plant (Gupta et al., 2015). Petroleum ether and ethanolic extracts show higher cytotoxic effect against BT-549 compared to the aqueous extracts. Because, the ethanol extract contains the highest concentration of luteolin than the aqueous extract. Due to the reason, the petroleum ether and ethanolic extracts induce promising anticancer activity and has the potential to be developed into a therapeutic option for the treatment of cancer (Bhagat et al., 2014).

1.2. *Leucas* R.Br.

The genus includes herbs, under-shrubs or shrubs with pubescent four angled branches showing opposite or whorled phyllotaxy. Flowers are white in colour and in axillary inflorescence. Bracts are many, linear or lanceolate. Calyx is tubular, 10-ribbed, equally or unequally 6-10-toothed. Bilipped corolla has upper erect and lower spreading lip. Stamens are four in number and didynamous. The ovary has four carpels that form dry nutlets after fertilization.

Leucas is mostly distributed over Africa, Iran, India, China, Japan, Indonesia and with a few species in Queensland and on various islands in the Indian Ocean. The plant is used traditionally as an antipyretic and insecticide. It possesses various pharmacological activities like antifungal, antioxidant, antimicrobial and cytotoxicity. Plant is the rich source of various phytochemical constituents viz. triterpenoids, oleanolic acid, ursolic acid, b-sitosterol, nicotine, sterols, glucoside, diterpenes, phenolic compounds etc. (Prajapati, 2010).

Anticancer activities: The presence of diverse bioactive compounds makes *Leucas* sp. more demandable for curing several diseases such as inflammatory diseases, diabetes and cancer. The different phytochemicals in methanol extract of *L. indica* leaves show remarkable antioxidant and anticancer activities (Susmi et al., 2022). The crude methanol extracts of

flowers exhibit antioxidant and anticancerous properties due to the cytotoxic effects against the selected cancerous cell lines viz. HeLa, HCT116, HL-60 and MCF-7. The important bioactive compound responsible for anticancer activity is 6-hydroxy-3-(4-hydroxyphenyl)-7-(3,4,5-trihydroxy-6-)(hydroxymethyl)tetrahydro-2H-pyran-2yl)-4H-chromen-4-one. Based on the antioxidant and anticancerous properties, *L. indica* might be a promising source of useful natural products and the newly bioactive compound might offer opportunities to develop new anticancerous drugs (Sowjanya et al., 2022). Presence of DPPH, flavoinds, FRAPS and phenol contents in water and methanol extracts of *L. aspera* induces antioxidant and anticancer activities as well as cytotoxicity in treated cells (Suruthi et al., 2016). The silver nanoparticles synthesized from aqueous leaf extract exhibit potent cytotoxic effect on cervical cancer cells and induce cell death through apoptosis (Chavata et al., 2019). Silver-copper bimetallic nanoparticles (Ag-Cu BNP) synthesized from the leaf extract act as a bioreducing agent that shows significant alveolar anticancer and antioxidant activity against human alveolar cancer cell line A549 than aqueous leaf extract (Yang et al., 2022). Moreover, ethyl acetate fraction shows cytotoxic effects in Dalton's lymphoma cell lines results in significant decrease in ascites tumour volume and viable cell count (Augustine et al., 2014).

L. biflora leaf extract fabricated silver nanoparticles (LbLE-Ag-NPs) act as a potential anticancer agent. LbLE-AgNPs exhibits an effective dose dependent anticancerous activity on MDA-MB-231 breast cancer cell line (Chitra et al., 2022). The leaf extract of *L. zeylanica* is mitodepressive and may be considered as a potential antitumour promoting agent (Sinha & Kumar, 2014). The methanolic extract contains phenol, flavonoid and tannin that are also responsible for cytotoxicity related antitumour activity (Abdullah et al., 2021). Ethanolic extract of *L. lanata* includes reducing sugars, alkaloids, cardiac glycosides, flavonoids and tannins. The plant also has 6-octadecenoic acid, cis-13-octadecenoic acid and l-(+)-ascorbic acid 2,6-dihexadecanoate as dominant phytochemicals in turn cause anticancer properties (Vijisaral & Arumugam, 2014; Vermaa et al., 2020). *L. martinicensis* has high inhibition of the cyclooxygenase-2 (COX-2) enzyme with IC_{50} values ranging from 3.79–25.80 µg/ml in turn induce anticancer activity against cervical and epidermoid cancer (Twilley et al., 2017).

1.3. *Leonotis* (Pers.) R.Br.

Leonotis is commonly called 'Lion's tail' and 'Wild dagga'. The plants may be herbs or shrubs with 4 angled stems having opposite phyllotaxy. The flowers with numerous bracts are yellow and axillary in position. Calyx is 10-ribbed while corolla bear 2 lips in which the upper lip is long and concave with a villous crown; and the lower lip is small 3 lobed with the largest mid lobe. Stamens are four in number and didynamous. The 4 partite ovary is end with subulate style that forms 4 dry nutlets after pollination and fertilization. The plants are the rich source of phenols, flavonoids, carotenoids, fatty acids and steroids (Oliveira, 2015). It is used in the treatment of haemorrhoids, eczema, skin rashes, boils, itching, muscular cramps, headache, epilepsy, chest infections, constipation, spider and snake bites due to the

presence of secondary metabolites (Nsuala, 2015).

Anticancer activities: *L. nepetifolia* root methanolic extract acts as a source of bioactive compounds with cytotoxic, genotoxic and proapoptotic activity against human melanoma cells (Merecz-Sadowska et al., 2022). It shows in vitro cytotoxic effects on HepG2 cell line. The methanol extract of leaves is to be more significant in scavenging free radicals that causes dose dependent damage to the breast and laryngeal cancer cell lines, MCF-7 and Hep2 (Veerabadran et al., 2013). While the ethanolic extract of the plant includes 1,3 propanediamine N (3- aminopropyl)-N-methyl, 1,3-methyl-2-(3,7,11-trimethyl dodecyl thiophene and benzoquinoline (n) quinoline 2,4-dimethyl shows cytotoxicity against Ehrlich Ascites carcinoma by activating the apoptotic pathway (Gurunagarajan & Pemaiah, 2011). Leaf extracts have various bioactive components including λ-sitosterol in methanol extract, 1-nonadecanol in petroleum extract and eicosane in hexane extract. Due to this, the leaves are significant in scavenging free radicals and causing damage to proliferative cells. Similarly, the different solvent extracts of flower buds contain a significant amount of various bioactive phytochemicals with antioxidant and anticancer activities; thus, the plant could serve as a potential source of pharmacological applications (Nagaraja et al., 2022).

1.4. *Isodon* (Schrad. ex Benth.) Spach

Isodon is native to the tropics and subtropics, especially in China. They are pubescent herbs with 4 angled branchlets with ovate leaves having truncate base and crenate-serrate margin. Panicled inflorescence is slender and terminal in position. Calyx is campanulate and 2 lipped with 3+2 condition. Corolla is white and 2 lipped with 4 + 1 condition. Stamens are four in number. Fruit is ovoid nutlets. The plants are used for treatment of acute hepatitis, trauma, dysentery, enteritis, bacterial infections and inflammation, treatment of sore throats, malaria, jaundice, pneumonia, gastrointestinal disorders and cholecystitis (Lianzhu et al., 2011).

Anticancer activities: The methanolic extract of *I. coetsa* treated DLA and EAC cell lines reveals cytotoxic activity that varies on basis of concentration. It induces cell death in dividing cells, an essential phenomenon in anticancer therapy (Neelamkavil & Thoppil, 2016). Melissoidesin G (MOG) is a diterpenoid purified from *I. melissoides*, uses in Chinese traditional medicine as antitumour and antiinflammatory agents. MOG specifically inhibits the growth of human leukemia cell lines and primary acute myeloid leukemia blasts via induction of apoptosis, with the evidence of mitochondrial ΔΨm loss, reactive oxygen species production, caspases activation and nuclear fragmentation (Yu et al., 2007). Water soluble flavanoids in *I. lophanthoides* var. *gerardianus* inhibit cell growth in HepG2 cells. It stimulates to increase the amount of iROS, mitochondrial membrane potential and the apoptotic relevant factors (cytochrome c, caspase-3) in HepG2 cells in turn induce apoptosis through downregulating apoptosis antagonizing protein (Bcl-2, Survivin, mcl-1) and upregulating apoptosis promoting proteins (Bax) (Feng et al., 2016). The ent-kaurene diterpenoid melissoidesin isolated from the leaves of *I. wightii* shows significant cytotoxicity against lung cancer and neurobla-

stoma cell lines. The prevention of DNA degradation activity of melissoidesin is prominently significant that promoting the anticarcinogenic activity in a dose dependent manner (Thirugnanasampandan & Jayakumar, 2009).

Diterpenoids isolated from *I. wightii* exhibits antibacterial, antiacetylcholinesterase, antioxidant and anticarcinogenic activities. Cytotoxic activity of ABA against cervical cancer cells (HeLa) promising it as a natural compound for herbal anticancer drug preparation (Ramnath et al., 2016). The compound, 3,4-*seco*-isopimarane isoamethinol D (4), isolated from *I. amethystoides* has toxicity to the cervical Hela cancer (Hela) cells and the lung (A549) cancer cells (Zhao et al., 2022).

Oridonin is the main bioactive constituent of *I. rubescens* which has anti-neoplastic effects against hepatocarcinoma HepG2 cells in a dose dependent manner. Treatment with oridonin induces apoptosis and G2/M cell cycle arrest. In addition, the up regulation of Hsp70.1, STRAP, TCTP, Sti1 and PPase as well as the down regulation of hnRNP-E1 by oridonin could be responsible for the apoptotic and G2/M arresting effects suppress the liver cancer cells (Wang et al., 2011).

1.5. *Hyptis* Jacq.

Hyptis is commonly known as 'Bushmints' and widespread in tropical North and South America as well as parts of West Africa. They are herbs or shrubs with opposite leaves and small or medium sized flowers. Calyx is tubular with 5 lobes and the five lobbed corolla tube is cylindrical. Didynamous stamens are 4 in number with free filaments. Ovary is 4 partite with sub-entire or shortly bifid stigma on the style. Fruit is dry nutlet. The plant shows antimicrobial, antidiabetic, antiulcer and antiinflammatory effects due to the presence of flavonoids and terpinoids.

Anticancer activities: Ethanolic leaf extract of *H. capitata* shows anticancer potential on T47D cells. The extract contains neophytadiene, hexadecanoic acid, methyl ester, ethyl ester and heptadecanoic acid, 16-methyl-, methyl ester that work synergistically to inhibit cell proliferation (Tobungan et al., 2022). *H. suaveolens* shows in vitro anticancer activity due to the occurrence of the major compounds of sabinene, trans caryophyllene, E-spathulenol, rimuene, 1,8 cineole, β-elemene, eucaliptol, bergamotol, α-selinene, caryophyllene oxide, γ-elemene and α-humulene. The compounds are very effective against human breast cancer cell line, MCF-7 (Poonkodi et al., 2017). *H. pectinata* hydro ethanolic extract includes a greater proportion of monoterpenes, cymene, thymol and β-terpinene in the essential oil and of a 2(5H)-furanone and α-pyrones in a dichloromethane extract. Thus shows moderate cytotoxicity against HCT-8 line cells and inhibits the sarcoma 180 (Barbosa et al., 2012). Isoquercitrin isolated from the aerial parts of *H. fasciculata* is effective to interfere with glioblastoma (Gbm) cell growth. Quercetin and rutin in the extract negatively affect Gbm cell proliferation after treatment times of longer than 24 h. Isoquercitrin did not induce Gbm cell death, but in turn cause marked reduction in cyclin D1 levels and an increase in p27 levels. Therefore, the compound reduces Gbm cell growth without inducing apoptosis, possibly by modulating the control of the cell cycle (Amado

et al., 2009). The extract of *H. mutabilis* leaves with different polarities viz. hexane, methanol, water and hot water; are against sarcoma 180 and Ehrlich solid tumour due to the anticancer activity. The extract includes steroids, saponins, flavonoids and catechins. The aqueous extract shows strong inhibition of tumour growth compared to other extracts (Ximenes et al., 2012). Moreover, *H. verticillata* and *H. tomentosa* are strongly effective against different cancer cell proliferation due to the effective secondary metabolites (Kingston et al., 1979; Picking et al., 2013).

1.6. *Gomphostemma* Wall. ex Benth.

The plant is native to Southeast Asia, China and the Indian subcontinent. The plants are herbs or undershrubs with salient morphological characters. The leaves are opposite, large, entire, dentate or crenate. Flowers are rather large, usually yellow with cymose inflorescence. Calyx is campanulate, equally 5 lobed, 10 ribbed; while corolla 2 lipped with slender tube. Didynamous stamens are four in number and ovary 4 partite with slender style and bifid stigma. After fertilization, the ovary forms nutlets. Normally, the plant is used to prepare medicines for rheumatism, dysentery and diorrohea by kurichia, kuruma and kattunaika tribes of Kerala due to the presence of alkaloids, flavonoids, terpenoids, phenols, tannins and saponins in the species.

Anticancer activities: The methanol extracts of selected species of *Gomphostemma*, viz., *G. heyneanum* and *G. eriocarpum*, consists a total of 72 volatile phytoconstituents belonging to various classes like terpenoids, flavonoids, phenolics, fatty acids, aldehydes etc.. Among them, the major components identified with prominent biological activities include α-thujene, neophytadiene, β-caryophyllene, limonene, eucalyptol, phytol, stearic acid, stigmasterol, quinic acid and tocopherol (Sajitha Menon & Thoppil, 2022). The cytotoxic potential of aqueous extract of *G. heyneanum* is the sign of apoptotic induction. Cytogenetic aberrations with apoptotic signs together with reduction in metabolic activity due to mitochondrial disfunction and cell death caused by the membrane damage are all indications of possible apoptotic potential of *G. heyneanum* extract (Sajitha Menon & Thoppil, 2018).

1.7. *Clinopodium* L.

Clinopodium is a genus of flowering plants in the mint family. It is commonly known as 'Wild basil' or 'Savory'. The genus includes several species of perennial herbs that are native to Europe, Asia and Africa. *Clinopodium* plants are typically low growing, bushy herbs with woody stems and small, oval shaped leaves that are arranged opposite each other on the stem. The leaves often have a pleasant aroma when crushed. The flowers of *Clinopodium* species are small and typically arranged in dense clusters at the tips of the stems or in the axils of the leaves. The flowers are usually tubular in shape, with a slightly curved or bent corolla that is typically two lipped. The corolla tube is often hairy or glandular, and the upper lip may be concave or hooded, while the lower lip is often three lobed. The flowers come in a variety of colors including white, pink, purple and blue. They are often used in traditional medicine to treat a range of ailments, including digestive issues, headaches and respiratory problems. Some species of *Clinopodium*, such

as *C. douglasii*, is also used as culinary herbs in certain cuisines.

Anticancer activities: The acidified, alkalized and lipophilic extracts of *C. vulgare* are very effective on the cell viability of cancer cell lines like CaOV (human testis cystadenocarcinoma), HeLa (human cervical adenocarcinoma), HT-29 (human colorectal adenocarcinoma) and FL (human amnion normal). The acidified and lipophilic extracts exert selective dose dependent cytotoxic activity against CaOV and HeLa cells, while the cytotoxicity of the alkalized extract against these cell lines is less pronounced. All extracts show very weak or lack of cytotoxic actions towards HT-29 and the normal FL cells. *C. vulgare* extracts possess selective anticancer activity and could serve as a source for isolation and development of new therapeutic anticancer agents (Batsalova et al., 2017). The petroleum ether, chloroform and methanol extracts of *C. umbrosum* have cytotoxic activity on HN-5 oral cancer cells after 24 h of treatment. The cytotoxicity of buddlejasaponin IVa and buddlejasaponin IV shows that buddlejasaponin IV possesses superior cytotoxicity. Both compounds show their cytotoxicity through the apoptotic pathway with increasing *Bax/Bcl2* ratio and the level of caspase 9. Similarly, HN-5 cells migration reduces with two saponin compounds (Sharifi et al., 2022). The essential oil from *C. sericeum* includes 73 compounds in which major components of the oil are -germacrene-D, caryophyllene and sabinene. The essential oil displays antibacterial activity against gram negative and gram positive bacterial strains in a dose range close to standard antibiotics. The antiproliferative activity in healthy non tumourigenic cells (HEK-293) and in three human cancer cell lines (T24, DU-145 and MCF-7) is positive by the essential oil (Benites et al., 2021).

1.8. *Ocimum* L.

Ocimum is a genus of aromatic annual or perennial herbs, undershrubs or shrubs native to the tropical and warm temperate regions of all 6 inhabited continents with the greatest number of species in Africa. It has strong aroma because of the presence of oil glands. Leaves are opposite or whorled, usually toothed and petioled. The flowers are small in whorls of 6-10 on the axis of elongate spikes or racemes which are sometimes panicled. The bracts are small and caducous. Calyx is 2 lipped in which upper lip broad and lower lip with 4 mucronate teeth. Corolla tube is short and 2 lipped. The upper lip is subequally 4 lobed and lower lip hardly longer than the upper. The didynamous stamens are four in number in which the filaments are free and connate below. Ovary is 4 partite with slender style and bifid stigma. A number of secondary metabolites such as nerol, eugenol, terpinene pinene and carvacrol are present in whole plant. The leaves are rich with ursolic acid, apigenin, luteolin and orientin which are used for the treatment of bronchitis, bronchial asthma, malaria, diarrhea, dysentery and skin diseases.

Anticancer activities: *O. gratissimum, O. basilicum, O. canum, O. kilimandscharicum, O. tenuiflorum* and *O. citriodorum* are found to reduce the proliferation of human breast cancer cells (Anusmitha et al., 2022). The ethanolic extract of *O. sanctum* induces cytotoxicity in human fibrosarcoma (HFS) cells. Biochemically

the extract treated HFS cells show depleted intracellular glutathione and increased levels of lipid peroxidation products. Administration of aqueous and ethanolic extracts in mice bearing Sarcoma-180 solid tumours mediates a significant reduction in tumour volume and an increase in lifespan (Karthikeyan et al., 1999).

Antioxidants and other bioactive compounds in *O. basilicum* leaves show important potential anticancer activity regards to cell death and viability inhibition, cytotoxicity, apoptosis, cell cycle arrest etc. Additionally, rosmarinic acid shows inhibition in DNA and protein synthesis in hepatoma derived cell line (HepG2) by lowering the suppression on caspase-3 activation to block apoptosis (Perna et al., 2022). Methanolic extract of *O. basilicum* contains ursolic acid which induces anticancer activity in HT-144, MCF-7, NCI-H460 and SF-268 cell lines. Ursolic acid induces a significant decrease in the percentage of cells in anaphase or telophase stages along with F actin aggregation and mitotic spindle distortion (Arshad Qamar et al., 2010). Beyond, the methanol extract of basil seeds is anticancerous due to the presence of potential source of stable bioactive compounds (Gajendiran et al., 2016). *O. tenuiflorum* essential oil significantly decreases AGS cell viability in a dose dependent manner and effectively inhibits cell migration and invasion. Essential oil induces cell shrinkage, chromatin condensation and fragmentation that are considered typical morphologies of apoptotic cell death. Proapoptotic genes including TP53, BAX and BAK significantly upregulate, while antiapoptotic genes like BCL2 and BCLxL significantly downregulate in presence of essential oil. In addition, significant increase of expressions of CASP8, CASP9 and CASP3 in AGS cells occurs when expose to the oil, rich with caryophyllene and α-pinene (Boonyanugomol et al., 2021).

1.9. *Mentha* L.

The plants are widely grown in temperate areas around the world, particularly in Europe, North America, North Africa, Asia Minor and Northern parts of Iran. Nowadays, it is cultivated throughout all regions of the world. The genus is strongly aromatic perennial herbs which is used remedy for respiratory diseases like bronchitis, sinusitis, tuberculosis and cold. Quadrangular stem is with opposite leaves of ovate-lanceolate shape and rounded or acute base bearing verticillaster inflorescence. Calyx of the flowers is glabrous with 13 nerves and corolla pale purple or pink in colour. Presence of the components like menthol, isomenthone, limonene, iso-menthanol, menthol acetate, carvone, β-pinene, α-pinene, 1,8-cineole, α-terpineol, isopulegol, pulegone, piperiton, piperitone oxide and β-phellandrene are boosting the antioxidant activities of the plant (Stefanaki, 2021).

Anticancer activities: *M. piperita* leaf extracts in petroleum ether, benzene, chloroform, ethyl acetate, methanol and water show anticancer effects on human cancer cell lines (HeLa, MCF-7, Jurkat, T24, HT-29, MIAPaCa-2). All the extracts show significant dose and time dependent anticarcinogenic activity leading to G1 cell cycle arrest and mitochondria mediated apoptosis, perturbation of oxidative balance, upregulation of Bax gene, elevated expression of p53 and p21 in the treated cells (Jain et al., 2011). The methanolic and aqueous extracts of whole plants of *M. arvensis, M. longifolia, M.*

spicata and *M. viridis* exhibit anticarcinogenic effect against eight human cancer cell lines like A-549, COLO-205, HCT-116, MCF-7, NCI-H322, PC-3, THP-1 and U-87MG from six different origins of breast, colon, glioblastoma, lung, leukemia and prostate. Beyond, the methanolic extracts display antiproliferative effect in the range of 70-97% against four human cancer cell lines namely COLO-205, MCF-7, NCI-H322 and THP-1; however, the aqueous extracts are found to be active against HCT-116 and PC-3 (Sharma et al., 2014).

M. piperita essential oil contains five major ingredients of menthol, menthone, camphane, menthofuran and iso-menthone. The essential oil has anticancer activity at various incubation periods against three human breast cancer cell lines. *M. piperita* possesses an antiemetic effect and green nanoemulsion could be used as an anticancer agent (Abedinpour et al., 2021). The cytotoxicity reveals considerable anticancer activity of AgNPs on HeLa and MCF-7 cancer cells (Kelkawi et al., 2017). The silver nanoparticles (NP) synthesized using an aqueous extract of *M. spicata* leaves show cytotoxicity and anticancer activity. The NP decreases cell viability and generation of reactive oxygen species in Chang and SiHa cells (Torres-Martinez et al., 2019). The anticancer and antioxidant activity confirmed in *M. citrata* and *M. longifolia* aerial parts. The extracts inhibit the growth of three tested cancer cells of liver, cervix and colon carcinoma due to the presence of phytosterols, phenolic compounds, unsaturated fatty acids and specific volatile constituents (Al-Okbi et al., 2015).

1.10. *Plectranthus* L. Her.

Plectranthus (Spur flower) is a genus of about 85 species mostly found in southern and tropical Africa and Madagascar. The species are herbs, undershrubs or shrubs with the 4 angled stem. Leaves are opposite with small flowers in panicle or raceme of 6-8 flowered cymes. Bracts are usually small, sometimes large and caducous. Two lipped calyx and corolla are with 5 lobes. The didynamous stamens are with free filaments. Tetra partite ovary ends with slender style and 2 fid stigma at the tip. Usually, the fruits are 4 orbicular ovoid or oblong nutlets. The plant is widely used in folk medicine to treat conditions like cold, asthma, constipation, headache, cough, fever and skin diseases due to the presence of 76 volatiles and 30 non volatile compounds belonging to different classes of phytochemicals such as monoterpenoids, diterpenoids, triterpenoids, sesquiterpenoids, phenolics, flavonoids, esters, alcohols and aldehydes. It has antimicrobial, antiinflammatory, antitumour, wound healing, antiepileptic, larvicidal, antioxidant and analgesic properties.

Anticancer activities: *P. ornatus* includes the phytochemicals viz. halimane (11R*,13E)-11-acetoxyhalima-5,13-dien-15-oic acid (HAL), the labdane diterpenes 1α,6β-diacetoxy-8α,13R*-epoxy-14-labden-11-one (PLEC) and forskolin like 1:1 mixture of 1,6-di-O-acetylforskolin and 1,6-di-O-acetyl-9-deoxyforskolin (MRC) that show anticancer properties in MCF-7 and FaDu cancer cell lines by increasing ROS production and mitochondrial damage in the ND1 and ND5 gene regions (Sitarek et al., 2022). The methanolic extract of *P. stocksii* leaf and stem shows higher concentrations of total phenolics and tannins that defend against MCF-7, Caco-2

and RAW 264.7 cancerous cell lines (Muniyandi et al., 2017). *P. amboinicus* treated TiO2 nanoparticles have better anticancer properties to treat oral cancer (Maheswari et al., 2021). The phytocompounds namely carvacrol, thymol, alpha pinene, limonene, vanillin, cineole and syringic acid include in *P. amboinicus* interact with the cancer target proteins (Sindhu et al., 2022). Moreover, the essential oil of the plant exhibits the potent chemotherapeutic or chemopreventive effect (Manjamalai et al., 2013). *P. strigosus* consists active ingredient of parvifloron D, a strongest antimicrobial and cytotoxic agent (Garcia et al., 2019).

1.11. *Pogostemon* Desf.

The plants are native to the island region of Southeast Asia including Sri Lanka, Indonesia, Malay Peninsula, New Guinea and Philippines. The plants are grown as herbs, under shrubs or shrubs, often aromatic with opposite leaves. The small flowers are in clusters of elongate spikes or raceme inflorescence. Calyx is more or less tubular and equally 5 lobed while the 2 lipped corolla tube includes the 3 lobed upper lip and the lower narrower and longer 2 lobed lower lip. The sub-equal four stamens and 4 partite ovary with slender style and 2 fid stigmatic lobes are prominent in flowers. The plant is used to treat colds, headaches, fever, nausea, vomiting, diarrhea, abdominal pain, insect and snake bites by the detection of secondary metabolites such as terpenoids, phytosterols, flavonoids, organic acids, lignins, alkaloids, glycosides, alcohols and aldehydes in plants (Swamy et al., 2015).

Anticancer activities: The aqueous leaf extract of *P. heyneanus* is effective cytotoxic agent inducing various clastogenic and non clastogenic aberrations including chromosome gaps, bridges, multipolar anaphase, fragments, nuclear budding and lesions, hyperchromasia, laggards and mitotic pairing in turn induce anticancer activity (Sheela & Thoppil, 2017). Patchouli alcohol (PA) is one of the important compounds isolated from the essential oil of *P. cablin* that exerts an anticancer activity by decreasing cell growth and increasing apoptosis in human colorectal cancer cells (Jeong et al., 2013). The methanol extract of *P. cablin* inhibits the growth of various cancer cells such as A549, HepG2, MCF-7 and HT29 by arresting the G1 phase of cell cycle (Yun et al., 2015).

1.12. *Salvia* L.

The genus shows maximum diversity in Central America and Mediterranean region. The plants are herbs or shrubs of various habits with small or large showy flowers having variously sized bracts. Calyx and corolla tubes are tubular with 3 lobbed upper lip and 2 lobbed lower lip. The lower pair of stamens shows fertility and the upper pair reduced to staminodes. The four partite ovary ends with bifid style. The plant normally uses for the treatment of different kinds of disorders including seizure, ulcers, gout, rheumatism, inflammation, dizziness, tremor, paralysis, diarrhea and hyperglycemia (Ghorbani et al., 2017).

Anticancer activities: The extracts of *S. africana-caerulea, S. africana-lutea, S. albicaulis, S. aurita, S. chamelaeagnea, S. disermas, S. lanceolata, S. muirii, S. namaensis, S. radula, S. repens, S. runcinata, S. schlechteri, S. stenophylla* and *S. verbenaca* have cytotoxic

effects on human colon cancer cells (HT-29) (Kamatou et al., 2008). Liposoluble compounds like tanshinone IIA [1,6,6-trimethyl-8,9-dihydro-7H-naphtho[1,2-g] [1] benzofuran-10,11-dione] and tanshinone I [1,6-dimethylphenanthro[1,2-b]furan-10,11-dione] are rich in *S. miltiorrhiza* and related species regards as having phytoestrogenic effects with antiproliferation of human breast cancer MCF-7 (Zhao et al., 2007). Daucosterol, a β-sitosterol glycoside, present in *S. sahendica* inhibits cell proliferation by inducing apoptosis (Esmaeili & Farimani, 2014). *S. miltiorrhiza* and *S. officinalis* contain the hydrophilic phenolic acids and the lipophilic tanshinones both show anticancer effects. *S. miltiorrhiza* and related species have specific effects on lung cancer cell lines. The methanol crude extracts of *S. menthaefolia, S. sclarea, S. dominica, S. spinos* and *S. palestina* exhibit antiproliferative activity against prostate cancer cell MDA Pca2b (Fiore et al., 2006). The protocatechualdehyde, a polyphenol in *S. miltiorrhiza* suppresses proliferation of breast cancer cell lines like MCF-7 and MDA-MB-231 via an estrogen dependent manner. The neo-tanshinlactone isolated from *S. miltiorrhiza* is active against ER positive human breast cancer cell lines (MCF-7 and ZR-75-1) and HER-2-overexpressing breast cancer cell lines (SK-BR-3, HER-2+) (Choi et al., 2014). Moreover, the aqueous extract from *S. miltiorrhiza* strongly inhibits the proliferation of hepatocellular carcinoma cells (HepG2). Linalyl acetate, α-terpineol and camphor, the main components of the essential oil of *S. libanotica* synergistically induces cell arrest and apoptosis resulting in the inhibition of the growth of two isogenic human colon cancer cell lines HCT-116 (p53+/+ and p53−/−) (Lee et al., 2014). Beyond, the acetone extract of *S. hypargeia* roots shows the highest activity against the human ovarian cancer cell line, A2780 (Topcu et al., 2008). Taxodione, ferruginol and 6-hydroxysalvinolone isolated from *S. chorassanica* exhibit cytotoxic and apoptotic effectiveness against the leukemic cancer cells, K562 and HL-60 (Tayarani-Najaran et al., 2013). The essential oils of *S. bracteata* and *S. rubifolia* from Lebanon exhibit an inhibitory effect on the human melanoma cells M14 through induction of apoptotic cell death (Cardile et al., 2009). Saprorthoquinone and taxodione of *S. hypargeia* show cytotoxic activity on human colon cancer, Col 2 (Ulubelen et al., 1999).

1.13. *Scutellaria* L.

The genus is commonly known as 'Skullcaps'. The generic name derived from the Latin word “Scutella” meaning "a small dish, tray or platter" or "Little dish". The plants may be mostly herbs or under shrubs with opposite leaves and small bract like floral leaves. Inflorescence is normally terminal raceme. Calyx and Corolla are 2 lipped in which the upper lip entire or notched and lower lip is broad and three lobed. Two paired didynamous stamens arranged as the lower longest pair and upper shortest pair in which anthers are connivent. Ovary is four partite on a curved gynophore with slender style and bifid stigma. The plants are usually using in the treatment of diarrhea, dysentery, hypertension, hemorrhaging, insomnia, inflammation and respiratory infections. Flavones such as baicalin, wogonoside and their aglycones baicalein wogonin are the major bioactive compounds. The flavones have pharmacological functions like anticancer, hepatoprotective, antibacterial,

antiviral, antioxidant, anticonvulsant and neuroprotective effects (Zhao et al., 2016).

Anticancer activities: The bioactive components of *Scutellaria* include flavones in which the major constituents are wogonin, baicalein and baicalin. These are cytostatic and cytotoxic to various human tumour cell lines in turn inhibit tumour growth (Li-Weber, 2009). The anticancer activity of the flavones in *S. baicalensis* extract is well known in human leukemia cell lines that connected with reduction of high level reactive oxygen species, inflammatory reaction and NFκB activation. The extract also shows antiprostate and antibreast cancer activity (Lamer-Zarawska et al., 2010). The gold nanoparticles synthesized from the *S. barbata* by green route method exhibits anticancer activity against pancreatic cancer cell lines (PANC-1) that may lead to the development of novel anticancer drugs to combat pancreatic cancer (Wang et al., 2019). The cytotoxic properties of methanol extract of *S. litwinowii* roots lead to the inhibition of different cancer cell lines including AGS, HeLa, MCF-7, PC12 and NIH 3T3 (Tayarani-Najaran et al., 2011). The methanol extract of *S. orientalis* contains apigenin, baicalein, chrysin, luteolin and wogonin which correlate with cyclin D1 and Cdc25A suppression and p21 induction in turn cause potent antileukaemic properties through the antiproliferative effect of baicalein and the genotoxic property of wogonin (Ozmen et al., 2010).

2.14. *Teucrium* L.

Teucrium is a wild growing flowering herb or shrubs found in various regions such as Europe, North Africa and South Western Asia. The leaves show opposite phyllotaxy. Flowers usually small in whorls of 2-6 in axillary or terminal spike, raceme or head inflorescence. Calyx may be 2 lipped, 10 ribbed and 5 toothed. Corolla tube is not annulate with 1 lipped limb. In didynamous stamens, the lower pair is longest with exserted and reniform anthers. The four lobed ovary ends with bifid style. The genus is used for treating different diseases such as diabetes, rheumatologic diseases, inflammation and gastrointestinal disorders. The antioxidant property of *T. polium* is due to the presence of ortho-dihydroxy substitutions in the flavone B ring (Rafieian-Kopaei, 2014).

Anticancer activities: Crude extracts with the phytochemicals show potential anticancer properties. A methanolic extract obtained from *T. persicum* potently inhibits viability of PC-3 cells. The viability of SW480 colon and T47D breast cancer cells significantly decreases in presence of the extract (Tafrihi et al., 2014). *T. polium* shows the identification of 29 phytochemical compounds belonging to 13 classes of compounds and 20 tripeptides. In the species, 13R-hydroxy-9E,11Z octadecadienoic acid, dihydrosamidin, valtratum and cepharantine are the main compounds. Using the malignant Walker 256/B and MatLyLu cell lines, *T. polium* methanolic extract shows a dose or time dependent antitumour activity (Noumi et al., 2020). The phenolic compounds of the *T. chamaedrys* and *T. arduini* show best cytotoxic effects in HCT-116 cells and also the high apoptotic percentage (Stankovic et al., 2011). The stable silver nanoparticles synthesized using the leaf extract of *T. polium* exhibits significant anticancer activity against MNK45 human gastric

cancer cell line helps for further development of anticancer drugs (Hashemi et al., 2020).

1.15. *Rosmarinus* L.

Rosmarinus is a small taxonomic clade of woody, perennial herbs or subshrubs with fragrant evergreen needle like leaves. It is native to the Mediterranean and Asia, but is reasonably hardy in cool climates. Calyx is densely white stellate and tomentose type. The flowers are white, pink, purple or blue in colour with upper bilobed lip and trilobed lower lip. *Rosmarinus* uses in folk medicine to cure several diseases including headache, dysmenorrhea, stomach ache, epilepsy, rheumatic pain, spasms, nervous agitation, memory boosting, hysteria, depression as well as physical and mental fatigue. The main constituents in the plants are carnosic acid, carnosol, rosmarinic acid etc. that in turn results in antiinflammatory, antioxidant, antinociceptive, neuroprotective, antidepressant and antihysteric properties (Rahbardar, 2020).

Anticancer activities: *R. officinalis* includes a variety of phenolic compounds essential for basic cellular processes or macro and micro nutrient metabolisms. The main compounds are carnosic acid and carnosol. The extracts are very effective in treatment of different cancers affecting various parts like human colon, gastric areas, pancreatic gland, hepatic cells, lungs, cervical cells, skin, mouth, breast, kidney etc. (Allegra et al., 2020).

2. Outlook

The species of the family Lamiaceae with active compounds have the potential to inhibit the growth of different human cancer cell lines of lung, breast, prostate, colon etc.. The whole extracts and essential oils effect at the molecular level and reduce the proliferation of the tumour cells by checking the cell cycle in turn inhibit the metastasis. Therefore, the members of Lamiaceae are the sources of crucial phytochemicals that may be important modulators of cancer related molecular targets and can be used as effective factors to support antitumour treatment in present era.

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