Traditionally Used Anticancer Plants in Rubiaceae

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Abstract: By considering the family Rubiaceae, there is many species with valuable secondary metabolites which can be used as anticancer and cytotoxic agents. Some of the plants are well known for camptothecin, genipin, genipodide, cisplatin, kaempterol, erithrodiole, quinine, caffeine, polyphenole, ursolicacid and phenolic compounds as anticancer agents. Cancer is a dreadful disease, and combating this disease is of great importance to public health. Phytochemical examination has been making rapid progress, and herbal products are becoming popular as sources of plausible anticancer compounds. The Rubiaceae members inhibit cancer in different human cell lines including A549, MCF-7, HeLa etc. by suppressing cell cycle and promoting apoptosis. The major plants which show the property are *Anthocephalus, Gardenia, Cinchona, Ixora, Chassalia, Coffea, Morinda* etc..

Keywords: Rubiaceae, anticancer, bioactive compounds, camptothecin, apoptosis

Globally cancer is one of the commonly life threatening diseases which severely affect the human being. It is recognized by the uncontrollable division of cells. There is a demand for new methods to prevent this disease. Conventional therapies have several adverse effects on the healthy cells; therefore, the alternative and effective medications are required to combat this disease. Benefits of using plant derived products over synthetic medicine have increased the importance of medicinal plants in the field of healthcare. Many plants derived products are potent in cancer treatment by inhibiting cancer activating enzymes, stimulating DNA repair mechanism, inducing antioxidant action and promoting protective enzymes production. As chemotherapy and radiation therapy causes various side effects, so there is a necessity to discover novel agents for the treatment of the disease; it could be possible with the use of naturally occurring compounds (Arpita & Navaneeta, 2017).

The chapter provides significant information regarding the plant resources of the family which can provide bioactive compounds for cancer treatment. The family is the main group of angiosperm represents one of the most species rich flowering plants with13, 548 species under 617 genera in Gentianales. The members are herbs, shrubs and trees, distributed primarily in tropical areas of the world. Several species are of economic

importance as sources of useful chemicals and a number are cultivated as ornamentals. The leaves are opposite each other with stipules or in whorls, unbroken leaf margins, and leaf like appendages at the base of the leafstalks. The plants may bear a single flower or many small flowers clustered together. The fruits can be berries, drupes, capsules or schizocarps (Michael, 2010).

The members of Rubiaceae as well as their isolated compounds possess diverse biological activities including antiinflammatory, antitumour, antimicrobial, larvicidal, antioxidant, gastrointestinal, antiulcer and hepato protective, with alkaloids and iridoids as the major active principles. About 3000 plants has anticancer properties are subsequently used as potent anticancer drugs (Srigiri, 2015). The members such as *Morinda, Gardenia, Ixora, Neurocalyx, Cinchona, Anthocephalus* etc., have shown potent cytotoxic activities in the previous studies.

About 12 species with anticancerous property which are almost common including the phytochemicals such as camptothecin, genipin, genipodide, cisplatin, kaempterol, erithrodiole, quinine, caffeine, polyphenole, ursolicacid and phenolic compounds. This can inhibit cancer in different cell lines. So the demand of natural pharmaceuticals made investigation in different plant groups of the family and also helps in conservation of them.

1. Anticancer plants in Rubiaceae

1.1. *Anthocephalus* A. Rich.

A. cadamba is one of the most precious medicinal evergreen tropical trees, native to South and Southeast Asia. It is a large tree with a broad crown and may reach a height of 45 m. The bark is gray, smooth in young trees, rough and longitudinally fissured in old trees. Leaves are glossy green, opposite, simple more or less sessile to petiolate, ovate to elliptical. Inflorescence is in clusters; terminal globose heads without bracteoles, subsessile, fragrant with orange or yellow flowers. Flowers are bisexual and 5 merous. Calyx tube is funnel shaped, corolla gamopetalous, saucer shaped with a narrow tube, the narrow lobes imbricate in bud. Stamens 5, inserted on the corolla tube, filaments short, anthers basifixed. Ovary is inferior, bilocular, sometimes 4 locular in the upper part, style exserted with a spindle shaped stigma. Fruitlets are numerous with their upper parts containing 4 hollow or solid structures. Seeds are trigonal or irregularly shaped.

Anticancer activities: The phytochemical screening of Cadamba reveals the presence of lupeol and betulinic acid type triterpene which have antineoplastic activity. It also has antitumour activity on Ehrlich ascites carcinoma (EAC) by defatted methanol extract of Cadamba (MEC). The antitumour potential of MEC shows influence on tumour volume, viable and nonviable tumour cell count, tumour weight, hematological parameters and biochemical estimations (Dwevedi, 2015). Despite several known pharmacological properties of *A. cadamba*, only few studies are available on antiproliferative activity of bark. The bark methanol extract shows the antiproliferative activity against human cervical cancer HeLa cells. By comparing with standard cisplatin drug, *A. cadamba* bark methanol extract have significant antiproliferative activity against

human cervical cancer cells due to induction of apoptosis which is credited to the phenolic contents. The phytochemical potency of the plant is due to high amount of total phenolic content.

1.2. *Borreria* G. Mey.

B. hispida is a creeping herb with tropical and subtropical distribution. Much branched prostrate perennial herb forms mats up to 23-40 cm wide; stems 10-20 cm long, tinged reddish, covered with spreading white hairs, with short internodes and rather congested foliage. Leaf blades are elliptic or oblong elliptic with white hairs on upper surface and particularly along the margins, also with hairs on midrib and nerves beneath. Flowers are 1-several, sessile, in most leaf axils. Calyx tube is oblong-ovoid, densely hairy; lobes 4, lanceolate, hairy along the margins. Corolla is pale blue or lilac; tube narrowly cylindrical; lobes oblong, hairy at the apex. Filaments exserted. Style exserted; stigma shortly bifid. Capsule is obovoid with spreading white hairs. Seeds are chestnut brown, oblong ellipsoid, sometimes narrowed to one end, finely reticulate, ventrally grooved.

Anticancer activities: The methanolic extract of the seeds of *B. hispida* shows the anticancer activity due to the presence of some bioactive elements like kaempterol and erythrodiol. The methanolic extract of seeds inhibits the growth of A549 and MCF-7 cells at the IC_{50} concentration of 3.125µg/mL and 1.56µg/mL respectively which show the anticancer activity of the extract against human lung carcinoma (A549) and breast carcinoma (MCF-7) cell lines. The F3 fraction cytotoxic protein of methanolic extraction of seed exhibits growth inhibition (in vitro cytotoxicity assay) and cell cycle arrest in sub-G0 population of human lung (A549) and cervical (HeLa) cancer cells (Rupachandra & Sarada, 2013).

1.3. *Cinchona* L.

C. officinalis is commonly known as 'Peruvian bark', native to South America specifically from the Andes mountain range. It can also be found in India, Java, Cameroon and Vietnam and in some other Asian and African countries. In India, it is mainly found in hilly areas. *Cinchona* is a 10 to 20 m tall tree with straight trunk about 30 cm in diameter. It has a dense and irregular globular crown; darkly green, oval shaped leaf with a thick central nerve with full margin. The color of flower is white or pinkish with white hairs found in panicles. The fruit is dark brown 2-4 cm long with 3-4 seeds. The brown bark of *Cinchona* is looked like a tube which is arched or curved during aging. Barks are usually visible in trunk or branches and after immediate collection the outside has a brown grayish color while the inside has a reddish brown.

Anticancer activities: The phytochemical screening of bark and leaves shows the presence of alkaloids known as quinine, cinchonine, quinidine, quinoline and cinchonidine. Quinine is more potent to inhibit the cell proliferation and induces apoptotic cell death in cancer cell line in a dose and time dependent manner (Krishnavedi & Suresh, 2015). ROS (Reactive oxygen species) is critical for the metabolic and signal transduction pathways associated with cell growth and apoptosis. Several anticancer agents including anthracyclines, cisplatin and bleomycin, currently used for cancer treatment have been shown to cause increased intrace-

llular ROS generation. Quinine also increases the intracellular ROS levels at time and dose dependent manner (Pranay & Puspal, 2017). Induction of cell death through indirect activation of the mitochondria dependent pathway is the conventional anticancer treatment but sometimes it is altered in drug resistant cancer cells. Effect of quinine induces typical morphological changes as the signal of apoptosis like cell shrinkage, membrane blebbing, chromatid condensation, nuclear fragmentation, apoptotic bodies and loss of adhesion. So quinine may be a strong anticancer agent in future due to its huge apoptotic activities in cancer.

1.4. *Chassalia* Comm. ex Poir.

The genus, commonly known as Curved flower Chasalis' or 'Curved flower woody *Chassalia*', consists of more than 110 species with paleotropic distribution, mainly in open areas forest edges in North East India. The plant erect, 1-2 m tall; branches weakly flattened to sub terete. Leaves opposite; petiolate, oblong-elliptic, glabrous; stipules persistent, united shortly around stem, with interpetiolar portion. Inflorescence cymose, pyramidal to rounded, several to many flowered, puberulent; bracts lanceolate to triangular or usually multifid. Flowers subsessile, trimorphic with anthers exserted and stigmas included, with anthers included and stigmas exserted or with anthers and stigmas both exserted. Calyx with hypanthium portion ellipsoid to obovoid. Corolla white with pink, violet on lobes, outside glabrous to sparsely puberulent; tube shallowly to markedly curved, straight or bent at base; lobes 4 or 5, ovate-triangular. Infructescence axes becoming swollen and red. Fruit purple, oblate to globose or weakly didymous.

Anticancer activities: The plant has various phytoconstituents such as steroids, terpenoids, alkaloids, tannins, phenolic compounds, flavonoids, carbohydrates, amino acids and other many bioactive compounds with medicinal property (Savitha et al., 2019). Ethanolic extract of leaves and roots of *C. curviflora* were possesses antiinflammatory, analgesic and hepatoprotective activity, and phytochemical analysis reveals that roots have high content of alkaloid. The antiinflammatory and immunomodulatory properties of a plant may contribute to its anticancer properties. Main alkaloid present in the plant is camptothecin. It can be treated against the 3 human cancer cell lines; breast cancer (MCF-7), lung cancer (A549), cervix cancer (HeLa) and normal fibroblast cell (3T3L1). The cytotoxic effect of the alkaloid rich extract (Chr-alk) on cancer cell lines shows a concentration and time dependent increase in the percentage of cytotoxicity. There is more cell death treatment of extract on in A549 lung cancer cells. The Chr-alk induces less toxicity in normal cells compared to cancer cells showing its specificity to cancer cells (Rajeswari et al., 2020).

1.5. *Coffea* L.

Members of the genus *Coffea* are evergreen shrubs or small trees and often inhabit the understory of tropical forests. The elliptical waxy leaves are borne oppositely along the stems and often feature prominent venation. Many species have a characteristic growth habit in which the upright trunks branch horizontally and may then repeat the pattern on secondary and tertiary branches. The small fragrant white or pink flowers

frequently open after a dry period and may last only a few days. The fruit, known as a "Coffee cherry," is a one or two seeded drupe and can be red, purple, yellow, orange, blue or black when mature, depending on the species. The "Coffee beans" are the rounded oblong seeds, each with a flat face marked by a lengthwise groove.

Anticancer activities: The epidemiological evidence consistently indicates that coffee protects against liver cancer, and also point toward protective effects for risk of colorectal cancers, overall risk of breast and prostate cancer. However, for subgroups such as postmenopausal breast cancers, advanced prostate cancers, and breast and prostate cancer survivors, an inverse association with coffee intake is indicated. Basically the coffee contains caffeine, chlorogenic acid (CGA) (which is caffeic acid bound to quinic acid), cafestol, kahweol, p-coumaroylquinic and feruloylquinic acid. Potential mechanisms for chemopreventive effects of coffee phytochemicals include inhibition of oxidative stress and oxidative damage, regulation of DNA repair, phase II enzymatic activity, apoptosis, inflammation, as well as having antiproliferative, antiangiogenetic and antimetastatic effects. The antiproliferative effect can be found as in human cancer cell line viability (breast carcinoma) significantly decreases in a concentration dependent manner. Similarly, the plant shows a comparable effect in cancer lines from colon (CHT116), brain (T98G) and bone (U2OS). Both green and dark coffee extracts inhibit the proliferation of MCF-7 and MDA-MB-231human breast cancer cell lines.

The two coffee lipids, cafestol and kahweol, are antigenotoxic compounds that prevent the deleterious effects of reference carcinogens such as N-nitrosodimethylamine, 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine, ferric ion-nitrilotriacetic acid and H_2O_2 in human hepatoma HepG2 cells. The ability of the caffeine and chlorogenic acids, 5-O-caffeoylquinic acid (5-CQA) and 3,5-O-dicaffeoylquinic acid (3,5-DCQA), to protect against ROS induced oxidation has investigated in HepG2 cancer cells (Ayelene et al., 2021). Both cafestol and kahweol are the inhibitors of cytochrome P450, an enzyme responsible for the activation of carcinogens and thus DNA damage (Jose et al., 2012).

1.6. *Gardenia* J. Ellis

Gardenia is a genus of more than 140 species of shrubs and trees in the Madder family, native to tropical and subtropical Africa, Asia, and Pacific islands. The plants have glossy evergreen leaves that usually are arranged oppositely or in whorls. The tubular flowers are white or yellow and are borne singly or in small clusters; the flowers are often strongly scented. The large berrylike fruits contain a sticky orange pulp. The fruits are used in Japan and China for dyeing food yellow. The colouring matter in the fruits contains glycoside, a compound similar to crocetin which is found in Saffron. The dye is also used to colour textiles yellow or scarlet. The flowers contain fragrant essential oils and are used in perfumery. It is also used in China for flavouring tea.

Anticancer activities: *G. jasminoides* is a natural plant, has many biological activities. Plant has the ability of apoptosis in HepG2 human hepatoma cells. It contains 1.03% genipin gentiobioside, 5.90% gardenoside,

1.26% crocin 1 and 0.17% crocin 2 in turn show significantly strong HepG2 cell inhibitory effects. Usually, species has the ability to increase the mRNA expression of caspase 3, caspase 8, caspase 9, Bax, TRAIL, Fas, Fas/FasL, p53, p21 and IκB-α, and decrease the Bcl-2, Bcl-xL, XIAP, cIAP-1, cIAP-2, survivin, NF-κB expression in HepG2 cells. The higher concentration of *G. jasminoides* shows the higher increasing or decreasing mRNA expression effects in HepG2 cells. So *G. jasminoides* had a strong anticancer effect through its apoptosis inducing abilities in hepatic cancer; it could be used for the treatment as a medicine or health product in daily human life for good liver health (Sook et al., 2012).

1.7. *Ixora* L.

I. coccinea is a small shrub. Stem is herbaceous, aerial, erect, branched, cylindrical, and differentiating into nodes and internodes. Leaves are cauline, simple, opposite, decussate, stipulate, sessile, ovate to elliptical, entire and acute with unicostate reticulate venation. Inflorescence is corymbose cyme. Flowers are bracteate, pedicellate, complete, hermaphrodite, actinomorphic, tetramerous, epigynous, large, showy with long corolla tube. Calyx made up of 4 sepals, gamosepalous, green, valvate, very short in comparison to corolla. Corolla made up of 4 petals, gamopetalous, twisted, long, slender, corolla tube with abruptly expanded corolla limbs. Androecium made up of 4 stamens, polyandrous, epipetalous and alternipetalous, anthers sagitate, dithecous, dorsifixed, introrse. Gynoecium composed of bicarpellary, syncarpous, bilocular, two ovules in each locule on axile placentation. The style is long and passes through the long corolla tube. Stigma is bilobed and simple. Fruit is berry with small endospermic seeds.

Anticancer activities: *I. coccinea* flowers show cytotoxic activity. The flower extract contains terpenoids, flavonoids, phenols, tannins and lupeol which have cytotoxic activity and kaempferol with antiplatelet aggregation potential. The compounds show cytotoxic activity against cancer cell lines namely, NCI H-460 (large cell carcinoma, lung), MCF-7 (adenocarcinoma, breast), HeLa and Hep3B (liver tumour) cell line.

The flower extract is effective against MCF-7, HeLa and NCI H-460 human cancer cell lines. 17 metabolites identified from *I. coccinea* flowers (yellow), which are mostly responsible for its cytotoxicity and growth inhibitory actions preferably towards cervical cancer cell line (Lubna et al., 2018). The flowers and leaves contain an anticancer drug camptothecin which having anticancer activity against Dalton's lymphoma (ascitic and solid tumours) and Ehrlich ascites carcinoma (EAC) tumours (Saravanan & Boopalan, 2011).

1.8. *Morinda* L.

M. citrifolia is a small, glabrous tree with straight trunk; smooth, yellowish white bark; branchlets obtusely quadrangular. Leaves are broadly elliptic, acute, acuminate or obtuse, bright green, glabrous, shining, one of the pair next the prominent peduncle, petiolate; stipules connate, short, broad, obtuse, membranous. Flowers are white in dense ovoid heads, peduncles solitary (rarely 2-3 together), usually leaf opposed. Calyx limb is truncate. Corolla is infundibuliform tube with hairy mouth, lobes 5, lanceolate, acute. Stamens are 5 in number,

filaments hairy, anthers about half exerted. Fruit is white when ripe, smooth, glossy, about a size of a small egg.

Anticancer activities: The ethyl acetate extract of noni fruit juice strongly inhibits the proliferation of MCF-7, MDA-MB-231 and HEK-293 cell lines with IC_{50} values of 25, 35, 60 µg/mL respectively. The extract shows increase in apoptosis of MCF-7 and MDA-MB-231 cells and arresting of the cell in the G1/S phase of MCF-7 and G0/G1 phase of MDA-MB-231 cells. Noni extract also decreases the intracellular ROS generation and mitochondrial membrane potential (Sharma et al., 2015). Concentrated components in noni juice may stimulate the immune system to 'possibly' assist the body fight to cancer, and kill a small percentage (0-36%) of cancer cells depending on the type (Amy, 2017).

The noni juice inhibits the A549 cells proliferation, migration and invasion. It also promotes cell apoptosis in A549 cells as well as effectively suppresses tumour formation of A549 cells in nude mice. The phosphorylation level of AKT, p50 and STAT3 proteins inhibits to different extents after noni juice treatment. It can be inhibited the expression of Ki67, PCNA and Bcl-2 protein in the tumour; while promoted the expression of caspase-3 protein. Additionally, the noni juice treatment could restrain the activity of AKT/NF- κ B signaling pathway in the tumour tissue (Ma et al., 2020).

More than 160 phytochemicals have been isolated from the plant Noni (Steroids, glycosides, phenol, tannins, terpenoids, alkaloids, resins, carbohydrates, flavanoids, anthraquinones, phylobatannins, saponins and protein) which makes it an amazing herbal remedy for the treatment of numerous disorders including cancer. Recently, the Noni juice has been in high demand in market as Complementary and Alternative Medicine (CAM) for its multidimensional health benefits. It is a potent antibacterial, antiviral, antifungal, antihelminthic, anticancer, analgesic, antiinflammatoiy, antioxidant, hypotensive, cardiovascular protective, wound healer, anxiolytic, sedative, antigout, antiobesity and immune enhancing agent. Anticancerous activity of *M. citrifolia* is attributable to its antiinflammatoiy, antioxidant and apoptosis inducing effects. Based on toxicological and mutagenicity assessment, Noni juice has been considered as safe.

1.9. *Neurocalyx* Hook.

N. calycina is a large herb endemic to South West India, found in evergreen forest. These are large pubescent herbs. Leaves are simple, whorled at tip, oblanceolate, acute at apex, rusty puberulus; nerves to 18 pairs, prominent below; stipule 2 cm long, obovate, 2 fid at apex. Racemes are 10-13 cm long, axillary, rarely branched; bracts lanceolate. Flowers white, pedicelled. Calyx tube is hemispherical, lobes 5, ovate. Corolla tube is absent, lobes 5 x 3 mm, ovate, twisted. Stamens are 5 in number, anthers connate into a conical tube. Ovary 2 celled, ovules many, style slender. Capsule irregularly bursting; seeds many, pitted.

Anticancer activities: The plant has wound healing, burn healing, anticancer, analgesic, antiinflammatory, immune enhancing, platelet augmentation and antioxidant effects. *N. calycina* has significant concentration of anticancer

alkaloid camptothecin, in the plant parts. Roots of *N. calycina* produce the highest content of camptothecin (CPT) and followed by stem and leaves. Plant derived monoterpene pyrrolidine alkaloid camptothecin, possessed to have unique antitumour activity. CPT inhibits the cell cycle at various stages and finally induces the cell death. Continuous exploration on the action of mechanisms of CPT, researchers have found out the compound inhibits the DNA replication in association of Topoisomerase I (Karuppuswami & Mohanaraj, 2021). Camptothecin and its derivatives are used as second or third line treatment for patients with endocrine resistant breast cancer (BC). These drugs convert nuclear enzyme DNA topoisomerase I (TOP1) to a cell poison with the potential to damage DNA by increasing the half life of TOP1-DNA cleavage complexes, ultimately resulting in cell death (Tesauro et al., 2019).

1.10. *Ophiorrhiza* L.

O. mungos is an annual erect herb form roots at lower nodes. Leaves 7-15 x 3-6 cm, elliptic or elliptic-lanceolate, base attenuate, apex acuminate, chartaceous, hirsute on veins below; petiole to 1.5 cm; stipules subulate, 3-5 mm long, 2 fid at tip. Flowers in dense terminal branched, scorpioid cymes. Peduncle is to 2.5 cm long, rusty pubescent. Calyx tube c. 1 mm long; lobes obscure. Corolla is 0.8-1 cm long, white with pink shades on lobes. Capsule 2.5-3 mm long, 4-6 mm wide, obcordate, laterally compressed, glabrous, dehiscence loculicidal. Seeds are many, angular.

Anticancer activities: *O. pumila* and *O. mungos* produce camptothecine in small quantity. The four other derivatives of CPT, which are currently in use, including topotecan, irinotecan, belotecan and trastuzumab deruxtecan, are also produced. The mode of action of CPT involves inhibition of topoisomerase 1 (TOP 1), which is known to be present in higher amounts in cancer cells when compared to normal tissues. The formation of TOP I-CPT complex leads to an irreversible strand breaks in the DNA eventually causing the death of cells. The initial usage of CPT and its derivatives are targeted to gastrointestinal tumours, and further slowly explored in the treatment of breast, ovarian, colon, lung and stomach cancers. It's low solubility and resistance by the cancer cells has reduced its usage (Madihalli et al., 2021).

1.11. *Pavetta* L.

P. indica, 'Indian *Pavetta*', is an erect, nearly smooth or somewhat hairy shrub, 2 to 4 meters or more in height. The leaves are elliptic-oblong or elliptic-lanceolate, 6-15 cm long, and pointed at both ends. The flowers are white, rather fragrant, and borne in considerable numbers in hairy terminal panicles which are 6-10 cm long. The sepals are very small and toothed. The flower tube is slender and about 1.5 cm long, with obtuse petals about half the length of the tube. The flowers attract butterflies and insects. The fruit is berry, black when dry, somewhat rounded, and about 6 mm in diameter.

Anticancer activities: Methanol extract of the leaves and branches of *P. indica* (MEPI) causes cell cycle arrest at the sub-G1 phase and induces apoptosis, as indicated by the activation of caspase 8, 3, 7, and c-PARP. The MEPI significantly reduces the expression of multidrug resistance associated protein 1 in triple negative breast cancer (TNBC). MEPI

causes nuclear fragmentation and chromatin condensation; thus, MEPI induces caspase dependent apoptosis of MDA-MB-231 cells. Moreover, the co-treatment with MEPI and doxorubicin results in a synergistic reduction in cell viability. MEPI also induces radiation sensitization of TNBC cells. The major constituent of MEPI is 5,6-dehydrokawain (DK). Doxorubicin (DOX) has enhanced the expression of MRP1 in breast cancer cells, leading to resistance. DOX significantly induces MRP1 expression levels in different non small cell lung cancer cells (H1299, A549, and CH27 cells) in a time dependent manner. Use of chemotherapeutics in combination with natural compounds can increase efficacy, reduce the dosage, minimize side effects and overcome resistance (Yen et al., 2019).

1.12. *Psychotria* L.

P. leptothyrsa is under shrubs up to 1 m tall with striate stem. Leaves are simple, opposite decussate; stipules 2x0.3 cm, foliaceous, linear-lanceolate; petioles 1.5-4 cm long, shallow-grooved; lamina 10-25x4-17 cm, ovate-lanceolate to elliptic-lanceolate, narrowed at base, acuminate at apex, obscurely crenate at margin; secondary nerves 10-15 paired. Inflorescences are in axillary or terminal 4-6 cm long umbellate cymes. Flowers are pale yellow; peduncles 2-3 cm long, slender puberulous; bracts subulate, 0.3 cm; pedicels 0.5 cm long; calyx lobes linear-lanceolate, 2x0.5 mm, ciliate; corolla tube very short; throat villous within. Fruits are 1x0.8 cm, ellipsoid with persistent calyx teeth, orange-yellow.

Anticancer activities: *P. leptothyrsa* var. *longicarpa* contains a suite of different cyclotides. Cyclotides, the largest known family of head to tail cyclic peptides, have approximately 30 amino acid residues with a complex structure containing a circular peptide backbone and a cystine knot. It displays cytotoxic, antiHIV, antimicrobial and inhibition of neurotensin binding activities and also has cytotoxic activity toward the human lymphoma cell line U937-GTB (Samantha et al., 2010). The another species, *P. serpens*, shows powerful activity against H460, HepG2, Hela and PC9/GR cell lines, and no toxic effects against normal 16HBE cell lines. The anticancer activity leading compounds are sevenetin, rutin, kaempferol-3-flavonoids, quercetin, tamarixetin-3-O-rutinoside, quercetin 3-O-(2G-β-D-xylopyranosyl-rutinoside), kaempferol and tamarixO- rutinoside. It can be often used as a substitute for *Caulis trachelospermi* to treat cancer in China (Chao-Zhang et al., 2015).

2. Outlook

The demand of bioactive plant derived compounds in pharmaceutical market is ever increasing due to its cancer potential and with their pharmacological efficacy of diverse natural chemical derivative. It is urged the identification of alternative source to meet out the pharmaceutical demand and conservation of high valued plant species. Total of 12 different species of family Rubiaceae have been reported in this chapter with bioactive compounds as their secondary metabolites which are active as anticancer molecules in different cell lines with different physiological properties. The major plant derived compouds, used as anticancer drug are camptothecin, lupiol, kaempterol, doxorubin, genipion, quinone, cyclotides etc., will become great demanded product in future.

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