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# A Review- Anti-Cancer Compounds from Medicinal Plants: Isolation, Identification, and Characterization

**Muhammad Atif Imran[1], Hira Shahid[1]**

*Department of Biochemistry, Government College University Faisalabad, Pakistan*

**Key words:** Cancer, Medicinal plants, Apoptosis, Anticancer compounds, Antioxidants.

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## Abstract

Cancer presently exists as the major pathological state in developed and emergent nations equally which is characterized by the uncontrolled division of cells and is fatal. People prefer anticancer plant products to treat cancer due to the increased mortality related to undetected growth in addition to its toxic reactions to chemotherapy and radiotherapy. In recent years, eastern medicine provided a profitable substitute for allopathic medicine against cancer. There have been considerable researches on plants for treating cancer, and many of the plant products have been sold as anticancer medicine, depending on the conventional uses and experimental reports. The anticancer property of medicinal plants is due to their antioxidant activity which has been described in many reports. Thus, after isolation (by using chromatographic and crystallization techniques) and identification using LCMS spectra, IR, and NMR, many combinations of the active components can be prepared and should be further evaluated for their synergic effects. The development of a systemized dose and dosage procedure may perform an exceptional role in the cure of tumors. The rate at which cancer develops is a necessary and effective endeavor for the good health of human beings. Further investigations are required to analyze the mechanisms of anti-malignant action of active compounds from new plants and the use of standard herbal remedies.

* **Corresponding Author:** Muhammad Atif Imran ✉ atifimran28@yahoo.com

**Introduction**

Cancer is the main source of death around the world, representing an expected 9.6 million deaths in 2018(Plummer *et al.* 2016). An array of strategies, including radiation treatment, medical procedure, or chemotherapy are applied for curing cancer. Nevertheless, every one of them has some disadvantages (Karpuz *et al.* 2018). The utilization of customary synthetic preparations bears consequences and damage(Nobili *et al.* 2009). In any case, as the difficult perseveres, new methodologies are required for the control of malignancies, particularly, as a result of the disappointment of regular chemotherapeutic methodologies. Subsequently, there are requirements for current procedures for the anticipation and fix of tumors to regulate the demise rate as a result of this sickness.

Cancer treatment has become a new field of research. Research investigations interpreted that plants especially act in fighting distinct tumors such as lung, hepatic, cervical, stomach, breast, oral, and cell lines of blood tumor. Plants have been served to treat diseases since the beginning of human civilization. Herbs perform an important role in cure and cancer prevention. Antioxidant phytochemical investigations have contributed somewhat to the introduction of advance anti-cancer fragments.

Herbal medicine (phytomedicine) has developed into a harmless, non-toxic, and current for the cancer treatment. It is accepted that herbs counteract the actions of diseases in the body due to the different characteristics contained in them. Many anticancer herbal plants like *Garcinia Indica*, *Scutellaria barbata*, and *Penthorum Chinense Pursh* have many active compounds like Garcinol, Triptolide, Pheophorbide a (Pa), and Polyphenols respectively which are traditionally used as the anticancer properties. Metabolites derived from plant components are used to activate apoptosis in tumor cells. For example, an aqueous isolated from *Fagonia cretica* induces cytotoxic actions (in vitro) against the epithelial cell lines of breast cancer which was not identified against natural mammary epithelial cells. Same as the natural molecule Angelicin, segregated from the historic Chinese herb *Angelica archangelica*, is one of the major active compounds which has been noted to apply anticancer actions by preventing cancer actions in distinct class of cancers, along with invasion, the development of the colony, proliferation, and migration.

A fruit extract of *P. macrocarpa* named Gallic acid was purified as an active compound that can show a main part in the introduction of cell death (apoptosis) in leukemia, lung cancer, and the A549 cell line (colon adenocarcinoma cell lines). Gallic acid (phenolic compound), a pure antioxidant with polyhydroxy activity. Many fruits like strawberries, grapes, bananas, green tea, and some vegetables are the source of Gallic acid. (Sun *et al.* 2002). This also take part actively in inhibiting malignant transformation and in the expansion of the cancer (Taraphdar *et al.* 2001). Likewise, various compounds such as podophyllotoxins, vinca alkaloids, and septin, are used to treat cancer are attained from different plants.

Many species of plants are already served to prevent or cure cancer. Most scientists are aware of state characteristic species combinations and need to investigate the organism's ability to "housekeeping" the organism to investigate plant survival and the death of cancer cell(Freiburghaus *et al.*, 1996; Kamatou *et al.*, 2008; Ochwang' i *et al.*, 2014).

However, herbal compounds are wrongly convinced that they have no concerns about protection and reactions. Many plant species are virulent to health. Likewise, otherwise friendly plants contain many compounds that result in cytotoxicity. Based on analyzing, it has been demonstrated that medicinal plants also have harmful actions(Ghorani-Azam *et al.* 2018).

A recently reported survey revealed that about 60% of patients suffering from cancer make use of vitamins or herbaceous plants as treatment. This review assembled several compounds with anticancer

combinations for different types of cancer. This review may help researchers to look over the herbicidal compounds at the clinical level and to level up other diseases and their studies. This article is designed to evaluate some of the therapeutic compounds from plants used for cancer treatment and gives information about the plants with anticancer properties, which are used by people everywhere around the world.

*Sources and methodology*

This investigation relies on a diligent writing review led through the hunt of pertinent keywords in computerized databases, including Google Researcher, Scopus, Web of Science, and PubMed. Keywords used in this literature are Cancer, Medicinal plants, Apoptosis, Anticancer compounds, and Antioxidants. Many articles were decided after the isolation and evaluation through the association of the said keywords. These relevant articles were based on distinct criteria including the selection of specific anticancer compounds from medicinal plants, traditional antioxidant abilities of compounds, origin of the compounds from which they are isolated.

For this purpose, 21 anticancer compounds were selected and studied assiduously to ascertain their antitumor and antioxidant properties. A few anticancer compounds from medicinal plants were chosen dependent on defined determination rules for their powerful antitumor characteristics.

The mode of action of these compounds is explained in their respective subheadings and is elaborated in the figures. All the data including the rest of the compounds are then summarized in the table below.

*Selected Anticancer Compounds from Medicinal Plants and Their Characterization*

Several compounds extracted from medicinal plants having antitumor abilities have been tested so far. And many of them have been recognized as an effective cure against distinct types of malignancies including colorectal cancer, liver cancer, and breast cancer, etc.

21 anticancer compounds are discussed here in this article and the remaining compounds are shortlisted in Table with basic information such as their sources, common names, the concentration of dosage, parts used in cancer treatment, their extraction, and their specificity.

*Angelicin from angelica archangelica*

Angelicin, 2-oxo-(2H)-furo (2,3-h)-1-benzopyran (Fig), the naturally present dynamic molecule segregated from Angelica archangelica, an herb with a traditional Chinese background. In different types of cancer, anticancer characteristics by suppressing malignant action have been reported by angelicin, including invasion, colony formation, migration, and proliferation. Cytotoxicity in distinct groups of malignant and non-malignant cells is activated by angelicin through genotoxic effects(Kavli *et al.* 1983; Lampronti *et al.* 2003).

(Mira and Shimizu 2015) identified that in different types of malignant cells along with colorectal cancer, hepatocellular cancer, and rhabdomyosarcoma the toxicity of cells by suppressing histone deacetylase 8 and tubulin polymerization activity is induced by angelicin.

The results showed in the recent study of (Y. Wang *et al.* 2019) determined that the cells of cervical malignancy were more responsive to angelicin instead of the epithelial cells of the cervix. Angelicin, at IC30, inhibited the multiplication of cells (SiHa and HeLa) by preventing the resting phase G0 or the first growth phase G1 of the cell cycle and impeding other malignant actions which include invasion and migration, the formation of the colony, and the formation of tumor in soft agar. Angelicin, at IC50, caused the death of cells by stimulating programmed cell death. By analyzing the sign of autophagy, it was noted that the treatment using angelicin induced the growth of microtubule linked protein 1 LC3B (light chain 3-β) in the cell's cytoplasm (SiHa and HeLa). Autophagy relevant proteins (Atg)12-5, (Atg)3, and (Atg)7 and split LC3B-II were upregulated succeeding angelicin treatment was showed by the protein

immunoblotting (western blot) results. Studies have been demonstrated that angelicin treatment activated the mTOR phosphorylation, Moreover, the suppressing of mTOR phosphorylation activated by angelicin did not distort the inhibitory action of angelicin on autophagy which specified that angelicin prevented autophagy-independent to mTOR. The findings of the recent study showed that angelicin may have promising chemotherapeutic properties against cervical cancer(Wang *et al.* 2019).

**Table 1.** Some anticancer active mixture isolated from medicinal plants and their in vivo activity.

| *No.* | Active Compounds (Source Plant) | Common name | Parts Used | Extract | Concentration of Dose | Applied to the cancer cell lines | References |
|---|---|---|---|---|---|---|---|
| *1* | Albanol A (*Morus alba)* | White mulberry | Root | N-hexane/ methanol | 30 µM | HL-60 and Crl 1579 i.e. cell lines of human leukemia and melanoma respectively. | (Kikuchi *et al.* 2010) |
| *2* | Allicin, flavonoids, and phenolic components (*Allium sativum)* | Garlic | Leaves | Aqueous | 20 mg per kg per 0.2 mL | Wehi-164 malignant cells | (Shirzad *et al.* 2011) |
| *3* | Angelicin (*Angelica archangelica)* | Wild celery, Garden/Nor-wegian angelica. | Root and rhizome | Ethanolic | 500 mg per kg | Cell lines of Mcf7 and 4t1 | (Oliveira *et al.* 2019) |
| *4* | Artemisinin (*Artemisia annua)* | Sweet worm wood/sweet sage wort | _ | _ | 0.02 percent. | Breast cancer | (Lai and Singh 2006) |
| *5* | Baicalin (*Scutellaria baicalensis)* | Baikal skullcap | Root | Aqueous | 100 µg per mL | Cell line of OSCC (Human oral squamous cell Carcinoma). | (SATO *et al.* 2013) |
| *6* | Benzophenones (*Garcinia preussii)* | _ | Fruits and leaves | Methanol | _ | Cell line of ht-29, du145, a431, and HeLa. | (Biloa Messi *et al.* 2014) |
| *7* | B-sitosterol (*Asclepia scurassavica)* | Tropical milkweed | Leaves i.e. shade dried. | Ethyl acetate and methanol. | 10–20 mg per kg BW. | Cell lines of monkey Vero including Human Colo 320. | (Baskar *et al.* 2010) |
| *8* | B-sitosterol and palmitic acid (*Nitraria retusa)* | Salt tree/Nitre bush | Leaves | Chloroform | 50 mg per Kg BW. | B16-f10 cells lines | (Boubaker *et al.* 2018) |
| *9* | Carbon tetrachloride (ccl4) (*Fagonia schweinfurthii)* | Bush candle | Whole plant | Ethanolic | 200 µg per mL | Cell line of Hep G2 | (Pareek *et al.* 2013) |
| *10* | Carvacrol and transcaryo-phyllene (*Wedelia chinensis)* | Chinese Wedelia | Leaves | Essential oils | _ | B16f-10 cell line of melanoma metastatic. | (Manjamalai and Berlin Grace 2012) |
| *11* | Chrysin (*Alpinia galangal)* | Greater galangal/blue ginger | Rhizomes | Ethyl acetate | 1.3 mg per kg | Murine dla (Daltons lymphoma ascites) and a549 (human lung cancer cells) | (Lakshmi *et al.* 2019b) |
| *12* | Clerodane Diterpenes (*Copaifera multijuga)* | Hayne oil, Copaiba | Trunk of the tree | Oil resin | 2 g per Kg | Melanoma cells of b16f10 | (Lima *et al.* 2003) |
| *13* | Curcumin (*Curcuma longa)* | Turmeric | _ | _ | 75 µM | Human colon cancer cells Ht-29 | (Goel *et al.* 2001) |
| *14* | Deoxyelephantopin (doe) (*Elephantopus scaber)* | Elephant's Foot | _ | Dimethyl sulfoxide | 25 mg per kg | Murine eac (ehrlich ascites carcinoma) | (Kabeer *et al.* 2019) |
| *15* | Diterpenes (*Andrographis paniculate)* | Green chireta | Ariel parts | Methanolic extract | 10 µg per mL | Cancerous cell line of a498 and sw620 | (Ajaya Kumar *et al.* 2004) |
| *16* | Garcinol (*Garcinia indica)* | Kokum | Fruits | Ethanol extract | <1 µM | Colon cancer cells hct-116 and Ht-29. | (Hong *et al.* 2007b) |
| *17* | Isoegoma-ketone (*Perilla frutescens)* | Beafsteak plant | Leaves | Methanol extract | 10 nmol per litter | hepatoma cell sarcoma Huh-7 | (Yan *et al.* 2018) |
| *18* | Oridonin (*Rabdosia rubescens)* | Bing Ling Cao/Blushred Rabdosia | _ | _ | 30 µmol per L | Cell lines sgc 996 of human gallbladder cancer and noz | (Bao *et al.* 2014) |
| *19* | Palmatine, berberine, epiberberine, and coptisine (*Zuojin wan)* | _ | _ | Aqueous extract | 10 mg per mL | Cancer cells (S180) | (Xu *et al.* 2014) |
| *20* | Phenolic compounds specially chlorogenic acid and Ascorbic acid (*Morus nigra)* | Black mulberry/black berry | Aerial parts | dimethyl sulfoxide extract | 1000 µg per mL | PC-3 i.e. human prostate adenocarcinoma | (Turan *et al.* 2017) |
| *21* | Platycodin D (*Platycodon grandifloras)* | balloon-flower | Root | Phosphate buffered saline with dissolved Platycodin d. | 8 µg per mL | mcf-7 cell line of human breast cancer | (Yu and Kim 2010) |
| *22* | Polyphenolic compounds (*Litchi chinensis)* | Litchi/lychee | Fruit pericarp | Ethanolic | 0.3 mg per mL | cell line of hepatocellular carcinoma i.e. Human smmc-7721 | (Wang *et al.* 2006) |
| *23* | Polyphenolic compounds (*Menyanthes Trifoliata)* | Bogbean and Marsh Trefoil | Aerial part and root | Aqueous methanol | 1.5 mg per mL | Glioma cells (Grade iv) | (Kowalczyk *et al.* 2019) |
| *24* | Polysaccharide (*Astragalus membranaceus)* | Mongolian milkvetch | _ | _ | 400 mg per kg | Hepatic cancer | (Yang *et al.* 2013) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *25* | Polysaccharides (*Scutellaria barbata)* | Barbed Skullcap | _ | _ | 40 µg per mL | cell line of 95-d | (Yang *et al.* 2014) |
| *26* | Quercetin-glycosides (*Tussilago farfara)* | Coltsfoot | Floral buds | Methanol | _ | Human colon cancer cells i.e. Ht-29 | (Lee *et al.* 2008) |
| *27* | Rosmarinic acid (*Perilla frutescens)* | Beafsteak plant | Leaf | _ | 105 µg per mL | Human hepatoma cells i.e. (HepG2) | (Lin *et al.* 2007) |
| *28* | Steroidal saponins (*Paris polyphylla)* | Herb Paris | Rhizomes | Methanol | 7.5 mg per kg | cell line i.e. A549 | (Li *et al.* 2013) |
| *29* | Tetracycline Diterpenoid oridonin (*Rhodamnia rubescens)* | Scrub stringybark/brown mallet wood | _ | _ | 50 µM | Human breast cancer cells i.e. mcf-7 and mda-mb-231 | (Wang *et al.* 2013) |
| *30* | Triptolide (*Tripterygium wilfordii)* | Thunder god vine | _ | _ | 250 nmol per L | Neuroblastoma cell lines (n2a and sknsh) | (Antonoff *et al.* 2009) |
| *31* | Xanthone (*Garcinia oblongifolia)* | Lignan garcinia | Branch | Methanol | 1000 µg per mL | cell line of breast cancer (Mcf-7) | (Li *et al.* 2016) |

*Artemisinin and It's Derivative from Artemisia annua*

Sesquatrin lactone with artemisinin 1,2,4-tyroxene round structure with derivatives (Fig). The endoperoxide compound was isolated from a Chinese herbaceous plant Qinghaosu, that has been utilized to treat fever for two millennia (Maude *et al.* 2010). It is known to be reactive against major derivative diseases, with extensive antimicrobial tasks, and demonstrated some remarkable antitumor action. Among the better compounds is artemisinin, which occurs with antichloric qualities(Efferth *et al.* 2001).

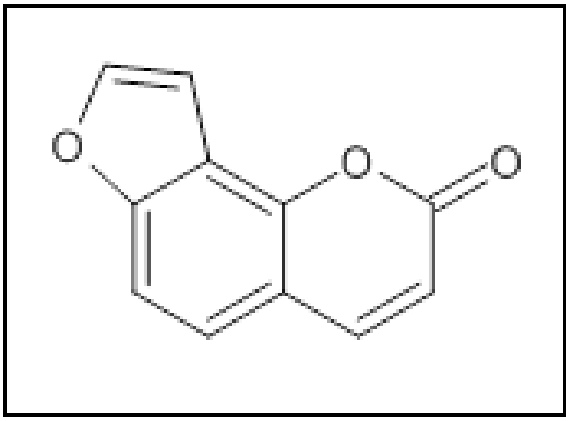

**Fig. 1.** *Structure of Angelicin.*

The Artemisinin with its derivatives, frequently used as the treatment of malaria, are one of the few drugs that are widely used as a drug- or radiation-resistant cell lines (Lee 2000; Reungpatthanaphong and Mankhetkorn 2002). Mainly Artemisinin does not have significant adverse reactions (Gordi and Lepist 2004). Even though tolerance is described(Dondorp *et al.* 2009).

In the primary cell lines along with cancer cultures, antitumor behavior was prevented by a proliferation of cancer, angiogenesis, and metastasis. In the xenograft model, exposure to the artemisinin significantly decreases the tumor size and the development. However, the justification of the usage of artemisinin in the treatment of anticancer should be a better interpretation of the basic procedures elaborated in their toxic actions.

The purpose of this article is to give an outline of the progress in this category of drugs or medicine as dormant anticancer agents.

While researching cancer, a persistent finding of genes and their interaction is derived. As the immunological hallmarks are tangled in the production of cancer, the research of how the artemisinin control malignant may become more arduous. Immunological properties in cancer cells involve the potential to produce a chronic irritant reaction, malignant identity theft, and tolerance(Cavallo *et al.* 2011).

*Subsequent development as anticancer drugs*

Artemisinins have been commonly served to treat malaria for many generations(Betram *et al.* 2008). This drug has revealed a lot of biological enterprise and a strong anticancer development activity. Many verifications showed that compounds like artemisinin may be a curative substitute in extremely metastatic and belligerent cancers(Xu *et al.* 2011) with short-term effective therapy (Morrissey *et al.* 2010; Xu *et al.* 2011) and commonly developing drug opposing effects(Wang *et al.* 2010). Additionally, endo-peroxides against malaria may work with different anticancer medicine having no side effects.

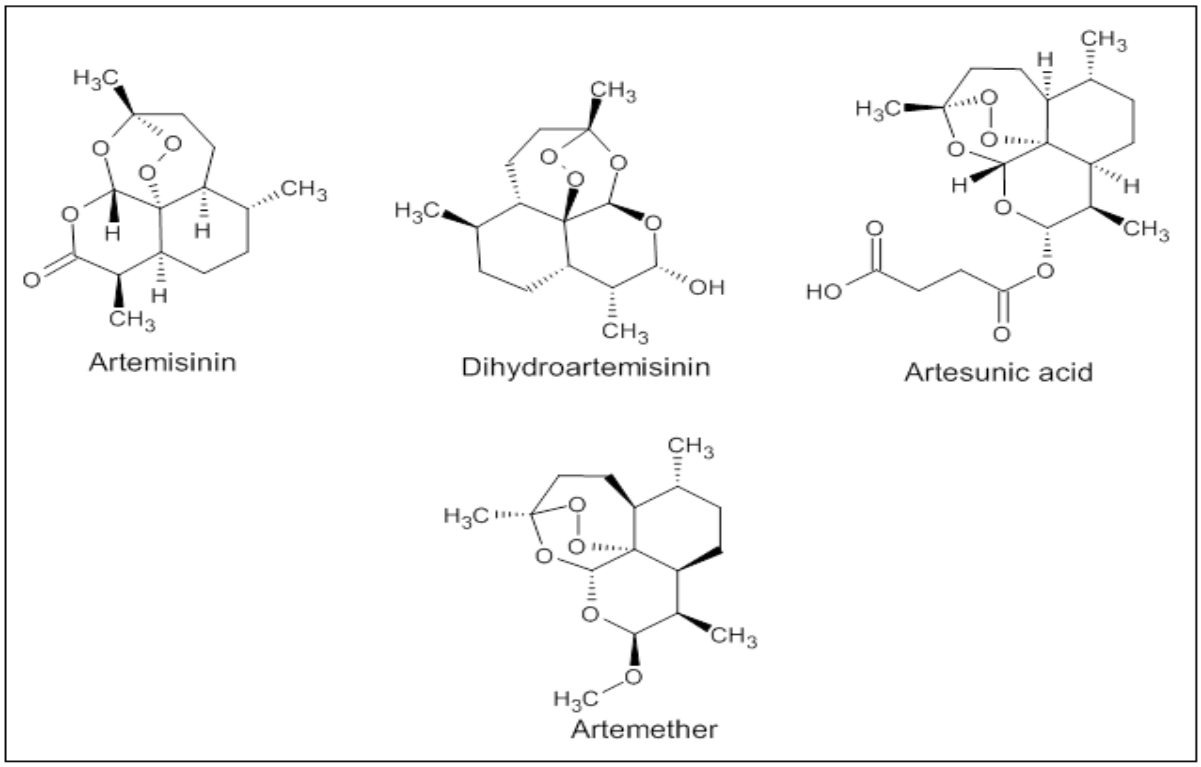


**Fig. 2.** *Artemisinin, Dihydroartemisinin, Artesunic acid, Artemether, and Artemotil.*

*Brassinosteroids*

Naturally existing compounds, brassinosteroids (BRs) especially brassinolide (Fig) present in plants that perform roles in the elongation of the cells of root and steam, signaling of the hormone to organize growth and differentiation of cells, and play other actions like tolerance and resistance towards stress and disease.

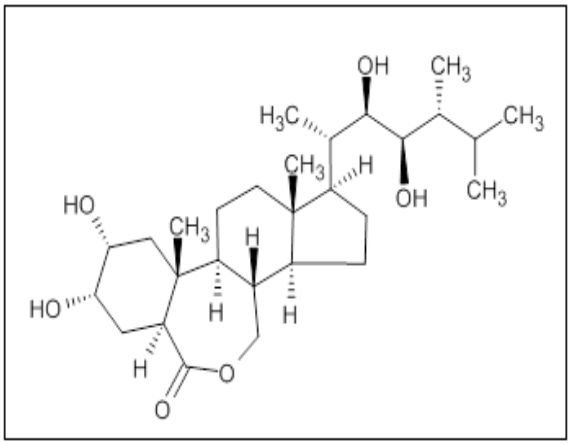

**Fig. 3.** *Brassinolide.*

Two naturally occurring BRs (brassinosteroids) have been served in analyzing with cancer cells to determine the antitumor abilities that these both compounds acquire.

It has been demonstrated that 24-epibrassinolide (24-epiBL) along with 28-homocastassterone (28-homoCS) showed anti-tumor actions on distinct cancer cell lines and confirmed to be active at micromolar concentrations. Prostate cancer cell lines and breast cancer cell lines are also included(Malíková *et al.* 2008).

*Camptothecin*

Camptothecin along with its by-products (Fig) belongs to quinoline alkaloids (pentacyclic group) are extracted from *Camptotheca acuminate* having anticancer characteristics(Khazir *et al.* 2014). In the fruit, cortex, and wood of the plant *Camptotheca acuminate*, Camptothecin is widely present.

The anticancer property of this compound is due to the development of DNA strand breaks (reversible) in the cell-division cycle of normal cells. Camptothecin can prevent the redevelopment of the DNA strand of a single chain by binding to a complex involving topoisomerase I and DNA. By-products of Camptothecin are used to treat rhabdomyosarcoma, cervical cancer, Ewing's sarcoma, and gliomas(Pommier 2006; Robati *et al.* 2008).

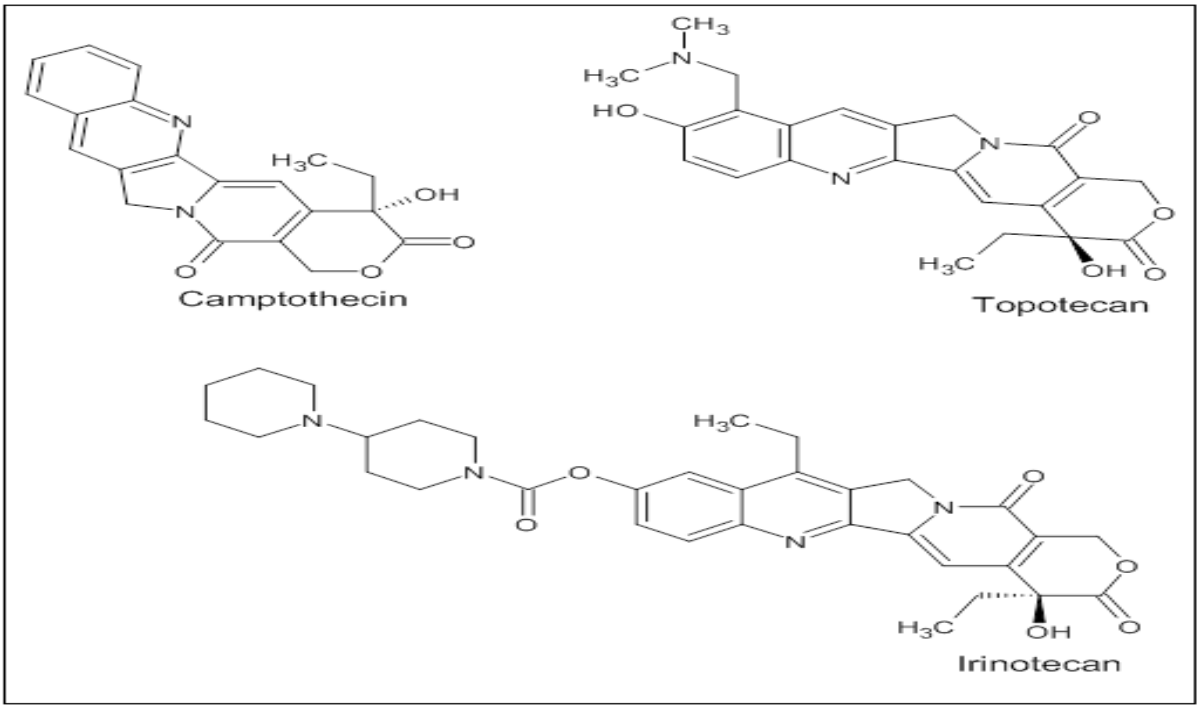


**Fig. 4.** *Camptothecin including its derivatives.*

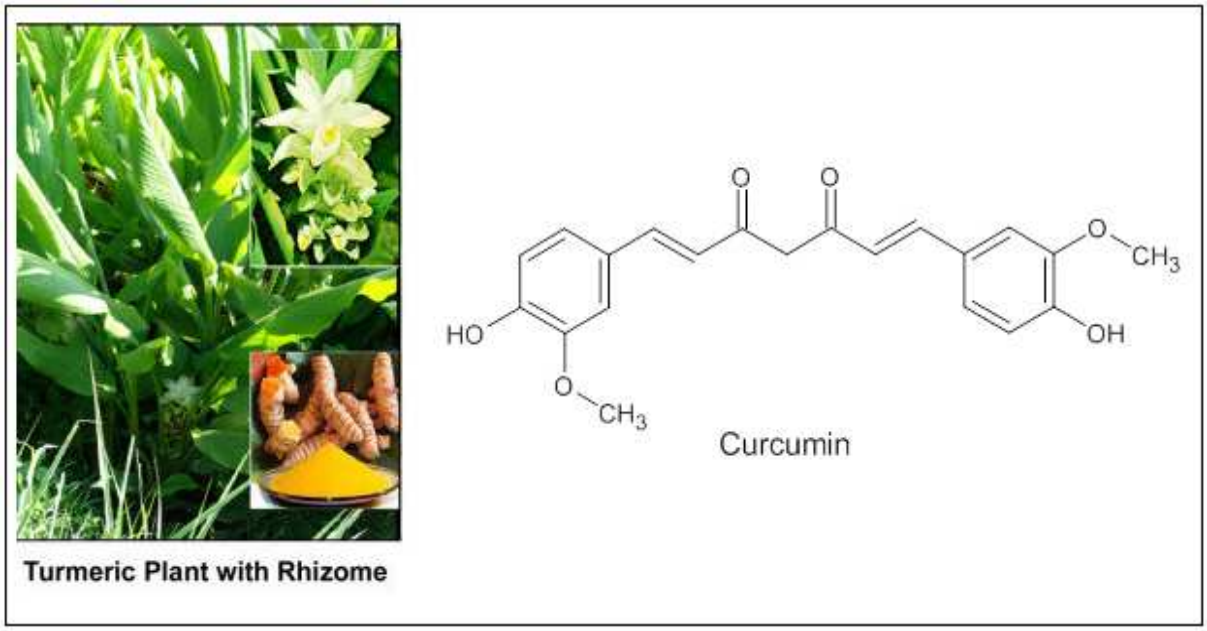


**Fig. 5.** *Curcumin and Turmeric plant.*

*Curcumin from Curcuma longa*

Curcumin is the vital element of plant (Curcuma longa) that has collected much concentration above the past twenty years as of its anti-inflammatory, antioxidant property, and anticancer agent. Curcumin (Fig) has many more applications in other diseases that are not discussed here in this article but have been explained elsewhere (Goel *et al.* 2008; Aggarwal *et al.* 2015a). The derivatives and curcumin itself have gained considerable focus over the previous twenty years because of their anti-inflammatory, anticancer, and antioxidant activities (Nagahama *et al.* 2016). These features are the key elements of curcumin structure(Aggarwal *et al.* 2015b). The major procedure by which curcumin displays its distinctive anticancer property is to induce cell apoptosis and inhibit tumor proliferation along with the invasion by defeating a diversity of the channels of cellular

signaling (Holder *et al.* 1978). Numerous studies have reported antitumor activity of curcumin on breast tumor, squamous cell carcinoma of the neck including head, lung tumor, brain cancer, and prostate cancer (Hassaninasab *et al.* 2011), which shows an ability to target numerous cell lines of cancer. Despite all these benefits, the functions of the curcumin are short because of its low solubility in the water, resulting in oral bioavailability and low chemical strength(Donaldson 1981).

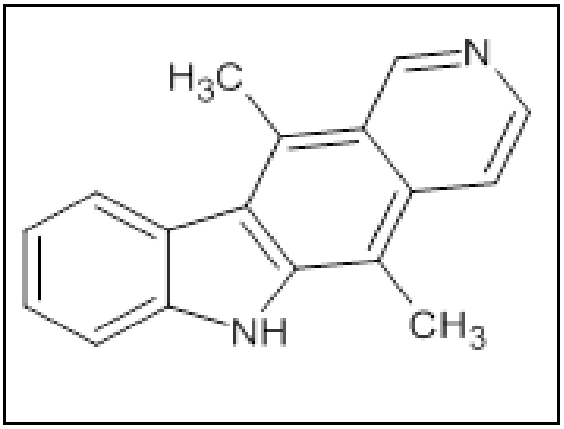


**Fig. 6.** Ellipticine.

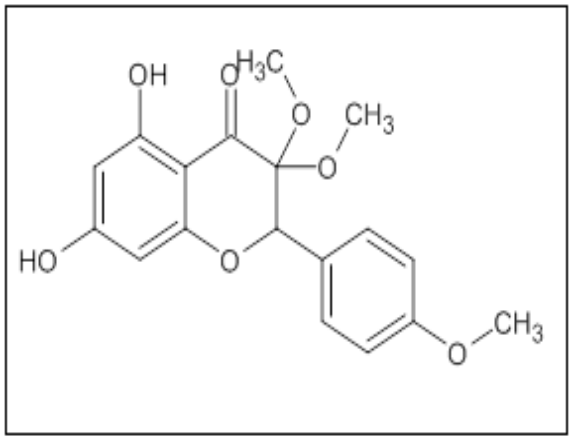


**Fig. 7.** *5, 7-dihydroxy- 3,'4',5'-trimethoxy flavone.*

While entering the cell membrane, curcumin molecule binds with chains of the fatty acyl of lipid membrane via the hydrophobic interactions and the hydrogen bonding, resulting in the less availability of the curcumin in the cytoplasm(Lin *et al.* 2000; Usta *et al.* 2007). To defeat these barriers and to defeat these barriers and to enhance the anti-tumor action of curcumin, certain constitutional moderations have been suggested to boost the bioavailability of selected toxins to specific cancer cells (Prasad *et al.* 2014), and to increase sustainability(Kwon and Magnuson 2007; Aggarwal 2010). Another perspective is to utilize a variety of distribution systems to upgrade the physicochemical properties of curcumin and its anticancer action.

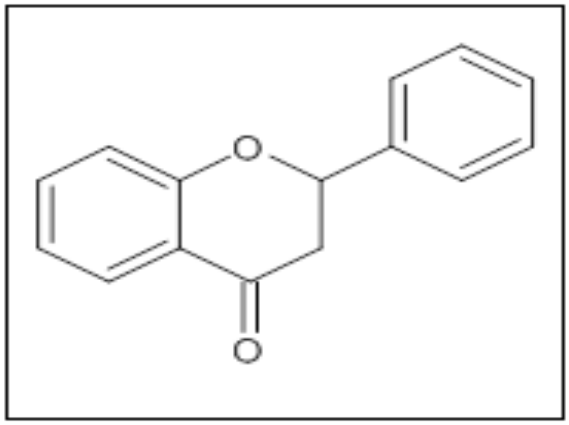


**Fig. 8.** *Flavanone (Flavonoids).*

The latest literature on the curcumin, its analogs, and their anticancer activities on various cancerous cell lines, human clinical trials, and animal models along with the various curcumin distribution systems used to treat malignancy. Additionally, the latest advancement in the transport system for the curcumin transfer to the cells of cancer is nominated(Tomeh *et al.* 2019).

*Diterpenoid lactones from andrographis paniculata*

An herbaceous plant Andrographis paniculata, the family Achantasi, locally present in India and Sri Lanka and planted in South Asia, which is used to cure inflammations and specific infections, before the formation of antibiotics.

The major goal is to separate and distinguish a molecule from leaves of Andrographis Paniculata that can show anticancer effects or other biological affairs. Major classes of compounds include flavones, flavonoids, flavone glycosides, diterpenoids, cloacons, xanthones, chocone glycosides, dimeric diethypes, and sterols, which are separated from different potions of the Andrographis punctata of the family Ascensi. Ayurvedic medicine, Siddha, and sadham traditional medicine, which is present in South Asia (India) and many other countries, various clinical administering essentially antiprolifiratory, anti-

inflammatory, anti-hepatic, antisnake venom, anti-thrombogenic has been shown for Andrographis Paniculata, but only a few of separated compounds have been analyzed. It prompted us to segregate diterpenoid lactone from the plant Andrographis penicillate and analyze it for the anticancerous activities.

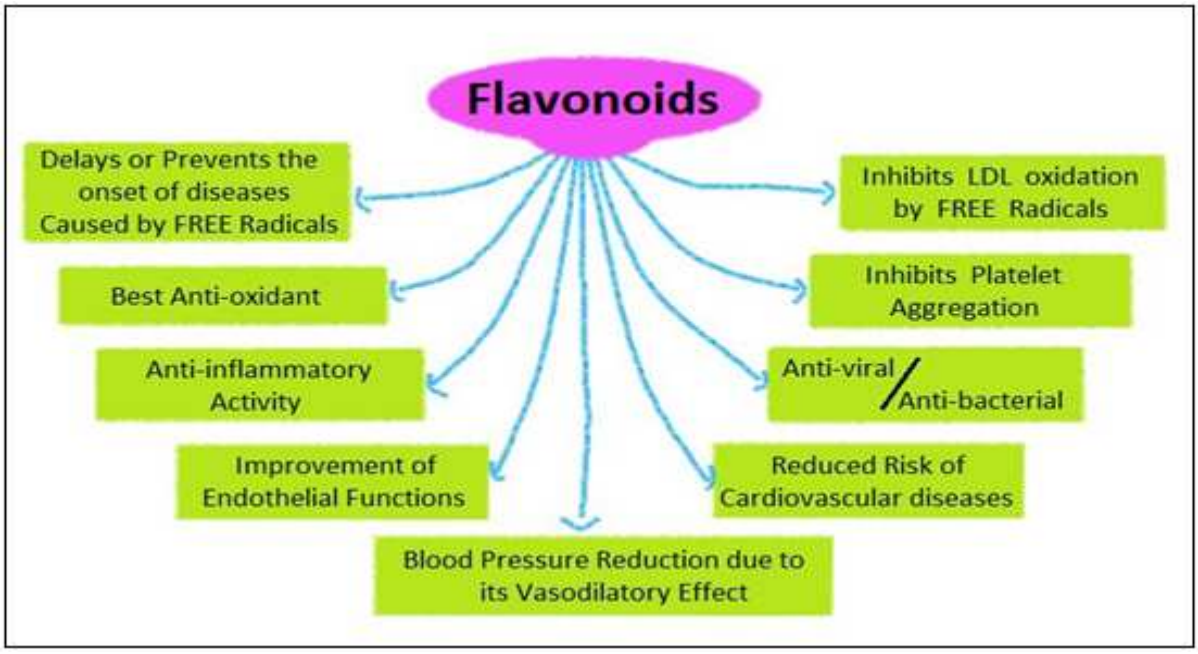


**Fig. 9.** *Actions of Flavonoids.*

The extracts like chloroform and the petroleum ether were produced from the leaves of the Andrographis paniculate chromatographed in a row of the silica gel, separated by the purification and by the gradient-elution technique and crystallized using compounds ethyl acetate and methanol.

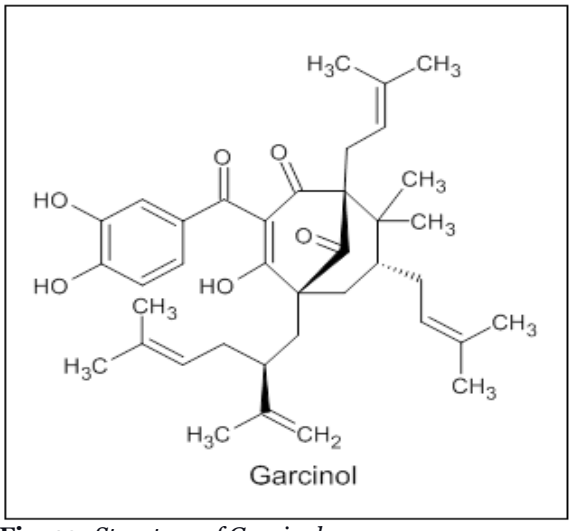


**Fig. 10.** *Structure of Garcinol.*

These compounds were detected using LC-MS spectra, IR, NMR, and compared with standard models for detection of the andrographolide (1), 14-deoxy andrographolide (2), and the neoandrographolide (3).

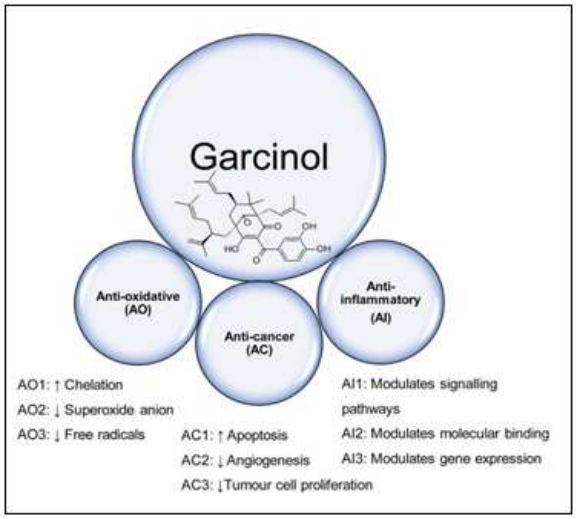


**Fig. 11.** *Garcinol and its actions.*

Recognized compounds were examined using MTT-amplification assays at distinct concentrations on different cell lines of cancer, for instance, Hepat2 (Hepato Cellular) and HCT-116 (Human Colorectal). Besides, DAPI STAINING and ACRIDINE-ORANGE

STAINING methods have been confirmed. Both compounds showed significant activation in micro-molar fields(Mulukuri *et al.* 2011).

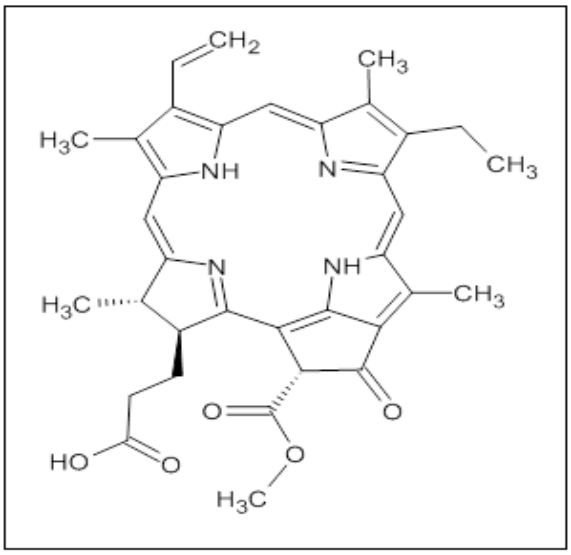


**Fig. 12.** *Pheophorbide a (Pa).*

*Ellipticine*

An alkaloid, the ellipticine (5,11-dimethyl-6H-pyrido-(4,3-b)-carbazole) (Fig) present in *Apocyanaceae* species. Ellipticine was isolated from the plant (leaves), Ochrosia elliptica Labill. Ellipticine acts as a cytotoxic agent in cells of CCRF-CEM and HL-60 (leukemia), along within the cells of human breast cancer (MCF-7). The strong anticancer activity of ellipticine (genotoxic side effects and pharmacological ability) are dependent on its P450 cytochrome a peroxidase-related activation to the species producing covalent adducts of DNA(Stiborová *et al.* 2011).

*Flavones (5, 7-dihydroxy) from Alpinia galanga (L.)*

Alpinia galanga from the family Zingiberaceae which has been extensively analyzed for their qualities related to biological and medicinal.

Research showed that chrysin separated from the A. galanga was tested for the existence of the 5, 7-dihydroxyflavone flavonoid compound (Fig. ). Chrysin has been shown to affect toxicity and apoptosis in cancerous cells of lungs in humans and is found in normal fibroblast cells and lymphocytes that leave the marmalade lymphoma cells at the 25,50 concentrations, and the 75 µg/mL. Cell cycle study by making use of flow cytometry has shown that there is a rise in the collection of S-phase cells, leading chrysin to induce G1 / S-phase at the concentrations mentioned above. Annexin V- and activated caspase-3 positive cells both increased the dose dependence in the cells as indicated by the flow cytometry.

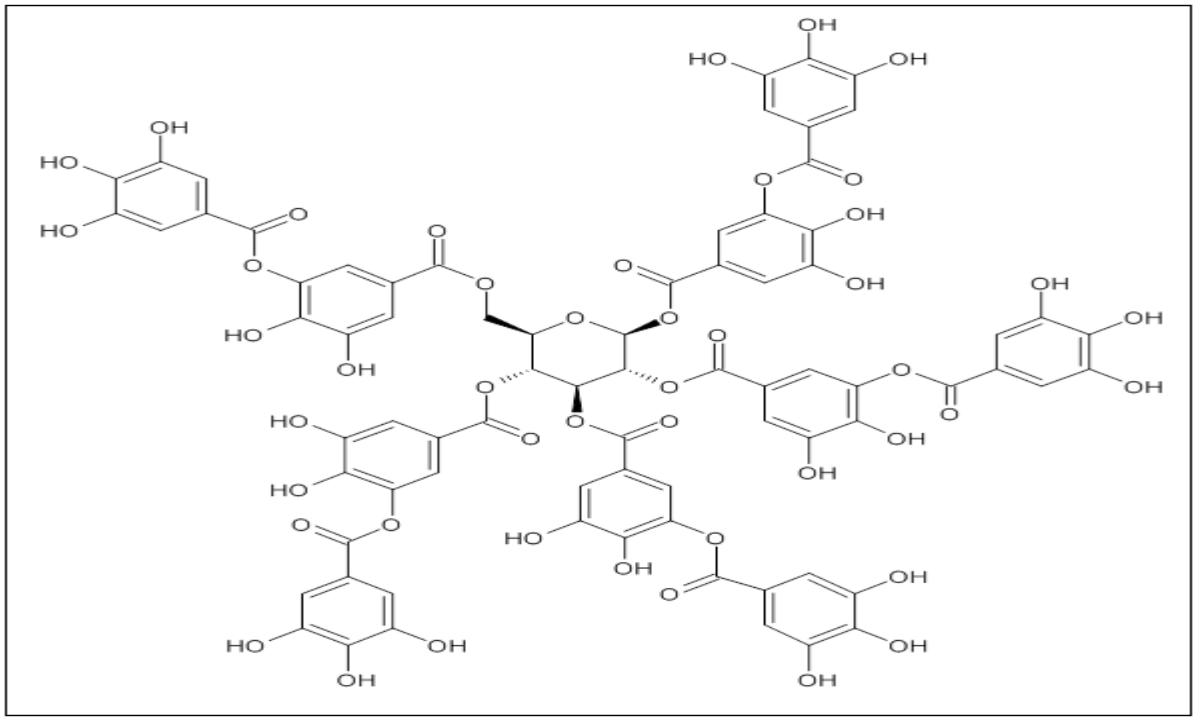


**Fig. 13.** *Polyphenols from Penthorum Chinense Pursh.*

Reduction in tuberculosis studies in a sample of mice with Dalton's lymphoma ascites significantly reduced tumor size by 1.3 mg per kg weight of the body and increased rat life expectancy by 52.6%. Besides, the compound has been shown to have chemical effects whenever administered with cyclophosphamide, by decreasing the toxic actions.

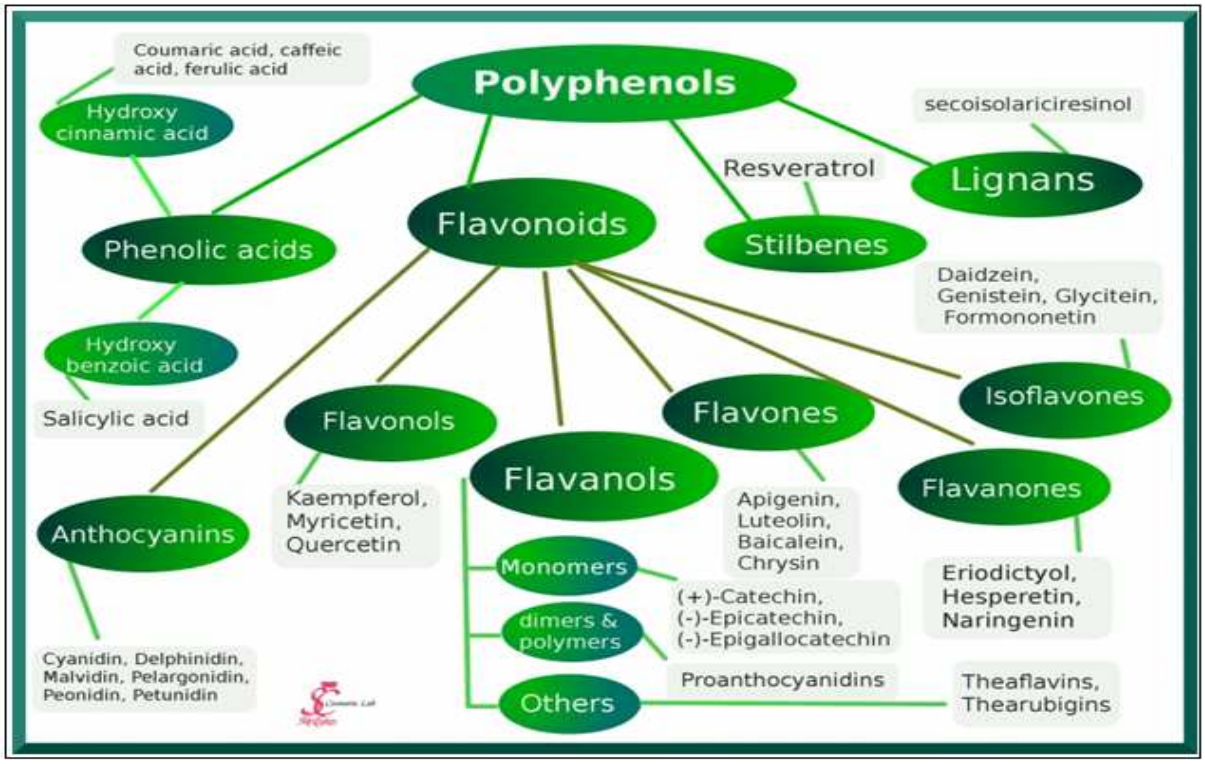


**Fig. 14.** *Polyphenols.*

The synergistic reaction of chrysin including cyclophosphamide in the matter of decreasing the size of the tumor and prolonging the lifetime of the mice as compared to separate therapy recommends the probability of decreasing cyclophosphamide amount during the treatment(Lakshmi *et al.* 2019a).

*Flavonoids*

Flavonoid compounds like chalcones, flavones, flavanols, and anthocyanins, and many more can be present only just in the seed of the plant(Wen *et al.* 2014). It has been shown that flavonoids (Fig. ) in purified form can exhibit anticancer actions (Fig) towards more human cancers including; breast cancer (MCF-7), hepatoma (Hep-G2), and cervical cancer (Hela). The regulations of other agents and proteins which may be involved in the survival of the cancer cells can be altered or inhibited by polyphenols. AIF and MLF prevent the representatives of this family of proteins by inhibiting their phosphorylation essential for the survival of malignant cells(Kumar and Pandey 2013).

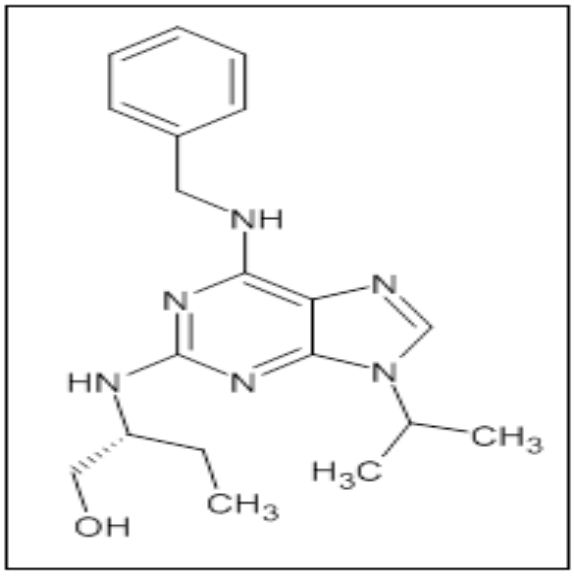


**Fig. 15.** *Roscovitine (Seliciclib).*

*Garcinol*

Garcinol (Fig) from *Garcinia Indica*, a mangosteen family generally known as kokum, has normally been used in the tropics and has been praised for years.

However, the biological characteristics of garcinol are beginning to clarify (Fig).

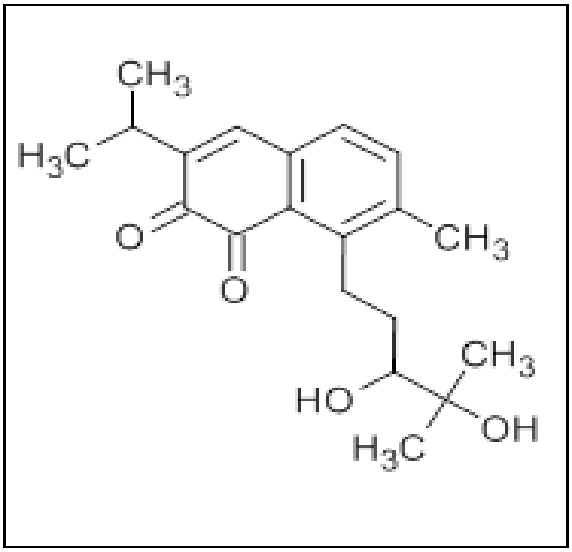


**Fig. 16.** *Salvicine.*

After 3 days of treatment vigorous growth-inhibiting properties on every intestinal cell have values of IC50 between the extent of 3.2–21.4 μM showed by Garcinol and its derivatives. Compared to normal immortal cells it has been found that Garcinol inhibits the multiplication of tumor cells more effectively. These outcomes propose that Garcinol and its by-products can prevent the production of the cells of colorectal cancer leaving the natural cells unaffected. However, garcinol at its low concentration induces the growth of cells(Hong *et al.* 2007a).

Garcinol exhibits practical epigenetic effects associated with carcinogenesis through miRNA profiles inhibited by histone acetyltransferase (HAT300) and post-transcriptional protein modification (Padhye *et al.* 2009). Several in vivo tests have indicated the efficacy of garcinol across distinct types of cancers, along with colorectal cancer, pancreatic cancer, leukemia, and breast cancer.

*Pheophorbide a (Pa) from Scutellaria barbata*

Pheophorbide a (Pa), a derivative of chlorophyll from the plant *Scutellaria barbata* also known as barbed skullcap, a flowering plant species belonging to *Lamiaceae* (mint family), which can initiate notable antiproliferative results in certain cancer cell lines (Fig). The mechanism of action of Pa-PDT (Pheophorbide a moderated photodynamic therapy) has been investigated on liver cancer (hepatocellular carcinoma/Hep3B cells) in humans. Notable prevention of the development of ep3B cells can be achieved by Pa-PDT which has an IC50 value of 1.5 μM. Moreover, Pheophorbide a moderated photodynamic therapy could decrease tumor size (57%) after 336 hours of treatment in a mice model(Tang *et al.* 2007).

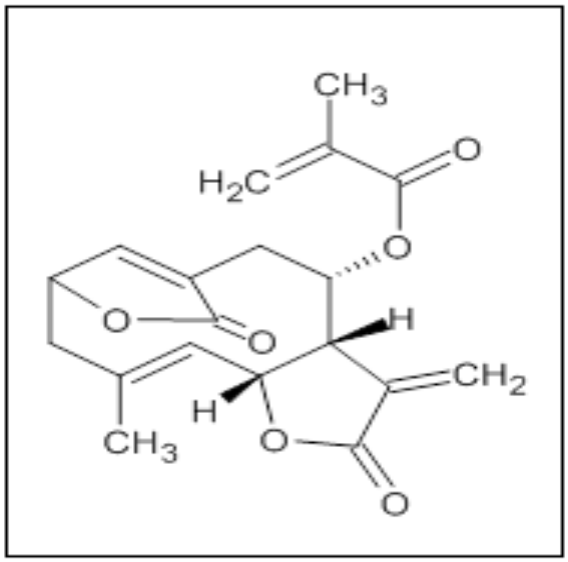


**Fig. 17.** *Structure of isodeoxyelephantopin.*

*Polyphenols from penthorum chinense pursh*

P. Chinese Pursh (Oriental penthorum), a plant extensively present in eastern Russia, Japan, Korea, and China (eastern Asia)(Ikeda and Itoh 2001) (Fig). Anti-cancer and antioxidant characteristics have been exhibited by the metabolites from Penthorum Chinese Pursh (Sigurdsson *et al.* 2004; Mahesh and Menon 2004; Moon *et al.* 2006; Wang *et al.* 2008). Based on the recent research EtOAc part carries powerful inhibitory characteristics as compared to other parts of P. Chinese Pursh. New polyphenols i.e. 2,6-dihydroxyacetophenone-4-O-[4',6'-(S)-hexahydroxydiphenoyl]-β–D-glucose and Penthorumin C as well as polyphenols thonningianin B, pinocembrin–7-O-[3"-O- galloyl-4",6'-hexahydroxydiphenoyl]-β-D-glucose, thonningianin A, and pinocembrin- 7 - O -[4",6"-hexahydroxydiphenoyl]- β -D-glucose were extracted from P. Chinese Pursh. In the cells of HSC-T6, antiproliferative activities were assessed by these compounds, and with IC50 values of 19.2 μM and 12.7

μM thonningianin B and 2,6 - dihydroxyacetophenone- 4- O -[4',6'-(S)-hexahydroxydiphenoyl]- β– D -glucose showed symbolic activities respectively(Lu *et al.* 2012)(Sanli *et al.* 2002; Ferreira *et al.* 2016)(Huang *et al.* 2014).

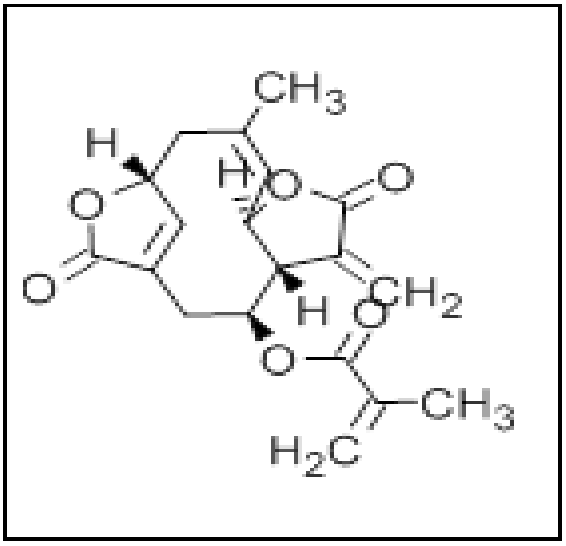


**Fig. 18.** *Structure of deoxyelephantopin.*

*Polyphenols*

Polyphenolic compounds involve antitumor compounds which are flavonoids, curcumin, tannins, gall catechins, and resveratrol (Fig). Resveratrol is present in foods like grapes, peanuts, and red wine. Gall catechins are extracted from green tea. By including polyphenols that are a natural antioxidant in the food of a person, we can lower the risk of the tumors and improve health(Azmi *et al.* 2006). Polyphenols show anticancer properties by inducing apoptosis which can be used to treat cancer. Cancer agents may be changed through the polyphenol regulating acetylation, methylation, or phosphorylation through direct bonding.

For instance, curcumin suppresses Tumor Necrosis Factor (TNF) expression to treat the cancer cells in different cell lines on interaction with other stimuli(Apostolou *et al.* 2013).

*Roscovitine*

Roscovitine

(

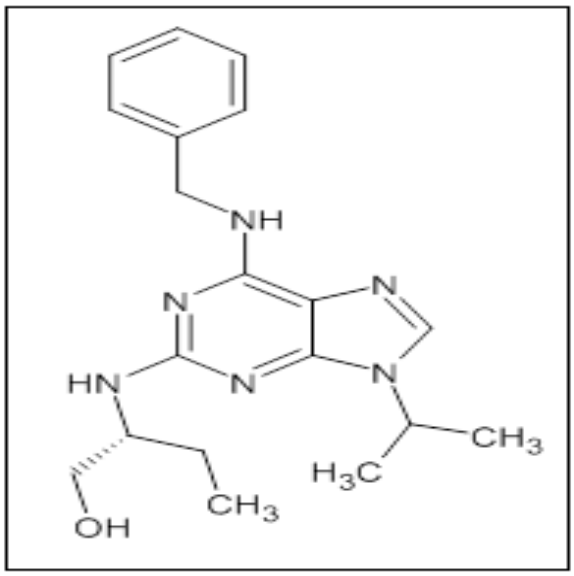


Fig), a purine based anticancer compound derived from olomoucine, a semisynthetic by-product of R-roscovitine, and was segregated from the cotyledons of the plant well-known as Raphanus sativus L. Roscovitine, a strong cyclin-depending kinase inhibitor (CDK/cyclin E) can show a vast spectrum of actions towards cancer, glomerulonephritis, neurogenerative diseases, and viral infections. In phase 1 clinical examination towards glomerulonephritis, and phase 2 clinical trials towards breast and lung cancer roscovitine was actively used(MacCallum *et al.* 2005).

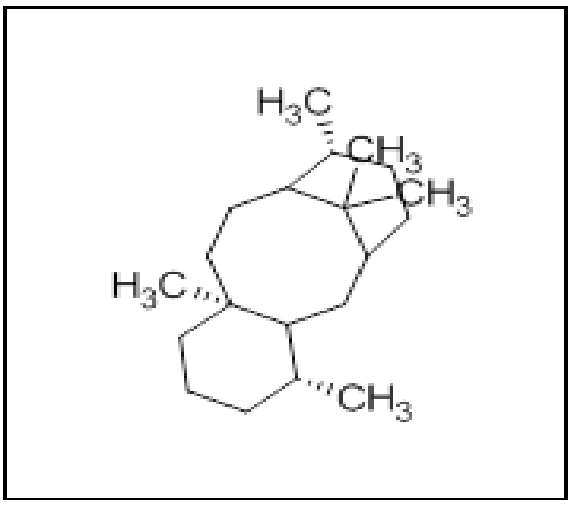


**Fig. 19.** *Taxanes.*

*Salvicine*

Salvicine, a modified derivative (diterpenoquinone) extracted from the Chinese vine Salvia pronitis Hanace. (Sheng *et al.*, 1999) In 1999 chemically synthesized salvicine which showed active inhibitory

action towards a large spectrum of tumor cells of humans in vitro and mice related human cancer xenografts(Meng and Ding 2007). Salvicine (

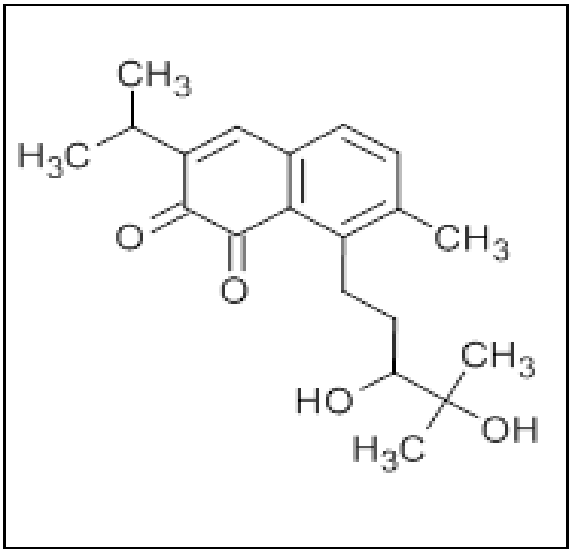


Fig) activate damage to distinct DNA genes, activating apoptosis.

*Sesquiterpene Lactones, deoxyelephantopin, and isodeoxyelephantopin Isolated from Elephantopus scaber L.*

Elephantopus scaber L. also referred to as *Asteraceae* (Daisy Family), an herb-related specie that is distributed worldwide, mostly in America. Researchers have shown that chloroform extract of Elephantopus scaber L. can exhibit anticancer and cytotoxic characteristics(Geetha 2016). Sesquiterpene lactone, deoxyelephantopin (

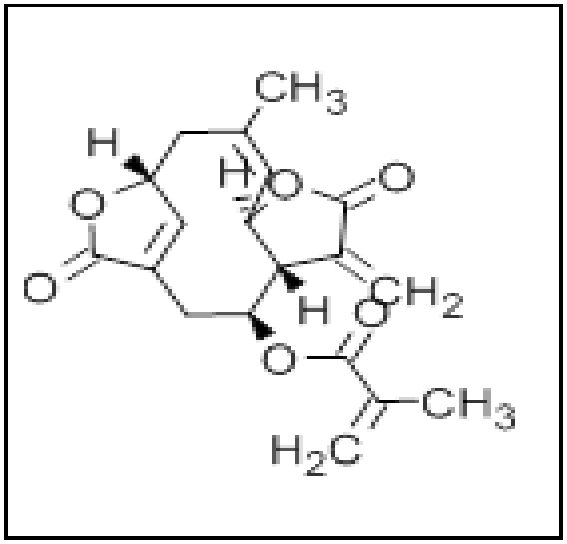


Fig), and isodeoxyelephantopin (Fig) can be extracted by the chloroform extract (whole plant) of Elephantopus scaber L. (South Indian) by Bioassay-mediated isolation whose chemical structures can be determined by spectroscopic techniques. These compounds with cell viability assay can cause a dosage depletion in the sustainability of cancer cells (L-929) in the culture of 3 days with the IC50 value (3.3 µg/mL and 2.7 µg/mL). In treating cancers with high proliferative potencies, the antiproliferative characteristics of isodeoxyelephantopin and deoxyelephantopin can be used because these compounds can selectively act on the Inhibition of integration of titrated thymidine into DNA (cellular) of Dalton's Lymphoma Ascites (DLA) cancer cells and PHA-mediated proliferating lymphocytes of human.

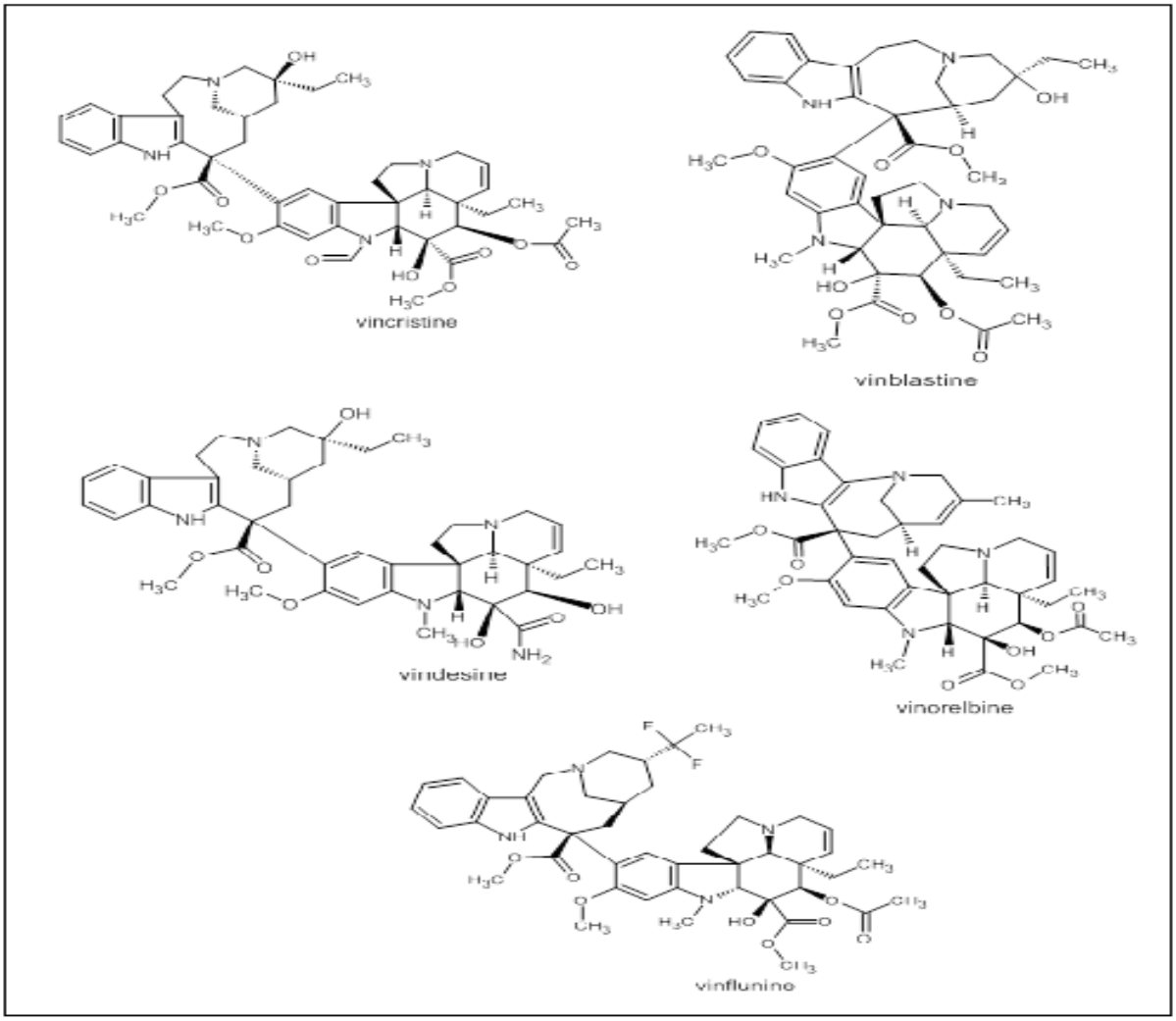


**Fig. 20.** *Catharanthus alkaloids: vincristine, vinblastine, vindesine, vinorelbine, and vinflunine.*

Deoxyelephantopin with 3 µg/mL concentration can cause the highest apoptotic cells and display remarkable in vivo anti-cancer potency against Lymphoma Ascites (DLA) cancer cells(Geetha *et al.* 2012).

*Taxanes (Taxus baccata)*

Paclitaxel (PTX) is taken from the tree needles of Taxus baccata (European yew) and Pacific yew (Taxus brevifolia). It relates to a class of compounds famous as taxanes, which are inhibitors of the mitosis process. Paclitaxel and semisynthetic derivatives of paclitaxel, cabazitaxel (CTX), and docetaxel (DTX) are derived from 10- baccatin III or 10-deacetylbaccatin III (both contain property of the taxane skeleton three condensed homocyclic rings along with one heterocyclic ring. Taxanes (Fig) like paclitaxel and its look-alike docetaxel are also disruptors that disturb microtubule and stop cell cycle phase transitions from metaphase to anaphase which causes cell cycle arrest and programmed cell death.

- The formation of paclitaxel naturally from the Taxus is ecologically unbearable and economically impracticable. Later on, a new procedure for producing the precursor of paclitaxel 10-deacetylbaccatin III has been discovered(Zhang *et al.* 2018).
- Paclitaxel and docetaxel are commonly used alone or along with many other antitumor drugs that perform cell apoptosis and impede the process of mitosis.
- The antitumor pursuit of taxanes is alike the activity of vinca alkaloids on the microtubules, in which heterodimers of the Alpha-tubulin and the Beta-tubulin are present.

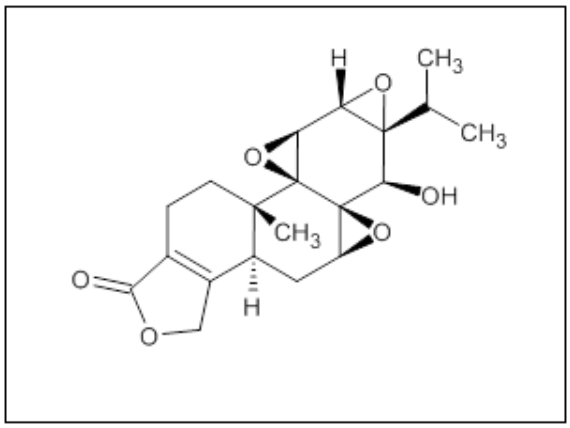


**Fig. 21.** *Triptolide.*

A dense collection of the taxanes causes polymerization of microtubule, while a high concentration of Catharanthus alkaloids impede it. The most efficient in compounds are taxanes that are used to cure ovarian cancers, breast cancers, and cell cancer (squamous) of the head as well as neck(Mody *et al.* 2016).

*The catharanthus alkaloids*

The Catharanthus alkaloids (Fig) contain a class of 130 terpenoid indole alkaloids(Barbosa-Filho *et al.* 2006). Robert Noble with Charles Beer from Canada isolated the first alkaloid in the 1950s known as Vinblastine from the plant Madagascar periwinkle. A group of plant medicines originate from vincristine including its derivatives are (indoloid) alkaloids, a heterodimeric found at the time of biosynthesis of the vindoline, and the catharanthine (both present in the pink Catharanthus roseus).

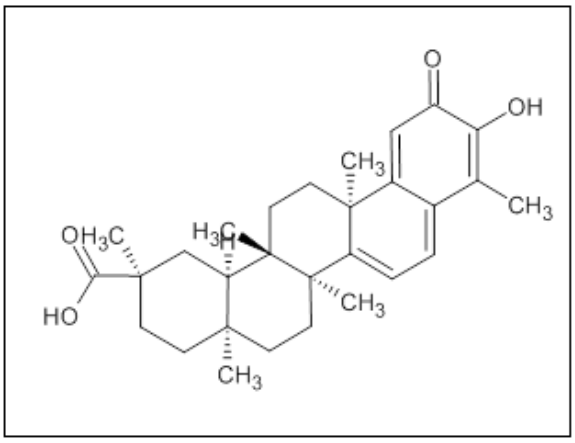


**Fig. 22.** *Celastrol.*

This group comprises of vinblastine, vincristine, the semisynthetic derivatives vindesine, anhydrous vinblastine, vinflunine (the fluorinated analog of vinorelbine), and vinorelbine (navelbine). Alkaloids of Catharanthus are used to cure ovarian cancer, soft tissue sarcoma (orphan), breast cancer, and lung cancer (non-small cell).

Vindesine is used more to treat acute lymphocytic leukemia and less used to treat colorectal cancer, breast cancer, and renal cancer, Vinflunine is served to cure bladder cancer, and Vinorelbine is served to cure non-small cell lung cancer(Kolb and Steinherz 2003).

*Triptolide and celastrol*

Triptolide and celastrol (also referred to as tryptrin) are the two essential compounds of Thunder God wine (also referred to as *tryptocargum vilfordi* and Lei Gong Teng), which have extensive bioactive activity, specifically anti-tumor activity(Jiang *et al.* 2015).

When combined, Tryptolide (Fig. ) and celestrol (Fig) have been reported to be anticancer by induction of programmed cell death (apoptosis) and cell-division cycle in various cancerous cells in vivo and in vitro (Kim *et al.* 2011, 2013; Li *et al.* 2012b, 2012a; Chen *et al.* 2014; Sai *et al.* 2014; Mi *et al.* 2014).

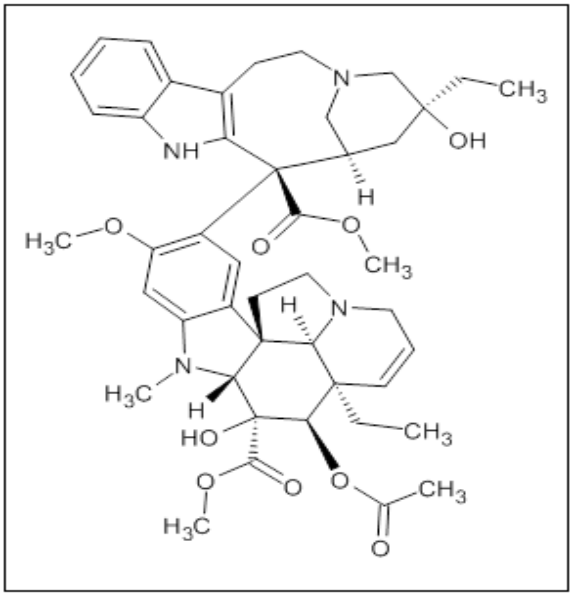


**Fig. 23.** *Vinblastine.*

As a specific inhibitor, Celastrol has been analyzed as a specific inhibitor of HSP90 and exhibits antitumor activity by initiating desensitization of HSP90 proteins, like, CDK, AKT, EGFR, p53, and IAP's. For known bioactivities, HSP90, and XPB has been distinguished as targets of triptolide and celastrol(Zhang *et al.* 2008, 2009). Collegial anticancer effects on different cancers as hepatocellular carcinoma, breast cancer, lung cancer, and melanoma are showed by Celastrol combined with chemotherapeutic agents(Raja *et al.* 2011; Lo Iacono *et al.* 2015; Ma *et al.* 2017).

Mechanistically, triptolide directly binds to excision repair cross-supplementation group 3 (XPB, also referred to as ERCC3), TFIIH (transcription factor 2), which suppresses its DNA-dependent ATS action, activating the inhibitory effect on RNA polymerase II-moderated transcription(Titov *et al.* 2011).

*Vinblastine and vincristine*

Vinblastine (Fig) as well as Vincristine (Fig) from *Fusarium* oxysporum isolated from *Catharanthus* roseus. Endophytic fungi can produce the exact natural compounds like their hosts by mimicking chemistry because of their relationship (symbiotic) with the host plants. Thus, endophytic fungi are being recognized to make important products such as podophyllotoxin, Taxol, and camptothecin, etc. Researchers have extracted *Fusarium oxysporum* (endophytic fungi) from the plant Indian Catharanthus roseus which gives the medicine (anticancer) vincristine and vinblastine in the concentrations of 67, 76, 67 µg per litter respectively with the same characteristics of the vincristine and vinblastine obtained from the plant.

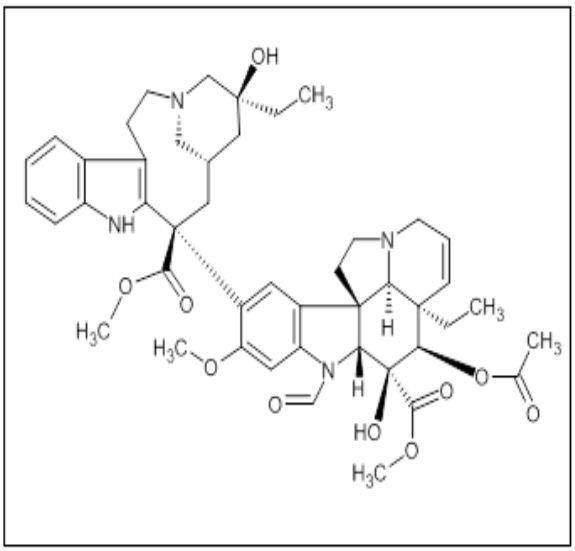


**Fig. 24.** *Vincristine.*

These are the wonder medicine for cancers and can be isolated from the leaves of the plant Catharanthus roseus with the help of techniques like cell culture, semi-synthesis, tissue culture, total synthesis, and shoot synthesis (Moreno *et al.* 1995; Kumar *et al.* 2013).

Vincristine and vinblastine are exceptional drugs with anticancer activity however the latest production of these products using plants is expensive and non-abundant(Kumar *et al.* 2013).

*Xanthones from Garcinia cowa (Leaves)*

In China mostly in the western and southern regions of Yunnan, *Garcinia cowa* belonging to the Guttiferae family which has diverse chemicals (Fig) with distinct bioactivities including xanthones (Fig), along with antibacterial and anticancer action(Panda *et al.* 2013).

*Anticancer plant-derived drugs*

Drugs derived from plants can be classified into 4 major types with the following properties: DNA damage defending drugs or antioxidants, mitotic disruptors, methyltransferase inhibitors, and histone deacetylases (HDAC) inhibitors(Amin *et al.* 2009). Compounds involving isothiocyanates, pomiferin, sulforaphane, and isoflavones are thought to be HDAC inhibitors.

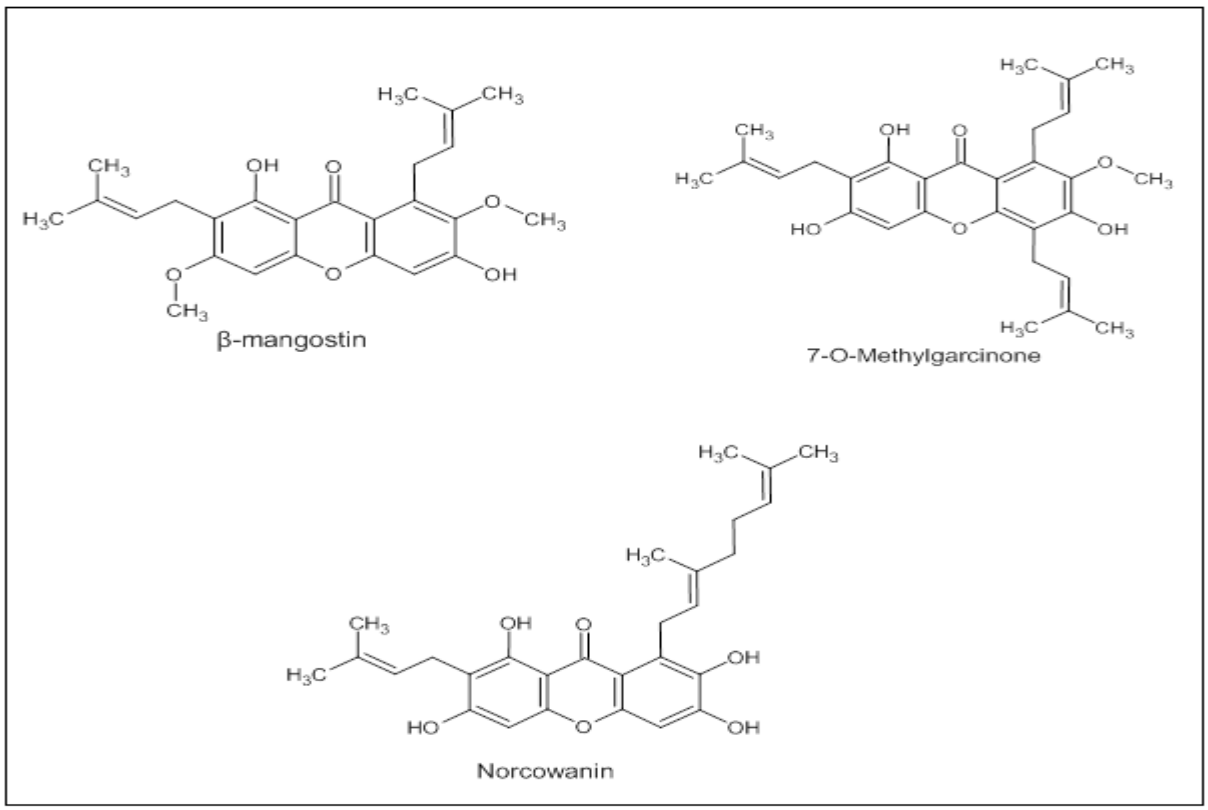


**Fig. 25.** *New and active compounds (Xanthones) from G. cowa.*

These compounds stop the working of the cancerous proteins. Compounds derived from plants show inhibition in HDAC working can increase chemotherapeutic sensitivity in the cancer in humans(Greenwell and Rahman 2015).

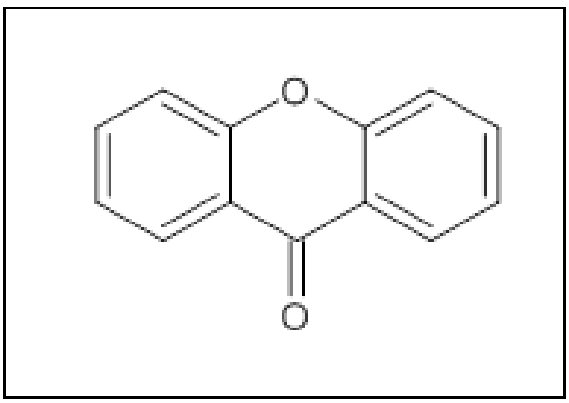

**Fig. 26.** *Xanthone.*

## Conclusion

This article intensively highlights the anticancer effects along with the mechanism of some of the essential compounds in the plants. This is achieved by modulating signaling pathways. These compounds have immunomodulatory and antioxidant activities which possess anticancer effect. These anticancer agents\compounds separated from medicinal plants are beneficial in distinct cancer treatment such as hepatic cancer, blood cancer, breast cancer, cervical cancer, stomach cancer, and lung cancer. The present review indicates the chemotherapeutic efficacy of the compounds extracted from medicinal plants. Now there is the need of the day to explore medicinal plants to more range and their utilization in different further disease and toxicity studies along with clinical trials. It is specified that the essential antitumor role via their distinct division of secondary metabolites (Table ) is played by these compounds. Nevertheless, the analysis of the above-mentioned compounds should not restrict the research of an abundance of antitumor compounds few of which are even undiscovered. Studies are required to specify the procedure of antitumor activity of numerous previously discovered and many undiscovered anticancer compounds from medicinal plants.

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