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Review

A Critical Review On Medicinal Plants With Anti-Cancer Activity

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Abstract

Cancer is known to be the second most common cause of death, surpassed only by cardiovascular disease. So there has been intense research on various plant resources to develop novel anticancer agents. From the past several years medicinal plants have been proven to be an important natural source for cancer therapy with fewer side effects. There are many natural cytotoxic drugs available, which need further improvement and development of new drugs. The basic aim of this review is to explore the potential of newly discovered anticancer compounds from medicinal plants, as a lead for anticancer drug development. It will be helpful to explore the medicinal value of plants and for new drug discovery from them for the researchers and scientists around the globe.

Keywords: anti-cancer agents, medicinal plants, cancer prevention, apoptosis

INTRODUCTION

Cancer is known to be the second most common cause of death, surpassed only by cardiovascular disease. Based on the ACS report 2014, nearly 1 in every 4 deaths can be attributed to cancer with a possibility of 585,720 deaths due to cancer this year [Ali et al., 1997]. In 2012 there were 14.1 million new cancer cases, 8.2 million cancer deaths and 32.6 million people living with cancer (within 5 years of diagnosis) reported by IARC worldwide. Breast and ovarian cancer are the major cause of cancer death in American women [Ambasta 2000] . Studies revealed that in India, 555,000 national cancer deaths in 2010. About 42% of male and 18% of female cancer deaths are due to tobacco-related products [Ambasta 2000]. Despite tremendous advances in the Cancer chemotherapy, search for new and better agents is continued. Compounds of natural origin have provided new and potential leads for cancer chemotherapy in the past; many of them are drug of choice in cancer treatment. For instance, Taxol for breast cancer, Vinca alkaloids for leukemia, Podophyllum, etoposides and capototheca etc.,are some of the natural products in clinical use. Herbs these days are also being used as chemo-protectant against cytotoxicity caused by anticancer drugs. So the present review aimed to explore the potential anticancer compounds obtained from plant sources..

MEDICINAL PLANTS WITH ANTICANCER ACTIVITY

The list of the plants having anticancer activity and the chemical constituents responsible for its activity are given in Table no:1. A brief discussion about each plant was given below

1. ***Allium sativum:*** commonly known as garlic, which contains chemical constitients likeallicin, alliin, sallyl-cysteine and diallylsulphide etc. pharmacological properties of allium id due to the presence of allicin which is a precursor for several compounds containing sulphar [Charfenberg K, 1990]. Due to the presence of alliin in galic oil, it inhibits prostaglandin dependent cancers. Metastasis in lung cancer was prevented by diallyl trisulphide present in it [Belman S., 1983]. Studies shown that the extract of garlic exhibited cytotoxicity against bladder, stomach, lung and breast cancer cell lines by MTT assay [Milner JA., 1996].
2. ***Actinidia chinensis:*** commonly known as kiwi fruit, its immune-modulatory and anticancer activities are due to the presence of polysaccharide known as ACPS-R.
3. ***Aloe vera:*** it contains aloe-emodin which inhibits the metastasis and activates the macrophages for anticancer activity [Pecere T et al., 2000]. Its immunostimulant activity against cancer cells is due to the presence of chemical known as acemannan[Wasserman et al., 2002].
4. ***Ananas comosus:***in the tratement of leukemias bromealin (mixture of protease + other enzymes] is used, which inhibits the growth of the cancer by enhancing the cytotoxic activity of macrophages and monocytes
5. ***Angelica sinensis:***used to treat cervical cancer. AR-4, a polysaccharide of the plant responsible for its immunomodulatory activities which includes stimulation of immunce cell proliferation, interferon production etc.
6. ***Annona species:*** acetogenins from the plant is effective in treatment of nasopharyngeal carcinoma and it shows cytotoxicity against sarcoma and leukemia.
7. ***Artemisia annua*****:** to treat leukemia and colon cancers. Furthermore, it was observed through these studies that the artesunate was more active than the drugs used for such cancers [Khan et al., 2019].
8. ***Astragalus membranaceus:*** used to treat advanced stage of liver cancer due to the presence of Swainsonine, a derivative of the plant. Studies shown that, using the plant with the combination of ginseng , shown a highest survival rate in liver cancer patients [Wang J et al., 1991].
9. ***Betula utilis:*** commonly known as birch, found to be effective in treatment of prostate cancer. Betulin is an active constituent, which can easily convert into betulinic acid responsible for its cytotoxic activity against liver and lung cancer cell lines .
10. ***Camellia sinensis:*** commonly known as green tea, it's a potential antioxidant because of the polyphenols present in it. It fights against cancer by removing free radicals from the body. Epigalloacatechin gallate (EGCG), a polyphenol in green tea decrease the number of leukemia cells in the patients with a form of blood cancer known as chronic lymphocytic leukemia (CLL). Daily consumption of (5gm/day) green tea protects the body against stomach, colon and lung etc cancers [Lea MA et al., 1993].
11. ***Catharanthus roseus:*** commonly known as Madagascar periwinkle, anticancer activity of the plant is due to the presence of major alkaloids known as Vincristine and Vinblastine. Vinblastine shows the anticancer activity by inhibiting the microtubule formation in cancer cells and its adverse effects includes loss of hair, bone pain and dizziness etc [Jean Bruneton, 1993]. vincristine sulphate inhibits the process of mitosis in cancer cells, and it is useful in treatment of acute leukemia in children and lymphocytic leukemia. It is also useful in treatment of Hodgkin disease, Wilkins tumor and reticular cell sarcoma [Nobel et al., 1990].
12. ***Colchicum luteum:*** colchicine, a tropolone alkaloid responsible for its anticancer activity by showing antimitoitic activity and used for dispersion of tumors and other neoplastic diseases [Jean Bruneton, 1993].
13. ***Combretum caffrum: C***ombretastatin, constituent of the plant responsible for its activity against cancer by inhibiting the blood supply to the tumor cells.
14. ***Curcuma longa: C***urcumin is the main constituent responsible for its anticancer activity by inhibiting the PGE-2 [Nagabhushan M et al., 1992]. The protective effects against cancer are due its direct antioxidant activity. Its antitumor activity is due to involvement in various pathways of cancer like NF-κB, AP-1 and transcriptional factor etc [Plengsuriyakarn et al., 2012]. It arrests the cancer cells proliferation in G2/S phase and induces apoptosis. It is also useful in the treatment of breast, stomach, skin, prostate and lung cancers [Kikuzaki H, 1993].
15. ***Echinacea angustifolia:*** by activating the macrophages arabinogalacton protects body from cancer. It is used in tratement of oseophagus and colon cancers [Jean Bruneton, 1993].
16. ***Fagopyrum esculentum;*** Amygdalin, a natural cyanogentic glycoside which contains benzaldehyde and cyanidine responsible for its anticancer activity. β-glucosidase a liver enzyme which breaks molecule into glucuronic acid. Glucuronidase, an enzyme present in higher concentrations in cancer cells, which helps to break glucuronic acid into cyanide which kills cancer cells[Jean Bruneton, 1993].
17. **Ginkgo biloba:** by regulating the platelet activating factor it inhibits the cancer growth [Tyler V, 1994]. Studies shown that it helps in protecting the DNA from nuclear radiations [Kleijnen J et al., 1992].
18. ***Glycine max:***Isoflavones such as genistein & daidzein and saponins isolated from the plant responsible for its activity. Genistein works by blocking angiogenesis, act as atyrosine kinase inhibitor and inducing

apoptosis. It helps in inhibiting the growth and spreading of various cancers such as uterus, breast, cervical, ovarian, testis, prostate and lung etc.

19. ***Glycyrrhiza glabra:***Licochalcone-A, compound isolated from the plant shows anticancer activity by inhibiting the growth and spreading of the cancer cells, specifically in prostate cancer by inhibiting the apoptosis and mitosis of cancer cells. Glycyyrhizin, a glycoside of the plant helps in inhibition of spreading and growing of lung cancer and fibrosarcomas [Ambasta, S.P, 2000].
20. ***Gossypium barbadense:*** gossypol, a constituent from the plant acts as an anticancer agent by inducing the apoptosis and arresting cell cycle at G0/G1 phase and it is useful in treatment of different cancers such as pancreas, adrenal gland, prostate, urinary bladder, breast, colon, liver, brain tumors and leukemias etc. The negative isomer of gossypol i.e., (-) gossypol which helps in inhibition of growth and spreading of radiotheraphy resistant cancers of breast, lung, head & neck and brain by inducing the apoptosis [Ambasta, S.P, 2000].
21. ***Lentinus edodes:*** Lentinan, a β-glucan present in the mushroom showed cytotoxicity against lung cancer cell line by MTT assay [Mizuno T, 1995] and it acts by increasing the production of natural killer cells and macrophages, which kills the cancerous cells [Mizuno T et al., 1995]. Other edible mushrooms belonging to the family shown anticancer activity, hypolipidemic activity and antithrombotic activity due to the presence of various steroids, terpens and polysaccharides.
22. ***Linum usitatissimum:*** commonly known as flax seed, which contains high amount of lignans. Breast cancer activity of the plant is due to conversion of lignans into enterolactone and enterodiol (mammalian lignans) by bacterial fermentation in colon [Thompson LU et al., 1991]which has structural similarity with estrogens and can bind to oestrogen receptors, thereby inhibits the growth of breast cancer cells [Serraino M et al., 1991, 1992].
23. ***Mentha species:*** essential oils of the plant species contains phenolic compounds which acts as a powerful antioxidants, by fights against free radicles it acts as an anticancer agent [Attele AS et al., 1999]. Monoterpene ketones present in *Mentha piperta*oil causes inhibition of carcinogen by acting directly on metabolites [Yun TK, 1996 andYun TK et al., 1990).
24. ***Ochrosia elliptica:*** Ellipticine and 9-methoxy ellipticine, monomeric alkaloids of the plants having potential cytotoxic activity by binding to DNAs of cancer cells [Yun TK et al., 1995]. Reports shown that this plant used in treatment of breast and kidney cancers.
25. ***Panax ginseng:***commonly known as ginseng, lowers the cancer risk in humans [Jeena KJ et al., 199]. Its main constituents are a group of 6 triterpenoid saponins known as ginsenosides [Cragg GM et al., 1991]. Its activity is due to induction of cell death by either necrosis or apoptosis [Yue et al., 2007]. Its cytotoxic studies were done on various cancer cell lines which include larynx, pancreas, stomach, bladder and breast etc [Ali M, 1991].
26. ***Picrorrhiza kurroa;*** commonly known as kutki and its active constituents are picrosides-I, II and III and kutkoside. Its shows activity against liver by acting as powerful antioxidant in liver.
27. ***Podophyllum:*** podohyllin is the active constituent of the plant species, which activity is similar to that of vinca alkaloids. It is used in teatement of Hodgkin's disease, non- Hodgkin's lymohoma, leukemia, braonchogenic carcinoma, ovarian and testicular cancers.
28. ***Taxus species:***commonly known as pacific yew and species includes Taxus brevifolia, Taxus yunnanensis, Taxus baccata and Taxus wallichiana. All the plant species contains taxanes which include paclitaxel and docetaxel are the constuents responsible for its activity. It activity is different from that of vinka alkaloids and podophyllin. By crosslinking the microtubules it stops the division of the cancer cells. It is usd in treatment of leukemia's, breast, ovarian, lung and colon cancers.
29. ***Tinospora cordifolia:*** recent studies reported that, ethanolic extract of the plant causes significant cytotoxicity and apoptosis effects on human breast cancer cell lines i.e., MCF-7 and MDA MB 231 [Maliyakkal N et al., 2013]. Palmitine , an alkaloid form the plant shown anticancer activity against DMBA induced carcinogenesis in Swiss albino mice model [Huma Ali et al., 2013]. Sesqiterpenoid and diterpenoid lactones from the plant shown cytotoxicity against throat, cervix and lung cancer ell lines.
30. ***Withania somnifera:***recent studies showed that ethanolic extract of the plant causes cell cycles arrest at G2/M phase in human breast cancer cell lines [Maliyakkal N et al., 2013]. Withanolide D and withaferin Aare compounds from the plant inhibit the growth and spreading of the cancerous cells. Cyototoxic potential of the plant is due to its free radicle scavenging activity [Devi PU. 1996]. When compared with Doxorubicin, withanolides of the plant showed significant inhibition in the growth of lung, breast and colon cancer cell lines [Devi PU et al., 1996].
31. ***Zingiber officinale:***cytotoxic activity of the plant id due the presence of pungent vallinoids like 6-gingerol, shagols, gingerone and 6-paradol. 6- shagol from the plant showed anticancer activity by inducing apoptosis and by inhibiting the formation of new blood vessels, particularly in patients with ovarian cancer [Kikuzaki H et al., 1993].

PLANT DERIVATIVES WITH ANTICANCER ACTIVITY

The list of the plant derivatives having anticancer activity and the particular constituents responsible for its activity are given in Table no:2. A brief discussion about each derivative was given below

1. **Berbamine:**a bisbenzyl isoqunoline alkaloid from Berberis amurensis. It was found that it inhibits the tyrosine kinase and induces apoptosis in chronic myeloid leukemia [Xie et al., 2009]. Recent studies proved that it acts by inducing caspase-3- dependent apoptosis of NB4 cells (leukemic cancer) [Xu et al., 2006].
2. **Berberine:** an isoquinoline alkaloid obtained from berberis species, *Tinospora cordifolia, Hydrastiscanadensis* etc. Recent studies showed its in vitro and in vivo anticancer activity in prostate, breast, lung, liver and osteosarcoma cancer cell lines [Wang et al., 2011; Patil et al., 2010].
3. **Betulinic acid:** is a pentacyclic triterpenoid from *Betula alba.* It acts by triggering the mitochondrial pathway in apoptosis, thereby causes the cell death [Fluda, 2008].
4. **Bruceatin:** studies shown that its activity against hela cell lines and rabbit reticulocytes by irreversible inhibition of protein and DNA synthesis [Liaoo et al., 1976].
5. **β- lapachone:** a water insoluble naphthaquinone from Tabebuia avellanedae [Li et al., 2000]. By inhibiting topoisomerase I and II, it showed its anticancer activity in pancreatic, lung and breast cancer cell lines. Because of its poor solubility and systemic toxicity the compound converted into gold nanoparticles for cancer therapy [Jeong et al., 2009].
6. **Camptothecin:** an alkaloid from *Camptotheca acuminate*, because of its poor solubility and toxicity new chemical moieties like itinotecan, topotecan, 9-amino camptothecin and rubitecan etc were chemically synthesized. Cytotoxicity of these compounds is due inhibition of topoisomerase I [Srivatsava et al., 2005]. As a second line treatment topotecans were used in ovarian and lung cancer patients [Creemers et al., 1996]. Irinotecan was used for colon cancer as a first and second line treatment [Fuchs et al., 2006].
7. **Colchicine:** an alkaloid from *Colchicum autumnale* and *Gloriosa superba.* It acts by arresting the cell cycle at mitosis. 3-demethyl colchicine, colchicoside, thiocolchicocide are the derivatives of colchicine synthesized chemically because of its toxic nature [Dubey et al., 2008].
8. **Combretastatin A-4:** a naturally occurring stilbene from *Combretum caffrum.* It acts by disrupting the tubulin and thereby changing the morphology of endothelial cells. It is developed into a nano formulation (2^{nd} phase of clinical trials) because of its poor solubility [Thomson et al., 2006; Ley et al., 2007].
9. **Cucurbitacin:**a tetracyclic triterpenoid from cucurbitaceae species. Their anticancer activity is due to inhibition of JAK 2 activity and transcriptor 3 activator (STAT3) in breast, prostate and nasopharynx cancer cell lines [Molavi et al., 2008]. Because of its water insoluble nature and non-specific toxicity, its polymeric form is used to deliver the compound [Bermard et al., 2010].
10. **Curcumin;** is a polyphenolic compound from turmeric. Its activity is by inducing apoptosis and modulation of cell cycle. But the exact mechanism of action of the compound is still not clear. 1^{st} and 2^{nd} clinical phase trails are going on the compound for colorectal cancer [Sa et al., 2010]. Studies showed that the compound in higher doses was safe and it was reported in 1^{st} phase of clinical trials [Goel et al., 2008].
11. **Daphnoretin:**is a coumarin derivative shown potent anticancer activity [Lu et al., 2011]. It shown cytotoxicity in human hepatoma Hep 3B cell lines by inhibiting hepatitis B surface antigen expression [Diogo et al., 2009].
12. **Diadzein and Genistein:**are the aglycon moieties found in isoflavones of soya and its activity is due to inhibition of 3A4- mediated metabolism [Moon et al., 2006]. Genistein used in breast and ovarian cancer due to inhibition of cell proliferation. These compounds also capable of chemically induced lung, prostate, bladder and blood cancers [Dixon et al., 2002].
13. **Ellipticine:**an alkaloid from Apocyanaceae family and its activity is due to inhibition of topoisomerase II and interclation of DNA. Reports shown that it inhibits growth and induces apoptosis in hepato carcinoma cells (HepG2) [Kuo et al., 2006].
14. **Emodin:**it is an antraquinone compound and it induces apoptosis in liver, lung, ovarian and blood cancer cell lines by different pathways [Huang et al., 2009].
15. **Flavopiridol:**is a semisynthetic derivative from plant alkaloid rohitukine. Its anticancer activity is due to the inhibition of cell cycle at G1 or G2 phase by interfering with cyclic dependent kinase. Presently it is under 1^{st} phase of clinical trials for treating solid tumors and 2^{nd} phase of clinical trials for treating renal cellular carcinoma and colorectal carcinoma [Mans et al., 2000].
16. **Harringtonine and Homoharringtonine:**are the esters of cephalotaxine alkaloid. By inhibiting the protein synthesis and chain elongation homoharringtone acts as an anticancer agent. Both these compounds are effective against acute and chronic myeloid leukemias [Cragg and Newman, 2005; Efferth et al., 2007].
17. **Indirubin and Meisoindigo:** its anticancer activity is due to inhibition of cyclin dependent kinase, which arrest the cell cycle and it also inhibit the proliferation of cancer cells. Clinically it is effective against chronic myeloid leukemia [Nam et al., 2005; Liu et al., 1996]. Because of its poor solubility and absorption, its derivative meisoindigo has been synthesized chemically.

18. **Ingenol 3-o-angelate:**is a diterpene ester and derivative of ingenol obtained from *Euphorbia peplus.* By activating the PKC it cause necrosis of the cancerous cells. Presently it is under 2nd phase of clinical trials for the treatment of actinic keratosis and basal cell carcinoma [Hampson et al., 2005].
19. **4-Ipomeanol:** is afuran derivative from *Ipomea batatus*. It acts by cytochrome p-450 mediated conversion into DNA-binding metabolite. It showed good cytotoxic potential against lung cancer in pre-clinical stages but unfortunately it showed poor results in human trails [Ancuceanu et al., 2004].
20. **Irisquinone:** is a benzoquinone derivative showed good anti-neoplastic potential against rodent tumors and acts as a chemosensitizer [Hazra et al., 2004].
21. **Phenoxodiol and Protopanaxadiol:** is a synthetic analogue of naturally ocuuring gensistein. It acts by inducing apoptosis by inhibiting the membrane electron transport and cell proliferation. Presently its under 3rd phase of clinical trials for ovarian cancer and initial stage of clinical trials for cervical and prostate cancer [Herst et al., 2009]. Protopananaxadiol is a tritepenoid analogue from ginseng saponins. It acts by inducing apoptosis and shows cytotoxicity against lung, breast and colorectal cancee cell lines. Presently it is under 1st phase of clinical trials for treatement of llung cancer [Pan et al., 2010].
22. Phodophyllotoxin: etoposide and teniposide are the semisynthetic analogues of phophyllotoxin,provedto be potential anti-neoplastic agents against lymphomas, bronchial and testicular cancers [Shoeb, 2006].
23. **Salvicine:** is a diterpenoid quinone from Salvia prionitis. Reports shown that it is a good anticancer activity in both *in vitro* and *in vivo*against malignant tumors by inhibiting topoisomerase II [Deng et al., 2011].
24. **Silvestrol:** was found to be effective against prostate and breast cancer. it revealed that mitochondrial pathway which triggers the extrinsic pathway of apoptosis of human prostate cancer cell lines (LNCaP). Episilvestrol is an epimer of silvestrol, proved to be less cytotoxic than silvestrol [Kinghorn et al., 2009; Kim et al., 2007].
25. **Taxanes:**they acts by binding to microtubles and stops the mitosis of the cancerous cells [Hait et al., 2007]. Paclitaxel and its semi-synthetic derivative docotaxel are important derivatives of taxanes and they are the choice of drugs as 1st and 2nd line treatment for lung, ovarian and prostate cancers [Kingston et al., 2007].
26. **Vinca alkaloids:** they act by inhibiting the cell proliferation by binding to tubulin during mitosis which leads to apopotosis of cancerous cells. Vincristine and vinblastine are the natural compounds; vinorelbine and vindensine are semisynthetic analogues of vinka alakaloids and presently they are in phase II clinical trials. In combination with chemotherapeutic agents these compounds are effective against advanced testicular cancer, lymphomas; leukemia's and breast cancers [Cragg et al., 2005]. Vinorelbine and vinflurine are the other two synthetic analogues which showed reduced cytotoxicity in animal models [Okouneva et al., 2003; Simeons et al., 2008].

Recent studies conducted through literature review showed that experimental studies are being explored on more plants for their anticancer activity for use as standard herbal medicines. Plants like *Coptis chinensis, fagonia indica, garcinica oblongifolia, garcinia indica, Hedyotis diffusa, Loranthus parasiticus, Scurrulus parasitica, Scutellaria barbata, morus alba, Paris polyphylla, Perilla frutescens, Platycodon grandifloras, Prunus armeniaca, Rabdosiae rubescens, Scutellaria baicalensis, Tripterygium wilfordii, Tussilago farfara, Wedelia chinensis* etc are studied extensively for their potential anti cancer activities [Khan et al., 2019].

Table 1: Herbal Medicinal Plants with Anicancer activity

S.No	Botanical name	Family	Common name	Active constituent
1	*Allium sativum*	Lilliaceae	Garlic	Alliin, allicin, alliinase, S-allyl-cysteine (SAC), diallyl sulphide (DADS)
2	*Actinidia chinensis*	Actinidiaceae	Kiwi fruit, china gooseberry	Polysaccharide known as ACPS-R
3	*Aloe ferax, Aloe barbadensis*	Lilliaceae	Aloe vera	Aloe-emodin, emodin, aloin
4	*Ananas comosus*	Bromeliaceae	Pine apple	Bromelain
5	*Angelica sinensis*	Umbelliferae	Angelica	Polysaccharide fraction known as AR-4
6	*Annona species*	Annonaceae	Monkey species	Acetogenins

7	*Arctium lappa*	Compositae	Burdock	Potential anticancer factors
8	*Astragalus membranaceus*	Papillonaceae	--	Swainsonine
9	*Betula utilis*	Betulaceae	Bhojpatra	Betulin
10	*Camellia sinensis*	Theaceae	Tea plant	Epigallocatechin gallate
11	*Catharantus roseus*	Apocynaceae	Vinca	Vincristine and Vinblastine
12	*Chlorella pyrenoidosa*	Oosystaceae	--	Lysine
13	*Colchicum luteum*	Lilliaceae	Colchicum	Colchicum democlocine
14	*Combretum cuffrum*	Combrittaceae	--	Combretastatin
15	*Curcuma longa*	Zinziberaceae	Turmeric	Turmerone, curcumine
16	*Echinacea angustifolia*	Asteraceae	Black Sampson	Arabinogalactan
17	*Fagopyrum esculentum*	Polygoneaceae	Vitamin P	Amygdalin, rutin
18	*Ginkgo biloba*	Ginkoaceae	Kew tree	Ginkgolide – B, A, C and J
19	*Glycine max*	Leguminosae	Soyabean	Isoflavones, protease inhibitors, saponins and phytosterols
20	*Glycyrrhiza glabra*	Leguminosae	Liquorice	Glycyrrhizin
21	*Gossypium barbadense*	Malvaceae	Raw cotton	Gossypol
22	*Gyrophora esculenta*	Umbellicariaceae	Mushroom	Polysaccharide β-glucans, α-glucans and galactomannans
23	*Lentinus edodes*	Agaricaceae	--	Lentinan
24	*Linum usitatissimam*	Linaceae	Flax seeds, linseed	Cynogentic glycosides, lignans
25	*Mentha species*	Labiateae	Pudina	Monoterpene ketones
26	*Ochrosia elliptica*	Apocynaceae	--	Ellipticine and 9-methoxy ellipticine are pyrindocarbazole alkaloids
27	*Panax ginseng*	Aralaceae	Ginseng	Ginsenosides, panaxosides
28	*Picrorrhiza kurroa*	Scrophulariaceae	Picrorrhiza (kutki)	Picrosides I, II, III and kutkoside
29	*Podophyllum hexandrum*	Podophyllaceae	Podophyllum	Podophyllin, astragalin
30	*Taxus brevifolia*	Taxaceae	Pacific yew	Taxanes, taxol cepholomannine
31	*Tinospora cordifolia*	Menispermaceae	Guduchi	Berberine, palmitine, tinosporside
32	*Withania somnifera*	Solanaceae	Ashwagandha	Withanolides, withaferin
			Ginger	Gingerols, shagols, zingerone

33	Zingiberaceae	
Taxus brevifolia		
Tinospora cordifolia		
Withania somnifera		
Zingiber officinale		

Table 2: Plant Derivatives as Anticancer agents

S.No	Semi-synthetic analogs of plant derivatives	Species and Genus name	Experiments on various cancer cells	Mechanism of action	Reference
1	Vindesine and Vinorelbine	*Catharanthus roseus*	Leukemia's, lymphomas, lung cancer, breast and advanced testicular cancer	Mitotic block	Cragg and Newman, 2005
2	Vinflunine	*Catharanthus roseus*	Reduced toxicity in animal models	Mitotic block	Okouneva etal.,2003; Simeons et al.,2008
3	Etoposide and Teniposide	*Podophyllum emodi* and *Podophyllum peltatum*	Lymphomas, bronchial and testicular cancers		Shoeb,2006
4	Taxol	*Taxus brevifolia, Taxus baccata*	Metastatic, breast, ovarian, lung, prostate cancer and lymphoid malignancies	Anti-mitotic	Kingston,2007
5	Taxotere	*Taxus brevifolia, Taxus baccata*	Used in patients resistant to placlitaxel	Anti-mitotic	Hait et al.,2007
6	Topotecan	*Camptotheca acuminate*	Epithelial ovarian cancer and small cell lung cancer	DNA topoisomerase I inhibition	Creemers et al.,1996
7	Irinotecan	*Camptotheca acuminate*	Metastatic and colorectal cancer	DNA topoisomerase I inhibition	Fuchs et al.,2006
8	Exatecan	*Camptotheca acuminate*	Potential anti-tumor activity both in vitro and iv vivo	DNA topoisomerase I inhibition	Mineko et al.,2000
9	LE-SN-38	*Camptotheca acuminate*		DNA topoisomerase I inhibition	Zhang et al., 2004
10	Berbamine	*Berberis amarensis*		Caspase -3-dependent apoptosis	Xie et al., 2009; Xu et al., 2006
11	Berberine			Not known	Wang et al.,2011; Patil et al., 2010

12	Beta-lapachone	*Hydrastis Canadensis L., Berberineeris sp & Arcungelisia flaw*	Various cancer cell lines	Inhibition of topoisomerase I and II	Li et al., 2000; De Almedia,2009
13	Betulinic acid	*Tabebuia Avellanedae*	Chronic myeloid leukemia	Triggers mitochondrial pathway of apoptosis	Fulda, 2008
14	Colchicine	*Betula alba*	Osteosarcoma, lung, liver, prostate and breast cnacer	Anti-mitotic	Dubey et al., 2008
15	Combretastatin A-4	*Colchicum autumnale and Gloriosa superba L.*	Breast cancer, prostate cancer, lung cancer, pancreatic cancer and promyelocytic leukemia	Tubulin structure disruption	Thomson et al., 2006; Ley et al., 2007
16	Cucurbitacin	*Combretum caffrum Kuntze*		Inhibits signal transducer/JAK 2 activity and activates STAT3 pathway	Molavi et al., 2008; Bernard and Olayinka et al., 2010
17	Curcumin	*Cucurbitaceae species*	Exhibits anticancer activity in humans	Exact mechanism of action is still unknown	Sa et al., 2010; Goel et al., 2008
18	Daphnoretin	*Curcuma longa*	Leukemia and solid tumors	Suppression of protein and DNA synthesis	Lu et al., 2011; Diogo et al., 2009
19	Diadzein and Genistein	*Wikstroemia indica*		Inhibits 3A 4 - mediated metabolism and oxidative metabolism	Kaufman et al., 1997; Moon et al., 2006; Dixon and Ferreira et al., 2002
20	Elipticine	*Lupinus species, Vicia faba, Glycine max, Psoralea corylifolia*	Phase II clinical trails	DNA intercalation and inhibition of topoisomerase II	Kao et al., 2006
21	Emodin		Various cancer cell lines	Apoptosis of cancer cells by several pathways	Huang et al., 2009
22	Flavopiridol	*Ochrosia borbonica, Ochrosia elliptica*	Colorectal cancer, multiple myeloma and pancreatic cancer	Inhibits cell cycle progression at G1 or G2 phase	Man's et al., 2000
23	Harringtonine and Homoharringtonine	Rhizome of rubarb	Ehrlich ascites carcinoma, Human hepatoma Hep3B cells	Inhibition of protein synthesis and chain elongation during translation	Cragg and Newman, 2005; Efferth et al., 2007
	Indirubin	*Amoora rohituka and Dysoxylum binectariferum*			Nam et al., 2005

24	Ingenol 3-o-angelate	*Cephalotaxus herrintonia*	Ovarian, breast cancer and chemically induced cancers of stomach, bladder and lung	Inhibits cyclin-dependent kinase	Hampson et al.,2005
25	4- Ipomeanol			Causes necrosis of tumor by the activation of PKC	Ancuceanu and Istudor, 2004
26	Irisquinone	Chinese herb, Danggui Lonehui Wan *Euphorbia peplus* L.,	Various cancer cell lines	Cytochrome p-450-mediated conversion into DNA-binding metabolites	Hazra et al., 2004
27	Phenoxodiol	*Ipomoeca batatas*	Lung, liver, ovarian and blood cancer	Acts as a chemosensitizer	Herst et al., 2009
28	Salvicine		Colorectal, non-small cell lung cancer, renal cell carcinoma and solid tumors	Inhibit plasma membrane electron transport and cell proliferation	Deng et al., 2011
29	Silvestrol	*Iridaceaclatca pallasii* and *Iris kumaoensis*		Inhibition of topoisomerase II	Kinghom et al., 2009; kim et al., 2007
30		Plant isoflavone, genistein	Acute and chronic myeloid leukemia	Apoptosome/ mitochondrial pathway was involved in triggering extrinsic pathway of programmed cell death of tumor cells	
		Salvia prionitis Hance	Chronic myeloid leukemia		
		Aglaia foveolata Panell	Actinic keratosis and basal cell carcinoma		
			Lung specific cancer in animal models		
			Good activity in transplantable rodent tumors		
			Ovarian, prostate and cervical cancer		
			Malignant tumors		
			Prostate, breast and lung cancers		

CONCLUSION

From the preceding review, it can be concluded that herbal medicinal plants and its derivatives are active against different type of cancers like lymphomas, breast, ovarian, lung, liver, stomach, prostate and testicular

cancers. Hence there is hope in the pharmaceutical industry, that even more powerful commercial drugs can be developed sooner, using plant derivatives, to effectively treat cancer and save mankind.

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CONFLICT OF INTEREST

We declare that we don't have any conflict of interest.

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