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REVIEW ARTICLE

A RECENT REVIEW ON ANTICANCER HERBAL DRUGS

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ABSTRACT:

Cancer is a leading cause of mortality in the world and it's the cause of more than 20% of all deaths. Plants are one of the main sources of biologically active ingredients. In the last few decades research has been focused on the use of natural products for cancer therapy. This is due to serious side effects associated with chemotherapy and radiation therapy, many cancer patients seek alternative complementary methods of treatment. In the present review an attempt has been made to study the plants that have been used in the treatment of cancer.

KEYWORDS: Cancer, Phytochemical constituents, anticancer plants etc.

INTRODUCTION:

CANCER is the abnormal growth of cells in our bodies that can lead to death. Cancer cells usually invade and destroy normal cells. These cells are born due to imbalance in the body and by correcting this imbalance, the cancer may be treated. Cancer is a leading cause of mortality, and it strikes more than one-third of the world's population and it's the cause of more than 20% of all deaths.

Causes of cancer are as follows -

1. Viruses such as *Epstein-Barr-Virus* (EBV), *Hepatitis-B-Virus* (HBV), *Human Papilloma Virus* (HPV).

2. Environmental and occupational exposure such as ionizing, UV radiation, exposure to chemicals including vinyl chloride, benzene and asbestos.

3. Life style factors such as high-fat, low fiber diets, tobacco, ethanol etc.

4. Medication such as alkylating agents and immunosuppressant's.

5. Genetic factors such as inherited mutations, cancer causing genes, defective tumour suppressor genes.[1]

For many years, scientists were searching for miracle cures for cancer using chemically synthesized or natural pure compounds. In the last few decades, research has been focused on the use of natural products such as crude plant extracts or a combination of different photochemical for cancer therapy.

CANCER BIOLOGY:

DNA damage causes conversion of normal cell into a cancer cell. Cancer cells lack the ability to communicate with their neighbouring cells. The first cancer cell starts to divide producing daughter cells, which in turn divide to produce more and more cancer cells. As cancer cells divide, they develop malignant characteristics including metastasis, immune system evasion, and induction of blood vessels formation (angiogenesis). Continuous cell division of cancer cells lead to the formation of tumours. In solid tumours, blood vessels become structurally and \ functionally abnormal; this abnormality leads to heterogeneous blood flow which creates chronically hypoxic and acidic regions in the core of the solid tumour. These hypoxic regions lead to the activation of angiogenesis and cell survival genes in addition to other genes that induce drug resistant. Furthermore, the low pH microenvironment of cancer cells in the tumour core may prevent the active uptake of some anticancer drugs. The two traditional therapies (chemotherapy and radiation) are not greatly efficient in treating hypoxic cancer cells. The killing effect of ionizing radiation depends on the presence of oxygen which is absent or very low in the tumour core and the poor vascularisation minimizes the delivery of chemotherapeutic agents. This makes the poorly vascularised regions of tumours a major obstacle to effective treatment and opens the door to other therapies that may use different mechanisms to targets highly resistant cancer cells.

ONCOGENES AND TUMOUR SUPPRESSOR GENES:

Two sets of genes are controlling cancer development. Oncogenes are the first set of genes and are involved in different cell activities including cell division. However, over expression of these genes transforms a normal cell into a cancer cell. On the other hand, the second set of genes (tumour suppressor genes) inhibits cancer cell formation by different mechanisms. Tumor suppressor genes are under expressed in cancer cells while, oncogenes are over expressed. Oncogenes and their products represent good targets for cancer therapy. Other targets include enzymes involved in cell division like topo isomerases that unwind the DNA during replication. The diversity of plant derived natural products can provide therapeutic products attacking different targets in cancer cells.[2]

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Table 1: Expression of genes with their funtions

Oncogenes	**Functions of their proteins**
Bcl-2	Inhibits apoptosis and protect cancer cell from free radicals.
c-myc	Initiate cell division and inhibits differentiation.
HER-2/neu(c-erb-2)	Facilitates signal transduction, expressed in 33% of breast cancers.
MDM2	Protect cancer cells from apoptosis by binding and inhibiting *p53* (tumour suppressor gene that induces apoptosis in damaged cells).
ras	Facilitate tumour invasion by stimulation of collagenase production and inhibits apoptosis by increasing *MDM2* expression.
fos and *jun*	Promote uncontrolled proliferation by their participation in cell cycle initiation.
Tumor suppressor genes	**Functions of their proteins**
Bax	An inducer of apoptosis
Cx32, *Cx 43* and other connexin producing genes	Inhibits carcinogenesis by restoring communication between cells through gap junctions.

Plants are considered as one of the main sources of biologically active materials. Recent records reported that medicinal herbs are used by 80% of the people living in rural areas as primary healthcare system. It has been estimated that about 50% of the prescription products in Europe and USA are originating from natural products including plants or their derivatives. These plants may promote host resistance against infection by re-stabilizing body equilibrium and conditioning the body tissues.[3]

CLASSES OF PHYTOCHEMICAL CONSTITUENTS:

- **Flavonoids**

Flavonoids are found in almost all plant families. Flavonoids are present in different plant parts including the leaves, stems, roots, flowers and seeds and are among the most popular anti-cancer candidates worldwide. Flavonoidic derivatives have a wide range of biological actions such as antibacterial, antiviral, anti-inflammatory, anticancer, and anti-allergic activities. Flavonoids are reported to inhibit specific enzymes, which include hydrolases, oxidoreductase, DNA synthases, RNA polymerases, lipoxygenase and gluthation *S*-transferase. They also block several digestive enzymes, including α-amylase, trypsin and lipase.

- **Tannins**

Tannins, phenolic photochemical, which are natural constituents of green tea, are considered to have cancer preventive properties Condensed tannins, isolated from black beans, did not affect the growth of normal cells, but induced cell death in cancer cells in a dose-dependent manner. This cell death was associated with a concentration-dependent decrease of ATP and a deterioration of cellular gross morphology.

- **Volatile oils**

Cancer-preventive constituents of fruits and vegetables may inhibit carcinogen activation, enhance carcinogen detoxification, prevent carcinogens from interacting with critical target sites, or impede tumour progression. Isoprenoids, a broad class of mevalonate-derived phytochemicals ubiquitous in the plant kingdom, suppress the proliferation of tumour cells and the growth of implanted tumours. Volatile isoprenoid constituents of food products spanning seven plant families have been characterized into 179 isoprenoids. Individual isoprenoids suppressed the proliferation of B16 and HL-60 promyelocytic leukemia cells with varying degrees of potency. Cell cycle arrest at the G0-G1 phase and apoptosis. geraniol, is an acyclic dietary monoterpene, found in aromatic herb oils. The anti-tumor efficacy of geraniol was evaluated on TC-118 human tumours, transplanted into Swiss nu/nu mice. Geraniol (150 "M) caused a two-fold reduction of thymidylate synthase and thymidine kinase expression in cancer cells.

- **Saponins**

Five saponins (diosgenin, hecogenin, tigogenin, sarsasapogenin, smilagenin) have been tested for their biological activities on human 1547 osteosarcoma cells. All examined saponins have shown a significant role on tested cell line in term of proliferation rate, cell cycle distribution and apoptosis induction.

- **Anthraquinone**

A number of new anthraquinones that exhibit in vitro antitumor effects against four human cancer cell lines has been identified. The anti-proliferative activity, the topoisomerase inhibitory and the cytotoxicity of these compounds have also been documented.

- **Coumarin**

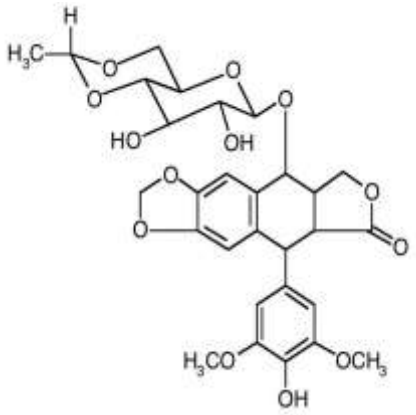
The diverse biological activities of natural and synthetic coumarin derivatives as anticoagulants and antithrombotics are well known. Many coumarin derivatives are also known as free radical scavengers and two naturally occurring coumarins have been found to

exhibit cytotoxicity against a panel of mammalian cancer cell lines

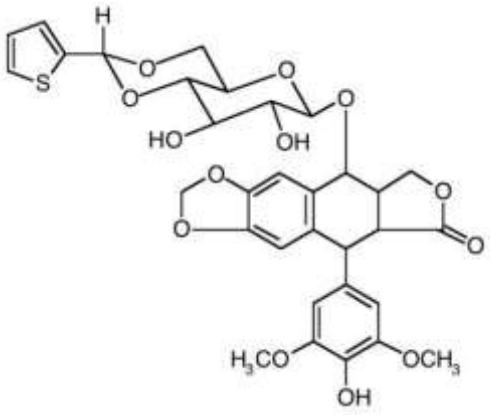
- **Sterols/ Triterpines**

Phytosterols, especially -sitosterol, are plant sterols that have been shown to exert protective effects against cardiovascular diseasesand many types of cancer. They have been reported to protect against cancer development. The inhibition of tumor growth could be explained by the effect of phytosterols on the sphingomyelin cycle and increased production of ceramide, which suggest an alteration of signal transduction pathways.[4]

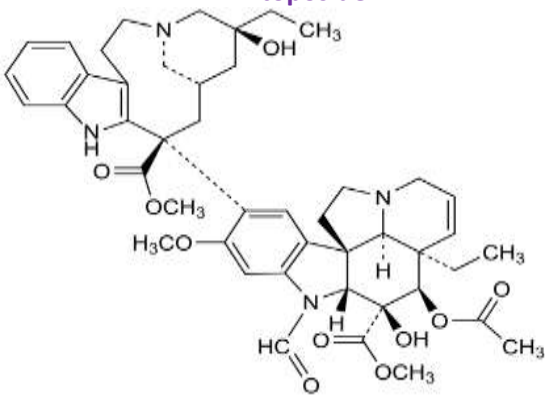
CHEMICAL STRUCTURES OF THE COMPOUNDS [5]



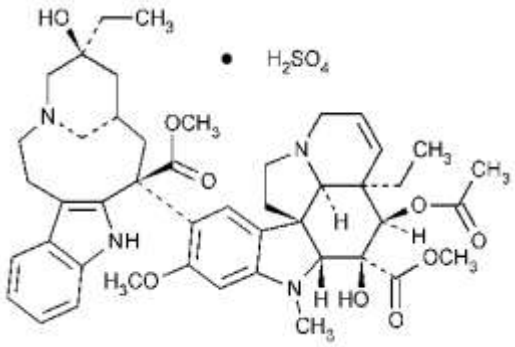
Etoposide



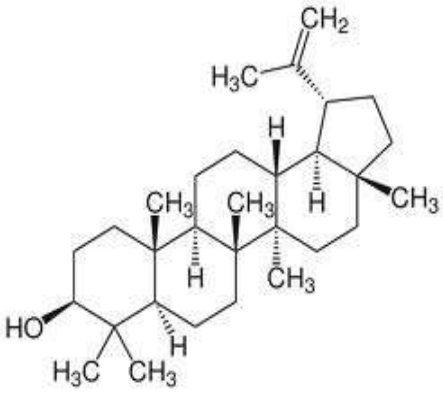
Teniposide



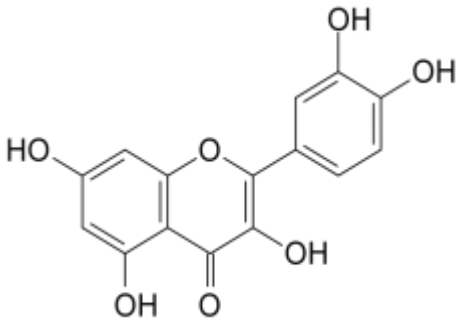
Vincristine



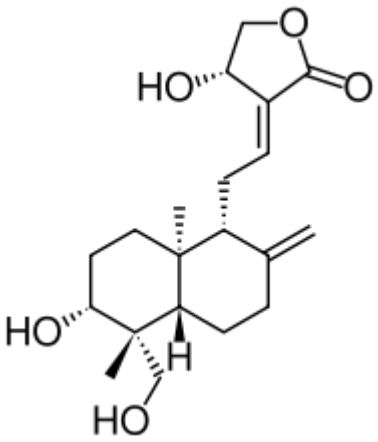
Vinblastine



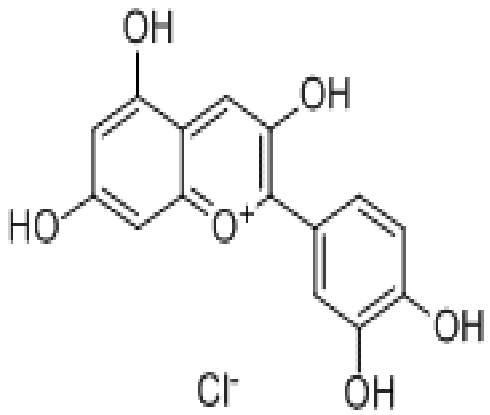
Lupeol



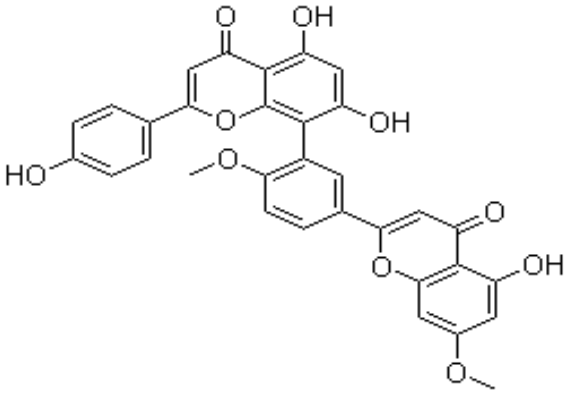
Quercetin



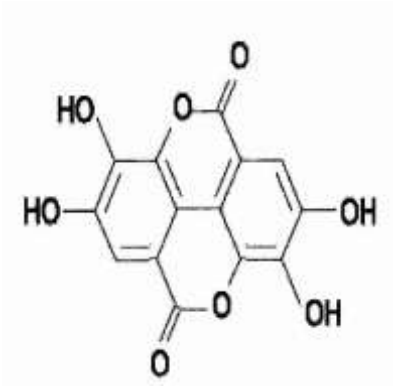
Andrographolide



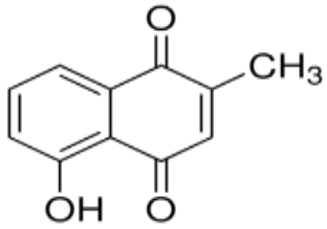
Cynidine



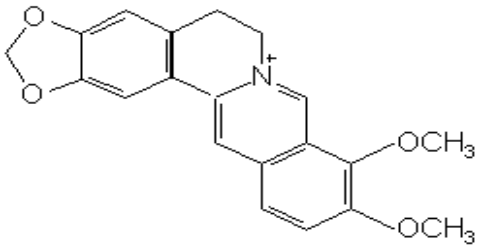
Ginkgetin



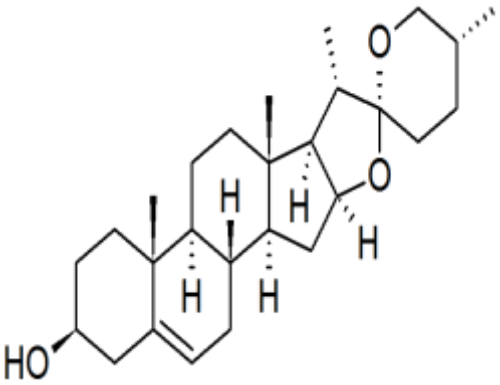
Ellagic acid



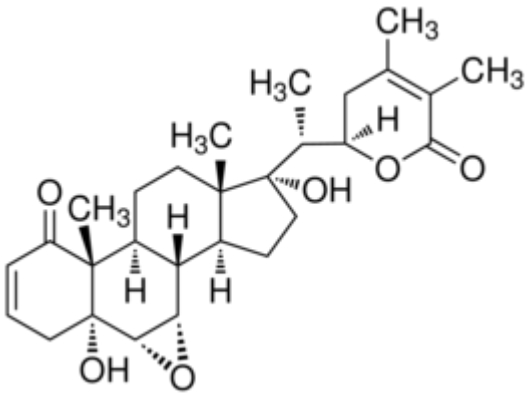
Plumbagin



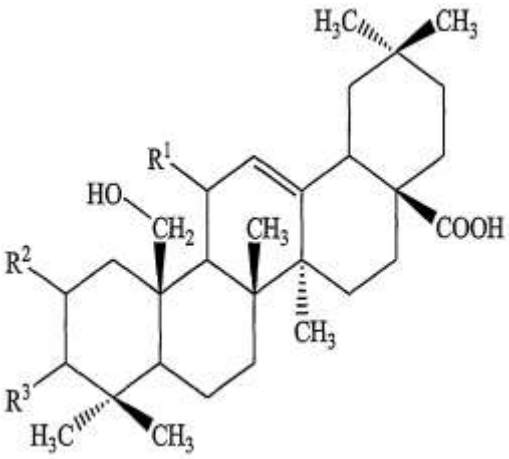
Berberin



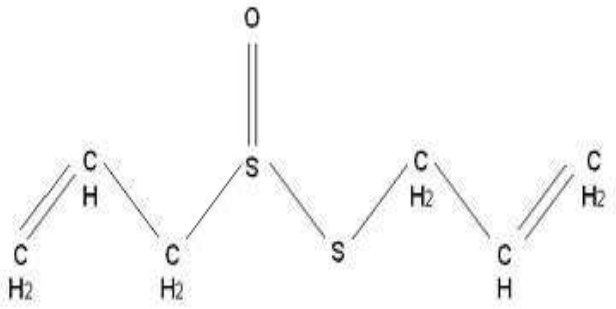
Diosgenin



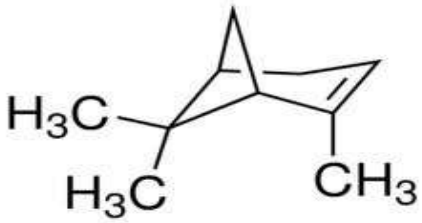
Withanone



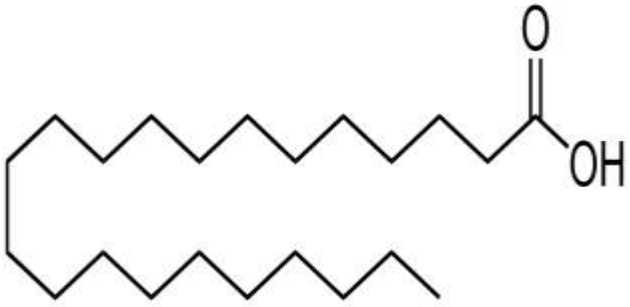
Amooranin



Allicin



Pinene



Behenic acid

Table 2: PLANTS WITH ANTICANCER ACTIVITY [6-10]

Sr. No.	Family & Botanical name	Class & Active constituents	Type of Cancer
1.	Rutaceae Aegli marmelos Roxb.	lupeol	Breast cancer & malignant lymphoma
2.	Liliaceae Allium cepa Linn.	Diallyl sulphide, quercetin, allicin, allin	Stomach cancer
3.	Zingiberaceae Alpinia galangal Willd.	Acetoxy, chavicol acetate	Breast, lung, prostate cancer, multiple myeloma
4.	Acanthaceae Andrographis paniculata Wall	andrographolide	Ovary, colon, kidney cancer
5.	Meliaceae Aphanamixis polystachya	amooranin	Breast & cervical cancer
6.	Caesalpiniaceae Bauhinia variegate Linn	Cyanidine glucoside,malvidine glucoside	Oral cavity & larynx cancer
7.	Berberidaceae Berberis vulgaris Linn	Berberin, berbaine, chelidonic acid, jacaranone, plamitine	Breast & oral cavity cancer
8.	Apocyanaceae Catharanthus roseus G	Alkaloids, vinblastin, vincristine	Breast, ovary, cervix, colon, rectum, kidney, testis cancers, malignant lymphoma, leukaemia
9.	Euphorbiaceae Embilica officinalis Gartin	Ellagic acid, gallic acid, embilicin	Liver cancer
10.	Rosaceae Fragaria vesca linn	Flavonoid, tannin, borneol	Kidney & breast cancer
11.	Ginkgoaceae	Ginkgetin, ginkgolides	Prostate, liver, ovary & colon

	Ginkgo biloba Linn		cancer
12.	Papillionaceae Glycine max Merril	Isoflavonoid- genistine, diazein, saponins	Pancrease, thyroid, urinary bladder, nasal cancer
13.	Fabaceae Glycyrrhiza glabra Linn	Flavones, flavonols, licochalcones	Lung & stomach cancer
14.	Rubiaceae Morinda citrifolia Linn	Damnacanthal, alizarin, morindone	Lung cancer, sarcoma
15.	Ranunculaceae Nigella sativa Linn	Thymoquinone. dithymmoquinone	Colon, prostate, pancrease, uterus cancer, malignant melanoma
16.	Meliaceae Azadirachta indica Linn	Liminoids, nimbolide, quecetin, β sitosterol	Stomach, prostate & skin cancer
17.	Zingiberaceae Curcuma longa Linn	Curcumin, genistein	Oesophagus,liver, colon, neck skin cancer
18.	Liliaceae Allium sativum Linn	Diallylsulphide, allicin	Stomach, liver, colon & breast camcer
19.	Lamiaceae Ocimun sativum Linn	Eugenol, linolenic acid, oleanic acid, orientin, vicenin, apigenin	Breast & liver cancer, fibrosarcoma
20.	Rubiaceae	Oldenlandosides, stigmasterol, ursolic acid	Brain, liver, colon cancer
21.	Araliaceae Panax ginseng Mey	Ginsenosides-panaxdiol	Breast, lung, ovary colon cancer
22.	Plumbaginaceae Plumbago zeylanica Linn	plumbagin	Fibrosarcoma,malignant ascites, leukaemia
23.	Berberidaceae Podophyllum hexandrum Royle	Podophyllotoxin, podophyllin	Urinary bladder, testes, brain, liver cancer & neuroblastoma
24.	Labiatae Prunella vulgaris Linn	Ursolic acid, oleanolic acid	Oesophagus, oral cavity intracranial tumors
25.	Pailionaceae Psoralea corylifolia Linn	Bavachinin, corylfolinin,psoralen	Osteosarcoma, fibrosarcoma, lung &liver cancer
26.	Punicaceae Punica granatum Linn	Anthocyanidine, vit.c	Solid tumour, ascites tumour
27.	Asteraceae Saussurea lappa Clarke	Sesquiterpines, costunolide, cynaropicrin	CNS, ovary, lung, colon cancer
28.	Solanaceae Solanum nigrum Linn	Flavonoids-quercetin, solasodine, solanine	Cyst cancer, choriocarcinoma, leukaemia
29.	Menispermaceae Tinospora cordifolia Willd	Berberine, tinosporine, giloin, giloinin, diterpenes	Lung, cervix, throat cancer, malignant ascites
30.	Viscaceae Viscum album Linn	Lectin alkalois, acetylcholine, lupeol, viscotoxin, viscumin	Malignant melanoma, lung metastasis, cervix & ovary cancer
31.	Solanaceae Withania somnifera Dunal	Withanone, withaferin A, saponins, ducitol	Breast, lung, colon & CNS cancer
32.	Lardiqabalaceae Akebia quinata	Limonene, eugerol, hexanol, palmitic acid	sarcomas
33.	Zingiberaceae Zingber officinale Rosc	eshogaol	Ovary, rectum, urinary bladder cancer, neuroblastoma
34.	Rubiceaceae Rubia cordifolia Linn	Rubidianin, rubiadin, rosemary acids, carnosic acid, purpurin, alizarin	Breast, ovary, colon, lung cancer
35.	Lardizabalaceae Akebia quinata	Limonene,eugenol, octanol,hexanol	sarcoma

36.	Asteraceae Taraxacum mongolicum	Sesquiterpene, saponins, polysaccharides	Ascites cancer, sarcoma, lug cancer
37.	Lamiaceae Vitex rotundifolia	Pinene, terpineol, vitexicarpin, vitricine,casticin, orientin, isovitexin	Lung tumour
38.	Fabaceae Sophora flavescens	Oxymatrine, sophordine,sophocarpine	Leukaemia, cervical cancer, sarcoma
39.	Leguminaceae Sophora subprostrata	Matrine, oxymatrine	sarcoma
40.	Lamiaceae Scutellaria barbata	Alkaloids, flavones, steroids	Ehrlichs ascites carcinoma, sarcoma
41.	Liliaceae Smilax chinensis	Diosgenin, parillin, sarsapic acid, sarsaponin	Sarcoma, ascites sarcoma
42.	Solanaceae Solanum lyrati	Aristolochic acid	Stomach cancer, sarcoma, ascites carcinoma
43.	Rosaceae Agrimonia pilosa	Tritepenoid, hydroxyursolic acid	Intestinal cancer, sarcoma
44.	Simaroubaceae Alianthus altissima	Oleic acid, octadeca, dienoic acid	Sarcoma, leukaemia
45.	Rosaceae Pyrus malus	nonasan	Lung, breast & intestinal cancer
46.	Pteridaceae Pteris multifida	Ludongnin, isoneorautenol	Yoshidas sarcoma
47.	Liliaceae Fritillaria thunbergii	Steroidal alkaloids, diterpenoids	Throat,chest, neck & breast cancer
48.	Thymelaeceae Phaleria macrocarpa	Kaempferol, myricetin, rutin,quercetin	Oesophageal cancer
49.	Vespidae Nidas vespae	polysacchaaride	Gastric & liver cancer
50.	Rutaceae Aegle marmelos	Limonene, ocimene, monoterpene hydrocarbon	Sarcoma
51.	Anacardiaceae Semecarpus anacardium Linn.	jeediflavone, semecarpuflavone, bhilavinol	hepatocellular carcinoma, oesophagus, urinary bladder, liver and leukemia cancer
52.	Fabaceae Trigonella foenum - graecum Linn.	Galactomannan, disogenin, gitogenin, neogitogenin, homorientin saponaretin,	neck squamous carcinoma, brain tumor, breast cancer
53.	Lythraceae. Lawsonia inermis Linn.	α- and β-ionones, behenic acid, arachidic acid	Melanoma, colon cancer

Dietary agents also consist of a wide variety of biologically active components that are responsible for the anti-cancer effects like curcumin, genistein, resveratrol, diallyl sulfide, S-allyl cysteine, allicin, lycopene, capsaicin, diosgenin, gingerol, ellagic acid, ursolic acid, silymarin, anethol, catechins, eugenol, isoeugenol, dithiolthiones, isothiocyanates, indole-3-carbinol, isoflavones, saponins, phytosterols, inositol hexaphosphate, Vitamin C, D-limonene, lutein, folic acid, beta carotene, selenium, Vitamin E and flavonoids. Many of which have been used in traditional medicines for thousands of years. These dietary agents are believed to suppress the inflammatory processes that lead to transformation, hyperproliferation, and initiation of carcinogenesis. Their inhibitory influences may ultimately suppress the final steps of carcinogenesis i.e angiogenesis and metastasis.[11]

Herbal medicines can be used in some countries based on both scientific and culture aspects. It may be a world-wide phenomenon that the use of herbal medicines depends on traditional culture and lessons from the forerunners

however, more and more scientific evidences have been obtained from *in vitro* studies and in animal models. The US patents have been issued for herbal compositions which were used in the treatment of cancer and cancer-related health problems in the past years. 69% of anticancer drugs approved were either natural products or developed based on knowledge gained from natural products between the 1980s and 2002, which may indicate that drug development based on the components with lead structures of potent bioactivity isolated from medical plants has been a major strategy for developing new anticancer drugs from herbal medicines.[12]

CONCLUSION:

Medicinal plants maintain the health and vitality of individuals, and also cure various diseases, including cancer without causing toxicity. These medicinal plants possess good immunomodulatory and antioxidant properties, leading to anticancer activities. The antioxidant phytochemicals protect the cells from oxidative damage.

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