MEDICINAL PLANTS FROM INDIA AS PROSPECTS OF ANTICANCER DRUG SOURCES: A COMPREHENSIVE REVIEW

Abstract

The incidence of cancer is steadily rising, making it one of the top causes of mortality in the world today. In many developing countries, including India, medicinal plants have been used to treat cancer and serve as an alternative to synthetic drugs known for their harmful side effects. The main objective of this review was to highlight the anticancer properties of 50 medicinal plants found in India. The review discussed the proposed anticancer pharmacological effects of these plants along with the specific bioactive compounds responsible for their anticancer effects. These plants have been found to inhibit various types of cancers such as prostate, lung,cervical,esophagus, skin,ovary, colon, blood, brain, breast,and kidney cancers. The molecular, physiological nature of cancer, stages of cancer proliferation and metastasis, different types of anticancer activity screening techniques and modern methods of cancer treatment were also discussed. Bioactive compounds identified in medicinal plants include polyphenols, flavonoids, alkaloids, saponins, triterpenes, tannins and quinones. Several major anticancer pharmacological effects have been attributed to these compounds, such as antiproliferative, cytotoxic, apoptotic, and antioxidant effects. Additionally, they have been found to induce cell cycle arrest, inhibit angiogenesis, and reduce cancer cell viability. In conclusion, the promising anticancer activity shown by the medicinal plants investigated in this study suggests that they have significant potential as a source of future readily available and affordable anticancer drugs in India. By exploring these natural alternatives, the adverse effects associated with synthetic drugs could be alleviated, offering new hope in the fight against cancer.

Keywords: Anticancer molecules, Apoptosis, cancer proliferation, Cytotoxicity and Medicinal plants.

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I. INTRODUCTION

Cancer, a severe metabolic disease, continues to be one of the leading causes of death, accounting for 18.1 million new cases and 9.6 million deaths in 2018. As the second leading cause of death worldwide, it has a huge impact on death and mortality. There are 36 types of cancer: stomach, liver, lung, prostate and stomach in men, breast, cervix, colon, lung and thyroid in women [1].The uncontrolled growth of normal cells leads to genetic instability and their transformation into malignant cells.Depending on the stage and type of cancer, treatment may involve surgery, radiation therapy, chemotherapy, biological therapy, and hormone therapy. However, these treatments have limitations [2].For example, chemotherapy can cause side effects such as fatigue, drowsiness, loss of appetite, hair loss, mouth sores, taste changes, fever, infections, anxiety pressure, anxiety, nausea and vomiting [3]. Because of these limitations, there has been interest in exploring alternative cancer treatments and therapies.

The ability of many substances found in the plant kingdom to inhibit cancer and promote apoptosis is currently being investigated [4]. Herbs have emerged as a safe, non-toxic and effective anti-cancer drug that is believed to fight diseases in the body through the various biomolecules they possess [5]. The ethnobotanical properties of medicinal plants are an important method for the discovery of new drugs [6].In recent years, interest in the use of plant-based drugs has increased due to the diversity of chemical structures and pharmacological activities of plant-derived compounds. These originating elements show promise in the treatment of cancer, with generally lower toxicity than conventional chemotherapy.

Ayurveda, a traditional Indian medicine uses plant-based drugs successfully totreat different cancers[7]. More importantly, a significant portion of FDA-approved anticancer drugs are derived from natural sources [8].There are many effective anticancer drugs derived from natural products, including vincristine, vinblastine, paclitaxel, Indicine-N-oxide, etoposide analogs, camptothecin, and analogs approved by the United States National Cancer Institute (NCI) through extensive research [9]. This review focuses on the anticancer potential of Indian medicinal plants and bioactive substances with anticancer properties as well as their pharmacological effects.

II. RESOURCES AND METHODS

The most important information was obtained by searching various electronic resources (such as Scopus, PubMed, Web of Science, and Google Scholar). The research included certain terms and phrases such as "medicinal plants", "antibiotic activity", "antibiotics", "antibiotics" pain", "mode of action" and "in vivo activity". A totalof 50 plants were chosen based on the availability of recent articles and relevant information was extracted and presented here.

III. CAUSES OF CANCER

Cancer is a complex, multifactorial disease with many causes. Factors that cause cancer can be broadly divided into genetic, environmental and lifestyle factors. Understanding these causes is important for the prevention and control of this deadly disease.

1. **Genetic Factors:** The chance of developing cancer may rise as a result of specific genetic modifications. For instance, a higher risk of breast and ovarian cancer is linked to mutations in cancer genes such as BRCA1 and BRCA2 [10]. Numerous malignancies can be brought on by mutations in DNA repair genes (p21, p27, p22, p51, and p53), tumor suppressor genes (NF1, NF2, and RB), and oncogenes (MYC, Bcl-2, RAF, and RAS) [11]. Tumor suppressor genes can be silenced by epigenetic modifications, such as hypermethylation of tumor suppressor genes in CpG islands [12], which also causes cancer.

2. **Environmental Factors:** Exposure to various environmental factors may also play an alarming role in cancer development. Environmental carcinogens include smoking, asbestos, solar ultraviolet radiation, ionizing radiation and certain chemicals [13, 14]that promote the formation of cancer cells.Prolonged exposure to these chemicals can cause genetic changes, cell damage and increases the risk of cancer.

3. **Lifestyle:** Cancer risk might rise as a result of unhealthy lifestyle choices. An elevated risk of malignancies such as stomach, breast, and pancreatic is linked to diet, physical inactivity, and obesity [15]. Additionally, drinking too much alcohol raises your risk of developing liver, esophageal, and breast cancer [16].

4. **Diseases:** Some types of cancer are associated with infectious diseases.Chronic infections from certain viruses, bacteria, and parasites can cause cell changes that promote cancer development. For example, human papillomavirus (HPV) causes cervical cancer, Helicobacter pylori cause stomach cancer and hepatitis B and C causes liver cancer [17].

5. **Hormone Factors:** Some cancer forms are largely influenced by hormones. For instance, a higher risk of breast cancer has been linked to extended estrogen exposure [18]. The development of prostate cancer has also been linked to elevated androgen levels.

IV. STAGE OF CANCER DEVELOPMENT

Cancer development is a complex process consisting of a series of stages in the progression of cancer.Knowing the stage of cancer is important for accurate diagnosis and effective treatment planning.

1. **Initiation**: The first stage of cancer development is the initiation in which genetic changes (called mutations) occur in a cell's DNA. These changes can be caused by many factors such as exposure to carcinogens, radiation, or genetic predisposition [19]. These changes lead to the formation of abnormal cells that grow out of control.

2. **Promotion:** Mutant cells are stimulated to proliferate and form clumps of abnormal cells, also known as tumors or neoplasms.

3. **Progression:** During progression, cancer cells continue to add genetic changes that lead to aggression and metastasis. Tumors attain the capability to produce blood vessels (angiogenesis) to support their growth and spread [20].

4. **Metastasis:** Cancer cells break off from the primary tumor and move to distant organs via the blood or lymphatic system. These cancer cells can form new tumors in different parts of the body, indicating that the cancer is in advanced condition and life-threatening [19]. The rate and pattern of cancer development can vary depending on the type of cancer and individual factors.

V. PATHWAYS OF ANTICANCER ACTIVITY SCREENING

For the discovery and development of anticancer medicines, screening techniques for anticancer activity are crucial. Testing different substances that can thwart the genesis and expansion of cancer cells is a part of this process. To assess the anticancer capabilities of natural and synthetic compounds, preclinical research employs several tests.

1. **Cell-Based Assays:** Cell-based assays are commonly used to examinethe anticancer activity of the drug. Cancer cells have grown and are subject to diagnostic testing.High-throughput screening (HTS), Tryptophan Blue Dye Exclusion Test, Lactate Dehydrogenase Test, MTT ([3-(4,5-Dimethylthiazolyl)-2,5-Diphenyltetrazolium Bromide]) test, XTT (2,3-bis)[2 -methoxy-4-nitro-5-sulfophenyl]-2H tetrazolium-5-carboxyaniline) assay and sulphorhodamine B assay are several in vitro cell-based methods that allow researchers to test the compounds for anticancer activities[21].

2. **Xenograft Model:** The xenograft model consists of the transplantation of human tumor cells into immunodeficient mice. These mice were treated with drugs to evaluate their effectiveness in inhibiting tumor growth in an *in-vivo* environment. Xenograft models provide valuable insight into the compounds' ability to inhibit tumor growth and metastasis [22].

3. **Enzyme Assays:** The Enzyme assaysare used to screen compounds against specific enzymes involved in the growth and development of cancer. These tests measure the inhibitory effect of a compound on the activity of the target enzyme. Inhibition of key enzymes can disrupt cellular processes important for cancer cell survival [23].

4. **In Silico Analysis:** In silico analysis is a type of virtual analysis that uses computational methods to predict interactions between compounds and cancer-related targets. This approach allows researchers to evaluate many compounds and prioritize those that have the potential to be effective anticancer drugs [24].

Analyzing ways to prevent cancer is an important part of the drug discovery process. These methods continue to evolvewith technology, leading to the discovery of advanced targeted treatments for cancer.

VI. MEDICAL PLANTS USED IN THE TREATMENT OF CANCER

Ayurveda and ethnomedicine have used medicinal plants for centuries to treat various cancers. Several natural compounds derived from various Indian plants have been demonstrated to possess anticancer properties. Flavonoids, terpenoids, and steroids are examples of plant-derived substances that have drawn a lot of attention for their wide range of therapeutic applications, including their cytotoxic and anticancer activities [25]. It was

made feasible by the discovery of vinblastine and vincristine (vinca alkaloids), the first medications to be used in a clinical setting to treat cancer [26].In this review, 50 medicinal plants from 33 families were discussed and provided detailed information about the parts used, the mechanism of action, and the tested cancer cell lines (Table-1). These plants are used to treat different types of cancers, including sarcomas, lymphomas, carcinomas, and leukemias.The structure of different phytochemicals with anticancer activity is shown in Figure 1.

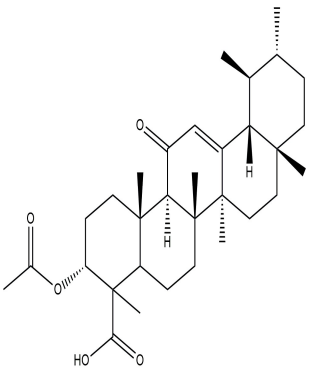
Table 1: Important Anticancer Medicinal Plants, and their Bioactive Compounds.

Family	Plants name	Parts used	Bioactive compounds	Cancer cell type
Acanthaceae	*Andrographis paniculata*	Aerialparts	5-hydroxy-7, 8-dimethoxyflavanone; 5-hydroxy-7	Lymphocytic, prostate, colon [27]
Amaranthaceae	*Aerva lanata*	Whole plant	Alkaloids and polyphenols	Breast, Cervical, Dalton's Ascitic Lymphoma[28-30]
Anacardiaceae	*Mangifera indica*	Leaves, fruits	Gallic acid, methylgallate and pyrogallol	breast cancer[31]
Annonaceae	*Annona reticulata*	Roots	Acetogenin	Lung, leukemia, Cervical, and adenocarcinoma [32]
Apiaceae	*Centella asiatica*	leaves	Asiatic acid, madecassic acid, asiaticoside, and madecassoside	adenocarcinoma (MK-1), uterine carcinoma (HeLa), and murine melanoma (B16F10) cells [33]
Apocynaceae	*Decalepishamiltonii*	Root	Saponins	hepatic cancer cells [34]
	Gymnema sylvestre	Leaves	Gymnemagenol	Cervical cancer (HeLa)[35]
	Ichnocarpus frutescens	Roots	Ursolic acid and amyrin	MCF-7, BEL-7402, SPC-A-1 and SGC-7901[36]
	Rauvolfia serpentina	The barkof the roots	Reserpine, Serpentine	Sarcoma and leukemia[37, 38]
	Wrightia tinctoria	bark	Polyphenols	Anderson-Metastatic Breast-231 Cells, and MCF-7 cancer cells[39]
Asparagaceae	*Drimia nagarjunae*	bulbs	C-glycosyl flavone, (5,7-dihydroxy-2-[4′-hydroxy-3′-(methoxymethyl) phenyl]-6-C-β-glucopyranosyl	Epidermoid carcinoma of the nasopharynx and Ehrlich ascites carcinoma[40.41]

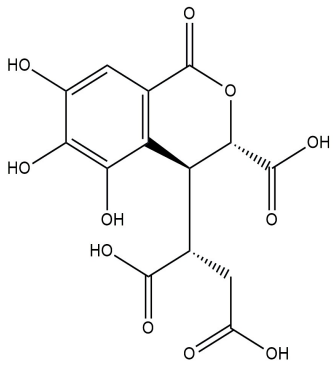
			flavone	
Asteraceae	*Chromolaena odorata*	leaves	Acacetin,quercetin3-O-rutinoside, kaempferide, and rhamnazin	Leaf Breast, lung, and blood [42-47]
	Eclipta alba	leaves	Wedelolactone,	Colon cancer[48]
Bignoniaceae	*Oroxylum* indicum	Aerial parts	Chrysin and Oroxylin	Abelson murineleukemia[49]
Bombacaceae	*Bombax ceiba*	Leaves	Tannins, alkaloids and flavonoids	Leukemia[50]
Burseraceae	Boswellia serrata	gum resin	β-boswellic acid	Anticancer[51]
Calophyllaceae	*Mesua ferrea*	Stem, fruits	Friedelin, lupeol	KB, MCF-7 and NCI-H187[52]
Colchicaceae	*Gloriosa superba*	Rhizome	Colchicine and peptides	Colon cancer [53]
Cucurbitaceae	*Momordica charantia*	fruits	Alpha memorcharin and beta memorcharin	prostate cancer cell lines, CNE-1 and HONE1 hepatocellular carcinoma [54, 55]
Combretaceae	*Terminalia chebula*	fruits	Chebulic acid, chlorogenic acid,	Cholangiocarcinoma [56]
Dipterocarpaceae	*Shorea robusta*	bark	Alpha and beta amyrin	Hepatocarcinoma [57]
Euphorbiaceae	*Cleistanthus collinus*	Leaves and fruits	Cleistanthin A and Cleistanthin B	Oral carcinoma (KB) and cervical carcinoma (SiHa)[58, 59]
	Euphorbia hirta	Whole plant	Quercetin	Ehrlich Ascites Carcinomaand Dalton Lymphoma Ascites[60]
	Ricinus communis	Fruit	Ricin	Breast cancer (MCF 7) and MDA-MB-231 [61]
Fabaceae	*Cajanus cajan*	Roots	Cajanol	Breast cancer [62]
	Desmodium gangeticum	Roots	Salicilin	Lung carcinomas [63, 64]
	Parkinsonia aculeate	Aerial parts	Vanillic acid hexoside, flavonols as 3,7-dimthylquercetin, and flavones as 30-hydroxymelanettin	Hepatocellular carcinoma and breast carcinoma[65]

	Pterocarpus santalinus	Heartwood	Benzofuran, pterostilbene Pterolinus K and pterolinus L	Cervical,breast,lung, colon, prostate and pancreatic cancers [66-68]
	Saraca asoca	Flower and bark	Catechin, and β-sitosterol	Dalton's lymphoma, lung cancerand Sarcoma [69, 70]
	Tamarindus indica	Seed kernels	Polysaccharide	A549, KB, and MCF-7 and murine cancer cell lines DLA and EAC [71]
	Tephrosia purpurea	Leaves, roots	Flavonoids	Hepatocellular carcinoma and breast cancer[72]
Lamiaceae	*Vitex negundo*	leaves	Phenolic compounds	Dalton's ascitic lymphoma[73]
Meliaceae	*Azadirachta indica*	Ripe Seeds, Leaves	3,5-Dihydroxy-6-methyl-2,3-dihydro-4 H-pyran-4-one; 4-ethylbenzamide; nimbolide	Breast, Ehrlichascites carcinoma[74, 75]
Malvaceae	*Sida cordifolia*	Leaf	[3-[(3E,7E)-3,7-dimethyl-9-(phenylsulfanyl)nona-3,7- dien-1-yl]-2,2-dimethyloxirane]	Human skin melanoma cell line colon cancer[76]
Menispermaceae	*Tinospora cordifolia*	Stem bark	Palmatine tinocordiside	Skin cancer, epidermal carcinoma[77, 78]
Moraceae	*Ficus racemosa*	fruit	Guaiol acetate	Breast cancer[79]
	Milicia excels	Roots and bark	Cudraxanthone I and neocyclomorusin	Cervicalepithelioid carcinoma [80]
Phyllanthaceae	*Phyllanthus amarus*	Aerial parts	Gallic acid, gereniin and rutin	Breast, lung, liver, leukemia and prostate cancer [81-83]
Piperaceae	*Piper longum*	Fruits	Piperine	Ehrlich ascites carcinoma,Breast cancer and Dalton's lymphoma ascites[84, 85]
Punicaceae	*Punica granatum*	seeds	Ellagic acid (EA, Urolithin A, Punicalagin	Prostate Cancer, colorectoal cancer[86, 87]
Rhamnaceae	*Ziziphus nummularia*	Leaves	Lapachol	Sarcoma-180 ascetic tumor cell[88]
Rubiaceae	*Rubia cordifolia*	leaves	Rubiaakane series peptides (RAs)	Myeloid leukemia and Histolytic lymphoma[89, 90]

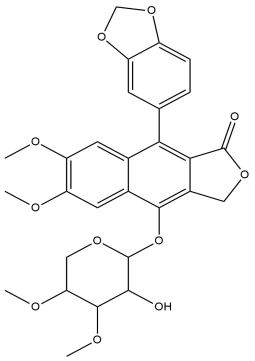
Santalaceae	Santalum album)	Heartwood	Sandal wood iol, α-santalol	skin cancer, Prostate, breast and liver cancers[91]
Solanaceae	*Solanum surattense*	Leaves	trans-Squalene, 9,12,15-Octadecatrienoic acid, Phytol Vitamin E,	Breast prostate, colorectal [92]
	Withania somnifera	Root stem leaves	Withanolide A, withanoside IV, withanoside V	Lung, colon and breast cancer cell lines, neuroblastoma[93, 94]
Stemonaceae	*Stemona tuberose*	tubers	Alkaloids	Lung and colorectal cancer [95]
Zingiberaceae	*Curcuma longa*	Rhizome	Ascorbic acid and curcumin,	Colon cancer and Leukemia [96]
	Zingiber officinale	Rhizome	β- elemene, gingerol	Lung and ovarian cancers [97]
Zygophyllaceae	*Balanites aegyptiaca*	fruit	Oleic, palmitic acids, β-sitosterol, ethyl iso-allocholate, Flavone-4'-OH,5-OH,7-di-O-glucoside	Prostate, breast, colorectal adenocarcinoma[98]
	Tribulus terrestris	Roots, fruits	Saponins	Liver cancer [99]



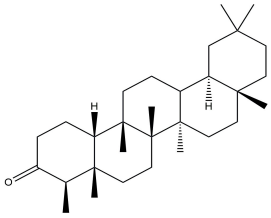
β-boswellic acid



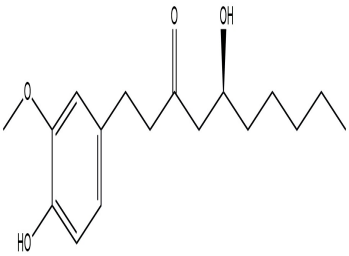
Chebulic acid



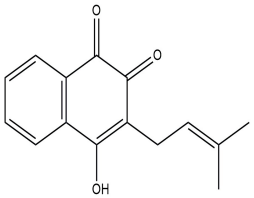
Cleistanthin A



Friedelin



Gingerol



Lappachol

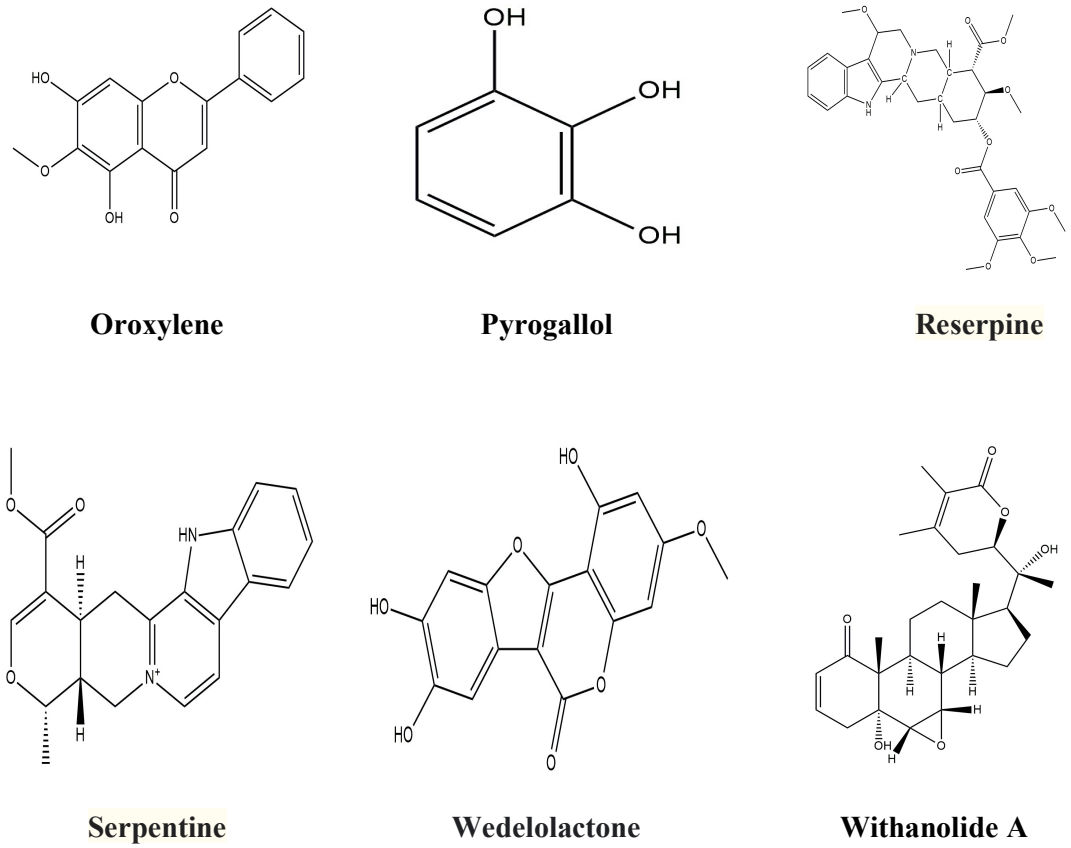


Figure 1: Molecular structures of some important phytochemicals presented in discussed in Table 1

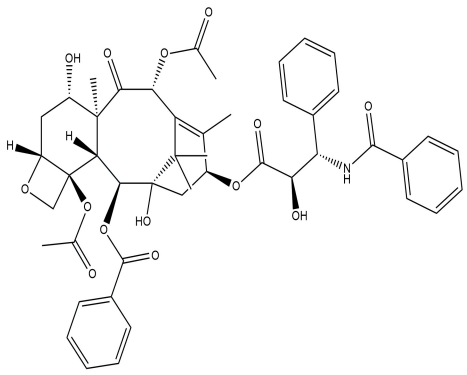
VII. IMPORTANT PHYTOCHEMICALS USED IN CANCER THERAPY

Based on available data, phytochemicals are effective against many types of cancer in humans, here discussing different groups such as alkaloids, flavonoids, phenols, tannins and saponins.

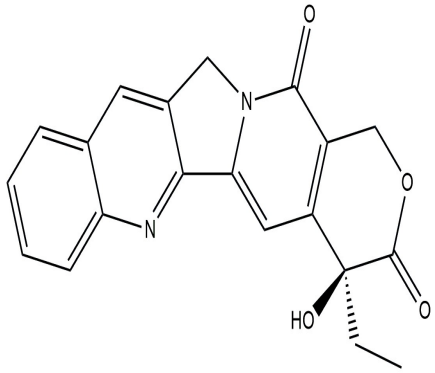
1. **Alkaloids:** Alkaloids inhibit cancer cell proliferation by inducing cancer cell autophagy, endoplasmic reticulum damage, cell apoptosis, and cancer cell termination in the G1 phase or G2/M phase. More than 21,000 different alkaloids have been identified, and many of them are important in medicine, particularly with anticancer activity [100].Many studies have shown that some alkaloids have significant anticancer properties, as shown in Table 2. Despite their great medicinal potential, alkaloids' clinical usage can be hampered by a variety of problems, including potential toxicity and difficulties in large-scale manufacture. However, continued research and progress in drug development aims to overcome these problems and improve the use of alkaloids in cancer therapy.

Table 2: A List of Some Alkaloids with Anticancer Properties.

Alkaloid name	Plant name	Cancer type	Mode of action
Paclitaxel	*Taxus brevifolia*	Breast, ovarian and lung cancer	Microtubule stabilization and causing apoptosis [111]
Camptothecin	*Camptotheca acuminata*	Colorectal and ovarian cancers	Inhibits the enzyme topoisomerase I, [112]
Berberine	*Berberis vulgaris*	Lung cancer	Sensitize cancer cells to radiation therapy and chemotherapy, thus improving treatment outcomes [113]
Vincristine	*Catharanthus roseus*	Acute lymphoblastic leukemia (ALL) and Wilms' tumor	Inhibition of spindle formation [114]
Cytisine	Cytisus and *Laburnum* sps	Lung cancer	Mitochondria-mediated apoptosis and cell cycle arrest [115]
Castanospermine	*Castanospermum australe*	Skin cancer	Inhibitor of the glycosidases [116]
Colchicine	*Colchicum autumnale*	Colorectal (HCT-116), chronic granulocytic leukemia, melanoma,	Stabilizes microtubule formation, arrest cell cycle [117]



Paclitaxel



Camptothecin

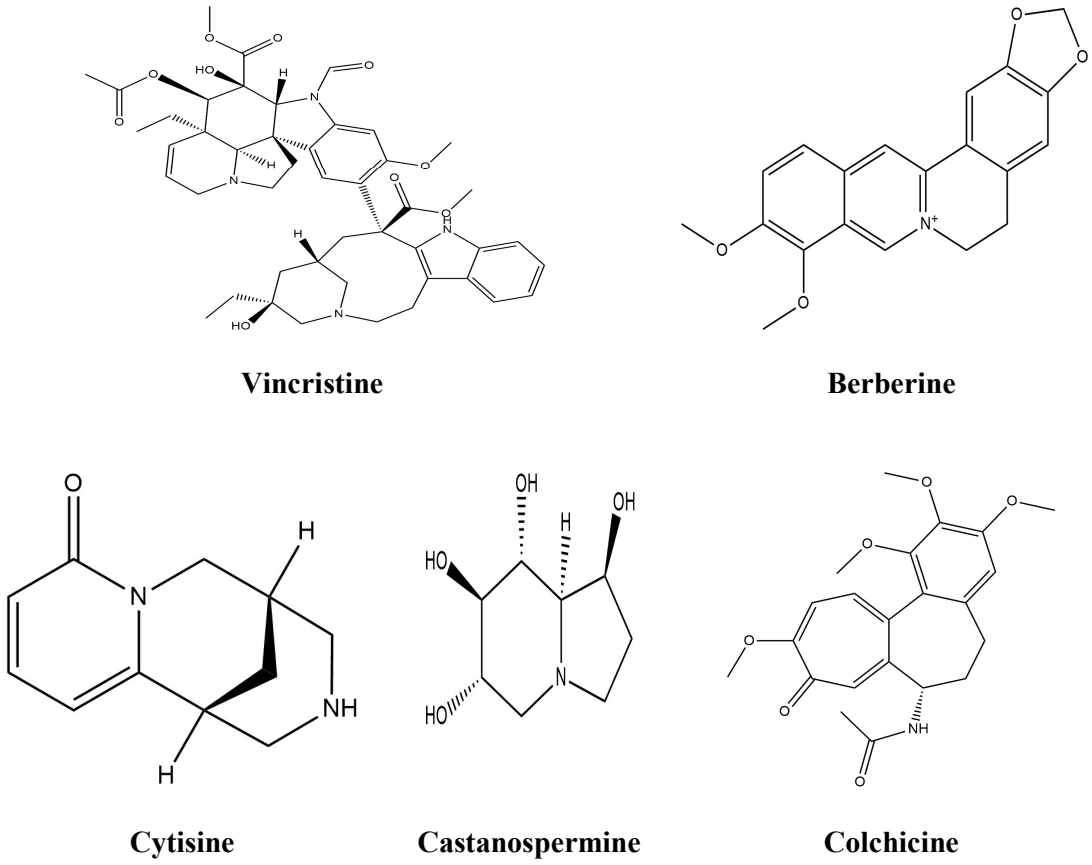


Figure 2: Chemical structures of alkaloids discussed in Table 2

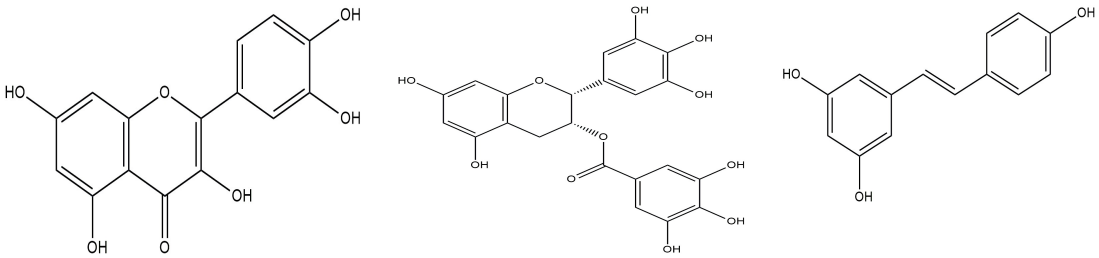
2. **Flavonoids:** Flavonoids are a diverse group of polyphenolic compounds with approximately 10,000 compounds found in a variety of fruits, vegetables, nuts, seeds, and other foods [118].

Known for their antioxidant and anticancer properties, these compounds have attracted great interest in cancer research. Polyphenols inhibit signal transducers and activators of the anti-apoptotic and cancer-promoting transcription (STAT) proteins, MLF and AIF, and inhibit NF necessary for the expression of cancer, angiogenesis and proliferation - κB [119]. Flavonoids inhibit DNA topoisomerase I and cyclooxygenase and are effective in the treatment of breast, lung and colorectal cancer [11].

Table 3 shows some of the most studied flavonoids with anti-cancer activity and their mode of action. Many studies have investigated the use of flavonoids as an adjunct to cancer treatment, such as chemotherapy and radiation therapy, to increase their effectiveness and reduce the risk of resulting pain.

Table 3: A List of Some Flavonoids with Anticancer Properties.

Flavonoid name	Plant source	Cancer type	Mode of action
Quercetin	apples, onions, berries, and green tea	Melanoma	Induce apoptosis in cancer cells, inhibit tumorproliferation, and angiogenesis [120]
Epigallocatechin gallate	green tea	Breast, prostate, and colorectal cancer.	Modulates cell signaling pathways, promote apoptosis and inhibit metastasis in different cancer types [121]
Curcumin	*Curcuma longa*	Pancreatic, colorectal, and breast cancer.	Inhibits inflammatory pathwaysand suppression of tumor cell proliferation [122]
Resveratrol	grapes and red wine	Skin cancer	Inhibitcell growth, induce apoptosis, angiogenesis and metastasis of cancer cells [123]
Flavopiridol	*Dysoxylum binectariferum*	Anaplastic thyroid cancer	Inhibit cyclin-dependent kinase[124]



Quercetin **Epigallocatechin gallate** **Resveratrol**

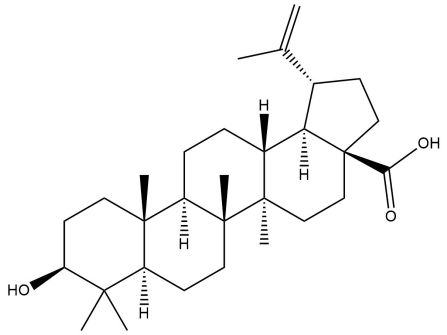
Curcumin **Flavopiridol**

Figure 3: Chemical structures of Flavonoids discussed in Table 3

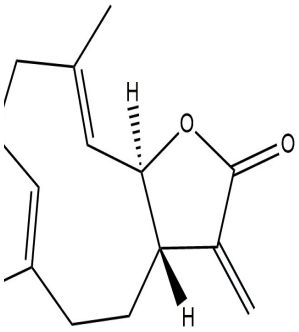
3. **Terpenoids:** Terpenoids, also known as isoprenoids, are a large and diverse group of compounds that occur in plants, fungi, and some animals. They show great promise in cancer treatment because of their different activities. Terpenoids have anti-inflammatory, antibacterial, and anticancer properties. In particular, triterpenoids exhibit anticancer activity by promoting apoptosis by regulating Bax and Bcl2 genes and promoting P53 release via the DR-5 pathway. The discovery of terpenoids in cancer therapy has led to the development of new drugs and treatment combinations.Additionally, scientists are investigating the possibility of terpenoids as adjuvants to increase the effectiveness of chemotherapy and reduce its side effects. Table 4 lists some terpenoids and their anti-inflammatory properties.

Table 4: A List of Some Terpenoids with Anticancer Properties.

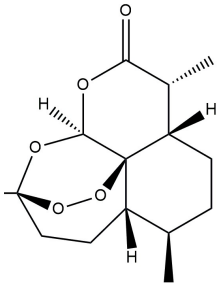
Terpenoid name	Plant source	Cancer type	Mode of action
Betulinic acid	*Ziziphus*and *Betula* Sp.	Wide range of cancer including human melanoma	Induce apoptosis [11]
Costunolide	*Saussurea lappa*	Breastcancer	Cell cycle arrest at G2/M phase [125]
Artemisinin	*Artemisia annua*	Leukemia, breast, and prostate cancers	Induce apoptosis [126]
Ursolic acid	Apples, basil, rosemary,	Pancreatic cancer	Apoptosis and inhibits tumor cell invasion and metastasis[127]
Andrographolide	*Andrographis paniculata*	Melanoma, breast, lung, leukemia, bladder, liverpancreaticand colorectal cancers	Suppresses tumor growthby inducing apoptosis [128]



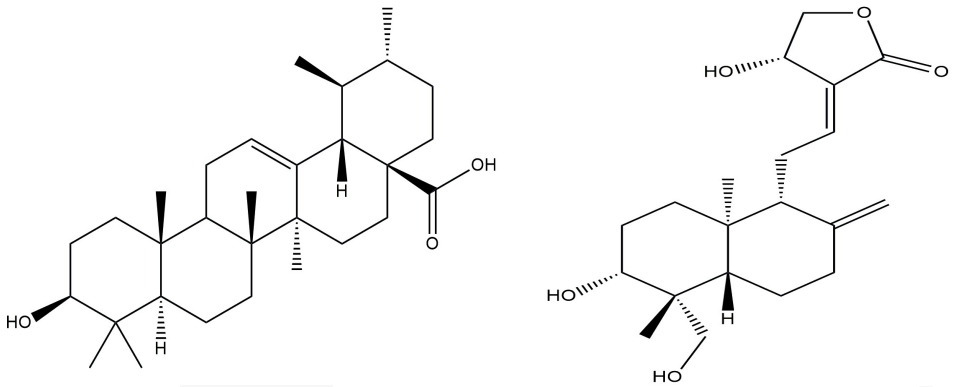
Betulinic acid



Costunolide



Artemisinin



Ursolic acid **Andrographolide**

Figure 4: Chemical structures of Terpenoids discussed in Table 4

4. **Saponins:** Saponins are natural components found in many plants, especially beans, ginseng, and many herbs. Saponins exhibit immunomodulatory activity through cytokine interactions [129]. Saponins accumulate in the S phase, show anti-inflammatory activity, inhibit p21 and cyclin-dependent kinase activity, and can induce apoptosis. Table 5 lists some important saponins with significant anti-inflammatory activities.

Table 5: Different Types of Saponins with their Anticancer Activities.

Saponin type	Plant source	Cancer type	Mode of action
Ginsenoside	*Panax ginseng*	Breast, lung, liver, and colorectal cancers	Inhibit cancer cell growth, induce apoptosis, and suppress tumor metastasis [130]
Quillaja saponins	*Quillaja saponaria* bark	Can used as adjuvants in several cancer immunotherapies.	Enhance the body's immune response against cancer cells [131]
Escin	*Aesculus hippocastanum*	Colorectal cancer	Inhibit tumor cell growth and metastasis [132]
Soy saponins	Soybeans	Colon cancer	Inhibit cancer cell proliferation and angiogenesis [133]
Dioscin	*Dioscorea alata*, *Smilax* and *Trigonella foenum graecum.*	Lung, esophageal, gastric, colon, cervix, ovarian, breast, prostate glioblastoma and leukemia	Triggering apoptosis, inhibiting tumor cell invasion [134]

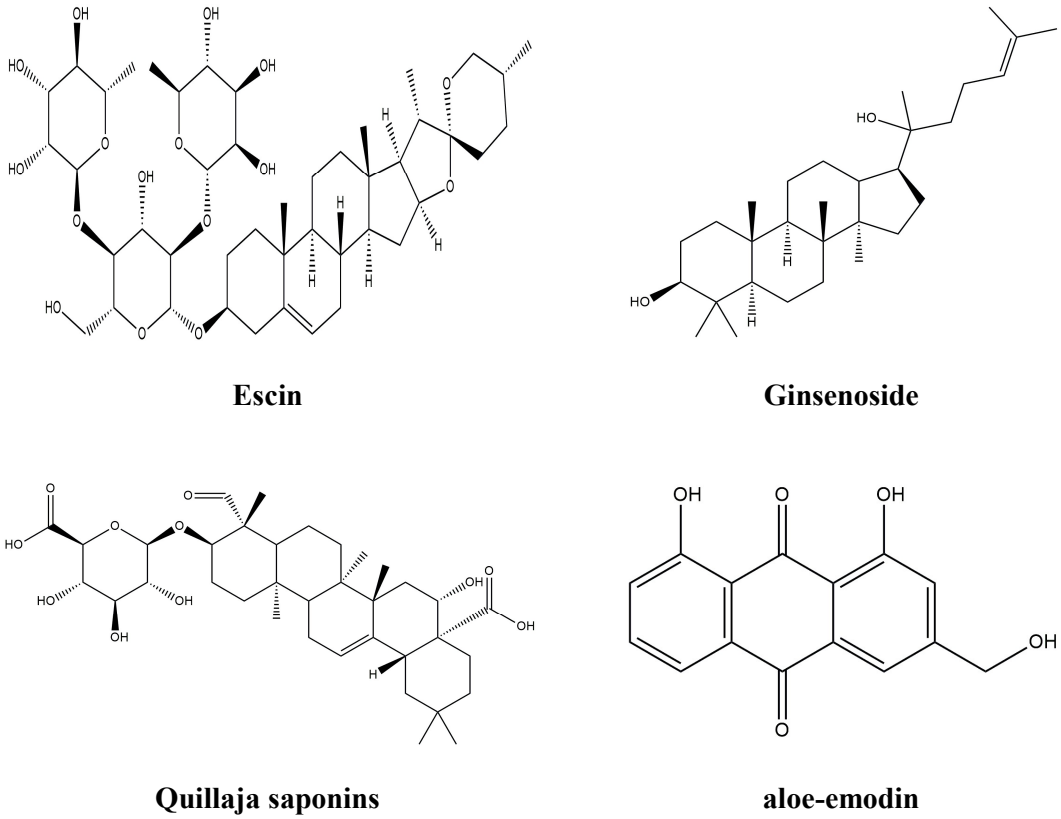


Figure 5: Chemical structures of saponinsdiscussed in Table 5 andaloe-emodin

5. **Brassinosteroids:** Brassinosteroids are a group of plant hormones that are crucial for numerous physiological processes, including controlling stem elongation, and plant senescence.Brassinosteroids also have anticancer benefits, making them potential candidates for cancer treatment. Recent studies have shown that brassinosteroids can inhibit cancer cells by inducing apoptosis, modulate of cell signalingpathways,regulating cell cycle genes and inhibiting tumor proliferation [135]. Brassinolide is among the most researched brassinosteroids.Brassinosteroids inhibit numerous cancer forms, including breast, prostate, and liver cancers byarrestingthe cell cycle and inducing apoptosis in cancer cells [136].

In addition to the molecules discussed above, tannins and quinones are also used in cancer therapy. Tannins such as ellagitannins also exert anti-inflammatory effects by modulating cyclins E, A and B1 and inhibiting the cell cycle in the S phase, inducing apoptosis, mitochondrial secretion of cytochrome C, and activating caspase-3 and caspase-9 [137]. Quinones such as aloe-emodin inhibit cancer cell proliferation by inhibiting the cell cycle in the G1, G2/M or S phase, or quinones stimulate apoptosis [138].

VIII. MODERN TRENDS IN CANCER TREATMENT

Cancer is still a major problem around the world, and scientists continue to find novel and effective treatments. Modern trends in cancer treatment are also under practicing to treat cancer effectivelyalong with conventional cancer treatments like ethno medicine, treatment with plant-based purified drugs, synthetic drugs, radiotherapy, and chemotherapy. Some of them are discussed here.

1. **Plant-Derived Nanomedicine:** Advances in nanotechnology have facilitated the development of plant-derived nanomedicine for the treatment of cancer. Nanoparticles loaded with plant-derived compounds can improve drug delivery, and bioavailability of drugs, and reduce off-target effects and toxicity by specifically targeting cancer cells [139].

2. **Immunotherapy:** Immunotherapy is a revolutionary approach to cancer treatment that uses the immune system to target and destroy cancer cells.This includes immune checkpoint inhibitors, CAR-T cell therapy, cancer vaccines, and adoptive T cell therapy. As they continue to be researched for broader applications, immunotherapies have demonstrated extraordinary efficacy in treating several forms of cancer [140].

3. **Precision Medicine:** Precision medicine, also known as personalized medicine, involves the treatment of cancer through the genetic modification of an individual tumor. Genomic profiling helps identify mutations in cancer cells so that the most likely treatments can be selected for the patient [141].

4. **Liquid Biopsy:** Liquid biopsy includes analysis of blood samples for tumor DNA (ctDNA), proteins, and other biomarkers. These non-invasive tests can provide information about the genetics of tumors and monitor treatment response (142).

5. **Combination Therapy:** Combination therapy involves the simultaneous or sequential use of multiple treatments to target different aspects of cancer biology. Combining immunotherapies with conventional chemotherapy or targeted medicines has the potential to enhance therapeutic results [143].

These contemporary patterns in cancer therapy are driving important developments in oncology, improving results and cancer patients' quality of life. It is essential to stay up to date on the most recent innovations and developments in cancer therapies as research advances.

IX. CONCLUSION

In this review, the molecular and physiological basis of cancer, cancer stages and anticancer activity screening methods are discussed. A total of 50 Indian medicinal plants with anticancer properties are discussed, including the compounds responsible for their anticancer activities and their mechanism of action. The rapid increase in cancer cases and the many limitations of conventional treatments have prompted scientists to develop alternative, environmentally friendly, biocompatible solutions.From the present review, it is clear that the use of phytochemicals in cancer treatment combined with modern technology is

a promising and effective research method for a cancer-free future. As research in this area continues, it is important to follow discoveries and developments in cancer treatment. While herbs are beneficial, their full potential as a cancer treatment must be rigorously tested in well-controlled clinical trials to ensure they are effective and safe in human patients.

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REFERENCES

[1] Bray, F.; Ferlay, J.; Soerjomataram, I.; Siegel, R.L.; Torre, L.A.; Jemal, A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 2018, 68, 394–424.
[2] Karpuz, M.; Silindir-Gunay, M.; Ozer, A.Y. Current and Future Approaches for Effective Cancer Imaging and Treatment. Cancer Biother.Radiopharm. 2018, 33, 39–51.
[3] Satyajit Halder, Prema Modak, Bidduth Kumar Sarkar, Ananya Das, Arghya Prosun Sarkar, Anita Rani Chowdhury, Sukalyan Kumar Kundu, Traditionally Used Medicinal Plants with Anticancer Effect: A Review, Int. J. Pharm. Sci. Rev. Res., 2020, 65(1), Article No. 01 1-13.
[4] M. Greenwell and P.K.S.M. Rahman, Medicinal plants: their use in anticancer treatment, International Journal of Pharmaceutical Sciences and Research, 2015; Vol. 6(10): 4103-4112
[5] Cheng, H. Advanced Textbook on Traditional Chinese Medicine and Pharmacology; New World Press: Beijing, China, 1995
[6] Quiroga R, Meneses L, Bussmann RW (2012) Medicinal ethnobotany in Huacareta (Chuquisaca, Bolivia). J Ethnobiol Ethnomed 8(1):29.
[7] Balachandran P, Govindarajan R. Cancer- an Ayurvedic perspective. Pharmacol Res 2005; 51: 19-30.
[8] Newman DJ, Cragg GM, Snader KM. Natural products as sources of new drugs over the period 1981-2002. J Nat Prod 2003; 66: 1022- 1037
[9] A M Shaikh, B Shrivastava, K G Apte, S D Navale, Medicinal Plants as Potential Source of Anticancer Agents: A Review, Journal of Pharmacognosy and Phytochemistry 2016; 5(2): 291-295.
[10] Kuchenbaecker, K. B., et al. (2017). Risks of Breast, Ovarian, and Contralateral Breast Cancer for BRCA1 and BRCA2 Mutation Carriers. JAMA, 317(23), 2402-2416.
[11] Javed Iqbal, Banzeer Ahsan Abbasi, Tariq Mahmood, Sobia Kanwal, Barkat Ali, Sayed Afzal Shah, Ali Talha Khalil, Plant-derived anticancer agents: A green anticancer approach, Asian Pacific Journal of Tropical Biomedicine, 2017; 7(12): 1129–1150.
[12] Esteller M. Epigenetic gene silencing in cancer: the DNA hypermethylome. Human Molecular Genetics. 2007; 16(1):50–59.
[13] Loomis, D., et al. (2018). Carcinogenicity of welding, molybdenum trioxide, and indium tin oxide. The Lancet Oncology, 19(5), 581-582.
[14] Kiecolt-Glaser, J. K., et al. (2011). Chronic stress and age-related increases in the proinflammatory cytokine IL-6. Proceedings of the National Academy of Sciences, 108(5), 18244-18249.
[15] Arnold, M., et al. (2015). Global burden of cancer attributable to high body-mass index in 2012: a population-based study. The Lancet Oncology, 16(1), 36-46.
[16] Bagnardi, V., et al. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. British Journal of Cancer, 112(3), 580-593.
[17] zur Hausen, H. (2009). Papillomaviruses and cancer: from basic studies to clinical application. Nature Reviews Cancer, 9(5), 342-350.
[18] Chlebowski, R. T., et al. (2018). Estrogen alone and joint symptoms in the Women's Health Initiative randomized trial. Menopause, 25 (10), 1023.
[19] Gupta, G. P., & Massague, J. (2006). Cancer metastasis: building a framework. Cell, 127(4), 679-695.
[20] Lopez-Otin, C., et al. (2013). The hallmarks of aging. Cell, 153(6), 1194-1217.
[21] Hughes, J. P., Rees, S., Kalindjian, S. B., & Philpott, K. L. (2011). Principles of early drug discovery. British Journal of Pharmacology, 162(6), 1239-1249.

[22] Houghton, P. J., Morton, C. L., Tucker, C., Payne, D., Favours, E., Cole, C.,& Houghton, J. A. (2007). The pediatric preclinical testing program: description of models and early testing results. Pediatric Blood & Cancer, 49(7), 928-940.
[23] Cohen, P. (2002). Protein kinases—the major drug targets of the twenty-first century? Nature Reviews Drug Discovery, 1(4), 309-315.
[24] Kitchen, D. B., Decornez, H., Furr, J. R., & Bajorath, J. (2004). Docking and scoring in virtual screening for drug discovery: methods and applications. Nature Reviews Drug Discovery, 3(11), 935-949.
[25] Abdullaev FI. Plant-derived agents against cancer. In: Gupta, S. K., editor. Pharmacology and therapeutics in the new millennium. Narosa Publishing House: New Delhi, India, 2001; p. 345-354
[26] Cragg GM, Newman DJ. Plants as a source of anticancer agents. J Ethnopharmacol 2005; 100: 72-79.
[27] Geethangili, M., Rao, Y.K., Fang, S.H., Tzeng, Y.M., 2008. Cytotoxic constituents from *Andrographis paniculata* induce cell cycle arrest in Jurkat cells. Phyther. Res. https:// doi.org/10.1002/ptr.2493
[28] R Krishnamoorthi and K Elumalai, In-vitro Anticancer Activity of Ethyl Acetate Extract of *Aerva lanata* against MCF-7 Cell Line, International Journal of Pharma Research and Health Sciences, 2018; 6 (1): 2286-89.
[29] K S Siveen and Girija Kuttan, Immunomodulatory and antitumor activity of Aerva lanata ethanolic extract, Immunopharmacology and Immunotoxicology, 2011; 33(3): 423–432.
[30] R. Rajesh, K. Chitra, Padmaa M. Paarakh and N. Chidambaranathan, Anticancer activity of aerial parts of *Aerva lanata* Linn Juss ex Schult against Dalton's Ascitic Lymphoma, European Journal of Integrative Medicine 3 (2011) e245–e250.
[31] Nemec, M. J., H. Kim, A. B. Marciante, R. C. Barnes, E. D. Hendrick, W. H. Bisson, S. T. Talcott, and S. U. Mertens-Talcott. 2017. Polyphenolics from mango (*Mangifera indica* L.) suppress breast cancer ductal carcinoma in situ proliferation through activation of AMPK pathway and suppression of mTOR in athymic nude mice. The Journal of Nutritional Biochemistry 41:12–9.
[32] H. M. Suresh, B. Shivakumar, K. Hemalatha, S. S. Heroor, D. S. Hugar, and K. R. S. Sambasiva Rao, In vitro antiproliferativeactivity of *Annona reticulata* roots on human cancer cell lines, Pharmacognosy Res. 2011; 3(1): 9–12.
[33] Dipankar C.R., et al., 2013, Current Updates on Centella asiatica: Phytochemistry, Pharmacology and Traditional Uses, Medicinal Plant Research, Vol.3, No.4, 20-36
[34] Gitanjali, J., Dinesh Ram, D. S., R, K., Amalan, V., Alahmadi, T. A., Alharbi, S. A., Kandasamy, S., Shanmuganthan, R., & Vijayakumar, N. (2023). Antimicrobial, antioxidant, anticancer, and antithrombotic, competency of saponins from the root of *Decalepis hamiltonii*.Environmental Research, 231, 116096.
[35] Khanna, G. (2010). Non-proliferative activity of saponins isolated from the leaves of Gymnema sylvestre and *Eclipta prostrata* on HepG2 cells-In vitro study. Int. J. Pharm. Sci. Res. 1 (8), 38–42. doi: 10.13040/IJPSR.0975-8232
[36] Kumar Singh, Narendra; Pratap Singh, Virendra Anticancer activity of the roots of *Ichnocarpus frutescens* R. Br. and isolated triterpenes. Pakistan Journal of Pharmaceutical Sciences . Jan2014, Vol. 27 Issue 1, p187-191.
[37] Belkin M., Hardy W.G. Effect of reserpine and chlorpromazine on sarcoma 37. Science.1957; 125: 233–234.
[38] Burton R.M., Goldin A., Humphreys S.R., Venditti J.M. Antileukemic action of reserpine. Science.1957; 125: 156–157.
[39] Fatima, N., Ahmad, M. K., Ansari, J. A., Ali, Z., Khan, A. R., & Mahdi, A. A. (2016). Anticancer, antioxidant potential and profiling of polyphenolic compounds of *Wrightia tinctoria* Roxb.(R.Br.) bark. Journal of Advanced Pharmaceutical Technology & Research, 7(4), 159-165.
[40] Alluri N, Majumdar M. Evaluation of α-glucosidase inhibition of *Drimia nagarjunae*, a medicinal plant from South India. Bangladesh J Pharmacol.2015; 10: 635-36.
[41] Bevara G.B., Kumar A.D.N., Koteswramma K.L., Badana A.K., Kumari S., Yarla N.S., Malla R.R. C-glycosyl flavone from *Urginea indica* inhibits growth and dissemination of ehrlich ascites carcinoma cells in mice. Anticancer Agents Med. Chem. 2017;17: 1256–1266.
[42] Kouamé PB, Jacques C, Bedi G, Silvestre V, Loquet D, Barillé-nion S (2012) Phytochemicals isolated from leaves of *Chromolaena odorata*: Impact on viability and clonogenicity of cancer cell lines. Phyther Res 27(6): 835–840 72.
[43] Hung TM, Cuong TD, Dang NH, Zhu S, Long PQ, Komatsu K (2011) Flavonoid glycosides from *Chromolaena odorata* leaves and their in vitro cytotoxic activity. Chem Pharm Bull (Tokyo) 59(1): 129–131.

[44] Block S, Baccelli C, Tinant B, Van Meervelt L, Rozenberg R, Habib Jiwan JH (2004) Diterpenes from the leaves of *Croton zambesicus*. Phytochem 65(8): 1165–1171.
[45] Singh RP, Agrawal P, Yim D, Agarwal C, Agarwal R (2005) Acacetin inhibits cell growth and cell cycle progression and induces apoptosis in human prostatecancer cells: structure-activity relationship with linarin and linarin acetate. Carcinog 26 (4): 845–854.
[46] Nath LR, Gorantla JN, Joseph SM, Antony J, Thankachan S, Menon DB (2015) Kaempferide, the most active among the four flavonoids isolated and characterized from *Chromolaena odorata*, induces apoptosis in cervical cancer cells while being pharmacologically safe. RSC Adv 5(122): 100912–100922.
[47] Yu Y, Cai W, Pei CG, Shao Y (2015) Rhamnazin, a novel inhibitor of VEGFR2 signaling with potent antiangiogenic activity and antitumor efficacy. Biochem Biophys Res Commun 458(4): 913–919.
[48] Nelson, V.k., Sahoo, N.K., Sahu, M. et al. In vitro anticancer activity of *Eclipta alba* whole plant extract on colon cancer cell HCT-116. BMC Complement Med Ther 20, 355 (2020).
[49] Rai, D., Aswatha Ram, H., Neeraj Patel, K., Babu, U., Sharath Kumar, L., & Kannan, R. (2022). In vitro immuno-stimulatory and anticancer activities of *Oroxylum indicum* (L.)Kurz.: An evidence for substitution of aerial parts for conservation. Journal of Ayurveda and Integrative Medicine, 13 (2), 100523.
[50] Neelima Sharma, Sneha Kispotta and Papiya Mitra Mazumder, Immunomodulatory and anticancer activity of *Bombax ceiba* Linn leaf extract, Asian Pacific Journal of Tropical Biomedicine, 2020, 10(9); 426-432.
[51] Khan, M. A., Ali, R., Parveen, R., Najmi, A. K., & Ahmad, S. (2016). Pharmacological evidence for cytotoxic and antitumor properties of Boswellic acids from *Boswellia serrata*. Journal of Ethnopharmacology, 191, 315-323.
[52] Sukanya Keawsa-ard, Boonsom Liawruangrath and Samart Kongtaweelert. Bioactive Compounds from *Mesua ferrea* Stems Chiang Mai J. Sci. 2015; 42(1) : 185-195
[53] Budchart P, Khamwut A, Sinthuvanich C, Ratanapo S, Poovorawan Y, T-Thienprasert NP. Partially Purified *Gloriosa superba* Peptides Inhibit Colon Cancer Cell Viability by Inducing Apoptosis Through p53 Upregulation. Am J Med Sci. 2017;354 (4): 423-429.
[54] Pan WL; Wong JH; Fang EF; Chan YS; Ng TB; Cheung RC Preferential cytotoxicity of the type I ribosome-inactivating protein alpha-momorcharin on human nasopharyngeal carcinoma cells under normoxia and hypoxia. Biochem. Pharmacol, 2014, 89, 329–339.
[55] Zhang CZ; Fang EF; Zhang HT; Liu LL; Yun JP *Momordica charantia* lectin exhibits antitumor activity towards hepatocellular carcinoma. Invest New Drugs, 2015, 33(1), 1–11.
[56] Chekdaengphanao, P., Jaiseri, D., Sriraj, P., Aukkanimart, R., Prathumtet, J., Udonsan, P., & Boonmars, T. (2022). Anticancer activity of *Terminalia chebula*, *Terminalia bellirica*, and Phyllanthus emblica extracts on cholangiocarcinoma cell proliferation and induction of apoptosis. Journal of Herbal Medicine, 35, 100582.
[57] M. C. Kamaraj, P. Manonmani, and R. ShanmugaSelvan, V. Kalaiselvan. In silico docking studies on the anti-cancer activity of isolated compounds, (alpha and beta amyrin) from methanolic bark extract of *Shorea robusta* .
[58] Pradheepkumar CP, Shanmugam G. Anticancer potential of cleistanthin A isolated from the tropical plant *Cleistanthus collinus*. Oncol Res. 1999; 11 (5):225-32.
[59] Kumar CP, Pande G, Shanmugam G. Cleistanthin B causes G1 arrest and induces apoptosis in mammalian cells. Apoptosis. 1998; 3 (6): 413-9.
[60] Sulaiman, C., Deepak, M., Praveen, T., Lijini, K., Salman, M., Sadheeshnakumari, S., & Balachandran, I. (2023). Metabolite profiling and anti-cancer activity of two medicinally important *Euphorbia* species.Medicine in Omics, 7, 100018.
[61] Munmi Majumder, Shibjyoti Debnath, Rahul L. Gajbhiye, Rimpi Saikia, Bhaskarjyoti Gogoi, Suman Kumar Samanta, Deepjyoti K. Das, Kaushik Biswas, Parasuraman Jaisankar & Rupak Mukhopadhyay Ricinus communis L. fruit extract inhibits migration/invasion, induces apoptosis in breast cancer cells and arrests tumor progression in vivo Scientific Reports volume 9, Article number: 14493 (2019)
[62] Luo, M., Liu, X., Zu, Y., Fu, Y., Zhang, S., Yao, L., & Efferth, T. (2010). Cajanol, a novel anticancer agent from Pigeonpea [*Cajanus cajan* (L.) Millsp.]roots, induces apoptosis in human breast cancer cells through a ROS-mediated mitochondrial pathway. Chemico-Biological Interactions, 188(1), 151–160.
[63] Chen YF, Lu YH, Tsai HY. Crude extract of *Desmodium gangeticum* process anticancer activity via arresting cell cycle in G1 and modulating cell cycle-related protein expression in A549 human lung carcinoma cells.Biomedicine (Taipei). 2022; 12 (2): 31-39.

[64] Preeti Srivastava, Gaurav Srivastava, B. D. Singha, Santosh Kumar Singh, Comparative evaluation of the anticancer activity of crude extracts and isolated compound salicin of *Desmodium gangeticum* (L) Dc against Ehrlich ascites carcinoma in swiss albino mice World Journal of Pharmaceutical Research. Volume 4, Issue 10, 2883-2898.2015

[65] Abdelaziz, S., Al Yousef, H. M., Al-Qahtani, A. S., Hassan, W. H., Fantoukh, O. I., & El-Sayed, M. A. (2020). Phytochemical profile, antioxidant and cytotoxic potential of *Parkinsonia aculeata* L. growing in Saudi Arabia. Saudi Pharmaceutical Journal, 28(9), 1129-1137.

[66] Wu SF, Chang FR, Wang SY, Hwang TL, Lee CL, Chen SL, et al. Anti-inflammatory and cytotoxic neoflavonoids and benzofurans from *Pterocarpus santalinus*. J Nat Prod. 2011;74:989–96.

[67] Mena S, Rodríguez ML, Ponsoda X, Estrela JM, Jäättela M, Ortega AL. Pterostilbene-induced tumor cytotoxicity: A lysosomal membrane permeabilization-dependent mechanism. PLoS One. 2012; 7:e44524.

[68] Wu SF, Hwang TL, Chen SL, Wu CC, Ohkoshi E, Lee KH, et al. Bioactive components from the heartwood of *Pterocarpus santalinus*. Bioorg Med Chem Lett.2011; 21: 5630–2.

[69] Dharshini, A. D., Elumalai, P., Raghunandhakumar, S., Lakshmi, T. and Roy, A. (2021) "Evaluation of Anti-Cancer Activity of *Saraca asoca* Flower Extract against Lung Cancer Cell Line", Journal of Pharmaceutical Research International, 33 (62A), pp. 423–431.

[70] Ahmad, S. R., & Ghosh, P. (2022). A systematic investigation on flavonoids, catechin, β-sitosterol, and lignin glycosides from *Saraca asoca* (ashoka) having anti-cancer & antioxidant properties with no side effect. Journal of the Indian Chemical Society.99 (1), 100293.

[71] Aravind SR, Joseph MM, Varghese S, Balaram P, Sreelekha TT. Antitumor and immunopotentiating activity of polysaccharide PST001 isolated from the seed kerinel of *Tamarindus indica*: an in vivo study in mice. Scientific World Journal. 2012; 2012:361382.

[72] Padmapriya R, Gayathri L, Ronsard L, Akbarsha MA, Raveendran R. In vitro Anti-Proliferative Effect of *Tephrosia purpurea* on Human Hepatocellular Carcinoma Cells. Pharmacogn Mag. 2017; 13 (Suppl 1): S16-S21.

[73] Chitra V, Shrinivas Sharma*, Nandu Kayande Evaluation of Anticancer Activity of Vitex negundo in Experimental Animals: An In Vitro & In Vivo Study Vol.1, No.4, pp 1485-1489, 2009.

[74] Kartik Chandra Guchhait, Tuhin Manna, Manas Barai, Monalisha Karmakar, Sourav Kumar Nandi, Debarati Jana, Aditi Dey, Suman Panda, Priyanka Raul, Anuttam Patra, Rittwika Bhattacharya, Subhrangsu Chatterjee, Amiya Kumar Panda and Chandradipa Ghosh, Antibiofilm and anticancer activities of unripe and ripe *Azadirachta indica* (neem) seed extracts, BMC Complementary Medicine and Therapies, 2022, 22:42, 1-18.

[75] Faten Zahran Mohamed, Amr Saad Mohamed, Fathy Mohamed Abd El-Galil and Noha Gamal Haikel, Antitumor activity of Neem leaf Extract and Nimbolide on Ehrlich Ascites Carcinoma Cells in Mice, Biochemistry Letters, 10(3) 2015, 27-41.

[76] Pratima M, Bhutkar V, Suganthi Milind, V Bhutkar and R Kothai. In vitro antiproliferative activity of ethanolic extract of *Sida cordifolia* Linn against various cancer cell lines Al Am een J Med Sci. 2020; 13(4): 234-241

[77] Bala M, Pratap K, Verma PK, Singh B, Padwad Y; Validation of ethnomedicinal potential of *Tinospora cordifolia* for anticancer and immunomodulatory activities and quantification of bioactive molecules by HPTLC. J Ethnopharmacol, 2015; 175(4):131–137.

[78] Ali H, Dixit S; Extraction optimization of *Tinospora cordifolia* and assessment of the anticancer activity of its alkaloid palmatine. Scientific World Journal, 2013; 28:376216.

[79] Dnyaneshwar SG, Moregaonkar SD, and Mhase AK, Cytotoxic and Anticancer Activity of *F. racemosa* Fruit Extract on MCF7 Human Breast Cancer Cell Line by SRB Method, Journal of Animal Research, 2016; 1(6): 43-47

[80] Oke-Altuntas, F., Kapche, G.D.F., Nantchouang Ouete, J.L. et al. Bioactivity evaluation of cudraxanthone I, neocyclomorusin and (9βh)-3β-acetoxylanosta-7,24-diene isolated from *Milicia excelsa* Welw. C. C. Berg (Moraceae). Med Chem Res 25, 2250–2257 (2016).

[81] Lee, S.H., Jaganath, I.B., Wang, S.M. & Sekaran, S.D. (2011). Antimetastatic Effects of *Phyllanthu*s on Human Lung (A549) and Breast (MCF-7) Cancer Cell Lines. PLoS ONE, Vol. 6, No. 6, 2011, pp. e20994.

[82] Huang, S.T., Yang, R.C., Lee, P.N., Yang, S.H., Liao, S.K., Chen, T.Y. & Pang, J.H.S. (2006). Anti-tumor and anti-angiogenic effects of *Phyllanthus urinaria* in mice bearing Lewis lung carcinoma. International Immunopharmacology, Vol. 6, No. 6, 2006, pp. 870–879.

[83] Tang, Y.Q., Jaganath, I.B. & Sekaran, S.D. (2010). *Phyllanthus* spp. induces selective growth inhibition of PC-3 and MeWo human cancer cells through modulation of the cell cycle and induction of apoptosis. PLoS ONE, 2010; 5 (9) 10) pp. e12644.

[84] Quijia, C. R., & Chorilli, M. (2022). Piperine for treating breast cancer: A review of molecular mechanisms, combination with anticancer drugs, and nanosystems. Phytotherapy Research, 36(1), 147-163.

[85] Sunila, E., & Kuttan, G. (2004). Immunomodulatory and antitumor activity of *Piper longum* Linn.and piperine. Journal of Ethnopharmacology, 90(2-3), 339-346. https://doi.org/10.1016/j.jep.2003.10.016

[86] Vicinanza R, Zhang Y, Henning SM, Heber D. 2013. Pomegranate juice metabolites, ellagic acid and urolithin a, synergistically inhibit androgen-independent prostate cancer cell growth via distinct effects on cell cycle control and apoptosis. Evidence-based Complementary and Alternative Medicine 2013: 247504.

[87] Seeram NP, Adams LS, Henning SM, et al. 2005. In vitro, antiproliferative, apoptotic and antioxidant activities of punicalagin, ellagic acid and a total pomegranate tannin extract are enhanced in combination with other polyphenols as found in pomegranate juice. J Nutr Biochem 16: 360–367.

[88] Kumar, S.; Garg, V.; Kumar, N.; Sharma, P.; Upadhyay, A. Pharmacognostical studies on the leaves of *Ziziphus nummularia* (Burm. F.). Eur. J. Exp. Biol. 2011, 1, 77–83.

[89] Lee, J. E., Hitotsuyanagi, Y., Kim, I. H., Hasuda, T., and Takeya, K. (2008a). A novel bicyclic hexapeptide, RA-XVIII, from *Rubia cordifolia*: Structure, semi-synthesis, and cytotoxicity. Bioorg. Med. Chem. Lett. 18 (2), 808–811. doi:10.1016/j.bmcl.2007.11.030

[90] Parag R. Patel1*, Bhuvan P. Raval2, Hamsraj A. Karanth1, Vishal R. Patel. Potent antitumor activity of Rubia cordifolia, International Journal of Phytomedicine 2 (2010) 44-46

[91] Sreevidya Santha and Chandradhar Dwivedi. Anticancer Effects of Sandalwood (*Santalum album*). Anticancer Research 35: 3137-3146 (2015)

[92] GC-MS Study on the Bioactive Components and Anti-Cancer Activities of *Solanum surattense* Hema R., S. Kumaravel and K. Alagusundaram Cancer Biology, 2011;1(1)

[93] Yadav B, Bajaj A, Saxena M, Saxena AK. In Vitro Anticancer Activity of the Root, Stem and Leaves of *Withania somnifera* against Various Human Cancer Cell Lines. Indian J Pharm Sci. 2010; 72 (5): 659-63.

[94] Mahendra Rai, Priti S. Jogee, Gauravi Agarkar, and Carolina Alves dos Santos Anticancer activities of *Withania somnifera*: Current research, formulations, and future perspectives Pharm Biol, 2016; 54(2): 189–197. 2015

[95] Evaluation of Anti-cancer activity of *Stemona tuberosa* lour. Thesis submitted to Department of Zoology, School of Life Sciences. March 2022.

[96] Ooko E, Kadioglu O, Greten HJ, Efferth T. Pharmacogenomic characterization and isobologram analysis of the combination of ascorbic acid and curcumin-two main metabolites of *Curcuma longa*-in cancer cells. Front Pharmacol 2017.

[97] Rhode, J., Fogoros, S., Zick, S., Wahl, H., Griffith, K.A., Huang, J. & Liu, J.R. (2007). Ginger inhibits cell growth and modulates angiogenic factors in ovarian cancer cells. BMC Compl Altern Shukla, Y., Pal, S.K. (2004). Dietary cancer chemoprevention: An overview. Int J Hum Genet.4: 265–276.

[98] Omer H. M. Ibrahim, Adel D. Al-Qurashi, Khalid A. Asiry, Magdi A. A. Mousa, Nabil A. Alhakamy and Kamal A. M. Abo-Elyousr, Investigation of Potential In Vitro Anticancer and Antimicrobial Activities of *Balanites aegyptiaca* (L.) Delile Fruit Extract and Its Phytochemical Components, plants, 2022; 11(19): 2621, 1-16.

[99] Chhatre S, Nesari T, Somani G, Kanchan D, Sathaye S. Phytopharmacological overview of *Tribulus terrestris*. Pharmacogn Rev. 2014 Jan; 8(15):45-51.

[100] Mondal, A.; Gandhi, A.; Fimognari, C.; Atanasov, A.G.; Bishayee, A. Alkaloids for cancer prevention and therapy: Current progress and future perspectives. Eur. J. Pharmacol. 2019, 858, 172472.

[101] MC, Taylor HL, Wall ME, Coggon P, McPhail AT. Plant antitumor agents. VI. The isolation and structure of taxol, a novel antileukemic and antitumor agent from *Taxus brevifolia*. J Am Chem Soc. 1971; 93 (9): 2325-2327.

[102] Bruin EC, Medema JP. Apoptosis and non-apoptotic deaths in cancer development and treatment response. Cancer Treat Rev. 2008; 34 (8):737-749.

[103] Samadi A, Sabzichi M, and Pourzand A. Berberine; a botanical alkaloid with a broad spectrum of anticancer properties.Biomedicine & Pharmacotherapy.2017; 87: 576–589.

[104] Pui CH, Relling MV, Sandlund JT, Downing JR, Campana D, Evans WE. Rationale and design of Total Therapy Study XV for newly diagnosed childhood acute lymphoblastic leukemia. Ann Hematol. 2004; 83 (1):S124-126.

[105] Xu, W.T.; Li, T.Z.; Li, S.M.; Wang, C.; Wang, H.; Luo, Y.H.; Piao, X.J.; Wang, J.R.; Zhang, Y.; Zhang, T.; et al. Cytisine exerts anti-tumor effects on lung cancer cells by modulating reactive oxygen species-mediated signaling pathways. Artif.Cells Nanomed.Biotechnol. 2020, 48, 84–95.
[106] Wojtowicz, K.; Januchowski, R.; Sosi ´nska, P.; Nowicki, M.; Zabel, M. Effect of brefeldin A and castanospermine on resistant cell lines as supplements in anticancer therapy.Oncol. Rep. 2016, 35, 2896–2906.
[107] Negia AS, Gautama Y, Alama S, Chandaa D, Luqmana S, Sarkarb J, et al. Natural anti-tubulin agents: Importance of 3,4,5- trimethoxyphenyl fragment. Bioorg Med Chem 2015; 23: 373-89.
[108] Cao J, Xia X, Chen X, Xiao J, Wang Q. Characterization of flavonoids from *Dryopteris erythrosora* and evaluation of their antioxidant, anticancer and acetylcholinesterase inhibition activities. Food and Chemical Toxicology.2013; 51:242–250.
[109] Kumar S, Pathania AS, Saxena AK, Vishwakarma RA, Ali A, Bhushan S. The anticancer potential of flavonoids isolated from the stem bark of *Erythrina suberosa* through induction of apoptosis and inhibition of STAT signaling pathway in human leukemia HL-60 cells. ChemicoBiological Interactions.2013; 205: 128–137.
[110] Yang B, Xia ZA, Zhong B, Xiong X, Sheng C, Wang YJ, Li MH. Quercetin attenuates doxorubicin cardiotoxicity by modulating Bmi-1 expression. Br J Pharmacol. 2012; 167 (2): e1-12.
[111] Siddiqui IA, Bharali DJ, Nihal M, Adhami VM, Khan N, Chamcheu JC, Khan MI, Shabana SM, Mousa SA, Mukhtar H. Excellent anti-proliferative and pro-apoptotic effects of (-)-epigallocatechin-3-gallate encapsulated in chitosan nanoparticles on human melanoma cell growth both in vitro and in vivo. Nanomedicine (Lond). 2014; 9(1): 100-9.
[112] Yallapu MM, Nagesh PK, Jaggi M, Chauhan SC. Therapeutic Applications of Curcumin Nanoformulations. AAPS J. 2015 Sep; 17 (5):1341-56
[113] Harikumar KB, Aggarwal BB. Resveratrol: a multitargeted agent for age-associated chronic diseases. Cell Cycle. 2008; 7 (3): 1020-35.
[114] Pinto N, Prokopec SD, Ghasemi F, Meens J, Ruicci KM, Khan IM, Mundi N, Patel K, Han MW, Yoo J, Fung K, MacNeil D, Mymryk JS, Datti A, Barrett JW, Boutros PC, Ailles L, Nichols AC. Flavopiridol causes cell cycle inhibition and demonstrates anti-cancer activity in anaplastic thyroid cancer models. PLoS One. 2020;15 (9): e0239315.
[115] Li, Q.; Wang, Z.; Xie, Y.; Hu, H. Antitumor activity and mechanism of costunolide and dehydrocostus lactone: Two naturalsesquiterpene lactones from the Asteraceae family. Biomed.Pharmacother.2020, 125, 109955.
[116] Efferth T, Dunstan H, Sauerbrey A, Miyachi H, Chitambar CR. The anti-malarial artesunate is also active against cancer. Int J Oncol. 2001; 18 (4):767-773.
[117] Li F, Liang J, Tang D, et al. Ursolic acid inhibits proliferation and induces apoptosis of cancer cells in vitro and in vivo. J Biomed Biotechnol. 2011; 2011: 419343.
[118] Li L, Sun P, Zhang C, Li Z, Wu B. Andrographolide induces apoptosis in human renal tubular epithelial cells through the ROS-mediated mitochondrial pathway. Am J Chin Med. 2020; 48 (6):1367-1382.
[119] Sun Y, Xun K, Wang Y, Chen X (2009) A systematic review of the anticancer properties of berberine, a natural product from Chinese herbs. Anti-Cancer Drugs 20 (9): 757–769
[120] Park HJ, Lee JH, Song YB, Park JH, Song H, Hong SH, Kim WS, Kim SH, Cho SH, Sung JH, Lee J. Aqueous extract of Panax ginseng C.A. Meyer induces apoptosis through a caspase-dependent pathway in A549 human lung cancer cells. J Ethnopharmacol. 2009 Jan 12; 121 (1): 108-16.
[121] Zentmyer J, Zhang X, Zhu Y.The Mechanism and Relevance of Lysis Efficiency of Quillaja Saponins in Vaccine Manufacturing. J Pharm Sci. 2021; 110 (5): 1986-1996.
[122] Yang Z, Sun Y, Xie X, Zhang T, Gong C. Anticancer effects of escin via regulation of miRNA/mRNA networks in a mouse model of colorectal cancer. Int J Oncol. 2018; 52 (3): 895-906.
[123] Lee SO, Li XH, Khan S, Safe S. Targeting NR4A1 (TR3) in cancer cells and tumors by novel NR4A1 antagonists.Mol Cancer Ther. 2013; 12 (12): 1950-60.
[124] He W, Zhang MF, Ye J, Jiang TT, Fang XF, Song Y. Dioscin induces prostate cancer cells apoptosis through inhibiting Vav3 phosphorylation. J Exp Clin Cancer Res. 2017 Oct 24; 36 (1):148.
[125] Wang Y, Xu W, Chen Z, et al. Brassinolide-mediated cell elongation is involved in suppressing rice infection by the parasitic weed *Striga hermonthica*. Plant Signal Behav. 2021; 16 (2): 1828701.
[126] Sharma I, Pati PK, Bhardwaj R. Brassinosteroids and their signaling in plant responses to abiotic stress. Front Plant Sci. 2016; 7: 1719.

[127] Larrosa M, Tomas-Barberan FA, Espin JC (2006) The dietary hydrolyzable tannin punicalagin releases ellagic acid that induces apoptosis in human colon adenocarcinoma CaCo-2 cells by using the mitochondrial pathway. J Nutr Biochem 17(9): 611–625.
[128] Chiu TH, Lai WW, Hsia TC, Yang JS, Lai TY, Wu PP, Ma CY, Yeh CC, Ho CC, Lu HF, Wood WG, Chung JG (2009) Aloe-emodin induces cell death through S-phase arrest and caspase-dependent pathways in human tongue squamous cancer SCC-4 cells. Anticancer Res 29 (11): 4503–4511
[129] Alfieri, M.; Leone, A.; Ambrosone, A. Plant-Derived Nano and Microvesicles for Human Health and Therapeutic Potential in Nanomedicine.Pharmaceutics 2021, 13, 498.
[130] Mellman I, Coukos G, Dranoff G. Cancer immunotherapy comes of age. Nature. 2011; 480 (7378): 480-489.
[131] Garraway LA, Verweij J, Ballman KV. Precision oncology: an overview. J Clin Oncol. 2013; 31 (15): 1803-1805.
[132] Siravegna G, Marsoni S, Siena S, Bardelli A. Integrating liquid biopsies into the management of cancer. Nat Rev Clin Oncol. 2017; 14 (9): 531-548.
[133] Topalian SL, Hodi FS, Brahmer JR, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. N Engl J Med. 2012; 366 (26): 2443-2454.

