Role of Herbal Medicine in Cancer Therapy

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Abstracts:

This review compiles comprehensive pharmacological data on plant-derived compounds with demonstrated anticancer potential across diverse cancer types, including carcinomas, sarcomas, leukemias, lymphomas, melanomas, central nervous system cancers, and bladder cancer. Notable phytoconstituents such as epigallocatechin gallate from *Camellia sinensis*, ginsenosides from *Panax ginseng*, and allicin from *Allium sativum* exhibit significant cytotoxic activity against breast cancer cells. Similarly, compounds like thymoquinone, parthenolide, baicalein, and flavonoids from various medicinal plants demonstrate potent anticancer effects in leukemia, lymphoma, and prostate cancers. Marine and fungal sources, including jasplakinolide, fucoxanthin, and polysaccharide-K, also exhibit promising results, particularly in melanoma and brain cancers. Extracts from *Moringa oleifera*, *Annona muricata*, and *Cannabis sativa* demonstrate effects on apoptosis, proliferation, and metastasis pathways. Across studies, IC_{50} values range from low micromolar to microgram levels, highlighting their therapeutic relevance. These findings support the potential of natural products as valuable leads in cancer treatment and warrant further clinical investigation.

Key Words: Herbal medicines, Cancer therapy, Marine sources, Plant sources, Natural Products

1. Introduction

Cancer remains one of the most pressing global health challenges, with common types such as breast, lung, gastric, colorectal cancers, etc., are accounting for a substantial proportion of cancer-related mortality.[1-2] Despite advancements in conventional treatments including chemotherapy, radiotherapy, and targeted therapies major limitations persist. These include systemic toxicity, development of drug resistance, lack of tumor selectivity, and adverse effects that compromise patient quality of life.

In recent years, there has been growing interest in the potential of herbal medicine as a complementary or alternative approach in cancer therapy[3-5]. Natural compounds derived from medicinal plants and marine organisms have shown remarkable therapeutic promise due to their structural diversity and bioactivity. Marine-derived compounds such as peptides, alkaloids, and terpenoids from sponges, algae, sea urchins, and cyanobacteria are exhibit potent cytotoxicity against cancer cells, often sparing normal cells and minimizing side effects. Several marine-based compounds have already progressed into clinical use, including cytarabine and trabectedin, underscoring their translational potential.

Similarly, phytochemicals extracted from medicinal plants, such as flavonoids, polyphenols, alkaloids, and terpenoids, possess a wide range of anticancer properties [6-7]. The sources of natural anticancer agents along with the structural profiles of their active constituents is present the table-1. These include induction of apoptosis, inhibition of cell proliferation and angiogenesis, disruption of cancer cell membranes, modulation of signaling pathways, reversal of drug resistance, and enhancement of immune responses. Notably, these compounds often exhibit selective toxicity towards cancer cells, thereby reducing the collateral damage associated with conventional chemotherapy[8]

Emerging evidence from clinical studies supports the integration of herbal medicine with standard cancer treatments, reporting improved survival outcomes, enhanced immune modulation, and better quality of life[9] (QOL) in cancer patients. Mechanistic studies also highlight how these natural compounds regulate key cellular processes such as autophagy[10], apoptosis, and gene expression, including up regulation of pro-apoptotic markers like BAX and down regulation of anti-apoptotic proteins such as BCL-2. Type of cancer and its target/mechanism is described in the table- 2.

This review aims to explore the evolving role of herbal medicine in cancer therapy, emphasizing both terrestrial and marine-derived natural compounds, their mechanisms of action, clinical relevance, and potential for integration into modern oncology.

2. PLANT AND ITS EXTRACT(S) /ACTIVE CONSTITUENT(S) HAVE ANTI-CANCER PROPERTIES:

2.1 CARCINOMAS (Cancer that starts in skin or tissues that line or cover internal organs).

2.1.1 Breast Cancer: *Camellia sinensis* (Green tea) leaves contain epigallocatechin gallate (EGCG), a potent antioxidant shown to inhibit breast cancer cell growth. The extraction is usually done using hot water (aqueous extraction). The Concentration amount used in green tea contains about 10-50% EGCG in dry weight, depending on the variety and preparation method. IC50 value of EGCG has an IC50 value of approximately 5-10 µM in some breast cancer cell lines[11]. *Panax ginseng* roots are rich in ginsenosides, which have shown anti-tumor effects in breast cancer studies. The roots are extracted using ethanol, followed by concentration. The concentration amount used in ginsenosides typically make up around 5-10% of the dried root extract. IC50 value of ginsenosides have an IC50 value in the range of 20-50 µM depending on the cancer cell line [12]. *Allium sativum (*Garlic) bulbs produce allicin, an active compound formed upon crushing the fresh cloves. Allicin can be extracted using water or ethanol. It has been reported to induce apoptosis in breast cancer cells. The Concentration amount used for Allicin is produced at concentrations of 1-5% in fresh garlic. Allicin showed anticancer activities IC50 values around 50-100 µM in various cancer cell lines[13].

2.1.2 Lung Cancer: *Moringa oleifera* (Drumstick Tree): The leaves contain the active constituent alkaloids, screened these extracted against lung cancer cells and results demonstrated that at the concentration used is 100–200 µg/mL, with an IC50 value of approximately 100–200 µg/mL against A549 lung cancer cells [14]. *Rhizophora mucronata* (Mangrove Plant), the leaves and stems contain flavonoids and alkaloids, extracted with methanol. The concentration is 127–376 µg/mL, with an IC50 value of 155 µg/mL (stems) and 376 µg/mL (leaves) against A549 cells [15]. *Camellia oleifera* (Tea Oil Camellia), the buds contain hesperetin and kaempferol, extracted using ethanol and screened for their lung cancer activities[16].

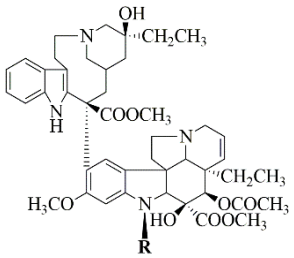
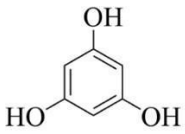
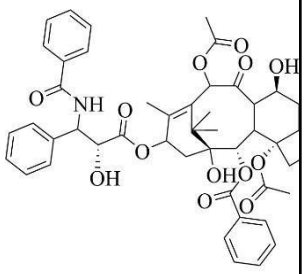
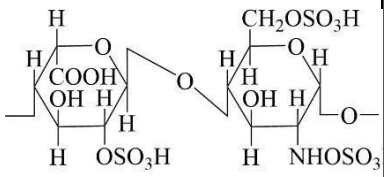
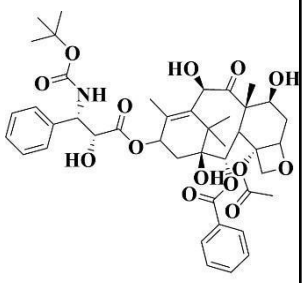
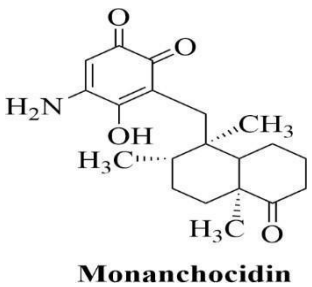
2.1.3. Pancreatic Cancer: *Nardostachys jatamansi* (Spikenard), the rhizome contains terpenoids, its cytotoxic activity has been studied against pancreatic cancer cell lines[17]. *Hypoxoside and Hyperoside*, these compounds have shown anticancer activity in pancreatic cancer cells. Hypoxoside has an IC50 value of ~25 µM, and Hyperoside has an IC50 value of ~50 µM[18]. This plant *Graviola* (Annona muricata) has been studied for its anticancer potential in pancreatic cancer[19].

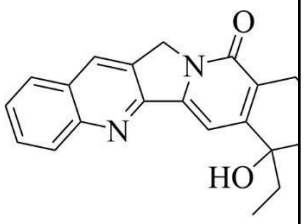
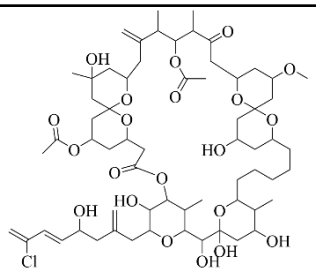
2.1.4. Prostate Cancer: The root *Scutellaria baicalensis* (Baikal Skullcap) contains baicalin and baicalein, extracted using hydroalcoholic extraction, screened for their anticancer against PC-3 cell line. The result displayed that IC50 value of 0.15 mg/mL against PC-3 cells [20]. The leaves *Hibiscus sabdariffa* (Roselle) contain anthocyanins and polyphenols, extracted via aqueous extraction, with a concentration of 8.58 ± 0.68 µg/mL and an IC50 value of 8.58 µg/mL [21]. *Calotropis procera* (Sodom Apple): The leaves contain cardenolides and flavonoids, extracted with hydroalcoholic extract, though the concentration against significant activity against prostate cancer [22]. The leaves *Ficus deltoidea* (Mistletoe) contain flavonoids and triterpenoids, extracted using chloroform extract[23]. The roots

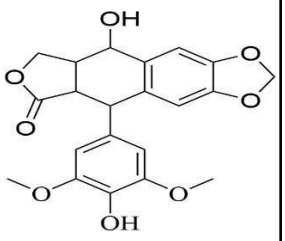
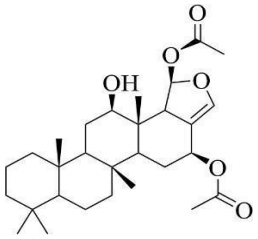
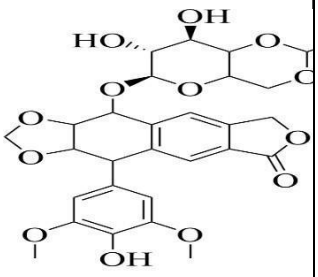
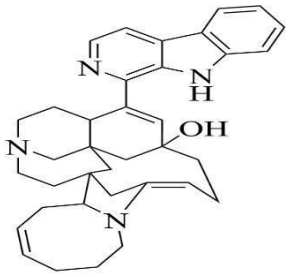
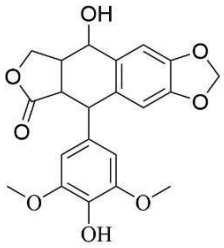
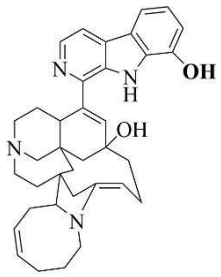
Levisticum officinale (Lovage) contain phenolic compounds and flavonoids, extracted with hydroalcoholic extraction[24]

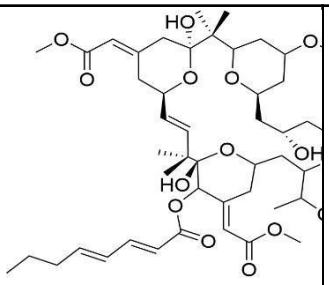
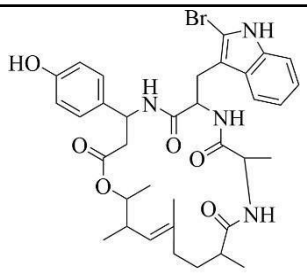
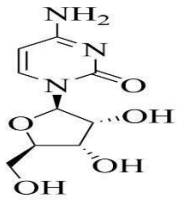
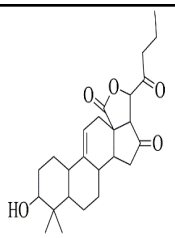
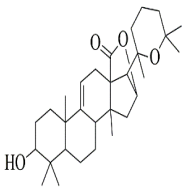
1.5.Esophagenal Cancer : The seeds *Nigella sativa* (Black Seed) contain thymoquinone, extracted using methanol. The methanolic extract exhibited cytotoxic effects against cancer cells, with an IC_{50} value of 0.48 mg/mL[25]. The rhizome *Zingiber officinale* (Ginger), contains 6-gingerol and 6-shogaol, extracted via reflux extraction at 76.9°C for 3.4 hours. The anti-cancer results of the extract showed an IC_{50} value of 20.9 µg/mL against HeLa cancer cells [26]. The leaves *Camellia sinensis* (Green Tea), contain epigallocatechin gallate (EGCG), extracted using hydromethanol. The extract demonstrated anticancer activity, significant activity against esophageal cancer cells line [27].

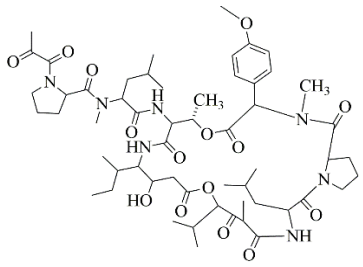
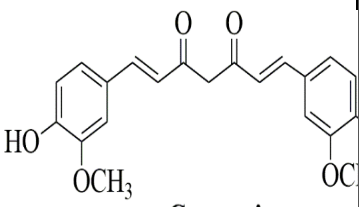
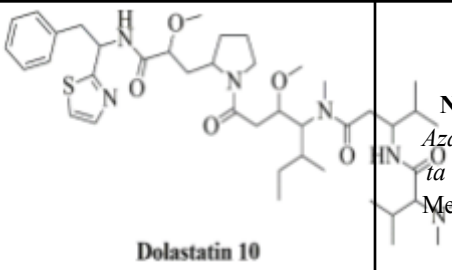
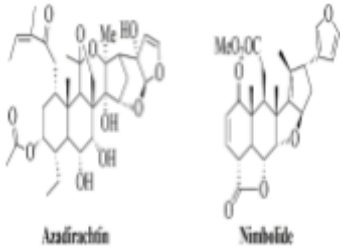
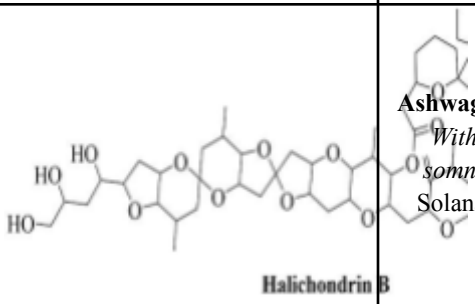
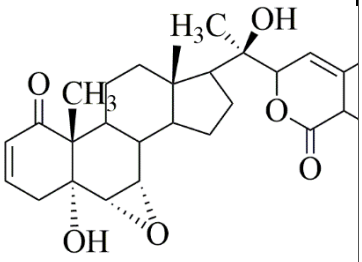
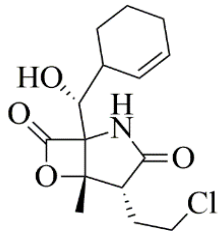
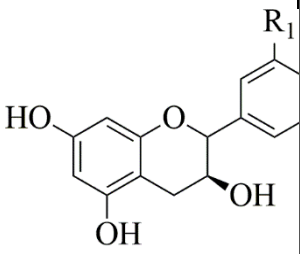
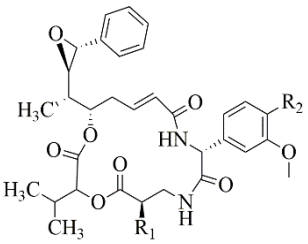
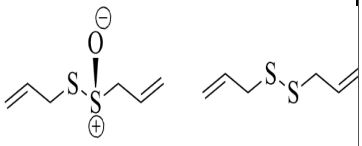
Table -1: Sources of natural anticancer agents and structural profiles of their active constituents

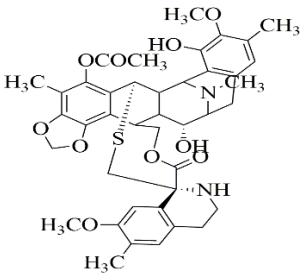
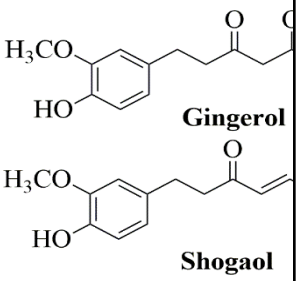
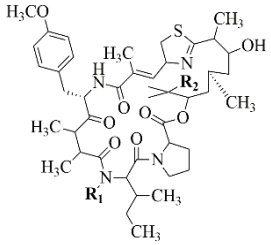
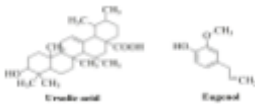
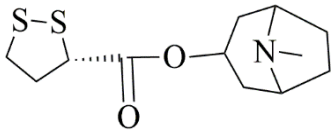
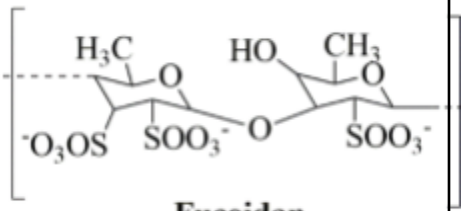
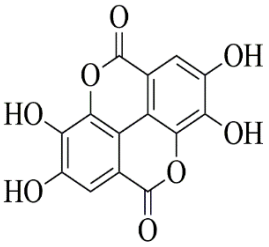
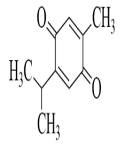
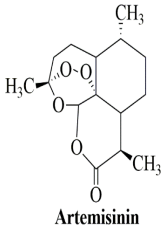
Common Name, Botanical Name and Family	Active constituents structures	Common Name, Botanical Name and Family	Active constituents structures
Periwinkle, *Catharanthus roseus* , Apocynaceae.	 **Vincristine: R=CHO** **Vinblastine: R=CH_3**	**Phloroglucinol,** Brown seaweed, Phaeophyceae.	 **Phloroglucinol**
Paclitaxel (Taxol), *Taxus brevifolia*, Taxaceae and also Semi-synthetic derivative of paclitaxel **(Docetaxel).**	 **Paclitaxel**	**Heparin,** *Dictyopteris delicatula,* Dictyotaceae.	 2-O sulfated iduronic acid 6-O Sulfated N-sulfated glucosamine **Heparin**
	 **Docetaxel**	**Monanchocidin,** *Monanchora pulchra,* Spongiidae.	 **Monanchocidin**

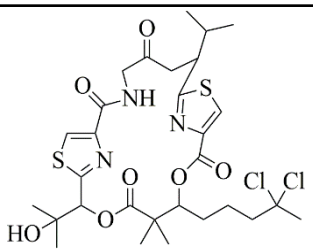
Camptothecin, *Camptotheca acuminate,* Nyssaceae.	 **Camptothecin**	**Spongistatin-I**, *Spongia* species, Spongiidae.	 **Spongistatin-I**

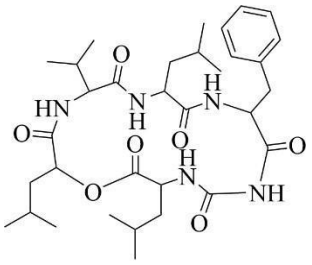
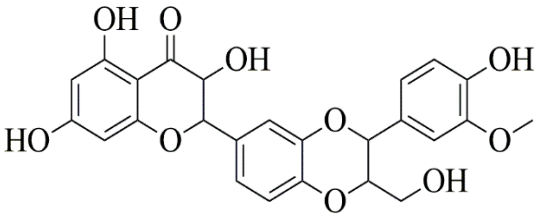
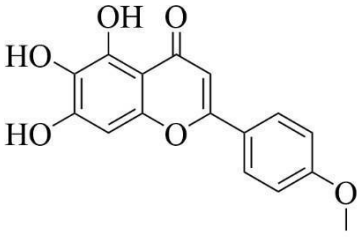
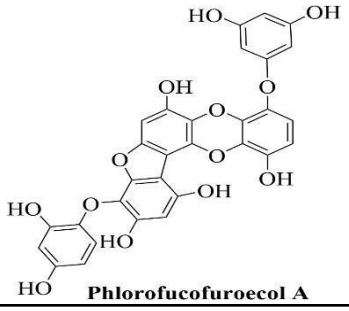
***Po*dophyllotoxin,** *Podophyllum peltatum*, Berberidaceae, and Semi-synthetic derivative of podophyllotoxin (**Etoposide).**	 **Podophyllotoxin**	**Heteronemin,** Marine sponges, Spongiidae	 **Heteronemin**
	 **Etoposide**	**Manzamine A,** Marine sponges, Spongiidae.	 **Manzamine A**
Podophyllotoxin, *Podophyllum peltatum,* Berberidaceae.	 **Podophyllotoxin**	**8-hydroxymanzamine A,** *Pachypellina* species, Spongiidae	 **8-hydroxymanzamine A**
Bryostatin 1, *Bugula neritina*, Bugulidae.		**Jaspamide**, *Jaspis* species, Spongiidae.	

	 Bryostatin 1		 Jaspamide
Cytarabine, *Cryptotheca crypta.*	 Cytarabine	**Holothuria atra,** *Holothuria atra,* Holothuriidae	 Cucumechinol  Philipnogenin B

Aplidine, *Aplidium albicans,* Didemnidae.	 Aplidine	**Turmeric,** *Curcuma longa,* Zingiberaceae.	 Curcumin
Dolastatin 10, *Dolabella auricularia,* Aplysiidae.	 Dolastatin 10	**Neem,** *Azadirachta indica,* Meliaceae	 Azadirachtin Nimbolide
Halichondrin B, *Halichondria okadai,* Halichondriidae	 Halichondrin B	**Ashwagandha,** *Withania somnifera,* Solanaceae.	 Withanolides
Salinosporamide A, Actinomycete *Salinispora tropica.*	 Salinosporamide A	**Green Tea,** *Camellia sinensis,* Theaceae.	 Epicatechin: R Epigallocatechin:
Cryptophycin, *Nostoc* species, Nostocaceae	 Cryptophycin A: R1=Me, R2=Cl Cryptophycin B: R1=Me, R2=H	**Garlic,** *Allium sativum,* Amaryllidaceae.	 Allicin Diallyl sulfide

Tunicate, *Ecteinascidia turbinate, Perophoridae*.	 **Ecteinascidin 743**	**Ginger,** *Zingiber officinale,* Zingiberaceae.	 **Gingerol** **Shogaol**
Apratoxin A, *Lyngbya boulloni,* Cyanobacteria.	 **Apratoxin A: R_1=CH_3, R_2=CH_3** **Apratoxin B: R_1=H, R_2=CH_3** **Apratoxin C: R_1=CH_3, R_2=H**	**Holy Basil,** *Ocimum sanctum,* Lamiaceae.	
Brugine, *Bruguiera sexangula,* Rhizophoraceae.	 **Brugine**  **Fucoidan**	**Amla (Indian Gooseberry),** *Phyllanthus emblica,* Phyllanthaceae.	 **Ellagic acid**
Fucoidan, *Ascophyllum nodosum,* Phaeophyceae.		**Black Cumin,** *Nigella sativa,* Ranunculaceae.	 **Thymoquinone**
Lyngbyabellin B, *Lyngbya majuscule,* Cyanobacteria.		**Sweet Wormwood,** *Artemisia annua,* Asteraceae.	 **Artemisinin**

	 **Lyngbyabellin B**		

Sansalvamide A, Marine fungi.	 Sansalvamide A	**Milk Thistle,** *Silybum marianum,* Asteraceae.	 Silymarin
Scutellarein 4′-methylether, *Osmundea pinnatifida,* Rhodophyta.	 Scutellarein 4′-methylether	**Phlorofucofuroecol A,** Brown seaweeds, Phaeophyceae	 Phlorofucofuroecol A

2.2. SARCOMAS (Cancer that starts in the bone, cartilage, fat, muscle, or other connective tissues).

2.2.1. Osteosarcoma (bone cancer): Pulsatilla *saponin D* is a bioactive saponin isolated from the root of *Pulsatilla chinensis* and *Pulsatilla koreana.* The active constituent is Pulsatilla saponin D. inhibited osteosarcoma growth by inducing apoptosis and cell cycle arrest at the G0/G1 phase[28]. Echinatin is a bioactive flavonoid compound found in the roots and rhizomes of licorice (Glycyrrhiza spp.). It's known for its various pharmacological effects, including antioxidant, anti-inflammatory, and anti-tumor properties. *Echinatin* compound has been shown to inhibit the growth and metastasis of human osteosarcoma cells [29]. The active constituent *Ziyuglycoside II* (from Sanguisorba officinalis) displayed significantly inhibit osteosarcoma cell proliferation and induce apoptosis [30]. Figure 1 presents the plant name, the type of cancer it targets, and its mechanism of action.

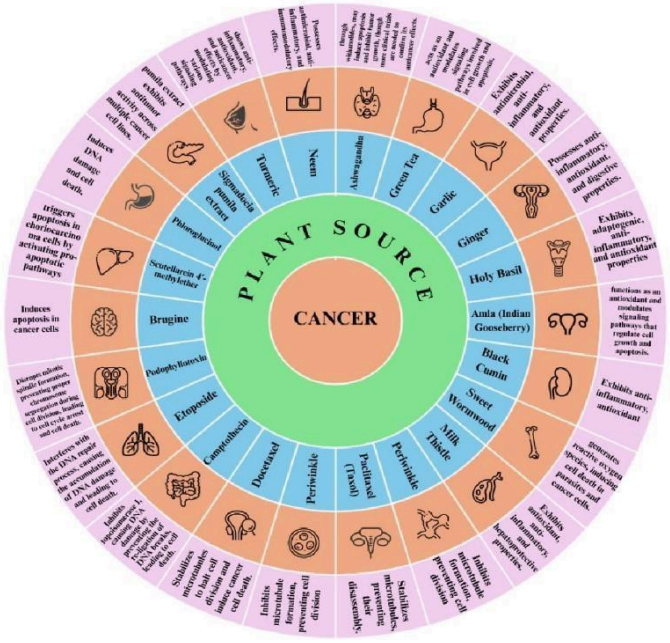


Figure-1: The plant name, the type of cancer it targets, and its mechanism of action.

2.2.2. Liposarcoma (Fat Tissue Cancer): *Fagonia indica* belong to *zygophyllaceae* family commonly known as dhamasa, contains flavonoids like quercetin, isorhamnetin, kaempferol, apigenin, as well as saponins, ursolic acid, ferulic acid, and arbutin, with stems and leaves used for aqueous extraction[31]. Kalanchoe pinnata, also known as the "miracle plant" or "cathedral bells," is a perennial plant belonging to the *Crassulaceae* family. *Kalanchoe pinnata* contains active compounds such as lupeol and stigmasterol, with leaves used for ethanolic extraction. The plant containing flavonoids, the potent water-soluble antioxidants and free radical scavengers, which prevent oxidative cell damage, have strong anticancer activity [32]. Berberis aristata, belonging to the family *Berberidaceae,* contains alkaloids and uses stems for methanolic extraction, showing effectiveness at 100 µg/mL with an IC_{50} value of 1.8964 µg/mL[33].

2.2.3. Rhabdomyosarcoma (Muscle Cancer): *Jasplakinolide,* a compound derived from the marine sponge *Jaspis species,* these extracts demonstrated predominantly against breast cancer and other cancer cell lines which include Rhabdomyosarcoma, by inducing actin polymerization and stabilizing actin microfilaments [34]. *Echinoside A*, extracted from the sea cucumber *Stichopus japonicus*, has demonstrated anticancer effects, including on RMS cells[35].

2.3. LEUKEMIA (Cancer of the blood or Bone marrow).

2.3.1. Acute Lymphocytic Leukemia (ALL): The leaves of *Madhuca longifolia* (Mahua) were extracted with water, containing myricitrin, which exhibited an IC_{50} value of 164.4 µg/mL against Jurkat ALL cells [36]. The leaves of *Prosopis cineraria* (Khejri) were aqueous-extracted, with the active compound vitexin**,** showing an IC_{50} value of 147 µg/mL against Jurkat ALL cells [37]. The bark of *Flacourtia indica* (Indian Plum) was extracted with water, yielding vanillin as the active compound, demonstrating an IC_{50} value of 29.22 µg/mL against Jurkat ALL cells[38]. Methanol extract of Flacourtia indica aerial parts induces apoptosis via generation of ROS and activation of caspases in human colon cancer HCT116 cells.

2.3.2. Chronic Lymphocytic Leukemia [CLL]: The aerial parts of *Tanacetum parthenium* **(Feverfew)** were extracted using ethanol**,** yielding parthenolide**,** which demonstrated an IC_{50} value of approximately 1.5 µM against CLL cells[39]. The aerial parts of *Eryngium stachyoides* were extracted with ethanol**,** containing luteolin and apigenin, but the specific IC_{50} value was not mentioned in the study[40]. Figure 2 presents the Marine source, the type of cancer it targets, and its mechanism of action.

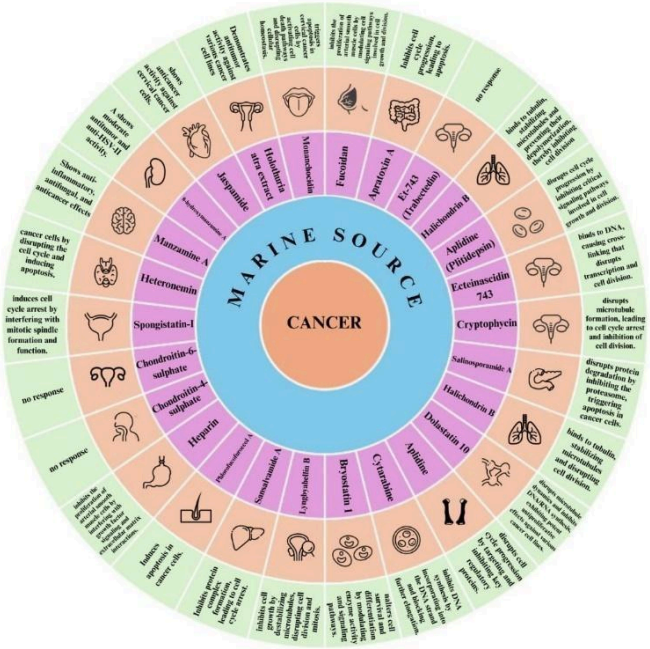


Figure-2: The Marine source, the type of cancer it targets, and its mechanism of action.

2.3.3. Acute Myelogenous Leukemia (AML): *Gleditsia sinensis* (Chinese Honey Locust) contains saponins, which are extracted using ethanol, and it shows an IC50 value of 12 µg/mL against the HL-60 AML cell line [41]. *Vernonia amygdalina* (Bitter Leaf) contains active constituents like Vernodaline and Vernolide, extracted with ethanol, and demonstrates 50–75% inhibition of AML and ALL leukemic cells[42]. *Madhuca longifolia* (Mahua) contains Myricitrin, which is extracted through aqueous methods, with an IC50 value of 164.4 µg/mL against HL-60 cells [43].

2.3.4. Chronic Myelogenous Leukemia (CML): Diosgenin (from *Dioscorea* species or fenugreek seeds) Dysgenic, derived from tubers/seeds via methanol extraction, induces ROS-mediated autophagy and apoptosis in CML cells, with significant cytotoxicity observed at concentrations of 10–40 µM [44]. Berbamine (from *Berberis* species bark), berbamine derivatives extracted from the bark using methanol show strong cytotoxic effects on imatinib-resistant K562 (CML) cells, with IC_{50} values ranging from 0.8 to 3.2 µM depending on the semi synthetic derivative[45]. Moringa oleifera (leaf extract), the leaves of Moringa oleifera extracted using aqueous or methanol methods demonstrated cytotoxicity in CML cells at concentrations around 10.7 µg/mL (IC_{50}), mainly due to its rich phenolic and flavonoid content [46]. Spirulina platensis (algae powder extract), extracts from dried biomass of Spirulina using ethanol or aqueous methods showed IC_{50} values of 15.77 mg/mL in K562 cells and 9.44 mg/mL in drug-resistant K562/ADR cells, attributed to phycocyanin and other antioxidants [47].

2.4. LYMPHOMAS (Cancers of the lymphatic system).

2.4.1. Hodgkin Lymphoma: *Catharanthus roseus* (Madagascar periwinkle) root extract, prepared using an aqueous method, contains active alkaloids such as serpentine, which showed promising anticancer activity with an IC_{50} value of 0.775 µM in vitro, indicating potential effects against Hodgkin lymphoma [48]. The roots of *Gypsophila* species are rich in saponins, and while not cytotoxic alone at concentrations up to 20 µg/mL, they significantly enhanced the anticancer effect of etoposide on lymphoma cells, reducing the IC_{50} to 93 µg/mL [49]. Coriolus versicolor (Turkey tail mushroom), when extracted from its fruiting body using water, yields Polysaccharide-K (PSK), which selectively inhibits lymphoma cell proliferation in a dose-dependent manner [50].

2.4.2. Non – Hodgkin Lymphoma: Piperlongumine, an active alkaloid extracted from the fruits of *Piper longum*, demonstrated potent cytotoxic activity against Burkitt lymphoma cell lines with IC_{50} values ranging from 2.8 to 8.5 µM[51].The whole plant of *Peperomia tetraphylla*, extracted using ethyl acetate, showed cytotoxic potential against lymphoma cells [52]. The leaves of *Murraya koenigii* were studied for their anti-cancer properties against lymphoma [53].

2.5. MELANOMAS (Cancer of the pigment-producing cells of the skin).

2.5.1. Skin Melanoma: Ocimum tenuiflorum (Holy Basil) leaf extract, obtained using various solvents like hexane, dichloromethane, and methanol, showed cytotoxicity against A375 melanoma cells with IC_{50} values less than 50 µg/mL [54]. The whole plant of *Euphorbia hirta* was extracted with ethanol and demonstrated cytotoxic potential, primarily due to its flavonoid content [55]. Morus alba (White Mulberry) leaf extract, with its active constituent Sanggenon C, exhibited IC_{50} values around 5 µM against melanoma cells [56]. Trametes versicolor (Turkey Tail Mushroom) mycelium extract showed significant cytotoxicity against melanoma cell lines (A375 and SK-MEL-5), with IC_{50} values of 114.5 µg/mL for A375 cells and 88.6 µg/mL for SK-MEL-5 cells, while fruiting body extracts exhibited higher IC_{50} values [57].

2.6. CENTRAL NERVOUS SYSTEM CANCERS (Cancers of the brain and spinal cord).

2.6.1 Brain Cancer: Trichobotrysin B, a compound derived from a marine fungus, inhibits glioma proliferation and induces apoptosis through the IL-6-mediated STAT3 signaling pathway [58]. Fucoxanthin, a compound from microalgae, induces apoptosis in glioma cells with an IC_{50} value of approximately 100 µM[59]. Ulva Lactuca extract, derived from green marine algae, has shown to induce apoptosis in glioma cells[60]. Psammaplin A, a compound extracted from marine sponges, inhibits aminopeptidase N, showing anticancer activity[61]. Fucoidan, found in brown seaweed, induces apoptosis and inhibits cell proliferation in glioma cells[62].

2.6.2.Spinal Cord Cancer: Cannabis sativa (Hemp), extracted using ethanol, contains cannabinoids like THC and CBD. These compounds demonstrate antitumor activity across various cancer types, including colorectal cancer (CRC). Cannabinoids have shown beneficial effects in CRC treatment by influencing key processes such as apoptosis, cell proliferation, metastasis, inflammation, angiogenesis, oxidative stress, and autophagy. Similarly, terpenes such as

β-caryophyllene, limonene, and myrcene have also been reported to exert antitumor effects in CRC by promoting apoptosis and inhibiting both cell proliferation and angiogenesis [63]. Ganoderma lucidum (Reishi Mushroom), with active constituents like polysaccharides and triterpenoids, is extracted using hot water and ethanol [64].

2.7. BLADDER CANCER:

Febrifugine, an active constituent, has demonstrated anticancer effects with IC_{50} values of 0.02 μM for T24 bladder cancer cells and 0.018 μM for SW780 cells[65]. Propolis (from poplar trees), extracted using a multi-dynamic extraction method, contains flavonoids and phenolic compounds, with an IC_{50} value of 81.9–86.7 μg/mL for osteosarcoma cells, although its effect on bladder cancer is not directly stated[66]. Thymoquinone, derived from the seeds of Nigella sativa, is an active compou

Table-2: Type of cancer and its Target/Mechanism

Type	Sub type	Target/Mechanism:
1. Carcinomas (cancer that starts in skin or tissues that line or cover Internal organs).	**Breast cancer[63]**	Estrogen receptor (ER), progesterone receptor (PR), Human Epidermal Growth Factor Receptor 2 (HER2), and Phosphoinositide 3-kinase (PI3K)/ protein kinase B (AKT)/ Mammalian Target of Rapamycin (mTOR) signaling pathways.
	Lung cancer[64]	EGFR, ALK, ROS1, BRAF, and PD-L1 pathways, focusing on inhibiting cell proliferation and immune evasion.
	Colon cancer[65]	KRAS, BRAF mutations, EGFR, and VEGF.
	Pancreatic cancer[66]	Inhibition of KRAS, c-MET, and PD-1/PD-L1 pathways to overcome resistance.
	Prostate cancer[67]	Androgen receptors, PI3K/AKT/mTOR pathways, and immune checkpoints (PD-1/PD-L1
	Esophageal cancer[68]	HER2 and EGFR are key targets; monoclonal antibodies and immune checkpoint inhibitors (like nivolumab) are used.
2. Sarcomas (cancer that starts in the bone, cartilage, fat, muscle, or other connective tissues).	**Osteosarcoma[69] (bone cancer)**	Targeting IGF-1R and p53 pathways for osteosarcoma
	Liposarcoma[70] (fat tissue cancer)	Targeting MDM2-p53 pathway and CDK4
	Rhabdomyosarcoma[71] (muscle cancer)	MYOD1 mutation and ALK inhibition
3. Leukemia (cancer of the blood or bone marrow).	**Acute lymphocytic leukemia[72] (ALL)**	Targeting CD19, CD22, and BTK; CAR T-cell therapy
	Chronic lymphocytic leukemia[73] (CLL)	Inhibition of B-cell receptor (BCR) signaling, targeting BTK and PI3K pathways.
	Acute myelogenous leukemia[74] (AML)	Targeting FLT3 mutations, IDH1/2 mutations, and BCL-2 inhibitors
	Chronic myelogenous leukemia[75] (CML)	Tyrosine kinase inhibitors (TKIs) targeting BCR-ABL1.
4. Lymphomas (cancers of	**Hodgkin lymphoma[76]**	Targeting PD-1/PD-L1 and CD30; nivolumab is a

the lymphatic system)		major therapeutic approach.
	Non-Hodgkin lymphoma[27]	Targeting CD20 with monoclonal antibodies (e.g., rituximab).
5. Melanomas (cancer of the pigment-producing cells of the skin)	**Skin melanoma**[78]	BRAF mutations, immune checkpoint inhibitors (PD-1/PD-L1).
6. Central Nervous System Cancers (cancers of the brain and spinal cord)	**Brain cancer** [79]	Targeting EGFR, IDH1/IDH2, and PD-1/PD-L1 pathways
	Spinal cord cancer[79]	Targeting specific genetic alterations like NF1, EGFR.
7. Bladder Cancer	**Cancer that starts in the bladder lining**[80]	Targeting FGFR3, PD-1/PD-L1, and EGFR.
8. Kidney Cancer		Targeting VEGF, mTOR, and immune checkpoint inhibitors (PD-1/PD-L1).
9. Liver Cancer		Targeting VEGF, mTOR, and PD-1/PD-L1 pathways.
10. Thyroid Cancer	**Cancer in the thyroid gland**[83]	Targeting BRAF mutations, RET fusions, and VEGF signaling pathways.

11. Ovarian Cancer	**Cancer that starts in the ovaries**[84]	Targeting BRCA mutations, angiogenesis, and PD-1/PD-L1 inhibitors
12. Cervical Cancer	**Cancer that begins in the cervix**[85] **(the lower part of the uterus)**	Targeting HPV, immune checkpoints, and VEGF.

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