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Review Article

MEDICINAL PLANTS FROM THE HIMALAYAS: INSIGHTS INTO THEIR ANTICANCER EFFECTS

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ABSTRACT

Management of cancer is a challenge to the modern system of medical practice despite of having an effective chemotherapy, radiotherapy, nuclear therapy and Surgery. While effective, these treatments have limited acceptance due to safety concerns. Herbal medicines, known for their minimal adverse effects, have shown promise in disease management and can provide high-quality nutritional and raw ingredients. Herbal therapies are also considered potential complementary treatments alongside conventional methods. The study was conducted by systematically reviewing the literature of various databases such as PubMed, Google scholar, Science direct and Wiley. In this study 4036 articles were reported from these tools and only 92 articles included after the exclusion due to duplication, irrelevant, non-full-text article, qualitative and quantitative analysis. Many herbal medicines described in this article contain numerous of these antioxidants. Recent researches showed the anti-oxidative and superoxide scavenging activities of individual active components of herbal medicine for their inhibitory activities on lipid peroxidation and anti-cancer properties. Individual herbal medicines show antipyretic, analgesic and anti-inflammatory and anti-cancer effects. Numerous *in vitro* studies of herbal medicine on different cell lines and *in vivo* study of herbal medicine have been reported. However, the mechanisms of actions remain unclear. This review aims to give an overview on the recent development of herbal medicine in the prevention and treatment of cancer. The report covers the possible mechanism of action of some of the herbal medicine. In addition, the common properties of herbal medicine are described. Finally, the study sheds lights on the pharmacological applications of herbal medicine in the treatment of cancer and its potential use as anti-cancer agents.

Keywords: Herbal drugs, Anticancer activity, Cancer cell lines

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INTRODUCTION

Management of cancer is a challenge to the modern system of medical practice despite of having effective chemotherapy, radiotherapy, nuclear therapy and Surgery. Although these methods of treatment are proven to be effective in some cases and useful in some other cases but, their acceptability is limited due to issues related to their safety [1]. Research is going on all across the world to find out an effective and safe medication therapy for the treatment of all types of cancer such as lung, breast, prostate, colonic, liver, leukemia, lymphatic, ovarian etc. However, the rate of success is very limited and number of drugs in pipeline are also limited. Therefore, scientists are looking at the medicines originated from natural resources either from plants or animals. There are thousands of compounds from traditional medicine are screened for their anticancer properties and validate their clinical use [2].

As per the WHO data about 80% of the world population use traditional medicine, especially of herbal origin in the management of multiple diseases and disorders. Herbal drugs are the part of various systems of medicine practice, such as Ayurveda, Siddha, Unani and even allopathy [3, 4]. Review of literature reveals that organic solvent extracts, decoctions, tinctures, powders, granules, mixtures and tablets have demonstrable anticancer activities both *in vitro* and *in vivo* [5]. Further, most of the preparations exhibited their significant antineoplastic activities as immunomodulatory and immunostimulants [6]. They also produced anticancer activities through differentiating cells, promoting apoptosis, inhibiting telomerase and affecting senescence [7-9].

The Himalayan region, due to its unique geographical, topographical, ecological, climatic, and physiographical conditions, is a treasure trove of valuable medicinal plants. The Himalayan regions are Garhwal Himalayas, Kumaon Himalayas, Bageshwar Valley, Terai Forest, Kashmir, Pauri Garhwal Himalayas, Himachal Pradesh and Sikkim Himalayas etc. The unique conditions of the Himalayas make it an invaluable resource for medicinal plants, contributing to the health and well-being of people not only in the region but around the world. The exact number of medicinal plants in the Himalayan region used for primary healthcare and livelihoods is not definitively established. However, researchers have documented that more than 10,000 medicinal plants from the Himalayas support approximately 600 million people in the region. This highlights the critical role of these plants in traditional medicine, healthcare, and the livelihoods of the local populations [10].

Herbal medicines and their products are proven to be effective with minimum adverse effects or no side effects. They are also known to have minimal drug-drug reactions, drug-food interaction, cautions, precautions and contraindications [11]. A population-based survey study conducted in United Kingdom indicated that more than 25% of cancer patients visited plant-based medicine practitioners for various types of cancer at different stages [12]. A study conducted in Canada shown that at least one herbal preparation was used by breast cancer patients during standard treatment [13]. It had been studied that about 80% of drugs used for the treatment of cancer are of herbal origin including anthracyclines, podophyllotoxins, taxanes and vinca alkaloids [14]. Despite use of herbal preparations extensively all across the continents, the evidence generated against cancer cells is non-scientifically generated, analyzed and or the models used in the preclinical study do not matches with clinical condition of cancer [15]. It is also believed that herbal medicine therapy could be a complementary therapy along with chemotherapy, surgical therapy, radiation therapy and nuclear therapy [16].

The main objective of this systematic review article is to review literature on cancer and/or herbal drugs and compile the information. There are about 80% of drugs used in the treatment of cancer are of herbal origin, including anthracyclines, podophyllotoxins, taxanes and vinca alkaloids.

It had been said that about 80% of drugs used in the treatment of cancer are of herbal origin, including anthracyclines, podophyllotoxins, taxanes and vinca alkaloids. Some herbal remedies have shown promise in these traditional systems. Many herbs contain compounds with anti-inflammatory and antioxidant properties (vitamins, enzymes, polysaccharides, polyphenols, flavonoids, minerals, lignins, xanthones, carotene etc.), which may help reduce the risk of cancer development by preventing DNA

damage and inhibiting the growth of cancer cells. Despite use of herbal preparations extensively all across the continents the evidence generated against cancer cells is non-scientifically generated, analyzed and or the models used in preclinical study do not matches with clinical condition of cancer.

Methods

The study was conducted by systematically reviewing the literature of various databases such as PubMed, Google scholar, Science direct and Wiley. Data was collected by using the keywords herbal drugs, anticancer, cancer cell lines, medicinal plants were added together or independent for each other. The articles only in English language published between 2000 and March 2022 were searched. In this study 4036 articles were reported from these tools and only 92 articles included after the exclusion due to duplication, irrelevant, non-full-text article (refers to an analysis of research articles where the full text of the articles is not available, and the analysis relies only on the abstract, summary, or metadata provided), qualitative (analyzing the content, themes, or patterns) and quantitative analysis (analyzing numerical data or measurable patterns from the available information). Then, the articles on anticancer activity of herbal drugs were selected, and demonstrating anticancer effect of these herbal drugs and their compounds.

Schematic presentation: Shown in fig. 1.

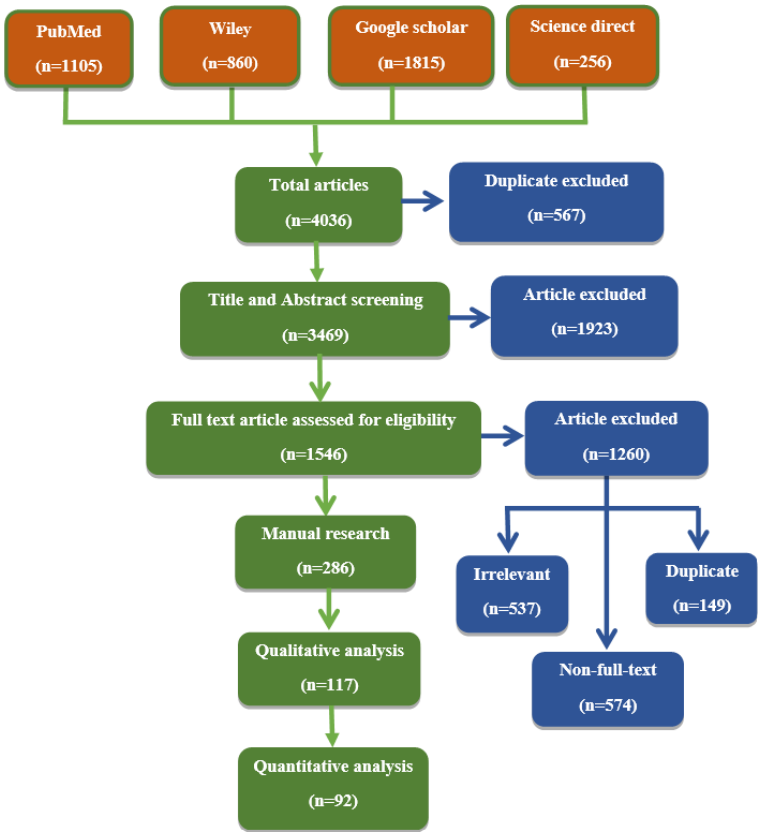

Fig. 1: Schematic presentation for methodology on literature survey

Anticancer activity of herbal drugs (table 1)

*Petroselinum sativum***,** commonly known as parsley, has been shown to induce cytotoxicity in various cancer cell lines, including prostate cancer cells (PC-3), Breast cancer cells (MCF-7, MDA-MB-231), lung cancer cells (NCI-H82), hepatocellular carcinoma cells (Hep-3B), Myeloid leukemia cells (K-562). The cytotoxic effects of *Petroselinum sativum* are attributed to the sensitization of these cancer cells, making them more vulnerable to treatment. This sensitization process enhances the effectiveness of therapeutic agents, leading to increased cell death and reduced tumor viability [17].

Phellodendron amurense, commonly known as the Amur cork tree, has been found to inhibit CREB (cAMP response element-binding protein) mediated COX-2 (cyclooxygenase-2) activation in lung cancer cell lines, specifically H1229 and A549. COX-2 is an enzyme that plays a significant role in inflammation and is often overexpressed in various cancers, including lung cancer. By inhibiting the CREB-mediated activation of COX-2, *Phellodendron amurense* potentially reduces inflammation and tumor growth [18].

Momordica charantia, commonly known as bitter melon, has been studied for its potential anticancer properties. Research indicates that it can induce cell cycle arrest and apoptosis in various cancer cell lines, including breast cancer (MCF-7) and cervical cancer (HeLa) cells. Bitter melon presents a promising natural compound for cancer therapy, particularly due to its ability to target cancer cells selectively while sparing normal cells [19].

Capsicum chinense, commonly known as habanero pepper, has been studied for its anticancer properties. The active compounds in this pepper, including capsaicin, have shown potential in inducing apoptosis and cell cycle arrest in various cancer cell lines such as hepatocellular carcinoma (HEPG2), colon cancer (Colo205), and glioblastoma (A172) cells [20].

Allium sativum, commonly known as garlic, and its derivatives have demonstrated significant anticancer properties. Research has shown that garlic and its active compounds, such as alliin, allicin, and allyl sulfides, can induce DNA repair, slow down cell division, and promote apoptosis in various cancer cell lines, including prostate cancer (DU145), breast cancer (MCF-7), human leukemia (HL-60), and cervical cancer (HeLa) [21, 22]. Alliin and allicin compounds can modulate the expression of DNA repair genes, ensuring the integrity of the genome. They increase the activity of enzymes involved in base excision repair (BER) and nucleotide excision repair (NER). Scavenge reactive oxygen species (ROS) that could otherwise cause DNA damage, thus reducing oxidative stress-induced mutations.

Allyl Sulfides enhance repair of damaged DNA by activating tumor suppressor proteins like p53, which is crucial for coordinating repair pathways.

Zingiber officinalis, commonly known as ginger, has been studied for its anticancer properties. Research indicates that ginger promotes apoptosis (programmed cell death) of cancer cells and has a preventive action against metastasis in various cancer cell lines, including prostate cancer, breast cancer, and cervical cancer [23].

Rosmarinus officinalis, commonly known as rosemary, has demonstrated significant anti-proliferative activity in various cancer cell lines. Studies have shown that rosemary extracts and its active compounds can inhibit the growth of prostate cancer (PC-3), breast cancer cells (MCF-7, MDA-MB-231), lung cancer cells (NCI-H82), liver cancer cells (Hep-3B), Myeloid leukemia (K-562), Adenocarcinoma cervical cancer cells (HeLa). Compounds like carnosol and ursolic acid obtained from rosemary disrupt mitochondrial membrane potential, leading to cytochrome c release and activation of caspase-9 and caspase-3. These triggers programmed cell death selectively in cancer cells. Rosemary compounds interfere with the G1/S and G2/M cell cycle checkpoints by inhibiting cyclins and cyclin-dependent kinases (CDKs) [17, 24].

Origanum vulgare, commonly known as oregano, has shown potential in preventing the spread of various cancer cells, including prostate cancer (PC-3), breast cancer (MCF-7, MDA-MB-231), lung cancer (NCI-H82), liver cancer (Hep-3B), and myeloid leukemia (K-562). Its anticancer properties can be attributed to several mechanisms: Compounds in oregano can induce programmed cell death (apoptosis) in cancer cells, thereby reducing their spread. Oregano may prevent the formation of new blood vessels that supply nutrients to tumors, inhibiting their growth. The high antioxidant content in oregano can neutralize free radicals, which can cause DNA damage, leading to cancer. Oregano may reduce the formation of carcinogenic heterocyclic amines that form when animal proteins are cooked at high temperatures, thus lowering cancer risk [17, 25].

Linum usitatissimum, commonly known as flaxseed, contains phytoestrogens called lignans, which have been shown to have beneficial effects in reducing the risk of estrogen-dependent breast cancer, such as the MDA-MB-435 cell line. By binding to estrogen receptors, lignans can block the stronger endogenous estrogens, leading to a decrease in the proliferative action of estrogen on breast tissue [26].

Triticum aestivum, commonly known as wheatgrass, contains various bioactive compounds, including the plant hormone abscisic acid (ABA). Abscisic acid is known for its role in plant physiology, particularly in response to stress and regulation of growth processes. Recent studies suggest that ABA may have potential anticancer properties. Research has shown that ABA can downregulate physiological processes and delay cell division in various cancer cell lines including: prostate cancer (PC-3), Breast cancer (MCF-7), lung cancer (A549), colon cancer (HCT-116), Pancreatic cancer cells (MIAPACA) [27, 28].

Aloe barbadensis, commonly known as Aloe vera, is a plant renowned for its medicinal properties. One of the key bioactive compounds in Aloe vera is acemannan, a polysaccharide that has been studied for its therapeutic potential, particularly in cancer treatment. Acemannan can stimulate the immune system to produce Tumor Necrosis Factor (TNF). TNF has been shown to target and destroy liver cancer cells (HEPG2). Studies have indicated that acemannan can induce apoptosis in breast cancer cells, including MCF-7 and BT-474 cell lines as indicated by DNA fragmentation [29].

Tancetum parthenium, commonly known as feverfew, contains several bioactive compounds, with parthenolide being one of the most notable. Parthenolide has been studied for its anticancer properties and has shown promising results in various types of cancer including lung cancer cells (A549) and Colon adenocarcinoma (HT-29). Parthenolide inhibits nuclear factor-kappa B (NF-κB), a protein complex that controls the transcription of DNA and plays a key role in regulating the immune response to infection. Inhibition of NF-κB can reduce inflammation and hinder cancer cell survival. Parthenolide induces oxidative stress and disrupts mitochondrial function in cancer cells, leading to the activation of apoptotic pathways. This results in the self-destruction of cancer cells [30].

Trifolium pratense (red clover) and *Genista tinctoria* (dyer's broom) contain phytoestrogens, which are plant-derived compounds that mimic the action of estrogens. These phytoestrogens can interact with estrogen receptors in the body and may help modulate the effects of endogenous estrogens. This modulation can be beneficial in certain hormone-related cancers like prostate cancer (IA8-ARCaPand LNCaP/HIF-1α), breast cancers (MCF-7 and MDA-MB-231), colorectal cancers (HT-29), as the phytoestrogens may downregulate the action of the body's estrogen, potentially inhibiting the growth and spread of cancer cells [31, 32].

Echinacea purpurea, commonly known as purple coneflower, is well-known for its immune-boosting properties. Research suggests that it can activate macrophages, increase T-cell activity, and stimulate the production of interferon, which are all crucial components of the immune response against cancer cells. *Echinacea purpurea* shows promise in enhancing the immune response against cancer and exerting direct anti-proliferative effects on certain cancer cell lines, such as colon cancer (COLO320) and pancreatic cancer (MIA-PaCa-2). These properties make it a potential complementary therapy in cancer treatment [33].

Artemisia annua, commonly known as sweet wormwood, is a plant that produces a compound called artemisinin. This compound has shown significant potential in cancer treatment due to its selective targeting of cancer cells. Artemisinin targets cancer cells selectively, such as prostate (PC-3, A549), breast (MCF-7, MDA-MB-231, T-47D), and pancreatic (MIA PaCa-2) cancer cells, without harming normal cells. This selectivity is primarily because cancer cells have a higher iron intake compared to normal cells. When artemisinin is combined with iron-carrying transferrin, it is more readily absorbed by cancer cells. Inside the cells, artemisinin triggers cytotoxic effects, leading to the destruction of cancer cells [34, 35].

Eugenia caryophyllata (also known as *Syzygium aromaticum* or commonly as clove) is a plant that possesses potent anti-cancer properties, particularly in targeting various types of cancer cells. Clove has shown effectiveness in targeting and killing several types of cancer cells, including prostate cancer cells (DU-145), breast cancer cells (MCF-7 and MDA-MB-231), Cervical cancer cells (HeLa). Clove extracts inhibit the proliferation of these cancer cells, preventing them from growing and spreading [36].

Glycyrrhiza glbra, commonly known as licorice root, is a medicinal plant with significant anti-cancer properties, particularly in the treatment of breast cancer cells (MCF-7) and Cervical cancer cells (HeLa) in humans. The extract influences the expression of Bcl-2 and Bax proteins, which are key regulators of apoptosis (programmed cell death). Bcl-2 typically prevents apoptosis, while Bax promotes it. By modulating the balance between these factors, licorice root encourages the apoptosis of cancer cells, aiding in their elimination [37, 38].

Berberis vulgaris, commonly known as barberry, has demonstrated significant anti-cancer properties, particularly against breast cancer (MCF-7). The extract from *Berberis vulgaris* effectively inhibits the proliferation of MCF-7 breast cancer cells, which means it prevents the cancer cells from multiplying and spreading [39].

Camellia sinensis, commonly known as tea, particularly green tea, contains powerful bioactive compounds that contribute to its anti-cancer properties. Tea is rich in vitamin C, which helps combat cancer-causing free radicals. It also has a low glycemic index and strong cleansing properties, contributing to overall health. Epigallocatechin Gallate (EGCG) is a potent antioxidant that helps neutralize harmful free radicals in the body. EGCG induces growth arrest in prostate cancer cells (DU-145) by affecting cell cycle regulatory proteins, effectively halting the progression of cancer cells. It activates killer caspases, which play a vital role in the execution of apoptosis and suppresses oncogenic transcription factors, which can turn normal cells into cancerous ones [40].

Allium cepa, commonly known as onions, are indeed rich in polyphenols and antioxidants, which contribute to their health benefits, including cancer prevention. Polyphenols are plant compounds that have been associated with a reduced risk of various diseases, including cancer, due to their antioxidant properties. One of the key polyphenols found in onions is quercetin, a flavonoid with potent antioxidant and anti-inflammatory effects. Research has shown that quercetin can inhibit the growth of cancer cells in various types of cancers, including colon cancer (specifically in SW-620 and HCT-116 cell lines) and breast cancer (in MDA-MB-231 cell lines). Quercetin has been observed to induce apoptosis (programmed cell death) in these cancer cells, which is a critical mechanism in preventing the spread of cancer [41, 42].

Digitalis purpurea l and Digitalis lanata induce apoptosis in prostate cancer (DU145, PC3), breast cancer cells (SK-MEL28, MDA-MB-435), and lung cancer cells (A549), colon cancer (HCT-116), ovarian cancer cells (OVCAR-3, OVCAR-5, and NCI-ADRES) by proliferation. It exhibited significant tumor growth inhibition in various cancers [43].

Annona muricata, commonly known as graviola or soursop, has gained attention for its potential anti-cancer properties. Graviola contains a group of natural compounds known as annonaceous acetogenins, which have been shown to have cytotoxic effects on various cancer cells including breast cancer cells (MCF-7), pancreatic cancer cells (FG/COLO357 and CD18/HPAF) [44, 45].

Silybum eburneum shows the Antiproliferative activity on Prostate cancer (LNCaP, DU145, and PC3), colorectal adenocarcinoma (HT-29), Lung cancer (NCIH-23), and Breast cancer (MCF-7) cells [46].

Curcuma longa, commonly known as turmeric, contains curcumin as its active compound, which has been extensively studied for its anti-cancer properties. Curcumin exerts its effects on cancer cells through various mechanisms, promoting apoptosis (programmed cell death) and inhibiting cell proliferation across several types of cancer: prostate cancer (PC3) cells, liver cancer (HEPG2) cells, colorectal cancer (LoVo and HT-29) cells, Glioblastoma cancer cells (A172), ovarian cancer (A2780 and CP70) [47]. Curcumin's ability to target multiple cancer types through various pathways, including oxidative stress, mitochondrial dysfunction, ER stress, and the activation of apoptotic proteins, makes it a promising compound in cancer therapy [48].

Polygonum cuspidatum, also known as Japanese knotweed, is a plant known for its bioactive compounds, particularly resveratrol, which has been widely studied for its potential anti-cancer effects. The anti-cancer properties of *Polygonum cuspidatum* are attributed to its ability to interfere with cellular processes critical for cancer cell survival and proliferation by inhibiting ERK1/2 cascade. Resveratrol has been found to block Prostate cancer cell (PC-3M-MM2 cells, DU145 and LNCaP), Breast cancer (MCF-7), lung cancer (NCI-H460, A549, A579, H1975), liver cancer (HEPG2), colorectal cancer (DLD1 and HT29, HCT-116 and CaCo-2), ovarian cancer (Pa-1, MDAH2774, SKOV3) cells [22, 32, 49].

Oryza sativa, commonly known as rice, particularly its bran and certain bioactive compounds found in rice, has been studied for its potential anti-cancer properties. Research has shown that rice and its components can exert anti-proliferative and pro-apoptotic effects on cancer cells, particularly in breast cancer (MDA-MB-231, MCF-7, and MCF10At). It reduces cell proliferation in hepatocellular carcinoma cell lines (HEPG2), Colorectal cancer cell lines (HT-29), Cervical cancer (HeLa), ovarian cancer (Caov-3) cell lines [22, 32, 50].

Garcinia Mangostana, commonly known as mangosteen, is a tropical fruit known for its bioactive compounds, particularly xanthones such as α-mangostin. These compounds have been studied for their potential anti-cancer properties, and research suggests that α-mangostin may induce apoptosis (programmed cell death) in various cancer cells by engaging the endoplasmic reticulum (ER) stress pathway: prostate cancer cells (LNCaP, 22RV1), liver cancer cells (Hep3B), cervical cancer cells (HeLa), ovarian cancer cells (HEY, A2780) [22].

Pimpinella haussknechtii, a plant belonging to the Apiaceae family, has been studied for its potential anti-cancer properties, particularly its effects on breast cancer cells. Research suggests that extracts or compounds derived from *Pimpinella haussknechtii* can induce apoptosis in breast cancer cells, specifically the MCF-7 cell line, through mechanisms involving protein aggregation and endoplasmic reticulum (ER) stress [22].

Salvia miltiorrhiza, also known as Danshen, is a traditional Chinese medicinal herb renowned for its diverse therapeutic properties, including its antitumor effects. Research has shown that *Salvia miltiorrhiza* exhibits anti-cancer activity across various cancer types including breast cancer, lung cancer (A549, H1975, PC9), liver cancer (SK-Hep-1, Bel-7404, HepG2HL-7702), Colorectal cancer (HCT116, HT29, HCT8), leukemia (THP-1, KG-1, Kasumi-1), ovarian cancer cells (SKOV3) [51]. The herb's ability to regulate the Bcl-2 family of proteins, which includes both pro-apoptotic and anti-apoptotic members, plays a significant role in balancing the survival and death of cancer cells.

Dioscoreae rhizome induce apoptosis in cervical cancer cells (HeLa, C33A) [22].

Catharanthus roseus, commonly known as the periwinkle plant, produces several important alkaloids, such as vincristine and vinblastine, which are well-known for their anti-cancer properties. The cytotoxicity of these vinca alkaloids, particularly in breast cancer cells like MCF-7, is primarily due to their effects on tubulin and microtubule dynamics [52, 53].

Sphaeranthus indicus, also known as the globe thistle, is a medicinal plant that has shown promising anti-cancer properties. Research has indicated that extracts from *Sphaeranthus indicus* are effective in inhibiting the proliferation of various cancer cell lines: prostate cancer cells (PC-3 and DU-145), breast cancer cells (MCF-7), lung cancer cells (A549), colon cancer cell (Colo-205) [52].

Radix sophorae, derived from the Sophora flavescens plant, is used in traditional medicine and has shown potential anti-cancer properties. Research indicates that its extracts can induce apoptosis in liver cancer cells, such as HEPG2, through both extrinsic and intrinsic pathways [52].

Saussurea lappa induce apoptosis in liver cancer (HEPG2), cervical cancer (HELA) [52].

Litchi chinensis, commonly known as lychee, has demonstrated notable antiproliferative effects against various cancer cell lines, including breast cancer cells. Research has shown that extracts from lychee fruit exhibit significant anti-cancer activity in breast cancer cell lines such as MCF-7 and MDA-MB-231 [52, 54].

Pinus densiflora, commonly known as the Korean red pine, has shown promising results in inhibiting the growth of various cancer cell lines, including breast cancer cells (MCF-7) and leukemia cells (HL-60).

Polyalthia longifolia inhibited cell proliferation of colon cancer cell lines (SW-620), Human leukemia cell (HL-60) lines [52].

Coffea canephora shows Antiproliferative effect against Breast cancer cells (MCF7 and MDA-MB-231), cervical cancer cells (HeLa) [32, 55].

Solanum nigrum shows induction of apoptosis in cervical cancer cells (HeLa) [56].

Table 1: Plant details along with their pharmacological activities

S. No.	Common name (fig. 2)	Chemical compound (fig. 3)	Biologcal source	Type of cancer (fig. 4)	Cancer cell models (fig. 5)	Mechanism of action	Ref
1.	Parsley	Myristicin, Luteolin, Apigenin	*Petroselinum sativum*	Lung cancer Myeloid leukemia Breast cancer Hepatocellular carcinoma Prostate cancer	NCI-H82 K-562 MCF-7, MDA-MB-231 Hep-3B PC-3	It sensitize cancer cells followed by cytotoxicity.	[17]
2.	Amur cork tree	Berberine	*Phellodendron amurense*	Lung tumor	H1229, A549	It inhibited CREB mediated Cox-2 activation.	[18]
3.	Bitter gourd, Karala	Alpha-eleostearic acid	*Momordica charantia*	Breast cancer Cervical cancer	MCF-7 HeLa	Arresting cell cycle arrest and activating apoptosis	[19]
4.	Habanero pepper	Capsaicinoids, Capsaicin	*Capsicum chinense*	Human hepatocellular carcinoma Colon cancer Human glioblastoma	HEPG2 Colo205 A172	Induce apoptosis and cell cycle arrest	[20]
5.	Garlic	Alliin, allicin, allyl sulfides	*Allium sativum*	Human leukemia Breast cancer Cervical cancer Prostate cancer	HL-60 MCF-7 HELA DU145	DNA repair, slowing down of cell division and apoptosis	[21, 22]
6.	Ginger	Gingerol, Shogaols, Zingerone	*Zingiber officinalis*	Prostate cancer Breast cancer Cervical cancer	LNCaP, C4-2, C4-2B, DU145, PC-3 MDA-MB-231, MCF-7 HeLa	Apoptosis of cancer cells and inhibition of metastasis	[23]
7.	Rosemary	Rosmarinic acid, Carnosol	*Rosmarinus officinalis*	Adenocarcinoma cervical cancer Lung cancer Myeloid leukemia Breast cancer Hepatocellular carcinoma Prostate cancer	HeLa NCI-H82 K-562 MCF-7, MDA-MB-231 Hep-3B PC-3	Inhibits growth and proliferation of cancer cells	[17, 24]
8.	Oregano	Carvacrol	*Origanum vulgare*	Hepatoma cancer Lung cancer Myeloid leukemia Breast cancer Prostate cancer	HEPG2 NCI-H82 K-562 MCF-7, MDA-MB-231 PC-3	Preventing metastasis, reducing carcinogenic heterocyclic amines	[25, 17]
9.	Flax seed	Omega-3 fatty acid, Secoisolariciresinol diglycoside(SDG)	*Linum usitatissimum*	Breast cancer	MDA-MB-435	Phytoestrogens down-regulate estrogenic action, reducing the risk of estrogen-dependent breast cancer.	[26]
10.	Wheatgrass	Abscisic acid	*Triticum aestivum*	Breast cancer Colon cancer Prostate cancer Lung cancer Pancreatic cancer	MCF-7 HCT-116 PC3 A549 MIAPACA	The plant hormone abscisic acid occuring in the wheatgrass is responsible for its anticancer activity. This hormone down regulates physiological processes and delays cell division.	[27, 28]
11.	Aloe-vera	Acemannan	*Aloe barbadensis*	Hepatocellular carcinoma	HEPG2	Acemannan induce the production of Tumor Necrosis Factor that destroys cancer cells.	[29]
12.	Feverfew	Parthenolide	*Tancetum parthenium*	Lung carcinoma Colon adenocarcinoma	A549 HT-29	Parthenolides inhibits the pro-inflammatory signalling pathway and activated apoptosis	[30]
13.	Red clover	Genistein	*Trifolium pretense/Genista tinctoria*	Breast cancer Colorectal cancer Prostate cancer	MCF-7 and MDA-MB-231 HT-29 IA8-ARCaP and LNCaP/HIF-1α	Phytoestrogens down-regulate estrogen mechanism preventing breast cancer, prostate cancers.	[31, 32]
14.	Echinacea	Arabinogalactan	*Echinacea purpurea*	Pancreatic cancer Colon cancer	MIA-PaCa-2 COLO320	Activate macrophages, increase T-cell activity and increase production of interferon.	[33]
15.	Sweet wormwood	Artemisinin	*Artemisia annua*	Breast cancer pancreatic cancer prostate cancer	MCF-7, MDA-MB-231, T-47D MIA PaCa-2 PC-3 and A549	Artemisinin shows cytotoxic by reducing uptake of iron	[34, 35]
16.	Clove	Anthocyanins, Eugenol, Caryophyllene, eugenyl, naphthalene, sesquiterpenes	*Eugenia caryophyllata/ Syzygiumaromaticum*	Cervical cancer Breast cancer Prostate cancer	HeLa MCF-7 and MDA-MB-231 DU-145	Anthocyanins and other high antioxidants show antiproliferative and apoptotic effect	[36]
17.	Liquoriceroot	Polyphenols, glycyrrhizin	*Glycyrrhiza glbra*	Cervical cancer Breast cancer	HeLa MCF-7	Antiproliferation and modulates the expression of Bcl-2/Bax apoptotic regulatory factors.	[37, 38]
18.	Barberry	Berberine	*Berberis vulgaris/Berberis aristata*	Breast cancer	MCF-7	Berberine induce cytotoxic effect	[39]
19.	Tea	Catechin	*Camellia*	Prostate cancer	DU-145	High levels of vitamin C, low	[40]

S. No.	Common name (fig. 2)	Chemical compound (fig. 3)	Biologcal source	Type of cancer (fig. 4)	Cancer cell models (fig. 5)	Mechanism of action	Ref
			sinensis			glycemic index acting as a powerful antioxidant. EGCG (Epigallocatechin Gallate) act as an antiangiogenic factor, promotes apoptosis and induces cell growth arrest via cell cycle regulatory proteins, it also activates killer caspases, and supresses oncogenic transcription factors.	
20.	Onion	Quercetin	*Allium cepa*	Colon cancer Breast cancer	SW-620 and HCT-116 MDA-MB-231	Polyphenols and quercetin are potent antioxidants preventing cancer development.	[41, 42]
21.	Foxglove	Digoxin, Acteoside	*Digitalis purpurea l and Digitalis lanata*	Breast cancer Prosate cancer Lung cancer Ovarian cancer Colon cancer	SK-MEL28, MDA-MB-435 DU145, PC3 A549 OVCAR-3, OVCAR-5, NCI-ADRES HCT-116	Antiproliferative and antimetastatic.	[43]
22.	Graviola	Annonaceousacetogenins	*Annona muricata*	Pancreatic cancer Breast cancer	FG/COLO357 and CD18/HPAF MCF-7	Cytotoxic and antimetastatic	[44, 45]
23.	Milk thistle	Mixture of flavonolignans such as silibinin, silidianin, silicristin, and isosilibinin.	*Silybum eburneum or silybum marianum*	Prostate cancer Colorectal adenocarcinoma Lung cancer Breast cancer	LNCaP, DU145, PC3 HT-29 NCIH-23 MCF-7	Antiproliferative effect on cancer cells	[46, 47, 48]
24.	Turmeric	Curcumin	*Curcuma longa*	Glioblastoma cancer Colorectal cancer Ovarian cancer Prostate cancer Hepatocellular carcinoma Lung cancer	A172 LoVo and HT-29 A2780 and CP70 PC-3 HEPG2 NCI-H460, H1975	Anti-proliferative, apoptotic and cytotoxic effect	[22]
25.	Grapes	Resveratrol, proanthocyanidins	*Polygonum cuspidatum (Grapes, Blueberries, Peanut)*	Hepatoblastoma Lung cancer Ovarian cancer colorectal cancer Prostate cancer Breast	HEPG2 NCI-H460, A549, A579, H1975 Pa-1, MDAH2774, SKOV3 DLD1 and HT29, HCT-116 and CaCo-2 (PC-3M-MM2 cells, DU145 and LNCaP) MCF-7	Arrest the cell cycle, trigger apoptosis by inhibiting ERK1/2 cascade and modulating the expression of p53 and cyclin-dependent kinases block cancer growth.	[22, 49, 32]
26.	Rice bran	Tocotrienols, Tocopherol, α-Tocopheryl succinate Phytic acid	*Oryza sativa*	Cervical cancer Ovarian cancer Breast cancer Liver cancer Colorectal cancer	HeLa Caov-3 MDA-MB-231 HepG2 HT-29	Inhibits cell proliferation	[22, 50, 32]
27.	Mangosteen	α-mangostin, γ-mangostin, and garcinone E	*Garcinia Mangostana*	Prostate cancer Ovarian cancer Hepatocellular carcinoma Cervical cancer	LNCaP, 22RV1 HEY, A2780 Hep3B HeLa	Pro-apoptotic activity of α-mangostin.	[22]
28.	Aniseed, Fennel	Pimpinelol	*Pimpinella haussknechtii*	Breast cancer	MCF-7	Induce apoptosis by increasing protein aggregation and ER stress	[22]
29.	Red sage, tan-shen	Salvianolic acid A and B	*Salvia Miltiorrhiza*	Lung cancer Breast cancer Leukemia Colorectal cancer Ovarian cancer Liver cancer	A549, H1975, PC9 MCF-7, MDA-MB-231 THP-1, KG-1, Kasumi-1 HCT116, HT29, HCT8 SKOV3 SK-Hep-1, Bel-7404, HepG2, HL-7702	Induce apoptosis through caspase activation, cell cycle arrest, anti-angiogenic effect, and Bcl-2 family regulation.	[22, 51]
30.	Yam rhizome	Protodioscin	*Dioscoreae rhizome*	Cervical cancer	HeLa, C33A	It induce apoptosis in cancer cells.	[22]
31.	Periwinkle, Sadabahar	Vincristine and vinblastine	*Catharanthus roseus*	Breast cancer	MCF-7	Interactions with tubulin and disruption of microtubule function causing metaphase arrest.	[52, 53]
32.	Gorakhmundi, Mundi	Spaeranthine, Stigmasterol, eugenol	*Sphaeranthus indicus*	Lung cancer prostate cancer colon cancer breast cancer	A549 PC-3 and DU-145 Colo-205 MCF-7	Inhibits proliferation of cancer cells.	[52]
33.	Lightyellowsophra root	Leachianone A	*Radix sophorae*	Liver cancer	HEPG2	Activation of both extrinsic and intrinsic pathways of apoptosis	[52]
34.	Kushta, Kutha	Costunolide,	*Saussurea*	Liver cancer	HEPG2	induction of apoptosis	[52]

S. No.	Common name (fig. 2)	Chemical compound (fig. 3)	Biologcal source	Type of cancer (fig. 4)	Cancer cell models (fig. 5)	Mechanism of action	Ref
		Cynaropicrin	*lappa*	Cervical cancer	HELA		
35.	Litchi fruit	Epicatechin, procyanidin	*Litchi chinensis*	Breast cancer	MCF-7 and MDA-MB-231	Antiproliferative effects.	[52, 54]
36.	Pine needles, Japanese red pine	Caryophyllene, spathulenol	*Pinus densiflora*	Breast cancer Human leukemia	MCF-7 HL-60	PNE inhibited the growth of cancer cells and antiproliferative effects.	[52]
37.	Ashok, Mast tree	Polyfothine, polylongine	*Polyalthia longifolia*	Colon Human leukemia	SW-620 HL-60	inhibited cell proliferation of various human cancer cell lines	[52]
38.	Coffee beans	Caffeic acid, Caffeine	*Coffea canephora/Coffea arabica*	Breast cancer Cervical cancer	MCF7 and MDA-MB-231 HeLa	Antiproliferative effect against cancer cells	[32, 55]
39.	Makoy, deadly nightsade	Solasodine, Solasonine	*Solanum nigrum*	Cervical cancer	HeLa	induction of apoptosis	[56]

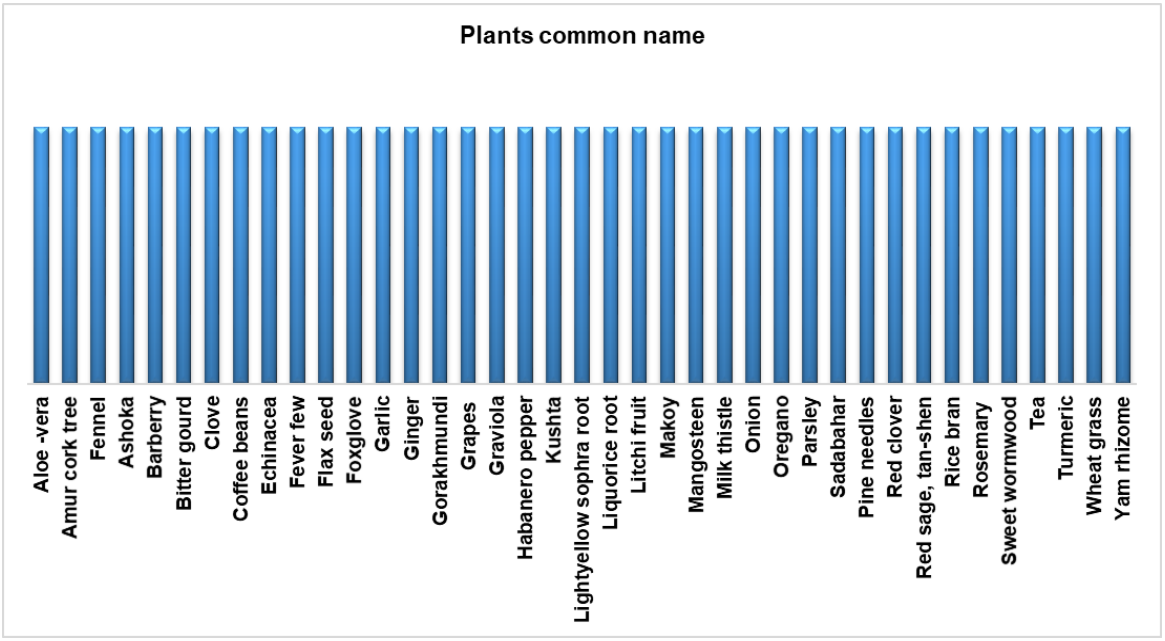

Fig. 2: Plants common name

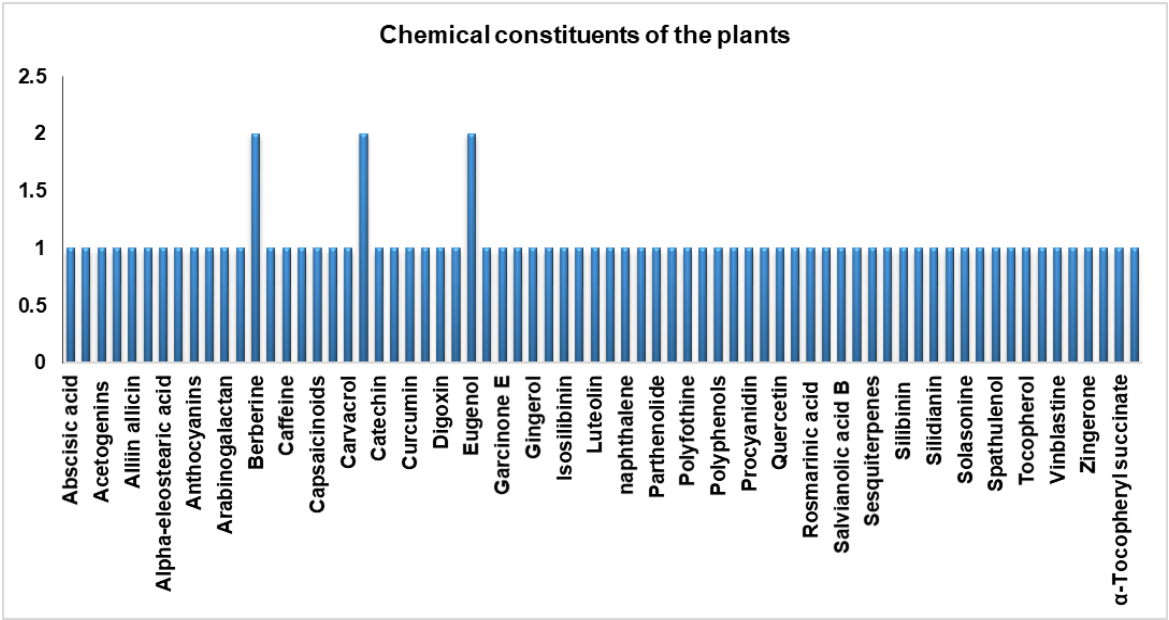

Fig. 3: Chemical constituents of the plants

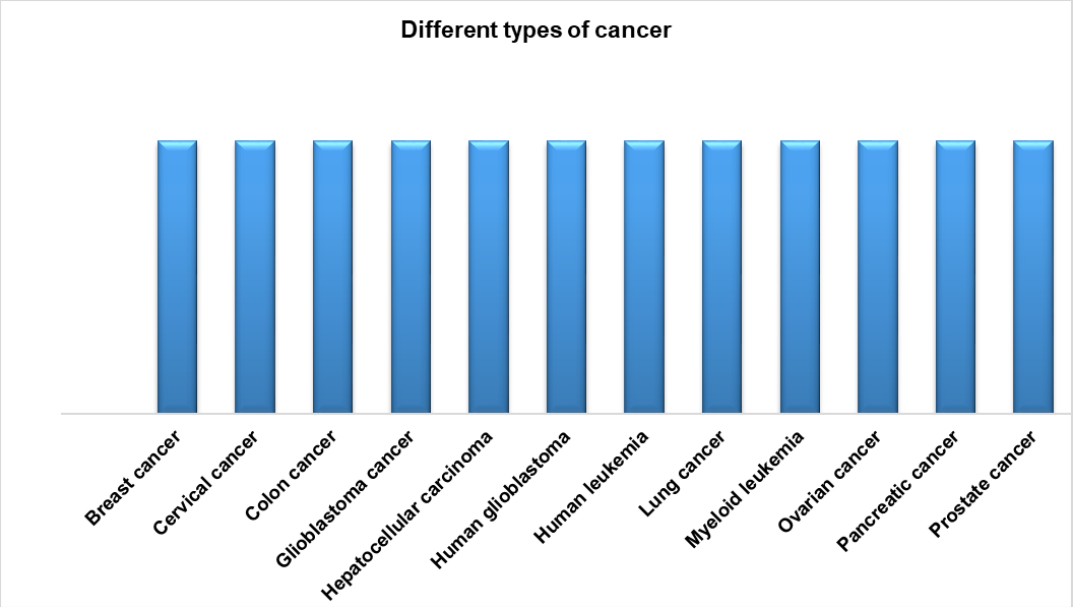

Fig. 4: Different types of cancer

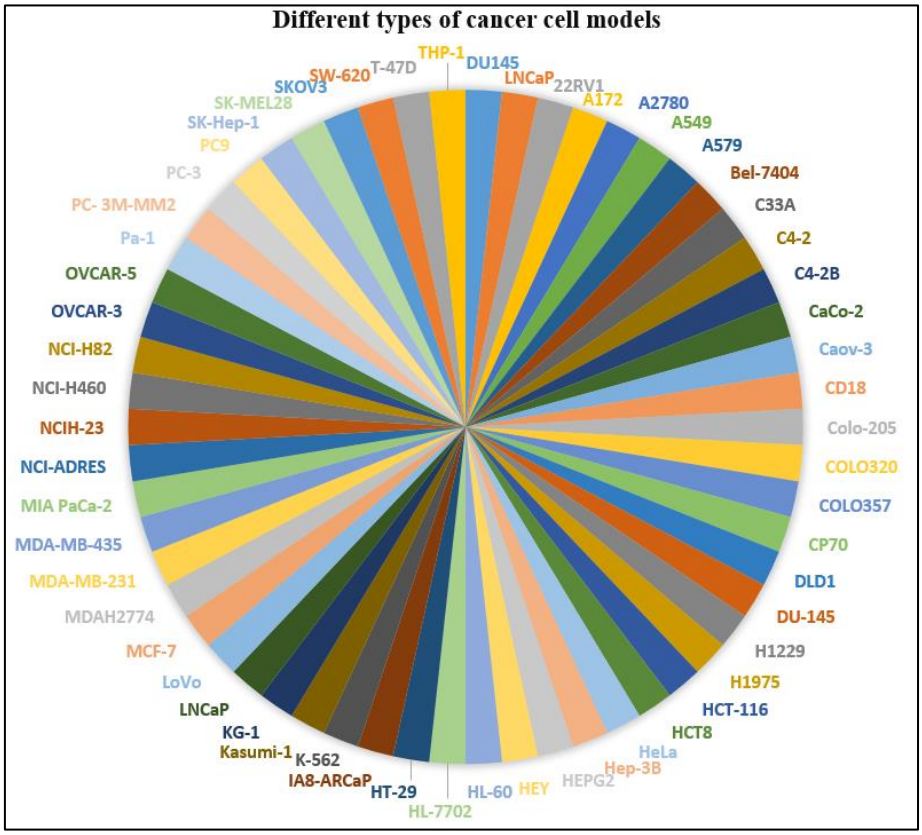

Fig. 5: Different types of cancer cell models

CONCLUSION

Herbal medicine has been used in traditional healing systems, such as Traditional Medicine and Ayurveda, for centuries to treat various health conditions, including cancer. It had been said that about 80% of drugs used in the treatment of cancer are of herbal origin, including anthracyclines, podophyllotoxins, taxanes and vinca alkaloids. Some herbal remedies have shown promise in these traditional systems. Many herbs contain compounds with anti-inflammatory and antioxidant properties (vitamins, enzymes, polysaccharides, polyphenols, flavonoids, minerals, lignins, xanthones, carotene etc.), which may help reduce the risk of cancer development by preventing DNA damage and inhibiting the growth of cancer cells. Despite use of herbal preparations extensively all across the continents, the evidence generated against cancer cells is non-scientifically generated, analyzed and or the models used in preclinical study do not matches with clinical condition of cancer. It is also believed that herbal medicine therapy could be a

complementary therapy along with chemotherapy, surgical therapy, radiation therapy and nuclear therapy.

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AUTHORS CONTRIBUTIONS

All authors equally contributed in the literature survey and preparation of manuscript. All authors participated in the design, interpretation of the studies and analysis of the data and review of the manuscript; Dr. Ritu Rani wrote the original review article, Mr. Sandeep and Mr. Abhay reviewed the manuscript.

CONFLICT OF INTERESTS

Declared none

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