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Review Article

Indian Medicinal Plants Having Anti-Cancer Properties

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ABSTRACT

These days, cancer is one of the deadliest disorders in the world, which has been estimated to cause 9.9 million passings in 2020. Customary medicines for cancer commonly include mono-chemotherapy or a combination of radiotherapy and mono-chemotherapy. In any case, the negative side impacts of these approaches have been broadly detailed and have provoked the look of unused helpful drugs. In this context, the scientific community has begun to look for inventive sources of anticancer compounds in conventional plants. Various studies have assessed the anticancer properties of common compounds inferred from plants, both in vitro and in vivo. In preclinical stages, a few promising compounds, such as the sulforaphane or diverse phenolic compounds, seem to be said. On the other hand, a few phytochemicals got positive results in clinical stages and were advanced and affirmed for cancer treatment, such as vinca. Alkaloids or the paclitaxel. These compounds are not excluded from confinements, such as low solubility, adverse side effects, etc. This review article aims to summarise some details about presently used phytochemicals in cancer treatment and promising candidates. In conclusion, more extensive research is required to develop efficient and safe phytochemical drugs in cancer treatment.

INTRODUCTION

Cancer is a disease in which uncontrolled abnormal cells grow by overlooking standard rules of cell division. Cancer cells create a degree of independence from these signals, coming about in uncontrolled development and multiplication. It can be deadly if this multiplication is permitted to proceed and spread. In reality, nearly 90% of cancer-related deaths are due to tumor spreading-a prepare called metastasis. Advanced cancer cell science is based on a simple principle: all mammalian cells share comparable atomic systems that control cell multiplication, separation and passing. Cancer is one of the deadliest diseases globally, especially in Western countries. According to the International Cancer

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Observatory, roughly 9.9 million people died in 2020 as a result of developing cancer.[1] Cancer credits a collection of disorders activated by the uncontrolled multiplication of malignant cells.

The global well-being burden has cleared out an intolerable passing toll worldwide. Conservative estimates show that cancer (of the liver, breasts, lungs, cervix uteri, stomach, and colorectal) causes almost 13% of yearly passings.[2] This unintended cell behavior may result from genetic hereditary qualities or an epigenetic-driven modification of essential qualities (oncogenes) related to the cell cycle and control of cell death (apoptosis). Cancerous cells are also characterized by dysregulation of modified apoptosis and abnormal behavior of microtubules, as they are included in the mitotic handle).[3,4]

Cancer initiation and development is a complex preparation that is subordinate to numerous steps, including hereditary modifications, growth/proliferation, vascularization, invasion, embolization, and survival/evasion of apoptosis. It may include one or more cellular changes that are spontaneous or start by presenting to a carcinogen. These changes make a potential for the influenced cells and cells to create into a cancer cell. Cancer depends on some external factors in environment like tobacco, chemicals, radiation and infectious organ. These factors are responsible for abnormal cell behaviour and uncontrolled multiplication.[5]

Medicinal plants have antioxidant and immunomodulatory qualities, as well as a variety of compounds with various anticancer effects.[6,7] The cells are shielded from oxidative damage by the antioxidant molecules. While there are already about 1500 known anticancer treatments and over 500 in clinical trials, there is still a need to produce many practical and efficient plant-based medications. India is known as the "Botanical Garden of the World" and is home to the greatest variety of medicinal plants. In India, there are around 8000 species of medicinal plants belonging to 400 families.[8] However, only a small number of them have been found to have therapeutic qualities. Three-quarters of people worldwide treat illnesses with traditional medicine or herbs, according to the World Health Organization (WHO). The usage of plants and phytomedicines has grown within the past 20 years.[9] About half of the medications used in clinical therapy today are derived from natural sources. Many of them can induce apoptosis in different types of human cancer cells.[10] More than 60% of anticancer drugs have been identified as originating from natural sources, such as microbes, plants, and marine life.[11,12]

The U.S. National Cancer Institute (NCI) launched the plan to discover plant anticancer medicines in 1957. Through the study of more than 35,000 plant species, the NCI program has discovered numerous promising therapeutic candidates, including vincristine, vinblastine, taxol, indicine-N-oxide, etoposide analogs, and camptothecin.[13] Vinca alkaloids, such as vinblastine and vincristine, derived from Catharanthus roseus and used to treat leukemia, bladder cancer, and testicular cancer, are among the significant and useful medications derived from higher plants. Paclitaxol (Taxol TM), initially developed from Taxus brevifolia, was used to treat breast and ovarian malignancies on the basis of the theory that it would bind the microtubule's tubulin component and stabilize it for normal disintegration.[14,15]

PLANTS HAVING ANTICANCER PROPERTIES –

This section summarizes currently available information regarding the medicinal plants having anticancer properties.

2.1] Plant name- *Allium sativum L.*

Active compound- Allicin

It is extracted from Allium species, including garlic (Allium sativum L.) and onions (Allium

cepa L.), as well as shallots (Allium ascalonicum L.). The sulfur-containing volatile oil known as Allicin, also known as diallyl thiosulfinate, is produced when tissue damage occurs to the non-proteinogenic amino acid S-allyl cysteine sulfoxide (alliin), which is catalyzed by the enzyme alliinase.[16,17]

Allicin has demonstrated potential as an antibacterial, antifungal, and anticancer agent.[17] It also demonstrates activity in cardiovascular disorders (CVD) by suppressing cardiac hypertrophy, preventing hyperlipidemia, inhibiting platelet aggregation, and inducing vasodilation.[18]

According to its anticancer potential, Allicin suppresses the Akt/mTOR signaling pathway, which starts autophagy-dependent cell death.[19] It has demonstrated that, via altering the p53 signalling pathway, Allicin causes apoptosis and controls biomarker expression in breast cancer in vitro.[20] Furthermore, it was discovered that Allicin can suppress VCAM-1 expression in MCF-7 cells.[21] Furthermore, Allicin can cause the SGC-7901 cells that represent stomach cancer to undergo apoptosis and suppress telomerase activity.[22] It was demonstrated that in glioma, Allicin effectively reduced proliferation, induced apoptosis, and improved the activation of both intrinsic and extrinsic apoptotic signalling pathways in U251 glioma cells vitro.[23] Furthermore, it has been demonstrated that Allicin suppresses the ability of U87MG cells to proliferate and induces apoptosis, which is mediated by the MAPK/ERK signalling network, the Bcl2/Bax mitochondrial pathway, and antioxidant enzyme systems. Allicin can activate the JNK pathway in ovarian cancer, which results in the translocation of Bax within the mitochondria and the release of cytochrome from the mitochondria, ultimately causing SKOV3 cell apoptosis in glioblastoma cancer cells.[24]

Allicin inhibits human glioblastoma cell development by causing G2/M and S phase cell cycle arrest, which slows the tumor cells' growth over time .[25] Allicin inhibits NRF2, which is primarily how it slows the migration and invasion of cervical cancer cells.[26] It was discovered that in lung carcinoma, it inhibits the TIMP/MMP balance and reduces the activity of the PI3K/AKT signalling pathway, hence preventing the invasion of lung adenocarcinoma cells.[27]

2.2] Plant Name- *Betula alba.*

Active Compound – Betulinic acid .

A pentacyclic triterpene, betulinic acid (B.A.) is present in the bark of white birches, Betula alba, and other plant species. B.A. has documented Numerous biological actions, including antiviral, antiparasitic, antibacterial, and anti-inflammatory properties. Notably, B.A. has been shown to inhibit cancer cell proliferation specifically.

According to reports, B.A. is an anticancer drug targeting neuroectodermal tumours. It has been shown to cause apoptosis in primary tumour cultures of neuroectodermal origin and in neuroblastoma cells resistant to doxorubicin.[28]

Additionally, it demonstrated activity against primary tumour cells isolated from individuals suffering from medulloblastoma and glioblastoma and against their cell lines. However, it was not cytotoxic against in vitro mouse neurones.[29]

It was recently reported that B.A. has a proapoptotic effect on different tumour cell lines. Human myelogenous leukaemia (K562), human breast cancer (SKBR), and human colon cancer (Colo-205) cell lines underwent apoptosis upon treatment with BA.[30]

2.3] Plant name-*Camellia sinensis Theaceae Gallate.*

Active compound-EGCG (Epigallocatechin)

EGCG, commonly called epigallocatechin gallate, is a naturally occurring flavonoid belonging to the catechin (Galvan-3-ol) subclass. It has a complicated structure and is classified as a

polyphenolic substance. Its flavanol core, or flavan-3-ols, is esterified with gallic acid.[31] Although several fruits, nuts, and cocoa-based items contain EGCG, green tea (Camellia sinensis Theaceae) is still considered the primary source of this substance.[32]

As per report EGCG functions as a metal chelating agent, inhibits angiogenesis, modifies redox reactions, induces apoptosis and cell arrest, inhibits certain proteins and factors involved in the development of cancer, stabilizes p53 for its antitumor activity, and affects cell proliferation in its capacity as an anticancer product.[33]

Furthermore, EGCG uses a variety of methods to cause cancer cells to undergo apoptosis and cell arrest. The MCF-7 breast cancer cell is one example of how the apoptosis-related proteins caspase-3, caspase-9, and PARP-1 are activated.[34] Through the production of apoptotic molecular markers, particularly in HuCC-T1 cholangiocarcinoma cells, such as Bax, caspases, and cytochrome c (cyt. c).[35] Decrease in the protein expression of Bcl-2 and adenosine triphosphate binding cassette subfamily G member 2 (ABCG2), while increasing the expression of Bax and caspase-3, particularly in human esophageal squamous carcinoma cells.[36] And, particularly in thyroid cancer, inhibition of the extracellular signal-regulated kinase (ERK)/mitogen-activated protein kinase (MAPK)/Ras/Raf signaling pathway.[37] By preventing the H1299 lung cancer cells' PI3K/Akt serine/threonine kinase 1 signaling pathway from becoming activated.[38]

In reports it is demonstrated that EGCG improved pathological lesions of the precancerous lesions of gastric cancer (PLGC) and enhanced the effect of apoptosis promotion in PLGC rats.[39]

Additionally, MMP-2 and MMP-9, which help facilitate cell invasion and damage the basement membrane and are frequently overexpressed in cancer, can be effectively inhibited by EGCG.[40]

In relation to breast cancer, it was discovered that EGCG inhibited rRNA transcription and cell proliferation by activating KDM2A in MCF-7 cells. Additionally, EGCG aids in the activation of KDM2A by stimulating the synthesis of ROS and 5' AMP-activated protein kinase (AMPK). Fundamentally, EGCG inhibited rRNA transcription and cell proliferation in MCF-7 cells, but it was not observed in non-tumorigenic MCF10A cells.[41]

2.4] Plant name- *Curcuma longa*

Active compound- Curcumin

Curcuma longa (Family: Zingiberaceae) and several other Curcuma species contain curcumin, diferuloylmethane, as its primary naturally occurring polyphenol. Turmeric is a yellow-coloured natural substance frequently used as a food spice and colorant. Due to the numerous health benefits of curcumin, it has been utilized as a medicinal herb for a long time in Asian countries. Anti-inflammatory, antiviral, wound-healing, antibacterial, antioxidant and perhaps anticancer and chemopreventive properties are a few of these.[42]

Preclinical research using a range of cell lines has demonstrated that curcumin inhibits cancer development. These cell lines include prostate, pancreatic, ovarian, oral epithelial leukaemia, hepatic, breast, cervical, gastric, and colon cancers.[43]

The antioxidant qualities of curcumin, which can raise serum concentrations of antioxidants such as glutathione peroxidase (GPx), superoxide dismutase (SOD), and lipid peroxides, are one of the primary mechanisms underlying its anticancer benefits. Additionally, curcumin suppresses the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) via lipoxygenase/cyclooxygenase and xanthine hydrogenase/oxidase, among other ROS-generating enzymes. Curcumin is a good scavenger for several kinds of free radicals.[44]

Furthermore, curcumin can alter several signalling pathways linked to cancer development, including those that decrease angiogenesis and induce apoptosis. Furthermore, it has been observed that curcumin also causes apoptosis in human acute monocytic leukemia THP-1 cells via activating the JNK/ERK/AP1 pathways. Curcumin can potentially inhibit cancer cells' lactate synthesis and glucose uptake by down-regulating pyruvate kinase M2 (PKM2), hence exerting its anticancer action.[45] Additionally, curcumin can cause cell cycle arrest at the G2/M phase, most likely through upregulating the expression of P21 and reducing that of CDC2 and CDC25. This outcome was noted in cases of haematological cancer.[46]

Furthermore, curcumin has impacted non-small cell lung cancer cell development and induced G0/G1 phase arrest through the inactivation of the Wnt/\-catenin pathway controlled by MTA1 (metastasis-associated protein1). Furthermore, several studies indicate that curcumin targets various microRNA (miRNA) expressions, including miR-181b, miR-203, miR-9, miR-19, miR-21, miR203, miR-9, and miR-208, to exhibit its anticancer characteristics.[47]

2.5] Plant name- Glycine max

Active compound- Genistein

As a phytoestrogen, genistein is an isoflavonoid with a skeleton consisting of 15 carbons. It was named after the genus of this plant, Genista tinctoria, after it was initially isolated from it in 1899. Nonetheless, it is the primary secondary metabolite in Glycine max (soybean) and Trifolium species. The most significant sources of genistein are soybeans, foods made with soy, and beverages made with soy.[48]

Recently a study has revealed it reduced tumor growth and development in the hepatocellular cancer models of nude mice and Wistar rats, as well as in the gastric cancer model of Wistar rats, demonstrating how genistein works against cancer by causing apoptosis, reducing proliferation, and inhibiting angiogenesis as well as metastasis.[49]

The relationship between genistein and prostate cancer has been thoroughly investigated in vivo using a variety of animal models, including the Lobund-Wistar rat, a special kind of rat in which 30% of the population develops metastatic prostate cancer on its own, and SCID mice that have been transplanted with human prostate carcinoma cells (LNCaP, PC3, and DU-145). In certain in vivo investigations, normal rats were utilized to assess the prostate's toxicity and the impact of genistein on androgen and estrogen receptor.[50]

It directly and indirectly inhibits cyclooxygenase-2 (COX-2) by squelching COX-2 activating factors such Nf-B and activated protein-1 (AP-1). Overexpression of COX-2 has been linked to lung, breast, colon, and pancreatic cancers; suppression of COX-2 has been associated with a reduction in the growth of malignant tumors in the colon and esophagus.[51]

It initiates cell cycle arrest in pancreatic cancer cells' G0/G1 phase.[52] In glioblastoma, melanoma, and breast cancer, genistein has been shown to downregulate matrix metalloproteinase-2 (MMP-2) expression levels. In prostate cancer cell lines, it has also been shown to regulate the caspase-3 and p38MAPK pathways.[53]

By blocking Akt and NF-B cascades in PC3 and MDA-MB-231 breast cancer cell lines and the IL-6/STAT3 pathway in MDA-MB-453 breast cancer cell lines, genistein can affect metastasis and trigger apoptosis.[54] This ultimately results in a reduction in cell proliferation. Additionally, in HT-29 colon cancer cells, LNCaP prostate cancer cells, cervical cancer cell lines, and other cancer cell cultures, genistein reduces phosphorylated Akt.[55]

2.6] Plant name- *Glycyrrhiza glabra*

Active Compound – Glycyrrhizinic acid.

Traditionally, liquorice, or Glycyrrhiza glabra (family: Fabaceae), has been used to cure many illnesses, such as cough, pharyngitis, laryngitis,

stomach and intestinal ulcers, etc. Additionally, a wide range of pharmacological properties, including antioxidant, anti-inflammatory, antitumor, antimicrobial, antiviral, antiprotozoal, antifungal activity, chemopreventive, antinephritis activity, antidepressant activity, anxiolytic, anticonvulsant activity, and antidyslipidaemic activity.[56]

It was reported that G.C. (Gastric cancer) proliferation was inhibited by G.A. (Glycyrrhizinic acid)[57]

Alcoholic extract of G. glabra showed decreased cell viability in the C6 glioma cell line, depending upon the dose. A molecular docking study showing possible binding pattern of these compounds against TOP I and TOP II.[58]

Numerous studies have detailed Gly's antiviral capabilities, which include broad-spectrum antiviral activity against viruses of both human and animal origin. Human immunodeficiency virus (HIV), herpes simplex virus (HSV), coronavirus, influenza virus, and other oncogenic viruses like human papillomavirus (HPV), Kaposi's sarcoma herpesvirus (KSHV), and Epstein-Barr virus (EBV) are among the viruses for which Gly has demonstrated antiviral activity.[59]

It is also believed that Gly's anticancer effect on cervical cancer cells is achieved through blocking the Notch signaling pathway, [60]

Furthermore, through directly binding and inhibiting HMGB1 (high-mobility group box-1), an immunosuppressive cytokine that aids altered cells in evading the immune system, Gly also helps regulate the cancer microenvironment.[61]

2.7] Plant name-*Morus alba (Moraceae)*

Active compound- Quercetin

Naturally lipophilic, quercetin is one of the most abundant flavonoids. Flavonoids, which are mostly found in plant seeds, bark, leaves, and flowers, are recognized for their low molecular weight and phenolic composition. There are six kinds of flavonoids, and quercetin is in the flavonol subclass.Many foods, including capers, apples, berries, grapes, brassica vegetables, pepper, asparagus, onions, broccoli, shallots, cherries, tea, and tomatoes, contain quercetin. Additionally, quercetin has been found in a number of therapeutic plants, including Hypericum perforatum, Ginkgo biloba, and Sambucus canadensis.[62]

According to reports, Quercetin has been demonstrated to have pharmacological properties, including antiviral, antibacterial, anti-inflammatory, and anticarcinogenic properties.[63] It plays a major role in anticancer such as the process of apoptosis induction through mitochondrial pathways, which includes activation of caspase-9 and caspase-3, cytochrome c (Cyt c) release, and poly-ADP-ribose polymerase (PARP) breakage.[64] Furthermore, quercetin triggers cell death via both the intrinsic and extrinsic routes of apoptosis by activating proapoptotic genes and inhibiting antiapoptotic ones. Additionally, in primary effusion lymphoma (PEL) cells, quercetin particularly inhibits the PI3K/AKT/mTOR and STAT3 pathways. This results in the downregulation of the production of pro-survival cellular proteins such c-FLIP, cyclin D1, and c-Myc.[65]

The anticancer action of quercetin was shown concerning thyroid cancer by lowering chymotrypsin-like proteasome activity and downregulating Hsp90 levels.[66] Regarding ovarian cancer, several in vitro investigations have shown that quercetin suppresses the ovarian cancer cell line PA-1's motility, adhesion, proliferation, and survival.[67] It also inhibits cancer angiogenesis. Quercetin, on the other hand, promotes the expression of E-, N-cadherin, β-catenin, and snail, and reduces the viability of colon 26 (CT26) and colon 38 (MC38) cell lines in instances of colon cancer. Furthermore, by altering the expression of

certain genes, quercetin prevents the CT26 cell line from migrating and invading.[68]

2.8] Plant name - *Nigella sativa L*

Active compound – Thymoquinone

It has many biological activities; traditional medicine in the Middle East and Southeast Asian countries has made considerable use of thymoquinone (T.Q.), a non-toxic main bioactive component derived from the essential oil of black seed Nigella sativa L.[69] Being harmless, thymoquinone is used to treat a variety of illnesses in humans, such as diabetes and cancer. Antioxidant, anti-inflammatory, immunomodulatory, hepatoprotective, antihistaminic, antibacterial, antidiabetic, anti-epileptic, chemo-sensitizing, and extremely promising anticancer potential are among the pharmacological actions of TQ.[70]

T.Q. induces apoptotic mechanisms, including caspase activation, downregulation of precancerous genes, inhibition of the nuclear factor kappa-light-chain enhancer of activated B cells (NF-B), antitumor cell proliferation, hypoxia, anti-metastasis, and a reduction in side effects when using traditional chemotherapeutic drugs, it has unique anticancer properties.[71]

T.Q. induces cell arrest in human mammary breast cancer epithelial cell lines, MCF-7, at different phases depending on the concentration (25 and 50 μM) in vivo.[72] By raising p21 and p53 levels and markedly lowering cyclin A, cyclin B1, and cyclin E expression, T.Q. promotes G2/M phase cell cycle arrest in esophageal cancer.[73] It also causes DNA damage, apoptosis, elevated iROS, and cytotoxicity in C6 glioma cells.[74]

Reports have shown that T.Q. effectively inhibits tube formation, decreases endothelial cell migration, and suppresses tumor angiogenesis. In HCT 116 human colon cancer cells, T.Q. significantly lowers the phosphorylation of EGFR at tyrosine-1173 residues and JAK2 in vitro. It also downregulates the Jak2/STAT3 signalling pathway in human melanoma cells and HL60 leukaemia cells.[75]

2.9] Plant name - *Polygonum cuspidatum*

Active compound- Resveratrol

A polyphenolic substance called resveratrol is generated by plants in reaction to environmental stress and is present in at least 72 different plant species, including grapes, mulberries, peanuts, cranberries, and blueberries.[76]

According to studies, resveratrol demonstrates a wide range of functions, such as anti-aging, anti-inflammatory, cardiovascular protective, and anticancer effects.[77]

Resveratrol in colon cancer actually promoted G1 phase cell cycle arrest. That was accomplished by boosting p53 in a dose-dependent manner and decreasing cyclin D1 and E1.[78] Furthermore, resveratrol administration led to decreased cyclin B gene expression and increased levels of p27 and p21 gene expression.[79]

Resveratrol has been demonstrated to target the AMPK/mTOR signalling pathway, reduce glycolysis, and prevent the growth of ovarian cancer cells by inducing apoptosis.[80] Furthermore, resveratrol blocks the spread of cancer by interfering with many mechanisms. Resveratrol inhibits the ability for metastatic spread in vitro in pancreatic cancer cells by modifying variables associated with epithelial-mesenchymal transition through the PI3K/Akt/NF-B signaler.[81]

It was reported that resveratrol had been demonstrated to prevent prostate cancer cells from spreading and invading other areas by suppressing glioma-associated oncogene homolog 1, a transcription factor involved in the Hedgehog signalling cascade.[82] According to recent research, resveratrol's antitumor effects may also be mediated by boosting antitumor immunity and reversing the immunosuppressive tumor microenvironment. This is achieved by inducing the secretion of cytokines and chemokines and the

expression of multiple other immune-related genes.[83]

2.10] Plant name- *Reseda luteola*

Active compound-Luteolin

One flavone chemical that is a member of the flavonoids group is luteolin. It is typically present in flowers, vegetables (celery seeds, onion leaves, cabbages, sweet bell peppers, carrots, and broccoli), herbs (parsley, peppermint, oregano, and thyme), and spices (cardamom and anise).[84]

Many cardio-protective properties of luteolin have been suggested, in addition to its antimicrobial, anti-inflammatory, antioxidant, and anticancer properties[85]. Additionally, luteolin exhibits anticancer properties against skin, breast, liver, colon, and lung cancers. However, luteolin demonstrated a broad spectrum of safety with respect to normal cells.[86]

According to reports, By inhibiting the activity of epigenetic targets like SIRT1, several traditional histone deacetylases, and DNA methyltransferases, luteolin demonstrates its anticancer capabilities in a variety of ways.[87] In addition, it suppresses invasion, network formation, and migration and promotes autophagy and cell death. For instance, this substance can prevent the migration and carcinogenesis of U-251 cells.[88] In accordance, it triggers apoptosis in breast cancer that is resistant to tamoxifen by activating proteins linked to apoptosis (cleaved poly (ADP-ribose) polymerase, cleaved-Caspase-7, 8, 9).[89] Furthermore, luteolin suppresses the proliferation of hepatocellular carcinoma (HCC) cells by upregulating microRNA-6809-5p.[90] In HCC cells, overexpression of miR-6809-5p inhibits flotillin1 production and deactivates signalling pathways such as Erk1/2, p38, JNK, and NF-B/p65.[91]

As a result, it inhibits the growth of cancer. Similarly, luteolin functions in cancer therapy by upregulating and downregulating autophagy.[92] An in vitro study has demonstrated that luteolin induces autophagy in the HCC cell line SMMC 7721, which has an anticancer effect.[93] Similarly, luteolin has enhanced the host system in mice with liver cancer through a variety of ways, including altering the levels of marker enzymes and alpha fetoprotein, as well as lowering glutathione and inflammatory cytokines.[94]

According to a study, the proliferation of colon cancer cells from the drug-sensitive LoVo cell line and its drug-resistant LoVo/Dx subline is inhibited by luteolin and baicalein (5,6,7-trihydroxyflavone).[95]

According to recent research, luteolin inhibits the growth of stomach cancer by regulating cyclin D1, cyclin E, p21, and Bcl2. Furthermore, luteolin regulates the expression of MMPs and the EMT process to control metastasis.[96]

It was shown that in prostate cancer, luteolin significantly reduces the protein stability of the Anoctamin1 (ANO1) chloride channel and potently inhibits its activity.[97]

It is known that excessive expression of ANO1 contributes to the development of epithelial malignancies. Furthermore, luteolin inhibits the Akt/mTOR/c-Myc signalling pathway in cancer cells, which drastically lowers the production of ribosomal protein S19.[98]

2.11] Plant name- *Tanacetum parthenium*

Active compound- Parthenolide

Parthenolide (PTL) is the most notable member of its subclass of germacranolides. It is a naturally occurring substance that falls under the class of germacrane sesquiterpene lactones. Plants belonging to the Asteraceae/Compositae family (daisies) and Magnoliaceae family (magnolias) generate PTL as a secondary metabolite. It is taken from feverfew, a medicinal plant, leaves.[99]

According to a different study, PTL dramatically reduced the migration and proliferation of two lung cancer cell lines (A549 and H1299). Regarding the mechanism at play, PTL can prevent Akt, the insulin-like growth factor 1

receptor, from becoming phosphorylated.[100] It has also been demonstrated that PTL effectively inhibits the MAPK/Erk signalling pathway and targets B-Raf in human non-small cell lung cancer cells. PTL is therefore a novel therapeutic approach for renal cell cancer.[101]

Furthermore, in both MCF-7 and MDA-MB-231 cells, PTL therapy reverses the epithelial to mesenchymal transition (EMT) process by substantially reducing the mesenchymal marker vimentin and increasing the epithelial marker E-cadherin protein expression.[102]

The decrease in TGF protein, gene expression, and the EMT-inducing transcription factor TWIST1 expression all occurred simultaneously with the reversal of EMT.[103] Consequently, it stops the spread and metastasis of cancer. Furthermore, PTL reduced the viability of human uveal melanoma cells C918 and SP6.5.[104]

PTL inhibits miR-375, which causes cell cycle arrest in prostate cancer cells.[105] Furthermore, PTL can directly interact with and block the deubiquitinating enzyme ubiquitin-specific peptidase7. Ubiquitination is essential for a number of biological processes within cells, and that its dysregulation can result in the development of cancer.According to a study, 106 PTL suppresses USP47, which controls colorectal cancer stem cells (CCSCs). Consequently, PTL may effectively inhibit the renewal and maintenance of stemness in CCSCs, offering a possible treatment for colorectal cancer.[107]

2.12] Plant Name- *Taxus chinensis*

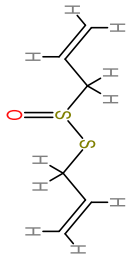
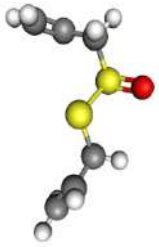
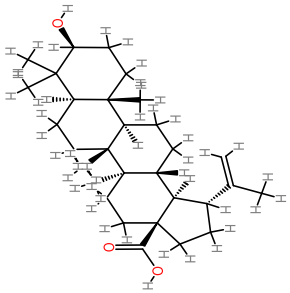
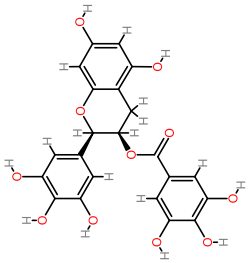
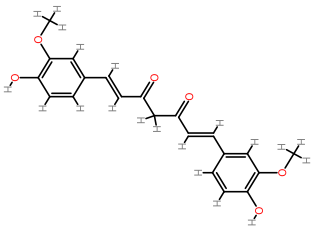
Active compounds- Paclitaxel (taxol)

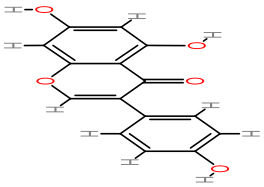
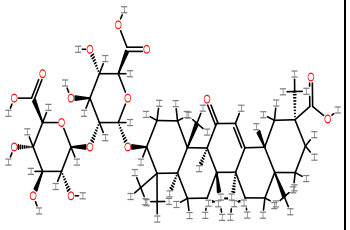
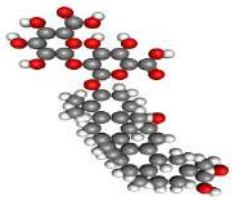
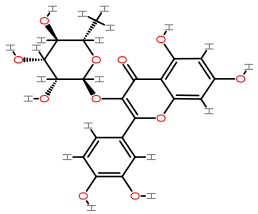
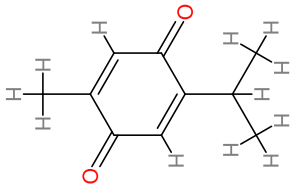
One of the most often found herbal medicinal components in T. chinensis is paclitaxel (PTX), which is a well-known first-line chemotherapy treatment for cancer diseases like breast and ovarian cancer. [108]

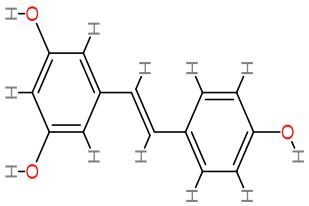
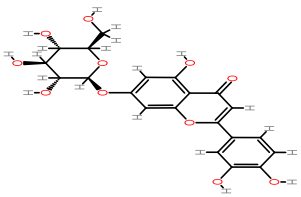
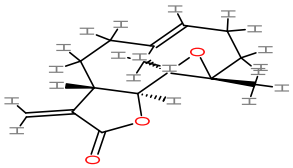
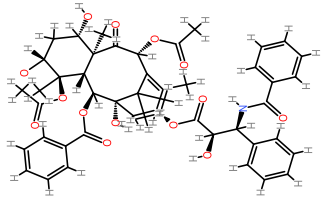
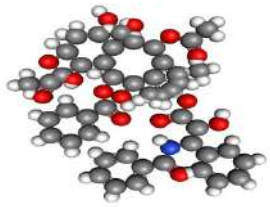
Many studies have shown that PTX can induce cell cycle arrest and apoptosis by increasing microtubule polymerization and inhibiting microtubule depolymerization. PTX's unique structure and anticancer potential have also drawn interest from researchers worldwide.[109]

An extremely potent anticancer medication, taxol treats a wide range of cancers, including ovarian, lung, breast, head, and AIDS-related Karposi's carcinoma. Cancer cells proliferated because of aberrant cell division and proliferation, which increased the total number of cells.[110]

A globular protein called tubulin is found in the cytoskeleton of eukaryotic cells and is essential to the mitotic process of cancer cells. Chromosome separation during mitotic division depends on the dynamics of microtubules, which include depolymerization (shrinking) and polymerization (growing). Heterodimer microtubules, which are put together to form protofilaments, are created when two different types of tubulins polymerize together. It has been discovered that 13 protofilaments are organized parallel to the microtubule axis in living cells. It inhibits microtubule depolymerization and stops the cell cycle by interacting with tubulin through an amino-terminal stretch of amino acids (31 amino acids). In the presence of taxol, microtubules arranged to have 12 proto filaments instead of 13.[111]

Plant name	Active Compound	2D structure	3D structure	Distribution
Allium sativum L	Allicin			China, Korea, India, USA, Spain, Argentina
Betula alba	Betulinic acid			Afghanistan, Northern Pakistan, Himalaya in India, western northern China
Camellia sinensis Theaceae Gallate.	EGCG (Epigallocatechin gallate)			Indian subcontinent, EastAsia, Southeast Asia.
Curcuma longa	curcumin			

Plant Name	Active Compound	2D structure	3D structure	Distribution
Glycine max	Genistein			Russian Far East to China
Glycyrrhiza glabra	*Glycyrrhizinic acid*			Eurasia, northern Africa and western Asia
Morus alba (Moraceae)	Quercetin			China and India, Pakistan, Zambia, South Africa, United States, Mexico, Australia, Kyrgyzstan, Argentina, and Turkey.
Nigella sativa L	Thymoquinone			eastern Europe (Bulgaria and Romania) and western Asia (Cyprus, Turkey, Iran, and Iraq)

Plant Name	Active Compound	2D structure	3D structure	Distribution
Polygonum cuspidatum	Resveratrol			China, Japan and Korea, North America.
Reseda luteola	Luteolin			Asia: India, Pakistan; Africa; Europe; North America: United States of America
Tanacetum parthenium	Parthenolide			Australia, Europe, China, Japan, and North Africa
Taxus chinensis	Paclitaxel (taxol)			all countries of Europe (except Iceland), the Caucasu, Turkey, Iran. Morocco, Algeria in North Africa

DISCUSSION

Plants have been a valuable source of medicinal compounds, many of which have demonstrated potential in cancer treatment. Phytochemicals derived from plants exhibit various anticancer properties, such as inhibiting tumor growth, inducing apoptosis (programmed cell death), and suppressing metastasis. Over the years, numerous plant-based compounds have progressed to clinical trials, showcasing their potential as alternative or complementary therapies for cancer. In the case of allicin, a double-blind, randomized controlled trial involving individuals with colorectal adenomas revealed that high doses of aged garlic extract were linked to a significantly reduced risk of developing new adenomas.[112] Clinical trials have also investigated its effects on stomach cancer, prostate cancer, and esophageal squamous cell carcinoma.[113,114]

Betulinic acid underwent phase I/II clinical trials, though the results have not been disclosed.[115] Similarly, numerous trials have been conducted on EGCG (epigallocatechin gallate) to assess its effects on gastric, esophageal, pharyngeal, colorectal, and locally advanced non-inflammatory breast cancers.[116-121]

Curcumin has been the subject of many clinical trials, evaluating its efficacy in treating colon and pancreatic cancers, as well as its role in minimizing the side effects of chemotherapy and radiation therapy.[122,123] Curcumin has also been tested in combination with chemotherapy drugs such as paclitaxel and docetaxel, with several trials still ongoing.[124,125]

Genistein has been tested in breast, prostate, and pancreatic cancers through various clinical trials.[126,127] A clinical trial on glycyrrhizinic acid, the active compound in liquorice root, is set to begin soon. This trial will involve patients recently diagnosed with prostate cancer, and researchers will monitor the compound's impact on tumor growth during the period between diagnosis and surgery.[128]

Few clinical trials have been conducted on quercetin; their results remain unpublished. However, a phase I clinical study demonstrated that quercetin can be safely administered as an intravenous bolus injection and inhibits lymphocyte tyrosine kinase.[129]

Despite extensive in vitro and in vivo research showing its anticancer potential, Thymoquinone has yet to be tested in clinical trials. Luteolin (nano-luteolin) has been evaluated in a single clinical trial for its effectiveness in treating tongue cancer, but the trial's status is currently unknown. No clinical studies are available on parthenolide's anticancer activity.

Resveratrol has been studied for its safety in healthy individuals, with doses up to 5 grams per day found to be safe. It has shown positive activity against colon, breast, and multiple myeloma cancers. Resveratrol continues to be examined for its effectiveness in treating breast, colon, and colorectal cancers.[130,131]

CONCLUSION

Natural bioactive chemicals derived from medicinal plants have had a major impact on human health. As specifics contested in this evaluation, emphasis was placed entirely on creating new anticancer medications or innovative therapeutic approaches strategy against different cancers. Consequently, several naturally occurring bioactive substances or metabolites might be looked at or studied to examine the precise structure and mechanistic activity of creating innovative anticancer medications. Nevertheless, the process of finding new drugs involves the isolation, characterization, preclinical testing, biological activity assessment, and Clinical studies are an expensive and time-consuming process, but green cancer treatment options with no side effects are worth any expense. This review has highlighted the diverse array of plant species

that exhibit potential anticancer effects through various mechanisms, including the modulation of cell signaling pathways, induction of apoptosis, and inhibition of tumor growth and metastasis. Notable examples include the use of compounds derived from plants such as Taxol from Taxus chinensis, and Curcumin from Curcuma longa, which have demonstrated significant efficacy in preclinical and clinical studies.Despite the considerable progress made, challenges remain in translating these findings into effective and widely applicable treatments. Issues such as the complexity of plant-derived compounds, potential toxicity, variability in bioavailability, and the need for extensive clinical trials must be addressed. Advances in technology, such as high-throughput screening and molecular docking, alongside improved understanding of plant-based bioactive compounds, will be crucial in overcoming these hurdles. Future research should focus on elucidating the precise mechanisms of action of these plant-derived compounds, optimizing their formulations, and exploring synergistic effects when combined with conventional therapies. Additionally, integrating traditional knowledge with modern scientific approaches could yield novel insights and accelerate the development of new anticancer agents. By bridging these gaps, the potential of plant-based anticancer therapies can be fully realized, offering new hope for more effective and targeted cancer treatments.

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