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Novel Application of Traditional Medicinal Plants for the Management and Treatment of Cancer

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Abstract:- Cancer is the second largest cause of mortality worldwide. The prevention and treatment of cancer progression still has a great deal of room for improvement despite enormous advancements. When having chemotherapy, a number of unfavourable side effects might possibly occur. Unfavorable side effects may be reduced by using natural therapies, such as using cancer therapy components derived from plantsCurrently, a small number of plant-based products are used to treat cancer. However, a variety of plant substances have demonstrated highly promising anti-cancer properties in vitro but have not yet been tested on people.. The effectiveness of these plant compounds in treating human tumours needs to be further investigated. The focus of this review will be on the numerous conventionally used medicinal herbs and the chemical substances they contain that have recently proved promise as anticancer agents. It will examine the possible mechanisms of action for such compounds. The medicinal plant and patents for cancer chemotherapy and chemoprevention are covered in this article. Future research emphasizing on the natural anticancer agents which can provide a new horizon in cancer treatment, This will significantly increase the likelihood that cancer patients will survive.

Keywords:- *Phytoconstituents, Anticancer, Apoptosis, Medicinal Plants.*

I. INTRODUCTION

Cancer is still one of the leading causes of illness and death in the global. Among non-communicable illnesses, cancer places second in terms of fatality rates, just after cardiovascular disease. The sum of cancer-related demises worldwide stands anticipated toward rise from 7.1 million in 2002 to 11.5 million in 2030. [1–4]. More people worldwide die of cancer than from AIDS, Tuberculosis, and malaria combined [5]. In general, Western Europe, North America, Australia and New Zealand have greater rates of cancer prevalence and mortality than that of the rest of the world. [6, 7]. One in four casualties in the US is related to cancer. [8].

Chemotherapy is widely used to treat cancer. Cancer cells divide without normal cells not doing so because they lack many of the control frameworks that govern them. Cancer cells are more vulnerable to chemotherapy because of this characteristic. An extensive library of helpful chemotherapeutic medicines has been established as a result of about 5 decades of systemic medication research and development. Chemotherapeutic regimens do not, however, come without some inherent issues. Chemotherapeutic treatments may result in a variety of toxicities. For instance, the frequent chemotherapy drug 5-fluorouracil is identified to produce myelotoxicity. [9], cardiotoxicity [10] and has even been shown to act as a vasospastic agent in rare but documented cases [11]. Another broadly used chemodrug, doxorubicin causes cardiac toxicity [12–14], renal toxicity [15], and myelotoxicity [16]. Similarly, bleomycin a known as chemotherapeutic agent, is known for its pulmonary toxicity [17–19], and bleomycin shows cutaneous toxicity [20]. The medication cyclophosphamide, used to treat a variety of malignant illnesses, has been linked to myelotoxicity, immunosuppression, alopecia, and bladder toxicity in the form of hemorrhagic cystitis at larger doses. [21]. When treating cancer with allopathy or conventional medicine, the toxicity of chemotherapy medicines occasionally poses a severe challenge. For the treatment of cancer, numerous medicines have been proposed, many of which incorporate compounds derived from plants. There are four types of plant-based cancer treatments currently on the market: epipodophyllotoxins (etoposide and teniposide), taxanes (paclitaxel and docetaxel), vinca alkaloids (vinblastine, vincristine, and vindesine), and camptothecin derivatives (camptotecin and irinotecan). Plants are a rich source of natural compounds that may have chemoprotective properties against cancer and still hold excessive promise for the development of novel medications. Taneja and Qazi have proposed a number of plant-based molecules with potential anti-cancer properties. [22].

In this study, we'll discuss about a few plant items that have recently undergone testing and may have application in cancer treatments. Also mentioned is the potential mode of action for such plant products.

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II. MEDICINAL PLANTS WITH ANTICANCER PROPERTIES

Many plants are used for their health advantages in developing countries, and populations in Asia and Africa have utilized medicinal plants for thousands of years in traditional remedies. The World Health Organization (WHO) reports that some countries still mainly rely on plant-based treatments for medical care, and developing countries are making therapeutic use of the advantages of organically produced substances [23]. The following is a list of plants having potential anticancer qualities.

- ***Achyranthus aspera***

The anti-cancerous and cytokine-based immunomodulatory effects of the polyphenolic compounds in Achyranthus aspera extract are investigated. The plant extract includes both known and unidentified phenolic acid and flavonoid components, including mixtures of chlorogenic acid, quinic acid, , kaempferol, chrysin and quercetin. For 30 days away, Achyranthes aspera was administered orally to mice to lung cancer after just being exposed to urethane (ethyl carbamate) 100 milligrammes per kilogramme of body weight. 100 milligrammes of A powder. 2.4 milligrammes of phenolic acid and 1.1 mg of flavonoid are present in aspera (2:1 ratio). As related to polyphenolic non-feed urethane primed lung carcinogenic tissues, PCA feed urethane primed lung cancerous tissues revealed enhancing effect and expression of antioxidant enzymes GST, GR, CAT, and SOD, as well down-regulated expression and activation of LDH enzymes. Pro-inflammatory cytokines IL-1, IL-6, and TNF- along with TFs, NF-B, and Stat3 were found to be down-regulated in PCA nourish urethane primed lung tissues, while pro-apoptotic proteins Bax and p53 were shown more prominently in polyphenolic feed urethane primed lung tissues. In accordance with the current research, the components of Achyranthus aspera exhibit synergistic anti-cancerous, cytokine-based immunomodulatory, and DNA conformation restoring properties. To effectively treat and prevent lung cancer and other malignancies, further study is needed to demonstrate the effects of each element both individually and in combination. [24].

- ***Allium sativum***

According to epidemiologic studies, consuming garlic reduces the risk of dying from stomach cancer in Chinese populations. Based on this research, garlic may help prevent human cancer. It has been demonstrated that garlic prevents the growth of transplantable tumours and lowers the frequency of some tumours that develop on their own. Components of garlic have also been shown to block the activity of several chemical carcinogens during both the initiation and propagation phases of carcinogenesis. There is more proof that the active ingredients in garlic affect both specific and nonspecific anti-tumor immunity. Recent research proposes that a variety of pathways can explain the biological effects of garlic. [25].

- ***Andrographis panniculata***

According to the current study, human cancer cells and immune cells exhibit anticancer and immunomodulatory activities of Andrographis paniculata methanolic extract. methanolic extract of Andrographis paniculata's was fractionated into dichloromethane, petroleum ether, and aqueous extracts before being tested for bioactivity. According to our results, the methanolic extract's dichloromethane fraction still contains the dynamic substances that contribute to its anticancer and immunostimulatory activities. At low concentrations, the dichloromethane fraction greatly reduces the HT-29 (colon cancer) cells proliferation, while increasing the proliferation of HPBLs. We are able to isolate three diterpene molecules, including andrographolide, 14-deoxy andrographolide, and 14-deoxy-11,12-didehydroandrographolide, after further fractionating the dichloromethane extract. On a variety of cancer cells that represented various forms of cancer in humans, andrographolide shown anticancer efficacy. However, all three compounds increased HPBLs' ability to proliferate and to induce the inflammatory cytokine interleukin-2 (IL-2). [26].

- ***Annona muricata***

In particular, cancer and parasite illnesses are treated with traditional medicines made from the A. muricata tree. The main purpose of the current research is to investigate the leaf extract's ethyl acetate fraction's anticancer activity. FTIR and GC-MS have been used to assess the bioactive component of the ethyl acetate fraction. In response to a low medication concentration of 200µg/ml, A. muricta demonstrated 82% cell death. [27].

- ***Bidens pilosa***

Some South American civilizations regard the plant Bidens pilosa as having therapeutic properties. It has polyacetylenes, which may be the main ingredient behind its anticancer effects. Antitumor efficacy and the presence of polyacetylenes in the extracts prepared by hydroethanol maceration (HCE) and supercritical fluid extraction (SFE) were detected. While the SFE extract shown better cytotoxic activity, both extracts killed the MCF-7 cells in culture in a concentration-dependent manner. Incubation after 24 hours, the SFE had an IC50 of 437 (428-446) µg/mL, which fell to 291 (282-299) µg/mL after 48 hours. While the HCE began producing DNA cleavage at a concentration of 160 µg/mL, the SFE extract began at a concentration of 40 µg/mL, which was sufficient to start the in-vitro cleavage. By combining TL chromatography with UV-vis studies, it was demonstrated that polyacetylenes were the predominant components in SFE. The anticancer investigation was conducted using mice bearing Ehrlich ascites carcinoma. The following factors were taken into consideration: body weight, abdomen circumference, ascites fluid and tumour cell volume, viable and nonviable tumour cell count, mean persistence time, and enhanced life expectancy. Both extracts exhibited anticancer action, but SFE induced longer mean survival times (17 days) and increased lifespan expectancy (~31%). It also reduced ascites fluid and tumour cell volumes more significantly (4 ± 1 and 1± 0.4 mL, respectively). The findings point to the significance of *B. pilosa* polyacetylenes as leader molecules

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for developing a novel anticancer medication employing supercritical technology. [28].

- ***Bolbostemma paniculatum***

One of the most prevalent malignant tumours of the nervous system is malignant glioblastoma. A novel cyclic bisdesmoside called tubeimoside V, which is derived from the tubers of the plant Bolbostemma paniculatum, has not yet been identified, but it appears to have a number of biological properties, including an anticancer impact. In the current work, we looked at how human glioblastoma U87MG cells proliferated after being exposed to Tubeimoside V at various concentrations (0.9–14.8 μM) over a set period of time. Tubeimoside V considerably reduced U87MG cell growth, and this effect was time and dose-dependent (IC_{50} = 3.6 μM). based on the data. Tubeimoside V brings the protruding appearance of a sub-G1 peak in the cell cycle that is expressive of apoptosis, according to a flow cytometric analysis of DNA in U87MG cells. Additionally, nuclear condensation of apoptotic bodies were seen by both fluorescence and electron microscopy after Tubeimoside V treatment of U87MG cells. An annexin V/PI assay result revealed that phosphatidylserine externalisation started after treatment and then intensified over the course of the next 24 hours. Tubeimoside V was found to cause molecular alterations that resulted in a decrease in Bcl-2 protein expression and an increase in Bax protein expression. According to the novel findings, Tubeimoside V's cytotoxic effects on U87MG cells are caused by the stimulation of cell death. Inclusive, our results show that Tubeimoside V is a highly effective inducer of apoptosis in glioblastoma cells and indicate that this mechanism may be crucial in anti-tumor chemotherapy. [29].

- ***Apis Mellifera***

A promising potential for cancer therapy is melittin, a significant peptide found in bee venom. Various anti-cancer effects of this substance have been found in preclinical cell culture and animal model systems. In spite of having strong evidence of its effectiveness against a number of cancers, non-specific cytotoxicity, degradation, and hemolytic activity have made it challenging to apply to humans. To get around the problems, a number of optimization techniques have been used, such as Melittin delivery via nanoparticles. Here, we provide a summary of our current knowledge of the anticancer effects of Melittin and bee venom on numerous cancer types. Additionally, we include the information that's also currently available regarding the possible mechanism of action of Melittin and/or bee venom. [30].

- ***Cannabis sativa***

A serious issue with public health is colon cancer. Cannabis-based medications are effective complementary therapies for cancer patients. In this study, we looked at how standardized *C. sativa* extracts with high levels of cannabidiol (CBD), also known as CBD BDS or CBD botanical drug substance, affected colorectal tumor cell proliferation and in vivo colon cancer models. [31].

- ***Astralagus hedysarum***

Astralgus hedysarum polysaccharide has demonstrated anticancer efficacy. After two hours, an intraperitoneal injection of 500 mg/kg increased the deposition of macrophages' C3, the third component of their complement. When *Astralagus hedysarum* was injected five times, more C3-positive macrophages were present than with a single injection. According to the findings, *Astralagus hedysarum* may be helpful in cancer chemotherapy because of its immuno-potentiating properties. [32].

- ***Centaurea ainetensis***

In human colon tumor cells, the cytotoxic potential of *C. ainetensis* extracts has been investigated. Numerous cancer cells originating from the colon were prevented from proliferating by the crude extract of Centaurea ainetensis. *In-vivo*, the crude extract, given intraperitoneally beforehand giving a subcutaneous injection of 1, 2-dimethylhydrazine (a significant carcinogen), decreased the mean size of aberrant crypt foci and the number of tumours. Salograviolide-A, a bioactive sesquiterpene lactone molecule, was isolated and characterised as a result of additional fractionation experiments on the crude extract. Salograviolide-A may be related to the colon growth inhibition. Salgraviolide-A reduced the growth of colon tumor cell lines at non-cytotoxic concentrations when administered to normal human intestinal cells. Additionally, salograviolide A showed significant cytotoxic effect against formation of epidermal squamous cell carcinoma. [33].

- ***Camellia sinensis***

Saponins from the flowers of Camellia sinensis have a variety of biological characteristics. However, there hasn't been much research done on how saponins work against cancer. Here, we examined human ovarian cancer cell lines to evaluate the anti-cancer effects of bioactive. A2780/CP70 and OVCAR-3 cells were significantly inhibited from proliferating by saponins (1.5 g/ml) via causing p53-dependent apoptosis and S phase arrest. Further research revealed that the p53 inhibitor PFT-reversed the saponin-induced reduction of cell growth and death, lowered the potential of the mitochondrial membrane, and stimulated the activities of caspase-3/7, caspase-8, and caspase-9. Additionally, Camellia sinensis elevated Cyclin E and Cyclin A while downregulating Cdc25A, Cdk2, and CyclinD1 expression, indicating that the Cdc25A-Cdk2-Cyclin E/A pathway was involved in *C. sinensis* induced S phase arrest. Also, a Chk2-Cdc25A DNA damage response was linked to the S phase arrest. These findings showed that Camellia sinensis has a hopeful future as a functional dietary ingredient for ovarian cancer prevention. [34].

- ***Hypericum perforatum***

Serotonin-reuptake inhibitors (SSRI) and serotonin antagonists have shown to have an antiproliferative effect on prostate cancers. In this study, we examined the impact of therapy with *Hypericum perforatum* extract on the proliferation of human prostate cancer cells both in-vitro and in vivo since components of the plant serve as serotonin-reuptake inhibitors and have lethal effects on a number of cancer cell lines. This study revealed a considerable reduction in the size of the tumour and a

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number of metastases, indicating that this natural substance might be helpful in the management of prostate cancer. [35].

- ***Daphne mezereum***
  A plant entitled Daphne mezereum is commonly used as a folk medicine to treat cancer-like symptoms. In mice having lymphocytic leukaemia, a hydro-alcoholic extract of *D. mezereum* exhibited substantial antileukemic action. A plant commonly used as a folk treatment for treating symptoms of cancer led to the isolation and characterisation of mezerein as a powerful antileukemic component through further fractionation investigations on the extract. Mice with lymphocytic leukaemia were treated with a Daphne mezereum hydro-alcohol extract, which demonstrated strong antileukemic properties. Mezerein, a powerful antileukemic molecule, was isolated and characterised as a result of the additional fractionation investigations on the extract. [36].
- ***Gossypium hirustum*** *or* ***Gossypium herbaceum***
  It also known as Gossypol or cottonseed oil, and it is used as a male contraceptive, to treat ovarian or endometrial metastatic cancer, and to cure HIV. Gossypol has been shown to have anticancer characteristics in both *in-vivo* and *in-vitro* studies on a variety of cytosolic and mitochondrial enzyme systems that are essential for the growth of tumour cells, including melanoma, endometrial, colon, lung, prostate, breast, brain, and adrenocortical cancers. Gossypol self-medication is not safe due to its potential toxicity, and no typical dose has ever been recommended for the treatment of cancer.[37].
- ***Mangifera indica***
  Gold nanoparticles (AuNPs) must attracted a lot of responsiveness in nanomedicine over the past few decades and have increased their use in treatments and clinical diagnostics. The utilization of plant extract in the synthesis of gold nanoparticles demonstrates that it is an environmental friendly technology for large-scale production. In this work, aqueous *M. indica* seed extract was used as a reducing agent to create AuNPs using a straightforward one-step procedure. Due to its innate capacity to produce reactive oxygen species (ROS), AuNP's effectively inhibited the development of E. coli and S. aureus and had negative impacts on the tested bacterial species. Intriguingly, the biocompatibility assessment revealed that AuNPs were non-toxic to mesenchymal stem cells at a concentration of 25 µg/ml and inhibited the development of human gastric cancer cells in in vitro culture. By inhibiting the Ang-1/Tie2 pathway, AuNPs significantly exhibited anti-angiogenic properties in the chick chorioallantoic membrane model (CAM). It can be used to inhibit the growth of tumours, treat inflammatory conditions that require for the inhibition of angiogenesis, and its antibacterial activity is appropriate for medical use to prevent infections carried over by surgery. [38].
- ***Nervilia fordii***
  In-vitro selection of the most effective petroleum ether extract and ethyl acetate extract parts was followed by anticancer experiments using the S180- and H22-mice models. To S180-mice and H22-mice, petroleum ether extract and ethyl acetate extract components both had noticeable anticancer effects that might also lengthen H22-mice life. They could enhance the mice's immune regulation in the interim. The effectiveness of the Nervilia fordii petroleum ether and ethyl acetate extracts as anticancer fractions in vivo has only recent times been proven. On the basis of this, additional research is required to determine the active principles or principle group responsible for the anticancer effect in Nervilia fordii. [39].
- ***Oroxylum indicum***
  There is still a need for novel anticancer metabolites with higher efficacy and fewer side effects despite clinical advancements in anticancer therapy. Using MDA-MB-231 cancer cells and WRL-68 non-tumor cells, the chemopreventive capabilities of hot and cold non-polar extracts (petroleum ether and chloroform) of O. indicum were examined in the current work. After compared to WRL-68 cells, all of the extracts, but especially the petroleum ether hot extract (PHO), significantly ($P<0.05$) increased cytotoxicity in MDA-MB-231. Using cellular DNA fragmentation ELISA, PHO was next examined for its ability to induce apoptosis in oestrogen receptor (ER)-negative (MDA-MB-231) and ER-positive (MCF-7) breast cancer cells. It showed a higher level of effectiveness in the MDA-MB-231 cells. PHO also demonstrated positive outcomes when tested for anti-metastatic potential in a cell migration inhibition assay. Thus, ER-negative breast cancer cells can be effectively targeted by non-polar extracts of O. indicium (especially PHO) to cause apoptosis without causing harm to normal cells due to cancer-specific cytotoxicityAs a result, it might be thought of as an extract with potential precursors to slow or stop the progression of ER-negative breast cancer, even in its advanced stages of malignancy. [40].
- ***Salvia miltiorrhiza***
  Miltiorrhiza Salvia Bunge polysaccharides (SMP) were comprehensively investigated in this study. High purity ethanol precipitation and water boiling were used to extract the polysaccharides. Using the established HPLC-UV protocol with PMP precolumn derivatization, the monosaccharide composition of SMP was determined. The results show that the polysaccharides are primarily made up of d-galactose (Gal), d-glucose (Glc), and d-galacturonic acid (GalUA), with mole percentages of 64.5%, 31.1%, and 4.4%, respectively. The antioxidant capacity of SMP was also assessed in terms of its scavenging power, ability to neutralise DPPH, superoxide, and hydroxyl free radicals, and reducing power. The findings show that S. miltiorrhiza Bunge polysaccharides exhibit unique antioxidant effects in a dose-dependent manner. Additionally, in a dose- and time-dependent way, SMP is observed to have a significant inhibition ratio against LoVo cells (typical tumour cells). According to FCM analysis, SMP can cause LoVo cells to undergo apoptosis, stop the cell cycle in the S phase, and increase intracellular reactive oxygen pressure. These findings indicate that SMP may serve as a natural anticancer

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drug with reduced cost and cytotoxicity as well as a bioactive factor for the creation of functional foods, revealing for the first time the potential anti-tumor mechanism of SMP. [41].

- ***Scutellaria***

Numerous chemotherapeutic drugs from natural sources have been discovered as a result of the extensive usage of plants as readily available anticancer medicines. For thousands of years, the famous flowering plant species Scutellaria has been used to treat a variety of human diseases. Scutellaria possesses in-vitro and in-vivo anti-metastatic, anti-proliferative, anti-invasion, anti-angiogenic, and apoptotic properties. Despite multiple studies on the plant's cytotoxic-antitumor potential, there are certain concerns that require more research. The use of plants as anticancer treatments may need to be reconsidered due to factors including incorrect interpretations, disregard for the pharmacokinetics profile, and poor study design. The possible health advantages of Scutellaria and its active ingredients, as well as the underlying mechanisms of cytotoxicity and anticancer activity, have been outlined in this study. Meanwhile, we talked about potential issues that may affect the precise outcome. [42].

- ***Picrorrhiza kurroa***

Mice were used to study the anti-tumor and anti-carcinogenic properties of Picrorrhiza kurroa extract. In contrast, the oral treatment of P. kurroa extract at doses of 150 and 750 mg/kg body weight, respectively, substantially reduced tumour incidence and tumor-related mortality in control mice after 20-methylcholanthrene (20 MC) administration. Additionally, it was discovered that the extract lengthened the lives of mice with ascites tumours and decreased the size of transplanted solid tumours caused by Dalton's lymphoma ascites (DLA) tumour cell lines. *Yeast topoisomerase I and II enzyme activity was decreased by P. kurroa extract when evaluated on Saccharomyces cerevisiae mutant cell cultures. The cdc2 kinase enzyme, which controls the cell cycle, and the enzyme responsible for carcinogen activation were not inhibited by the extract.* [43].

- ***Rubia cordifolia***

Three new cyclic hexapeptides, termed as rubicordins A–C (1–3), together with 7 known ones (4–10) were isolated from the roots and rhizomes of *Rubia cordifolia*. Through spectroscopic research, their structures were clarified, and the actions of the cytotoxic and NF-B signalling pathways were examined. According to the findings, cancer cell lines SGC-7901, A549, or Hela were all sensitive to 1–10, and 1–3 suppressed the NF-B signalling pathway. [44].

- ***Silybum marianum***

Hepatocellular carcinoma (HCC), which has few effective treatments and a dreadful prognosis, is a major worldwide health burden. Silibinin, an antioxidant obtained from the Milk Thistle plant (Silybum marianum), is thought to have hepatoprotective and antitumorigenic effects both in-vitro and in-vivo by inhibiting oxidative stress and proliferation. This study investigated the impact of dietary silibinin supplementation alone or in conjunction with chronic ethanol intake on the development of HCC using a DEN-initiated mouse model. Our findings show that silibinin had little hepatoprotective benefits in the early stages of hepatocarcinogenesis, but when given in combination with ethanol, it increased ethanol's pro-tumor effects in HCC-bearing mice, but only in males. [45].

- ***Smilax china***

By using the MTT assay and the clonogenic assay to test eight crude extracts of Smilax china L. rhizome against HeLa cells, the fraction rich in flavonoids shown excellent effectiveness against these cancerous cells. This extract was subjected to a bioassay-guided separation that resulted in the discovery of kaempferol-7-O-D-glucoside (KG), a flavonoid glycoside with strong anticancer properties. By using the MTT assay and the clonogenic assay, we assessed its in vitro cytotoxicity and antiproliferative impact in a panel of known cancer cell lines. Apoptosis induction by KG was shown to occur in A375 and HL60 cells using morphological modifications, DNA fragmentation, and flow cytometric analyses. Our findings showed that one way KG exerts its antiproliferative impact is by producing cell cycle arrest at the G1 phase and inducing apoptosis.[46].

- ***Withania somnifera***

Men frequently get prostate cancer, a noncutaneous tumour. Globally, the occurrence of PC is rising at an alarming rate. Elevated interleukin-8 (IL-8) and cyclooxygenase-2 (COX-2) levels in cancerous cells are linked to PC progression. Chronic inflammation, enhanced angiogenesis, proliferation, migration, and apoptosis inhibition are all brought on by the overexpression of these playersFurthermore, the disease's transition from an androgen-dependent to an androgen-independent state is aided by their higher circulating levels. Therefore, IL-8 and COX-2 expression inhibition would be a viable target in the creation of PC therapies. In this work, we looked at the inhibitory effects of withania somnifera extract on a prostate cancer cell line that was highly metastatic and androgen-independent (PC3). Additionally, in prostate tissue samples, we contrasted the real-time expression of IL-8 and COX-2. [47].

- ***Strychnos nuxvomica***

Strychnos nuxvomica, is a member of Loganiaceae family, its mostly gathered from forests in Northern Australia and the Indian subcontinent. Strychnos nuxvomica has been found to have cytotoxic action against the ROMI 8226 multiple myeloma cell line. The same cell lines were used for screening Strychnos nuxvomica's root extract, and it demonstrated anticancer activity in a dose- and time-dependent manner. Major components of Strychnos nuxvomica are alkaloidal in nature and inhibit the proliferation of HepG2 cells. Brucine alkaloid causes the death of HepG2 cells via apoptosis, which is mediated by caspase-3 and cyclooxygenase-2. [48].

- ***Taraxacum officinale***

Women's health issues, including liver and gallbladder diseases as well as cancers of the breast and uterus, have commonly been treated with taraxacum officinale. Taraxacum officinale appears to have anti-tumor properties, according to a number of earlier studies, the exact mechanism is still unidentified. In this study, we looked at how Taraxacum officinale affected a human hepatoma cell line's cytotoxicity and cytokine productionHep G2. According to our findings, Taraxacum officinale greatly

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enhanced the production of tumour necrosis factor (TNF)- and interleukin (IL)-1 when compared to medium control (approximately 1.6-fold for TNF-α and 2.4-fold for IL-1α, P 0.05). It also dramatically lowered the viability of cells by 26%. By using flow cytometry, it was also discovered that Taraxacum officinale substantially caused apoptosis in Hep G2 cells. Increased levels of TNF-α and IL-1α were a factor in the apoptosis that Taraxacum officinale caused. Anti-TNF-α and IL-1α antibodies nearly eliminated it. These findings imply that Taraxacum officinale causes cytotoxicity in Hep G2 cells via secreting TNF-α and IL-1α. [49].

- ***Terminalia chebula***

The effects of a 70% methanolic extract of the *Terminalia chebula* fruit on the proliferation of many malignant cell lines, including the human (MCF-7) and mouse (S115) breast cancer cell lines, were investigated, human osteosarcoma cell line (HOS-1), human prostate cancer cell line (PC-3) and non-tumorigenic, immortalised human prostate cell line (PNT1A), utilising tests for proliferation ([3H]-thymidine incorporation and Colter counting), cell viability (ATP determination), and cell death (flow cytometry and Hoechst DNA staining). The extract reduced cell viability, slowed cell growth, and caused cell death in each of the cell lines that were examined. These effects were dose-dependent. The extract did elicit some apoptosis at lower dosages, according to flow cytometry and other tests, however, necrosis was the primary mechanism of cell death at higher concentrations. Three known antigrowth phenolics of Terminalia, ethyl gallate, gallic acid, luteolin, and tannic acid, were tested by ATP assay on the HOS-1 cell line in comparison to ellagic acid, 2,4-chebulyl-β-D-glucopyranose (a new natural product), and chebulinic acid, which were obtained through chromatographic fractionation of the extract guided by the ATP assay. The highest growth-inhibitory phenolics found in T. chebula fruit were Chebulinic acid (IC_{50}=53.2 μM±0.16)>tannic acid (IC50=59.0 μg/ml±0.19)> and ellagic acid (IC_{50}=78.5 μM±0.24). [50].

- ***Zingiber officinale***

Medication-induced nausea, vomiting, and emesis, its a common side effect of cancer treatment, despite substantial advancements and the creation of innovative antiemetics. The different ginger extracts and the ginger juice have been demonstrated to have anti-emetic properties against chemotherapy-induced nausea, vomiting in preclinical investigations using experimental animals (dogs and rats). The active ingredient in ginger, gingerol, has been shown to have anti-emetic effects in minks. While most human research have supported the preclinical discoveries, a few have provided conflicting results. However, the ginger phytochemicals, particularly 6-gingerol, 8-gingerol, 10-gingerol, and 6-shogaol, may serve as a 5-hydroxytryptamine (5-HT3) antagonist, NK1 antagonist, antihistaminic, and have prokinetic actions. The precise mechanism underlying ginger's anti-emetic properties is unknown. For the first time, the current analysis makes an effort to examine anti-emetic observations and the heterogeneity in how ginger's anti-emetic properties respond to chemotherapy for cancer. Additionally, an attempt is made to fill in any gaps in the published studies and highlight areas that require additional research in order for ginger to be used as an anti-emetic medication in clinics in the future. [51].

- ***Vernonia amygdalina***

Amygdala Vernonia In Cameroon, delila is a common vegetable that is also utilised as a folk remedy for a number of human diseases. To our knowledge, however, no prior papers have examined its therapeutic effectiveness against human prostate cancer. With human androgen-independent prostate cancer (PC-3) cells as a test model, the goal of the current study was to assess the anticancer properties of *V. amygdalina* methanolic extract in the prevention and treatment of prostate cancer. We used different Vernonia amygdalina dosages to treat PC-3 cells for 48 hours in order to accomplish our objective. The trypan blue test and MTT assay results showed that Vernonia amygdalina extracts significantly inhibited the proliferation of PC-3 cells. Additional research involving cell morphology, lipid peroxidation, comet assays, and apoptosis analysis revealed that Vernonia amygdalina inhibited PC-3 cell growth by inducing cell growth arrest, DNA damage, apoptosis, and necrosis *in-vitro* and might shield against oxidative stress-related illnesses due to its high antioxidant content. [52].

- ***Agave angustifolia***

While moderately little is known about branched fructans, linear inulin-type fructan (ITF) prebiotics have a putative role in the prevention of colorectal cancer With the Simulator of the Human Intestinal Microbial Ecosystem (SHIME) model, the purpose of this work is to examine the fermentation characteristics and possible prebiotic action of branching fructans produced from *A. angustifolia* Haw. By using MTT, Comet, and transepithelial electrical resistance (TER), three different methods were used to evaluate the impact of the fermentation supernatant on the bioactivity of the sample. The addition of agave fructan to the SHIME model significantly ($P < 0.05$) raised the proximal and transverse bifidobacteria populations, the proximal, transverse, and distal SCFA concentrations, and lowered the distal vascular ammonia concentrations. Also, the fermentation supernatant expressively ($P < 0.05$) increased the TER of a Caco-2 cell monolayer (%) and reduced fluorescein-based paracellular flux, signifying enhanced barrier function and reduced epithelial barrier permeability (proximal and distal vessel).While cytotoxicity and genotoxicity persisted unchanged in response to the presence of Agave fructans. As a result of improving gut barrier function, a crucial factor in colon carcinogenesis, branching Agave fructans appear to have prebiotic action, especially in connection to colon health. [53].

- ***Agrimonia pilosa***

To evaluate the anticancer effectiveness of the root methanolic extract of A. pilosa, many transplantable mice tumours were used. Mice bearing S180, Meth-A fibrosarcoma, and MM-2 mammary carcinoma had significantly longer survival when Agrimonia pilosa was administered intraperitoneally (i.p.) before or after treatment. Agrimonia pilosa also reduced the development of 5-180 solid type tumours. On the other hand, in mice with S-180 ascites type tumours, pretreatment with cyclophosphamide dramatically decreased or abolished the extending of life span caused by *A. pilosa*. When tested in

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vitro on MM-2 cells, *A. pilosa* displayed exceptionally powerful cytotoxicity, then the effect was diminished by the addition of merely one-tenth as much serum. After receiving an intraperitoneal injection of AP-M for 2 to 5 days, mice's peripheral white blood cells significantly increased as compared to the host animals. On the fourth day after receiving an injection of AP-M, the number of peritoneal exudate cells exhibiting in vitro cytotoxic activity against MM-2 cells increased to approximately 5-fold that of the untreated control. The cells in the mice's spleens could absorb 3H-thymidine and their spleens were larger. [54].

- ***Ailanthus altissima***

Ailanthus altissima's stem bark is used in traditional Asian medication to treat a variety of illnesses, with cancer. This investigation's goal was to recognize and investigate compounds with tumoricidal action from the stem bark of A. altissima. The -carboline alkaloid 9-hydroxycanthin-6-one significantly repressed the growth of all three of the ovarian cancer cell types tested when it was isolated from the ethyl acetate fraction of *A. altissima* stem bark. 9-hydroxycanthin-6-one activated caspases 3, 8, and 9 to induce apoptosis. Because of 9-hydroxycanthin-6-one, cellular reactive oxygen species (ROS) were increased, and their pro-apoptotic activity was decreased by pre-treatment with the antioxidant N-acetyl-L-cysteine (NAC). Furthermore, it was demonstrated that 9-hydroxycanthin-6-one inhibited the synthesis of MCP-1 and RANTES, two essential elements that influence macrophage movement to tumour sites, in ovarian cancer cells. Treatment with 9-hydroxycanthin-6-one decreased the levels of M2 phenotypic indicators and many cancer-promoting chemicals in macrophages conditioned with ovarian cancer medium, such as VEGF, MMP-2, and MMP-9.These results suggest that 9-hydroxycanthin-6-one, isolated from the stem bark of *A. altissima*, prevents the activation of tumor-associated macrophages and induces cell death in human ovarian cancer cells via caspase- and ROS-dependent mechanisms. [55].

- ***Alpinia galangal***

One such well-illustrated chemical is 1'S-1'-Acetoxychavicol acetate (ACA), which is produced from the rhizomes of *A. galanga*. With this work, the purification process for ACA from *A. galanga* rhizomes is advanced and made simpler. Additionally, it investigates ACA's cytotoxicity and antiproliferative effects in Dukes' type B colorectal cancer (SW480). The purification of ACA from Alpinia galanga rhizomes involved HPLC standardization. To determine the IC_{50} value of ACA against the SW480 cell line, the MTT assay was used. Acridine orange/ethidium bromide, DAPI, and JC-1 staining were utilised to examine this value in order to analyse apoptosis, nuclear morphological alterations, and mitochondrial membrane penetrability. At an IC_{50} of 80μM, ACA markedly reduced the proliferative ability of SW480 cells (48h). The initial diagnosis of SW480 cell death caused by ACA was apoptosis, with significant DNA damage and mitochondrial depolarization occurring at the G0/G1 phase. Comparing ACA treated to control, the expression of p21 was upregulated while Cyclin D was downregulated. According to this study, 1'S-1'-Acetoxychavicol acetate exhibits strong anti-colorectal cancer action. [56].

- ***Coix lachryma-jobi***

Traditional Chinese medicine uses of seeds of gramineous plant Coix lachryma-jobi L. var. ma-yuen Stapf because they have anticancer properties. To determine the anticancer components, an acetone extract of the seeds was fractionated using the aqueous alkali technique and silica gel column chromatography. An acidic fraction was shown to have antitumor effect when an *in-vivo* growth inhibition test was performed on a transplantable mouse tumour. This acidic fraction contained four free fatty acids: palmitic, stearic, oleic, and linoleic acids, according to infrared spectroscopy and gas-liquid chromatography. [57].

- ***Dryopteris crassirhizoma***

To determine its anti-cancer characteristics, the mode of action and the inhibitory impact of *D. crassirhizoma* on the growth of PC3-MM2 (human metastatic prostate cells) were investigated. On PC3-MM2 cells, the extract's impact on cell cycle progression and its lethal result when coupled with tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) were also examined. [58].

- ***Vitex rotundifolia***

Three polymethoxyflavonoids, 2′,3′,5-trihydroxy-3,6,7-trimethoxyflavone (Vx-1), vitexicarpin (Vx-5) and artemetin (Vx-6), from the fruit of *V. rotundifolia*, were observed for their ability to inhibit the proliferation of human myeloid leukaemia HL-60 cells. They observed a dose-dependent slowing of HL-60 cell proliferation. After 96 hours, the concentrations of Vx-1, Vx-5, and Vx-6 needed to completely suppress growth was 4.03 μm, 0.12 μm and 30.98 μm for Vx-1, Vx-5, and Vx-6, respectively. The flavonoids caused morphological modifications in HL-60 cells that are indicative of apoptosis. The grade of apoptosis was determined by a double-antibody sandwich ELISA and by flow cytometric analysis. We determined the initiation of apoptosis by the detection of DNA fragmentation in agarose gel electrophoresis. It was discovered that the C-3 hydroxyl and C-8 methoxyl groups were not necessary for the action, but that the antiproliferative and apoptosis-inducing effect was reduced when the C-3′ methoxyl group was used in place of the hydroxyl group. These findings imply the potential for the polymethoxyflavonoids extracted from *V. rotundifolia* is employed as chemopreventive and chemotherapeutic medicines. [59].

- ***Thymus vulgaris***

This emphasises the necessity for complementary therapies, including herbal medications, to treat this illness. *Thymus vulgaris* L. is a widely used herb that reportedly has a great therapeutic potential. However, little is known about how this plant affects human colorectal cancer cells' ability to behave malignantly. The purpose of this study was examine the ability of *T. vulgaris* extract (TVE) to kill colorectal cancer cells. According to our findings, TVE inhibits proliferation in a way that depends on both concentration and time. As shown by increased caspase3/7 activity, this reduced proliferation was accompanied by an increase in apoptotic cell death. Additionally, TVE reduced fibronectin adherence in a concentration-dependent manner. TVE greatly reduced the ability of HCT116 cells to migrate and

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invade. Together, these studies imply that the TVE prevents colon cancer cells from developing a malignant phenotype. T. vulgaris may thus have an anticancer impact, and some of its bioactive chemicals may prove to be valuable as therapeutic agents for treating human colorectal cancer cells. [60].

- ***Thuja occidentalis***

Thuja occidentalis crude alcoholic extract is used in traditional remedy and as a homoeopathic mother tincture (TOΦ) to give a variety of conditions, including moles and tumours. The malignant melanoma cell line A375 has been used to test the anti-proliferative and apoptosis-inducing abilities of TOΦ and the thujone-rich fraction (TRF) that was isolated from it. The three main fractions separated by chromatography have little to no effect on the A375 cell line during the initial trial using the S-diphenyltetrazolium bromide assay; as a result, only TRF was further characterised and subjected to various other assays in order to pinpoint its precise anti-proliferative and apoptotic potentials. TRF was said to have a molecular weight of 152 and the chemical formula C(10)H(16)O. Comparing TRF of *T. occidentalis* toTOΦ, in-vitro exposure to A375 cells revealed higher cytotoxic, anti-proliferative, and apoptotic effects, but had no influence on normal cell growth (peripheral blood mononuclear cell). In addition, both TOΦ and TRF significantly reduced cell viability, induced inter-nucleosomal DNA fragmentation, mitochondrial transmembrane potential collapse, increased ROS generation, released cytochrome c, and activated caspase-3, all of which are directly linked to the induction of apoptosis in A375 cells. TRF exhibited and matched all of TOΦ anti-cancer actions as a result, and it may be the major bioactive fraction. [61].

- ***Scrophularia striata***

Scrophularia striata extract's impact on the development of an astrocyte cancer cell line (1321). To ascertain their potential anticancer effects in contrast to etoposide, the 1321 cell line was seeded in 96-well culture plates with varying doses of either leaves and seeds filtered or unfiltered extracts of *S. striata* (chemical anticancer reagent). In comparison to the control group (cells not exposed to the extracts) and even the group (adenocarcinoma gastric cell line) treated to etoposide, the filtered leaf extract of S. striata significantly inhibited the growth of the 1321 cell line. The seed extract, as opposed to the leaf extract, induced cell growth in every experiment. Results from flow cytometry showed that the leaf extract reduces cell growth through apoptosis. Our research shows that S. Striata seeds and leaves both contain substances that inhibit cancer growth and promote cell proliferation. [62].

- ***Rubus idaeus***

Due to its positive effects on health, raspberries (Rubus idaeus L.) have been the subject of significant research all over the world. According to recent findings, Rubus idaeus (RIE) crude extracts exhibit antioxidant and anticancer properties.. The aim of this study was to analyse how the antimetastatic properties of the substance worked on oral cancer cells. In this work, RIE was used to treat SCC-9 and SAS oral cancer cells. The impact of RIE on migration and invasion was then examined. Oral cancer cells' capacity for invasion and migration was reduced by the addition of RIE. Matrix metalloproteinases-2 (MMP-2) mRNA, protein expression, and enzyme activity were all down-regulated by RIE, according to zymography, western blot, and real-time PCR analyses. Further, RIE therapy decreased the phosphorylation of the extracellular signal-regulated kinases (ERK), src, and focal adhesion kinase (FAK). These findings presented that RIE inhibited oral cancer cells' migration and invasion and changed metastasis by reducing MMP-2 expression through the FAK/Scr/ERK signalling pathway. [63].

- ***Pygeum africanum***

Prostate cancer is a great candidate for chemoprevention since it normally grows slowly and is frequently found in older individuals. *African prune (plum) trees, Pygeum africanum,* are indigenous to tropical Africa. In Europe *P. africanum* bark extract has been utilised for the treatment and prevention of prostate diseases, such as benign prostatic hypertrophy (BPH). *P africanum* and saw palmetto phytotherapeutic formulations have recently been sold in the USA for prostate health, including the prevention and treatment of prostate cancer. [64].

- ***Phaleria macrocarpa***

In this work, we use a bioactivity-guided DLBS1425, an extract of Phaleria macrocarpa, on the MDA-MB-231 breast cancer cell line to assess its molecular mechanism. In a dose-dependent manner, DLBS1425 demonstrated inhibition of MDA-proliferative, MB-231's migratory, and invasive potential. Additionally, DLBS1425 significantly reduced phosphoinositide-3 (PI3)-kinase/protein kinase B (AKT) signalling by lowering PI3K transcript levels, which in turn resulted in a decrease in AKT phosphorylation. In addition, it stimulated pro-apoptotic genes including BAX, BAD, and PUMA, which in turn caused caspase-9 to become activated, causing DNA fragmentation and the cellular death signal. Our findings indicate that the anticancer drug DLBS1425 targets genes involved in cell survival and death in MDA-MB-231 breast cancer cells. [65].

- ***Olea europaea***

According to epidemiological research, consuming fruits and vegetables on a daily basis—many of which are high in polyphenols—can help lower your chance of developing chronic illnesses like cancer and cardiovascular disease. O. europaea L phenolic compounds, which are abundant in leaves and have been linked to cancer prevention, the antioxidant activities of the crude extracts and its isolated compounds by using various in-vitro assays, including total antioxidant capacity (TAC), DPPH radical scavenging capacity, xanthine oxidase (XO) inhibitory effect and the capability to delay the linoleic acid peroxidation process, the main goal of this study was to identify the major components in the *O. europaea* L. leaf preserved during the decoction preparation (ALP). The aqueous decoction was divided into four extracts, and the n-butanol extract had the greatest levels of phenolic content and antioxidant activity. 13 secondary metabolites, including flavonoids, secoiridoids and simple phenolics are isolated as a result of phytochemical research and their structures are clarified by spectroscopic data (1D and 2D NMR) and spectrometric methods. Fraxamoside (1) (EC50 62.6 µM) and taxifolin (5) (EC50 50.0 µM), which was separated for the first time

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from the decoction of water, have been revealed to have a considerable free radical scavenging action against DPPH. The 3,4-dihydro-phenyl glycol (8), which has a 0.90 caffeic acid equivalent, was the most active substance in the TAC assessment. Taxifolin and fraxamoside, on the other hand, were shown to be the most effective inhibitors of XO activity (IC50 values of 2.7 and 5.2 µM, respectively). The maximum ALP activity was seen in secoxyloganin (4), oleuropein (2), and tyrosol (6). [66].

- ***Lonicera japonica***

  Lonicera japonica Thunb. (Indongcho) dried flower decoctions have been used in traditional treatments for inflammatory illnesses. PELJ, or isolated polyphenols from lyophilized Lonicera japonica Thunb, has recently been studied for its potential to treat cancer in U937 cells. Here, we showed that upregulating DR4 and Fas and suppressing XIAP greatly enhanced PELJ-induced apoptosis. Additionally, inhibiting the PI3K/Akt pathway is at least partially responsible for the PELJ-induced apoptosis. These results imply that PELJ could have anticancer actions on U937 cells. To ascertain whether PELJ give more solid proof that PELJ which may provide a good impact for treating cancer, further research for the precise mechanism and the effects on animal models is required. [67].
- ***Lantana camara***

  Ultraviolet-Visible spectroscopy, X-ray diffraction, fourier transform infrared, high resolution transmission electron microscopy, selected area electron diffraction pattern, and energy dispersive X-ray analyses were used to characterise the gold nanoparticles (Au NPs) produced by the Lantana camara Linn root extract. Gallic acid and gold nanoparticles had inhibitory concentrations (IC50) of 24.17 and 5.39µg/ml, in the DPPH assay, respectively, but the IC50 of gold nanoparticles in the cytotoxicity assay was 17.72 and 32.98µg/ml, on MBA-MB-231 and Vero cells, respectively. Because of their strong in-vitro antioxidant and cytotoxic characteristics, Au NPs might be used as a viable alternative to traditional anticancer medication development in the future. [68].
- ***Juncus effusus***

  A phenanthrene called dehydroeffusol (DHE) was discovered in the Chinese medicinal plant Juncus effusus. DHE has anticancer properties both in vitro and in vivo, according to biological examination. We used liquid chromatography-tandem mass spectrometry to conduct a shotgun proteome study to look at how DHE therapy affected the protein profiles in cancer cells. Cancer-related signalling pathways such asNF-κB, β-catenin, and endoplasmic reticulum stress were all impacted by DHE. Activating transcription factor 2 (ATF-2) and c-Jun kinase (JNK) were discovered to be the essential elements in DHE's regulated biological pathways using quantitative route and key node analysis of the proteomics dataThe route analysis and chemical resemblance to estradiol support the hypothesis that DHE is a phytoestrogen. With specific cell-based assays, the proteomic, bioinformatic, and chemoinformatic analyses were further validated. [69].
- ***Hydrastis canadensis***

  The potential anti-cancer properties of Hydrastis canadensis ethanolic extract have been investigated in mouse models of hepatocarcinogenesis caused by p-dimethylaminoazobenzene (p-DAB). For 1, 2, 3, and 4 months, respectively, mice was chronically given p-dimethylaminoazobenzene (p-DAB) and phenobarbital (PB), two hepato-carcinogens., and were divided into sub-groups: i) fed normal low protein diet (Gr. I, normal control); ii) fed diet mixed with 0.06% p-DAB at a daily dose of 165 mg/kg b.w. per mouse plus 0.05% PB plus 0.06 ml 90% alcohol (vehicle of the crude extract) (Gr. II, carcinogen treated); iii) fed diet mixed with p-DAB and PB at the same daily dose plus crude extract of *Hydrastis canadensis* (Gr. III, drug treated). In different groups of treated and control mice, the activities of lactate dehydrogenase, catalase, glucose-6-phosphate dehydrogenase, alanine amino-, aspartate amino-, and gamma glutamyl-transferases, lipid peroxidation, reduced glutathione content, and several other biochemical parameters were examined. The drug's anti-cancer potentials were found to be acceptable for usage as a supportive supplementary medication for liver cancer, according to a critical examination of the findings of these investigations. [70].
- **Achillea wilhelmsii**

  On colon cancer cells (HT-29), methanol extracts and the plant's essence show cytotoxic effects, and the essence's cytotoxic effects are stronger. In additional investigations, the effects of methanol extracts of plant leaves against the cell lineage of breast, stomach, and colon cancer are demonstrated. Plant phenol components, particularly flavonoids, are present in the methanol extract, which inhibits the growth of cancer cells by triggering apoptosis. 1,8-cineole and α-piene in plant leaf essence are two of the most significant monoterpene components of this plant that induce apoptosis in human melanoma cells. [71].
- **Ammi majus**

  This plant's ethanol extract was tested on HeLa and MCF7 cells, and the results indicated that it had a toxic effect on these cells. Comorian compounds, which are key constituents of phenol compounds, are responsible for the majority of this plant's biological functions. Apoptosis induction by these substances is researched and verified to cause cell toxicity in coumarin compounds on cell lineagesThe most significant coumarin components of this plant that can block cytochrome p450 activity are called psoralens. [72]
- **Ammi visnaga**

  Different extracts from this plant's above-ground portion have been tested for their ability to kill T47D cancer cells. Additionally, pelvic rhabdomyosarcoma and L20B of mice, 2 human cell lineages, have demonstrated this plant's inhibitory and dose-dependent effects on them. The most significant components of this plant include khellol, visnadine, cimitugin, and beta-sitosterol. This plant's aqueous extract contains flavonoids including quercetin and kaempferol, and these substances can support the plant's anticancer properties .[73]

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- **Astragalus cytosus**
  In Iran, astragalus cytosus is found in more than 200 species. The toxicity of this plant's extract on cancer cells was shown in a study using HeLa cancer cells. Additionally, in a clinical trial involving 24 patients with lung cancer, 21 of them responded well to the plant's extract. Studies in vitro demonstrate that flavonoids from different species of this plant can trigger the apoptosis of cancer cells. [74].
- **Avicennia marina**
  A species of mangrove plant is called Avicennia marina. The halophyte mangrove plant is resistant to sea salt. The mangrove ecosystem's primary species is mangrove. With a height range of one to ten metres, this plant resembles a bush or shrub. Its leaves are pointed or oval, and its shell is either white, grey, or yellowish green. Its four petals might be white or golden orange. On human breast cancer BT-20 cells, flavonoid components of its leaf extract show an anticancer effect. Another study demonstrated the anticancer effects of naphthoquinone on laryngeal cancer cells (kb) by isolating it from the plant's leaves. 53 The extract has a demonstrated cytotoxic impact on breast cancer cells (row 231MDA-MB). [75].
- **Olea europae**
  The most significant leaf and its constituents, particularly oleic acid, are discussed in a study on the anticancer properties of olive oil. Pinoresinol, a component of olive oil, also possesses anti-colorectal properties. Oleuropein, a phenolic molecule found in olive oil, has a vital function and may directly affect the her-2 gene in breast cancer cells. The study also shown that some types of tumour cell growth and the activation of apoptosis can be inhibited by the acidic triterpenes contained in olive oil. Inhibiting tumour development and angiogenesis are crucial features, and two of these substances, maslinic acid and oleanolic acid, demonstrated adequate anticancer effects in a colon cancer model in rats. [76]
- ***Rosa damascenes* Mill**
  This essential oil has been found to be harmful to breast (MCF7) and lung cancer (A549) cell lines. The plant cell's ethanol extract has a lethal effect on cervical cancer cells (HeLa). Gastric cancer cells are affected by Rosa Damascena essential oil in two distinct ways: the soluble phase boosts cell viability, while the vapour phase reduces cell survival. Additionally, flow cytometry demonstrated that apoptosis is a key process involved in cell death.[77]
- **Viola tricolor**
  Viola tricolour is the scientific name for a violet plant. Violets are herbaceous plants that may reach a height of up to 25 cm and are resistant to cold throughout the year. These plant's tiny, colourful blooms, which come in shades of vivid purple, white, and yellow, bloom in the spring and summer and develop into fruit capsules. The active component of this plant, ethyl acetate, is responsible for the effect that this plant's aqueous extract has on the progression of cervical cancer. There are a variety of substances in this plant that have powerful cell-damaging actions. Studies have demonstrated the potential anticancer properties of flavonoids. [78]
- **Citrullus colocynthis**
  A study revealed that the extract of this herb (Hep2) may have harmful effects on cancer cells in the larynx. According to research, this plant's chemical components, such as cucurbitales, are employed as anticancer medications in malignancies including liver (HepG2) and breast (MCF7) tumours; quercetin and b-sitosterol have also been investigated as antitumor agents in several studies. These substances work by stopping the cell cycle in G2/M, and by inducing apoptosis, they can have anticancer effects. [79]
- **Myrtus communis**
  The herb was recommended because of its anticancer properties. On cancer cell lines MCF7, the plant also exhibits cytotoxic action. Some of the most significant components in this plant are polyphenols, myrtucommulone, semimyrtucommulone, 1,8-cineole, a-pinene, myrtenyl acetate, limonene, linalool, and a-terpinolene. Most studies attribute this plant's anticancer capabilities to its phenolic components (especially mitocomolon). The cell layer is affected by cytotoxic effects on cells. A strategy to combat cancer cells involves inducing apoptosis in cancer cells through both internal and external mechanisms. [80]
- **Boesenbergia pandurata**
  Boesenbergin, pinocembrin, pinostrobin cardamonin, , panduratin A, and 4-hydroxypanduratin A are the active ingredients in B. pandurata. These substances function as anti-inflammatory, anticancer, antibacterial, antifungal, antioxidant, and anti-tuberculosis agents. It has been demonstrated that Panduratin A, a cyclohexenylchalcone derivative found in B. pandurate, inhibits the growth of HT-29 colon cancer cells and causes them to undergo apoptosis. A study described that Panduratin A arrested the cancer cell lines A549 non-small cell lung cancer; PC3 and DU145 prostate cancer cells and MCF-7 breast cancer cells and illustrated proapoptotic activities. Mohd Isa et al. [10] explored the anticancer role of Boesenbergin a (BA) isolated from Boesenbergia rotunda in human non-small cell lung cancer (A549) BA accumulated cells in the sub-G1 phase to arrest the cell cycle. Caspases 3/7, 9 and 8 from the Bcl-2 family, which promote apoptosis, were stimulated by BA. Accordingly, the study's findings suggest that BA may be a promising agent for the treatment of lung cancer. [81]
- **Coptis chinensis**
  Coptis chinensis, the Chinese goldthread, is a herb used as a traditional medicine in China thus officially enlisted in the Chinese pharmacopeia. It is well known for its historical applications against a number of illnesses, including supportive infections, acute febrile illnesses, diarrhoea, and dysentery. C. chinensis' organic extract has anti-inflammatory and antioxidant qualities. Because of its potent antibacterial action, C. chinensis extract is widely used in the treatment of cholera, dysentery, diabetes, blood, and lung cancerThe most significant and potent elements are found in the Coptis genus, including an alkaloid called berberine (Figure 1). Berberines alkaloids cause human leukaemia HL-60 cells to apoptose by down-regulating nucleophosmin/B23 and telomerase activity, which is a

frequent criteria in the quality control of Rhizoma coptidis (Huang Lian) products. [82]

III. CONCLUSION

Many studies have been found that various medicinal plants having many novel compound which is responsible for the treatment of various kind of diseases. Here we discuss various plants having novel compounds which have been used in the treatment of cancer.

- **Conflict of Interest:** All author declare that they have no conflict of interest

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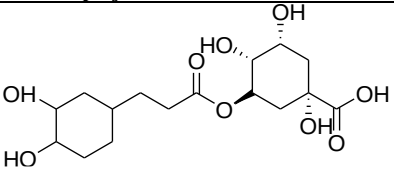
S.No.	Citing patent	Filing date	Publication date	Title	Assignee
1.	**KR20090033699A**	**2007-10-01**	**2010-03-11**	A cancer sensitizer comprising chlorogenic acid	Kim Soo-yeol Park Kang Seo Jeong Gyeong-chae
2.	**US7445802B2**	**2000-12-26**	**2008-11-04**	Site-specific in situ generation of allicin using a targeted alliinase delivery system for the treatment of cancers, tumors, infectious diseases and other allicin-sensitive diseases	Aharon Rabinkov Talia Miron David Mirelman Meir Wilchek
3.	**WO2013112186A3**	**2012-04-09**	**2013-08-01**	Organometallic anti-cancer complexes	Varattur Dayal Reddy
4.	**WO2007068071A2**	**2006-12-14**	**2007-08-02**	Process for obtaining an antineoplasic phytotherapeutic compound derived from an extract from the plant bidens alba and antineoplasic phytotherapeutic compound derived from an extract from the plant bidens alba	Universidade Estadual De Campinas - Unicamp
5.	**US20130059018A1**	**2013-03-07**	**2014-07-29**	Phytocannabinoids in the treatment of cancer	GW Pharma Ltd
6.	**JPH1036260A**	**1996-07-18**	**1998-02-10**	Enhancement of effect of anticancer agent	Chan Wan De Masahiko Hara Hoyoku Nishino Jun Chen Shu Su Zen Yon
7.	**WO2003094945A1**	**2003-05-06**	**2003-11-20**	Use of hyperforin and derivatives thereof for inhibiting angiogenesis	Christoph M. Schempp Jan C. Simon
8.	**KR101579371B1**	**2014-02-27**	**2015-12-22**	Anti-cancer composition comprising gossypol and phenformin	Kim Soo-yeol Kim Jong-heon Bae Young-gi Lee Ho Jang Hyun-cheol Hong Gyeong-man Hong Dong-wan Choi Beom-gyu
9.	**CN104958330A**	**2015-06-05**	**2015-10-07**	Oroxylum indicum general flavone extraction and purification method and application thereof	Meng Xiansheng Li Nannan Yang Yu Bao Yongrui Wang Shuai
10.	**WO2012108746A3**	**2005-06-16**	**2009-02-05**	Novel Anticancer Agent, Methods for Obtaining the Same and Pharmaceutical Compositions Thereof	MMI Corp
11.	**WO2011119625A1**	**2011-03-22**	**2011-09-29**	D. innoxia withanolides with specific anti-cancer activities	Julian Andrew SimonJeffrey Jerard Posakony Francisco Omar Holguin Mary Anne O'connell Richard Dean Richins

12.	**CN102293749B**	**2011-07-26**	**2012-08-22**	Brucine immune nanoparticles	Qin Jianmin Sheng Xia Yang Linsa Zhongqiu Huang Tao Li Qi Yin Peihao Zhang Min Hi-tech Climbing Chen Qinghua Ma Jingwei Shen Hebai
13.	**US6849604B2**	**2004-01-13**	**2005-02-01**	Phytochemotherapy for cancer	Jackson State University
14.	**CN102988517B**	**2011-09-15**	**2016-06-01**	Agrimonia pilosa ledeb anti-liver cancer active component and application thereof	Song Jingzheng He Yongcheng
15.	**KR101545507B1**	**2013-09-30**	**2015-08-19**	A Composition comprising an extract of Ailanthus altissima for treating or preventing cancer disease	Lee Sang-guk Park Heon-ju Kim Won-kyung Lee Jung-gu Lee Sang-woo Park Sang-hong
16.	**EP2952201A1**	**2014-12-05**	**2017-06-21**	Compositions of Alpinia galanga or Alpinia conchigera with high content of 1'S-1'-acetoxychavicol acetate suitable for pharmaceutical processing	Nerthus Aps
17.	**WO2008108647A2**	**2008-03-05**	**2008-12-04**	Enhancement of anticancer therapy by flavonoids	Wim J. F. Van Der Vijgh Aalt Bast Anna Maria Elisabeth Bruynzeel Cees J. Van Groeningen
18.	***CA2342403A1***	**2001-03-28**	**2002-09-28**	Sesquiterpene derivatives as anticancer agents	Jean Legault Andre Pichette
19.	***US20150216921A1***	**2008-03-05**	**2008-09-12**	Base powder from the red raspberry rubus idaeus and activated micronized zeolite for attenuating nicotine addiction, method for the preparation thereof and use thereof	Javier Isaias Alanis Ricardo Perez-Pasten Borja Santiago Filardo Kerstrupp Alfonso Atitlan
20.	***US8569382B2***	**2009-11-26**	**2011-10-20**	Isolated compounds from Phaleria macrocarpa as anti-cancer agents	PT Dexa Medica
21.	***US7527812B2***	**2006-09-26**	**2009-05-05**	Herbal composition for treating cancer	Sheng Foong Pharmaceutical Co Ltd
22.	***KR20140108796A***	**2013-02-28**	**2014-09-15**	Drug composition containing extract of Juncus Effusus L. for anti-oxidative and anti-tumor activity	Park Chan-ik

Table 1: Patents granted on anti-cancer Plants and phytoconstituents

S.N.	Name of the plant	Part used	Active phytoconstituent	Type of study	Mode of action	Ref.
1	***Achyranthus aspera***	Whole plant	 Chlorogenic acid	*In-vivo* lung cancerous mice	Enhanced activities and expression of antioxidant enzymes GST, GR, CAT, SOD,	[24]

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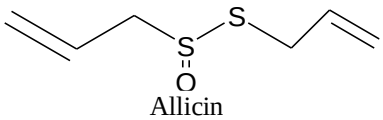
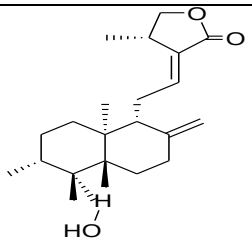
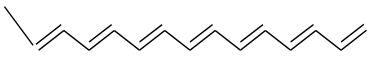
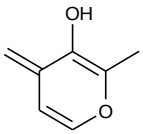
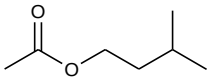
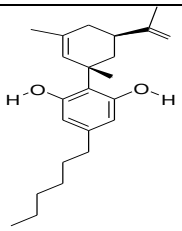
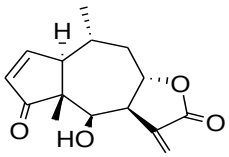
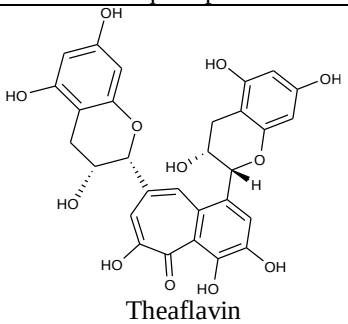
2	***Allium sativum***	bulb	 Allicin	human cancer, growth of transplantable tumors	inhibit the activity of diverse chemical carcinogens	[25]
3	***Andrographis panniculata***	Whole plant	 Andrographolides	inhibits the proliferation of HT-29 (colon cancer)	enhanced proliferation and interleukin-2 (IL-2) induction in HPBLs	[26]
4	***Bidens pilosa***	Whole plant	 Polyacetylenes	Ehrlich ascites carcinoma-bearing mice	concentration-dependently the MCF-7 cells	[28]
5	***Bolbostemma paniculatum***	tubers	 Maltol	proliferation change of human glioblastoma U87MG cells	Tubeimoside V significantly suppressed U87MG cell proliferation	[29]
6	***Apis Mellifera***	venom	 Iso-pentyl acetate	preclinical cell culture and animal model	BV inhibits proliferation of the cancer cells via induction of apoptosis	[30]
7	***Cannabis sativa***	Whole plant	 Canabidiol	colorectal cancer, colon cancer in vivo	colorectal cancer cell proliferation via CB1 and CB2 receptor activation.	[31]
8	***Centaurea ainetensis***	Whole plant	 Sesquiterpenes lactones	colon-derived cancer cells	inhibited the proliferation	[33]
9	***Camellia sinensis***	flower	 Theaflavin	human ovarian cancer cell lines	decreased mitochondrial membrane potential, activated Caspase-3/7, Caspase-8, and Caspase-9 activities, S phase arrest	[34]

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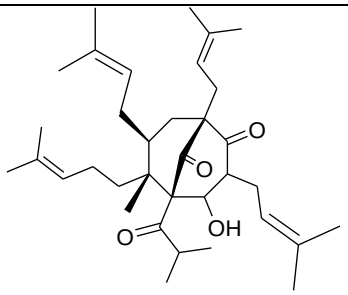
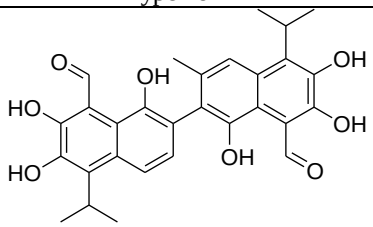
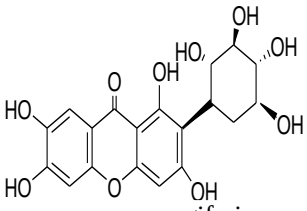
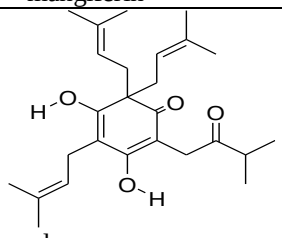
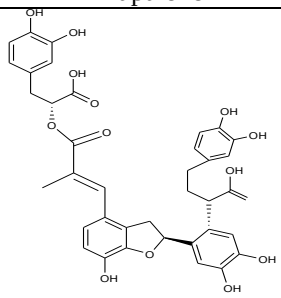
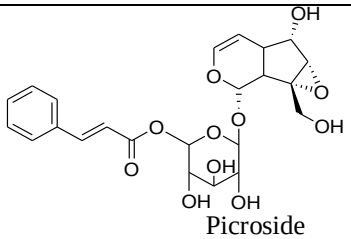
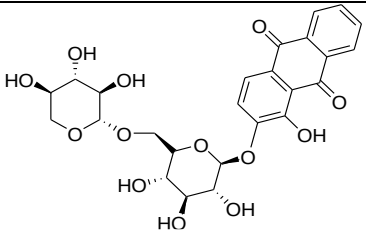
10	***Hypericum perforatum***	Whole plant	 Hyperforin	human prostate cancer cells *In-vitro* and *In- vivo*	serotonin-reuptake inhibitors	[35]
11	***Gossypium hirustum*** *or* ***Gossypium herbaceum***	seed	 Gossypol	metastatic carcinoma of endometrium	cytosolic and mitochondrial enzyme systems	[37]
12	***Mangifera indica***	seed	 mangiferin	human gastric cancer cells, chick chorioallantoic membrane model	downregulating Ang-1/Tie2 pathway	[38]
13	***Oroxylum indicum***	Whole plant	 Lupulone	MDA-MB-231 cancer cells	cell migration inhibition	[40]
14	***Salvia miltiorrhiza***	Whole plant	 Salvianolic acid	typical tumor cells	arrest the cell cycle at S phase	[41]
15	***Picrorrhiza kurroa***	Whole plant	 Picroside	sarcoma in control mice	inhibited yeast topoisomerase I and II enzyme activity	[43]
16	***Rubia cordifolia***	rhizomes	 Ruberythric acid	SGC-7901, A549 or Hela cancer cell lines	1–3 inhibited NF-κB signaling pathway	[44]

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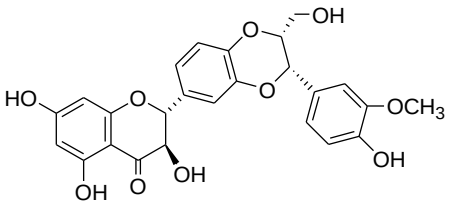
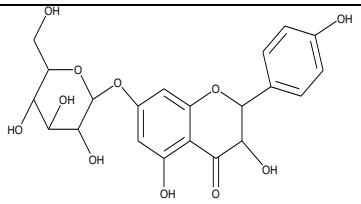
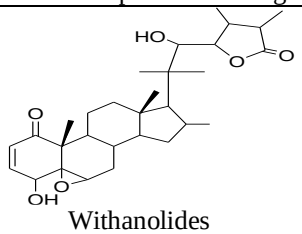
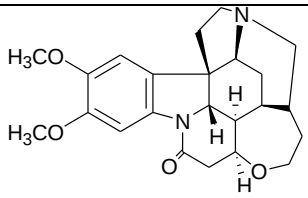
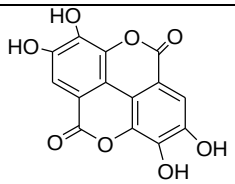
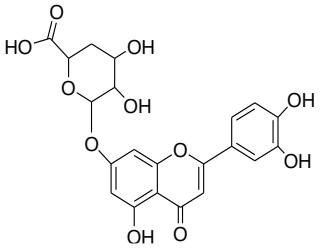
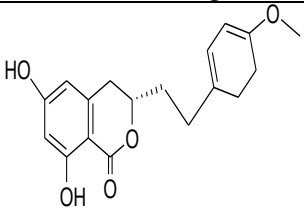
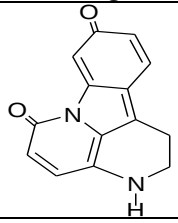
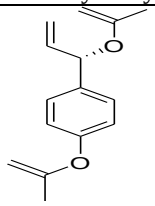
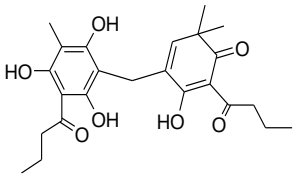
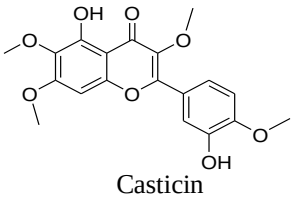
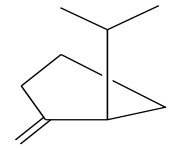
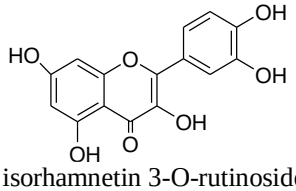
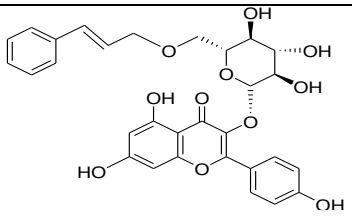
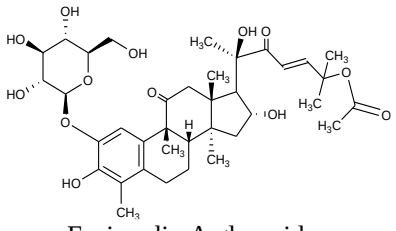
17	***Silybum marianum***	Whole plant	 Silibinin	DEN-initiated mouse model of HCC	suppressing oxidative stress and proliferation	[45]
18	***Smilax china***	rhizome	 kaempferol-7-O--d-glucosid	*In-vitro* cytotoxicity and antiproliferative effect in cancer cell lines	cell cycle arrest at G_1 phase	[46]
19	***Withania somnifera***	Whole plant	 Withanolides	prostate cancer cell line	inhibiting the expression of IL-8 and COX-2	[47]
20	***Strychnos nuxvomica***	root	 Brucine	myeloma cell line-ROMI 8226, HepG2 cells	apoptosis, through the participation of caspase-3 and cyclooxygenase 2	[48]
21	***Terminalia chebula***	fruit	 Ellagic acid	breast cancer cell line, human osteosarcoma cell line (HOS-1)	cell viability, inhibited cell proliferation	[50]
22	***Vernonia amygdalina***	Whole plant	 Luteolin-7-O-glucuronide	human prostate cancer	cell growth arrest, DNA damage, apoptosis	[52]
23	***Agrimonia pilosa***	root	 Agrimonolide	Meth-A fibrosarcoma and MM-2 mammary carcinoma-bearing mice	host-mediated actions and direct cytotoxicity.	[54]
24	***Ailanthus altissima***	Stem, bark		ovarian cancer cell	inhibits the activation of tumor-associated macrophages	[55]

			9-Hydroxycanthin-6-one			
25	***Alpinia galangal***	rhizomes	 1'-Acetoxychavicol acetate	colorectal adenocarcinoma	apoptosis and cell cycle halted at G0/G1	[56]
26	***Dryopteris crassirhizoma***	Whole plant	 Flavaspidic acid	human metastatic prostate PC3-MM2 cells	nduced apoptosis through the activation of caspase-3, -8, -9, bid, and PARP in PC3-MM2 cells.	[58]
27	***Vitex rotundifolia***	fruit	 Casticin	human myeloid leukemia HL-60 cells	induced morphological changes that are characteristic of apoptosis	[59]
28	***Thymus vulgaris***	Whole plant	 cis-Sabinene	human colorectal cancer cells	decreased adhesion to fibronectin in a concentration-dependent manner, increased caspase3/7 activity	[60]
29	***Scrophularia striata***	leaf and seed	 isorhamnetin 3-O-rutinoside	astrocyte cancer cell line	seed extract activated cell proliferation, leaf extract inhibits cell proliferation	[62]
30	***Rubus idaeus L***	Whole plant	 Tiliroside	oral cancer cells	inhibited the migration and invasion ability of oral cancer cells, alter metastasis of MMP-2 expression through FAK/Scr/ERK signaling pathway	[63]
31	***Phaleria macrocarpa***	Bark	 Fevicordin A glucoside	breast cancer cell line	reduced phosphoinositide-3 (PI3)-kinase/protein kinase B (AKT) signalling by reducing PI3K transcript level	[65]

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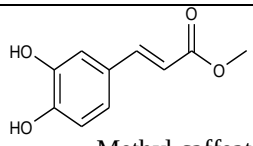
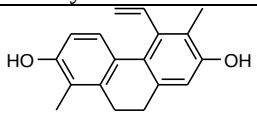
32	***Lonicera japonica***	flowers	 Methyl caffeate	U937 cells	induced apoptosis by upregulation of DR4 and Fas	[67]
33	***Juncus effusus***	Whole plant	 Juncusol	*In-vitro* and *In-vivo* anticancer effects	affected cancer-associated signaling pathways	[69]

Table 2: Plant and its Type of study