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Role of botanical weapon for controlling cancer-an update

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Abstract

Cancer is a leading cause of death and a vital health care challenge in the world. Men are mostly affected by skin cancer, liver cancer, blood cancer, lung cancer, colon cancer, rectum, and prostate cancer. Women are mostly affected by cervical, blood, liver, skin, breast, colon, rectal and stomach cancer. Oncology is the study of cancer. An oncologist is a doctor who treats cancer and provides medical care for a person diagnosed with cancer. An oncologist may also be called a cancer specialist. Cancer is the abnormal, uncontrolled division of cells in the body. The cancer cells when malignant, invade various parts of the body through the bloodstream and still remains an aggressive killer worldwide. However, adverse side effects of chemotherapy, radiation therapy, immunotherapy, surgery, and stem cell therapy has some negative effects on the patient suffering from cancer. Medicinal plants could also possess effective anticancer compounds that may be used as adjuvant to existing chemotherapy to improve efficacy and/or reduce drug-induced toxicity; such as chemotherapy-induced nausea and vomiting to improve patients' quality of life. Plant-derived anticancer agents are effective cancer inhibitors. Herbal medication offers very reasonable alternate to modern medicine against cancer. However, majority of plant extracts have been researched for cancer prevention rather than treatment, resulting in low efficacy and uptake in practice. Hence there is possible way to reduce the process of carcinogenesis with regular use of these plants along with a healthy lifestyle.

Keywords: Anticancer; Alkaloids; *Ayurveda*; Breast cancer; Cannabis; Cancer; Chemotherapy; Drug; Leukemia; Prevention; Medicinal Plants; Oncology; Tumors of Malignant

1. Introduction

Cancer has affected the human population. and remains a major global challenge in the health care system. The cancer disease is defined as the uncontrolled cell division in the human body and these cells are circulating in the blood stream and invade various parts of the body [1-265-313]. Cancer, a non-communicable disease, is a significant public health

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issue due to low survival rates, disease recurrence, drug resistance, toxicity, and the non-specificity of available drugs, resulting in approximately 15 million deaths in 2020 and a projected threefold increase by 2040. Defined as abnormal cell growth with metastatic potential, cancer involves uncontrollable cell division mediated by protein up-regulation and deoxyribonucleic acid (DNA) mutations, presenting a formidable treatment hurdle [1-284-305]. Addressing these challenges requires an urgent exploration of new strategies and therapies to enhance the overall survival rate and prognosis for cancer patients [1-284-313].

Cancer can be broadly classified into carcinoma, sarcoma, melanoma, lymphoma, and leukemia [1-200]. Carcinomas include almost 81% of overall cancer available, which originate in the skin, lungs, breasts, pancreas, and other organs and glands [1-200]. Carcinogenesis is a complex phenomena that involves many signaling cascades. Lymphomas are the cancers of lymphocytes. Leukemia is the form of cancer in blood. Sarcomas occur in bone, muscle, fat, blood vessels, cartilage, or other soft or connective tissues of the body [1-200]. Melanomas are cancers that arise in the cells that make the pigment in the skin [1-90]. The broad base of knowledge created by studying cancer cell helps to limit the progress of the disease [1-200]. Common treatments such as radiotherapy and chemotherapy can cause some complications[1-200]. Men are mostly affected by skin cancer, liver cancer, blood cancer, lung cancer, colon cancer, rectum, and prostate cancer. Women are mostly affected by cervical, blood, liver, skin, breast, colon, rectal and stomach cancer [1-200-305-313].

Cancer is the third leading cause of death worldwide following cardiovascular and infectious diseases[1-200]. With 100 different types, cancer mainly affects men in the form of colorectal, liver, lung, prostate, and stomach cancer and women in the form of breast, cervix, colorectal, lung, and thyroid cancer [1-200-313]. Breast cancer is the most common form of cancer in women [1-200]. It is the most frequent malignancy in women and accounts for 38.5% of all female cancers. About half (43.7%) of all breast cancers are detected in an advanced stage [1-200, 262]. Colon cancer is the second most common cause of cancer deaths in the US [1-200]. Prostate cancer is the most frequently diagnosed cancer among men in the US, and ranks second to skin cancer, with an estimated 180,000 new cases and 37,000 deaths expected to occur by the American Cancer Society each year [1-200-262].

More than 3000 plants have anticancer activity [1-200-313]. India is one among the 12 centers in the world that contain a diversity of plant producing novel bio-molecules. India is known as "the botanical garden of the world" and is the highest plant producer of the world [1-200-305]. The Western Ghats of India represent one of the world's ten biodiversity hotspots treasuring more than 700 medicinal plants [2-200]. *Ayurveda*, the traditional Indian medicine (TIM) and the traditional Chinese medicine (TCM), have provided most of the current knowledge related to medicinal plants [2-265, 311-313]. Herbal products such as plant extracts, dry powders and parts of plants, fungi, and algae have been used as complementary treatments alongside conventional drugs [2-265-280, 311-313].

The most important problem in cancer treatment is destroying tumor cells in the presence of natural cells, without damaging natural cells. Therefore, availability of natural products with higher effectiveness and lower side effects is desired. Medicinal herbs are important for cancer treatment due to their multiple chemical compound for discovering new active materials against cancer. Therefore, there is a constant demand to develop new, effective, and affordable anticancer drugs. Several factors, such as environmental factors, habitual activities, genetic factors, etc., are responsible for cancer [1-200]. Phytochemicals are considered suitable candidates for anticancer drug development due to their pleiotropic actions on target events with multiple manners[1-200-273]. On the other hand, medicinal plants with compounds include alkaloids, phenol compounds, and monoterpenes played an important role in controlling caner. In addition to these, indicators such as **vinblastine**, **vincristine,** curcumin, Taxol, boswellic acid, and umbelliprenin and compounds such as quercetin, catechin, cucurbitacin, kaempferol, thymol, carvacrol, 1 and 1,8-cineole, a-pinene, myrecene, and b-sitosterol have anticancer effects.

2. Cancer Treatment: Health Issues

Cancer incidence and mortality rates are increasing worldwide. Cancer treatment remains a real challenge for many countries, especially in developing countries where funding and resources are very limited[1-265-280]. High costs, side effects and drug resistance associated with cancer treatment have encouraged scientists to invest in research into new herbal cancer drugs[1-265-280]. Chemotherapy is one of the most common treatment methods, which uses one or more anticancer drugs to cure or prolong the life of the cancer patients [1-200]. Further, chemotherapy can also put patients under a lot of strain and further damage their health [1-200]. Chemotherapy, the primary choice for treatment of cancer, is often ineffective or/and presents itself with many debilitating side effects, including loss of appetite, nausea, insomnia, and anxiety [1- 104, 143-160-200]. Surgery at any stage of cancer is highly invasive and painful. Immunotherapy is the artificial stimulation of the immune system against cancer cells, a targeted therapy interfering with the molecules in the cancer block and inhibiting cancer growth [1-200]. Radiation therapy is the use of ionization radiation to kill malignant

cells [1-200]. Radiation therapy is known to induce unwanted DNA damage in normal healthy cells, leading to loss in cellular recovery, cell cycle arrest, loss of fertility and un-repairable damage [1- 104, 143-160-200]. Hormonal therapy inhibits the release of the hormones that facilitate the proliferation of cancerous cells [1-200]. Bone marrow transplantation is replacing of damaged or diseased bone marrow [1-200]. Surgery removes cancerous tumors [1-200]. Furthermore whereas chemotherapy is toxic to healthy tissues and so brings about short-term side effects such as hair loss, vomiting, diarrhea, coughing, swelling of the legs and weight loss [1-104-200]. The long term side effects from either radiation or chemotherapy include permanent abdomen, back or leg pain, trouble urinating, and feeling tired [1-104, 143-160-200]. Moreover, additional treatment options such as targeted immunotherapy are novel and so remain in clinical stage trials, whereby their overall effectiveness remains unknown [1-104, 143-160-200]. However, all these have toxic side effects, poor pharmaco-dynamics properties, resistance to metastasis, poor bioavailability and non-specificity limiting their clinical utility to a large extent. Therefore, it is important to search for new novel therapeutic agents that are naturally synthesized and cheaper, but still remain effective [1-200].

Today, solid tumors are surgically removed and patients receive adjuvant radiation treatment and chemotherapy that cause severe sides effects and dramatically reduce quality of life. In addition, the toxicity of some treatments restricts their use and effectiveness[1-265-280]. Many potential chemopreventive secondary metabolites in both plant extracts as well as purified molecules isolated from teas, herbs, spices, fruits and vegetables have been explored[1-200]. Various cancer therapies have been used to cure or increase the life span of the patient. Different synthetic medicines have been used for the treatment of different cancers, but these medicines are also associated with several health risks to the patient [1-200]. Therefore, the natural method of cancer treatment using plants or plant extracts has become a more popular method to cure cancer [1-200].

3. Cancer Treatment Approaches

Cancer is a global health problem responsible for one in six deaths worldwide. Treating cancer has been a highly complex process [1- 277]. Conventional treatment approaches, such as surgery, chemotherapy, and radiotherapy, have been in use, while significant advances are being made in recent times, including stem cell therapy, targeted therapy, ablation therapy, nanoparticles, natural antioxidants, radionics, chemodynamic therapy, sonodynamic therapy, and ferroptosis-based therapy[1-277].The chemotherapeutics, such as the taxanes and platinum compounds, being found to have a synergistic effect. Gene therapy is the insertion of a normal copy of a defective gene in the genome to cure a specific disorder. Current methods in oncology focus on the development of safe and efficient cancer nanomedicines [277]. Stem cell therapy has brought promising efficacy in regenerating and repairing diseased or damaged tissues by targeting both primary and metastatic cancer foci, and nanoparticles brought new diagnostic and therapeutic options[1-277]. argeted therapy possessed breakthrough potential inhibiting the growth and spread of specific cancer cells, causing less damage to healthy cells [277]. Ablation therapy has emerged as a minimally invasive procedure that burns or freezes cancers without the need for open surgery. Natural antioxidants demonstrated potential tracking down free radicals and neutralizing their harmful effects thereby treating or preventing cancer [277]. Several new technologies are currently under research in clinical trials, and some of them have already been approved [277].

4. Role of Botanical Medicine for Cancer

Plants have been used for medical purposes since the beginning of human history and are the basis of modern medicine [1-200-262]. Most chemotherapeutic drugs for cancer treatment are molecules identified and isolated from plants or their synthetic derivatives [1-265]. Medicinal plants constitute a common alternative for cancer treatment in many countries around the world [1-200]. At this time, more than 3000 plants worldwide have been reported to have anticancer properties [1-200-262]. In the traditional medicinal system, various medicinal plants have been reported to cure or treat infectious diseases, atherosclerosis, diabetes, cancer, etc. Traditional medicines are a first source of health care and traditional therapy throughout the world for around 80–90 % of people who utilize medicinal plants[1-200]. Bioactive plant-derived phytocompounds can be anticipated to play a more and more substantial function in the development of new drugs [1-200]. The most well-known plant-derived anticancer compounds of medical importance include those especially good at attacking the cytoskeleton system of cell microtubules which include the vincristine, vinblastine, and taxanes, e.g., docetaxel (Taxotere), paclitaxel (Taxol) and others [1-270]. Herbal medication offers very reasonable alternate to modern medicine against cancer [1-273].

Cancer is a disorder that rigorously affects the human population worldwide [1-200]. There is a steady demand for new remedies to both treat and prevent this life-threatening sickness due to toxicities, drug resistance and therapeutic failures in current conventional therapies[1-200]. Ellipticine, camptothecin, combretastatin, curcumin, homoharringtonine and others are plant derived bioactive phytocompounds with potential anticancer properties.

Researchers have improved the field further through the use of advanced analytical chemistry and computational tools of analysis [1-270]. These plant-derived natural resources have proved to be non-toxic and are potential modes of cancer management and therapy [1-270]. New technologies include nanoparticles for nano-medicines which aim to enhance anticancer activities of plant-derived drugs by controlling the release of the compound and investigating new methods for administration [1-19-270]. Three quarters of the prescribed anticancer drugs are plant-derived [1-200]. Classical examples include vinblastine, vincristine, taxol, camptothecin and podophyllotoxin [1-19-200].

The secondary metabolites in the plant kingdom such as polyphenols, flavonoids and brassinosteroids have been studied for their potential use as anticancer agents [1-19-200-313]. Collectively they have been shown to possess anticancer activities which include; antioxidant activity; inhibition of cancer cell growth; induction of apoptosis; target specificity; cancer cell cytotoxicity [1-19-200]. Many plant metabolites have been studied and reported to have anticancer characteristics, including isothiocyanate, resveratrol, genistein, soybean extract, vitamin A derivatives, luteolin, curcumin, green tea ex tract, and lycopene [1-200]. These herbal medications were studied in both vivo and in vitro settings. Nutraceuticals are gaining popularity due to their low risk of adverse effects and overall health benefits [1-200]. Currently, clinically approved anticancer compounds are vincristine, vinblastine, taxanes, and podophyllotoxin, all of which come from natural sources. With the triumph of these compounds that have been developed into staple drug products for most cancer therapies, new technologies are now appearing to search for novel biomolecules with anticancer activities [1-200-313]. Ellipticine, camptothecin, combretastatin, curcumin, homoharringtonine and others are plant derived bioactive phytocompounds with potential anticancer properties [1-200].

Diverse medicinal plants' anticancer properties have been evaluated in vivo using various animal models [1-200]. Clinical trials with phytochemicals in cancer are in their beginning, despite the fact that an enormous number of anticancer substances are now in research [1-200]. Plant-based isolated chemicals have been demonstrated to be less hazardous than laboratory manufactured compounds in previous studies and research [1-270]. Cancer is one of the main causes of mortality that affects a large proportion of population worldwide each year. Traditional and synthetic medications are less successful in cancer treatment [1-270-291]. Currently, plants are used because of their remarkable properties in the form of staple drugs. These plants gain huge attention as a safe treatment option with anti-tumor, chemo-protective and anti-proliferative properties than conventional harmful therapeutics[1-270-291]. The secondary metabolites extracted from medicinal plants lead to the production of innovative therapeutic strategies against cancer and other diseases [1-270-291].

5. Oncology Drug Marketing

Oncology drug development and marketing are governed globally by specialists and an advisory process mediated by regulatory organisations [1-274, 275]. The high cost involved in new drug development coupled with the threat of failure & adverse effects associated with cancer drug therapies poses to restrain the growth of oncology. The personalisation of medicine has transformed the oncology treatment landscape. One of the biggest challenges, and a lookout for marketers and market researchers, is differentiation [274-275]. The primary goal is to raise awareness about cancer treatments, products, or services and drive their adoption. Cancer is complex because it is one term that encompasses many different malignant diseases. There is no one cause of cancer, nor is there a single treatment protocol [274-276].

6. Botanical Weapon Treatment of Cancer: Problems and Disadvantages

The majority of plant extracts have been researched for cancer prevention rather than treatment, resulting in low efficacy and uptake in practice [1-200-192]. The problem is that there is insufficient information on the safety, quality, and efficacy of herbal drugs. The debate remains, however, because there have only been a few research on the plants anticancer effects [1-200-305]. Every proven medicine or its active ingredients (anticancer chemicals or isolated compounds) requires phase III clinical trials before it can be marketed [1-200]. Numerous challenging factors have created limitations in the development of natural anticancer biomolecules as drug products. Along with toxic side effects, lower water solubility, decreased absorption, lack of selectivity to targeted cancer cells, and sub-therapeutic activity are the major obstacles for anticancer drug development from natural sources [1-200-305]. Medicinal plants provide a huge reservoir of secondary metabolites – natural products produced by all life forms as a response to stress conditions – such as flavonoids, alkaloids, polyphenols and terpenoids[1-200-305].

It is generally established that the drugs including the anticancer compounds require phase III clinical research trials for marketing permissions. The Food and Drug Administration (FDA) and European Medicines Agency (EMA) guidelines require at least one controlled trial in Phase III with statistically significant results for the green signal to market them[1-

200-305]. This means that the drug is presented for approval with insufficient data on its quality, safety, and efficacy. Medicinal plants play a key role in cancer research. As scientific understanding grows, they may increasingly be used in conjunction with conventional cancer therapies to enhance patient outcomes and give patients new hope[1-200-305].

Plant-derived drugs have been developed through research and progressed to clinical trials. The first plant-derived anticancer substances used in clinical settings were **vinblastine** and **vincristine**, which were discovered in the leaves of *Catharanthus roseus* (Madagascar periwinkle) [1-200-305]. A number of indole alkaloids have been recently identified that efficiently suppressed human cancer cell lines under laboratory conditions. Human cancer-derived cell lines are the cancer cells taken from patients, the most widely used models to study the biology of cancer in laboratory conditions and test hypotheses to improve the efficacy of cancer treatment [1-200-305-311-313]. Nanoemulsions of essential oils have been used to increase solubility, stability and permeability in targeted cancer therapeutics[1-200-305]. Leaves of the Madagascar periwinkle, *Catharanthus roseus,* contain vinca alkaloids such as vincristine and vinblastine, which are used in chemotherapy to treat malignancies like leukemia and lymphoma. Paclitaxel (Taxol), a crucial chemotherapy medication used to treat breast, lung and ovarian cancers as well as Kaposi's sarcoma, can be found in the bark of the *Taxus brevifolia* (Pacific yew tree). [1-200-305-313].

Combinations of drugs derived from vinca alkaloids, obtained from the Madagascar periwinkle plant; Taxus diterpenes, derived from the yew; *Podophyllum lignans*, an antioxidant and anti-inflammatory compound found in the *Podophyllum* plant; and *Camptotheca* alkaloids, derived from the Campotheca tree, may enhance their anticancer effects and improve their efficacy as therapeutic agents[1-200-305]. Extracts from *Urtica membranacea,* belonging to the nettle family; *Artemisia monosperma*, or common mugwort; and *Origanum dayi*, or Desert Oregano, are also being tested for their effects on a wide range of cancer cell lines from lung, breast, colon and prostate cancers[1-200-305]. Plant-derived anticancer agents are effective inhibitors of cancer, putting them in high demand. Exploitation of these agents needs to be managed to keep up with this demand sustainably.

Although plant-based compounds have shown be less toxic compared to conventional synthetic compounds, there is growing evidence on the side effects of the unregulated use of these plants against different diseases[1-200-305]. The problem is that there is insufficient data available regarding the quality, safety, and efficacy of herbal drugs. *F. indica*, for instance, has shown potent activity against breast cancer when tested in the MDA-MB-231 cell line [1-200-305].

There are several regulatory framework models available for prescribing such drugs but there is a need for harmony among regulating agencies and improvement in the regulation process. It is, however, suggested that regulatory authorities, while bringing harmony with other agencies working for regulating anticancer herbal compounds, should increase the focus on combining information from traditional knowledge about that drug and the scientific studies on it [1-200-305]. Furthermore, adequate biopharmaceutical and clinical evidence is essential for delivering these bio-compounds from the laboratory to the patient. A number of natural phytochemicals have been reported as having significant anticancer properties and many of them have been investigated under clinical trials [1-200-292-305]. Many of them are proven to be safe, therapeutically effective, and biocompatible in clinical trials and are thus used in cancer treatments [1-200]. Potent therapeutic compounds such as colchicine, camptothecin, and podophyllotoxin showed severe side effects which limit their uses [1-200-313].

The use of herbal medicines offers a way to alleviate this crisis in drug development. There are three main advances for herbal medicine: (1) utilizing the traditional herbal medicine knowledge may give rise to an inexpensive and more rapid discovery of new drugs; (2) herbal remedies offer a holistic approach that complements the disease targeted approach of "Silver bullets"; (3) synergy between the various components of the herbs which are an important element of their overall medical effects[1-200-305]. The main **disadvantage** related to herbal medicines is the lack of international standardization in terms of methods for evaluating their composition, efficacy, safety, and quality, consistent manufacturing practices, regulation and approval processes [1-200-265-313].

7. List of Anticancer Plants

According to the literature survey by Malabadi et al., (2024) [312], some of the medicinal plants with anticancer activity listed are, 1) *Gloriosa superba* L. (*Colchicaceae*), 2) *Curcuma mutabilis* (*Zingiberaceae*), 3) *Colchicum autumnale* (*Colchicaceae*), 4) *Cannabis sativa* (*Cannabaceae*), 5) *Catharanthus roseus* (Madagascar Periwinkle) (*Apocynaceae*), 6) *Curcuma longa* (*Zingiberaceae*) (Turmeric), 7) *Ramphal* (*Annona muricata)* (Soursop) (*Annonaceae*), 8) Sitaphal (*Annona sqamosa*)(Custard apple) (*Annonaceae*), 9) *Acorus calamus* (Bauj) (*Acoraceae*), 10) *Ajuga parviflora* (Neelkanthi) (Lamiaceae), 11) *Aloe vera:* (*Asphodelaceae*), 12) *Asparagus racemosus* (Satavari) (*Asparaceae*), 13) *Artemisia herba-alba* (white wormwood) (*Asteraceae*), 14) *Boswellia serrata* (Guggul) (*Burseraceae*), 15) *Centella asiatica* (Brahmi) (Apiaceae), 16) *Dioscorea bulbifera* (Air Potato) (*Dioscoreaceae*), 17) *Saussurea costus* (Kuth/ Indian

costus) (*Asteraceae*), 18) *Taxus bacata* (Thuner) (*Taxaceae*), 19) *Tinospora cordifolia* (Amruthballi, Giloe or Guduchi) Menisermaceae), 20) *Withanaia somnifera* (Ashwagandha) (*Solanaceae*), 21) *Andrographis paniculata* (*Acanthaceae*), 22) *Camellia sinensis* (*Theaceae*), 23) European mistletoe (*Viscum album*), 24) *Phyllanthus amarus* (*Euphorbiaceae*) (Indian goose berry). 25) *Punica granatum* L. (Pomegranate) *(Lythraceae*, subfamily *Punicaceae*), 26) *Urtica membranacea* (Urticaceae), 27) *Artemesia monosperma* (*Asteraceae*), 28) *Origanum dayi post* (*Labiatae*), 29) *Soymida fembrifuga* (Roxb.)(*Miliaceae*), 30) *Lavandula bipinnata* (L.) (*Lamiaceae*), 31) *Helicteres isora* L. (*Sterculiaceae*), 32) *Allium sativum* (Allicin), 33) *Achyranthes aspera*, 34) *Apis mellifera*, 35) *Astralagus hedysarum*, 36) *Bidens Pilosa,* 37) *Bolbostemma paniculatum*, 38)*Centaurea ainetensis*, 39) *Gossypium hirustum* or *Gossypium herbaceumalso*, 40) *Hydrocotyle* 41) *Salvia miltiorrhiza,* 42) *Hypericin perforatum*, 43) *Annona muricata*, 44) *Daphne mezereum*, 45) *Picrorrhiza kurroa*, 46) *Mangifera indica*, 47) *Nervelia fordii*, 48) *Rubia cordifolia*, 49) *Silybum marianum*, 50) *Scutellaria,* 51) *Oroxylum indicum*, 52) *Smilax china*, 53) *Strychnos nuxvomica*, 54) *Terminalia chebula*, 55) *Vernonia amygdalina*, 56) *Taraxacum officinale*, 57) *Brugmansia suaveolens*, 58) *Zingiber officinale*, 59) *Artemisia annua* (*Asteraceae*), 60) *Fagonia indica* (*Zygophyllaceae*), 61) *Garcinia oblongifolia* (*Clusiaceae*), 62) *Garcinia indica*, 63) *Hedyotis difusa* (*Rubiaceae*)

8. Role of Botanical Weapon for Controlling Cancer

Cancer is the second leading cause of death worldwide. Although great advancements have been made in the treatment and control of cancer progression, significant deficiencies and room for improvement remain. Several undesired side effects sometimes occur during chemotherapy[1-200-305]. Natural therapies, such as the use of plant-derived products in cancer treatment, may reduce adverse side effects[1-200-305]. Globally, the number of cancer deaths is projected to increase from 7.1 million in 2002 to 11.5 million in 2030[1-200-305]. For cancer treatment, four classes of established anticancer drugs have been derived from plants: taxanes (e.g., docetaxel and paclitaxel), camptothecin (e.g., irinotecan), epipodophyllotoxins (e.g., etoposide and teniposide), and alkaloids (e.g., vincristine, vinblastine, and vindesine). Taxol, for example, a well-known drug extracted from the bark of the Pacific yew tree (*Taxus brevifolia*), is currently used to treat various cancers such as breast, lung, and ovarian cancer[1-200-305].

The herbal medicines are tested both in vitro and in vivo[1- 263-264]. The anticancer activities of the various medicinal plants have been tested in vivo using different animal models [263-264]. There are many studies available on in vivo experiments of the many different anticancer plants in mice models. For instance, di-hydroartemisinin was reported to inhibit tumor tissue, increase the level of interferon-gamma (IFN-γ), and decrease interleukin 4 (IL-4) in tumor-bearing mice[1-263-264]. Similarly, artesunate, a derivative of artemisinin is also reported to be a promising drug against angiogenic Kaposi's sarcoma, growth inhibition of A549 and H1299 lung tumors by 100 mg/kg dose, the suppression of human prostate cancer xenograft and the inhibition of leukemia growth in mice. Similarly, the artemisinin type compound can have anticancer activities against different types of tumors including leukemia, carcinomas of breast, kidneys, lungs, and ovaries, lymphoma, melanoma, and brain tumors [1-263-264]

Herbal medicines have a long history of comprehensive cancer treatment through various post-translational modifications (PTMs) [286]. **Stanford University, USA** researchers have discovered a rapid and sustainable way to synthetically produce a promising cancer-fighting compound right in the lab. The compound's availability has been limited because its only currently known natural source is a single plant species that grows solely in a small rainforest region of Northeastern Australia[1-200-305]. However, thanks to a clever process, the Stanford researchers demonstrated for the first time how to chemically transform an abundant, plant-based starting material into EBC-46[1-200-305]. Some of the anticancer compounds display teratogenic, mutagenic and/or oncogenic actions, which can block the synthesis of antibodies and also immune response mediated by cell[1-20-200-305]. Vinca alkaloids from *Catharanthus roseus* (pink periwinkle) of family *Apocynaceae* cause cytotoxicity by binding to betatubulin at a dissimilar spot than taxanes, blocking polymerization and microtubule assembly, ensuing in metaphase arrest and thus cell death [1-20-200]. Tea contains a significant amount of epigallocatechin gallate (EGCG) (*Camellia sinensis* ; family *Theaceae*). **Epigallocatechin gallate** (EGCG) is an important biochemical marker of Northeast Indian tea as it contributes 50% of total catechins [248] EGCG's anticancer efficacy is verified in numerous research using animal models and cell lines [1-20-200, 248].

Camptothecin is a quinolone alkaloid derived from the Chinese tree *Camptotheca acuminata.* [1-20-200]. Betulin and betulinic acid extracted from *Z. nummularia* exhibit anticancer properties [1-20-200]. The cancer cell lines being more susceptible than normal cells, betulinic acid glycosides create differential cytotoxicity [1-20-200]. Very recently research focused on collecting and analyzing plants native to Ethiopia is showing promise in the fight against cancer — specifically cervical cancer cells. Thanks to a new collaboration, a research team from Georgia State University is adding to the scientific literature about these valuable compounds. The research underway includes a collaboration among experts at Georgia State University and Georgia State's Perimeter College, Addis Ababa University in Ethiopia and the Winship Cancer Center at Emory University.

Ingenol mebutate found in Australian shrub *Euphorbia peplus*, family Euphorbiaceae can treat actinic keratosis topically caused by long- term UV exposure leading to squamous cell carcinoma if untreated [1-20-200]. Homoharringtonine is an alkaloid cephalotaxine from family *Cephalotaxaceae Cephalotaxus* genus[1-20-200]. Gingerol found in ginger rhizomes is a phenolic compound. In mouse model of spontaneous breast cancer metastasis, gingerol therapy enhanced caspase-3 activation and decreased orthotopic tumour formation and metastasis of 4T1Br4 mammary tumour cells to numerous lung, bone, and brain. Genistein is an oestrogen-like isoflavone found naturally in soy beans [1-20-200]. Taxanes found in Yew tree bark are prospective anticancerous drugs [1-273]. Taxanes suppress cancer growth by triggering aberrant mitosis and cell cycle detention by stabilising microtubules [1-273]. Paclitaxel derived naturally from *Taxus brevifolia* bark and leaves and docetaxel semi-synthetically derived are commonly used to treat ovarian, prostate, pancreatic, lung, and breast cancer [1-200]. All of the fundamental medicines are found in plants. Plant bioactive compounds have been shown to suppress cancer [1-200-273]. Several plant-based anticancer compounds have been evaluated using in silico and systems pharmacology tools [1-263-264]. The major challenge on this direction would be to predict the role of phytochemicals other than active compounds and are present in the traditional medicine [263-264].

Advancements in organic chemistry and analytical techniques have facilitated the extraction, purification, and identification of the bioactive components within plants that are responsible for their pharmacological effects. Notable examples include vincristine and vinblastine from Catharanthus roseus, codeine and morphine from *Papaver somniferum*, artemisinin from *Artemisia annua*, quinine from *Cinchona officinalis*, cocaine from *Erythroxylum coca*, paclitaxel from *Taxus brevifolia*, and digitoxin from *Digitalis purpurea* and *Digitalis lanata* [280-284]. Nanotechnology, an emerging multidisciplinary field in drug development, focuses on tiny particles in the nano range, from 0.1 to 500 nm. In cancer research, nanotechnology holds promise as an advanced system for drug delivery, diagnosis, and treatment for cancer, as well as for repairing damaged tissues and cells [1-284]. Nanotechnology application in medical care, known as nanomedicine, shows potential to enhance human health and well-being through precise diagnosis and targeted therapy [284].

- ***Gloriosa superba*** L. (Family: *Colchicaceae*) is herbaceous perennial semi-woody climber native of tropical Asia and Africa. In Karnataka, it is generally found growing all along the Western Ghats; it is also found growing in Madagascar, Sri Lanka, Indo-China and in the adjacent islands [1]. It is also known by its trade name 'Glory lily'; in English it is known as 'Malabar glory lily' and, in Hindi and Sanskrit as 'Kalihari' and 'Agnisikha [1]. The tubers of the plant are traditionally used to treat chronic ulcers, colic, bruises and sprains, haemorrhoids, leprosy, cancer, and also as a labour pain inducer [1-200].
- ***Curcuma mutabilis*** was collected from the Nilambur forest, Malappuram district of Kerala state, India [2-200]. The anticancer potential of petroleum ether extract from *C. mutabilis* rhizome (CMRP) and a novel labdane diterpenoid, (*E*)-14, 15-epoxylabda-8(17), 12-dien-16-al (Cm epoxide) isolated from it. CMRP was found to be a mixture of potent bioactive compounds including Cm epoxide [2-200].
- **Polyphenolic** compounds include flavonoids, tannins, curcumin, resveratrol and gallacatechins and are all considered to be anticancer compounds. Resveratrol can be found in foods including peanuts, grapes and red wine [3-200]. Gallacatechins are present in green tea. It is thought including polyphenols in a person's diet can improve health and reduce risk of cancers by being natural antioxidants [3-200].
- **Flavonoids** are from the polyphenolic compounds and constitute a large family of plant secondary metabolites with 10,000 known structures [1-100]. There is a high content of flavonoid compounds such as anthocyanins, flavones, flavonols, chalcones and many more which can be found in just one structure of the plant like its seed [3-9-200]. Purified flavonoids have also shown anticancer activities against other human cancers including; hepatoma (Hep-G2), cervical carcinoma (Hela) and breast cancer (MCF-7) [3-200].
- **Brassinosteroids** (BRs) are naturally occurring compounds found in plants which play roles in hormone signalling to regulate growth and differentiation of cells, elongation of stem and root cells and other roles such as resistance and tolerance against disease and stress [3-9-200]. Also, BRs are used for regulation of plant senescence. 28-homocastasterone (28-homoCS) and 24-epibrassinolide (24-epiBL) have demonstrated anticancer effects on various cancer cell lines 25-27 and proven to be effective at micromolar concentrations [3-9-200].
- **Plant-derived drugs** are desired for anticancer treatment as they are natural and readily available [3-9-210]. Plant-derived drugs can fall under four classes of drugs with the following activities; methytransferase inhibitors, DNA damage preventive drugs or antioxidants, histone deacetylases (HDAC) inhibitors and mitotic disruptors [3-9-210]. Compounds including sulforaphane, isothiocyanates, isoflavones and pomiferin are considered to be HDAC inhibitors. They inhibit the activity of carcinogenic proteins. Plant-derived compounds which show inhibition of HDAC can enhance chemotherapeutic sensitivity in human cancers [3-9-210]. Derivatives of vinca alkaloids, vincristine, vinblastine, vinorelbine, vindesine and vinflunine are drugs which will inhibit the dynamics of microtubules by binding to β-tubulin [3-9-200].

- **The field of nanotechnology** the use of nanoparticles (NPs), as a delivery system for drugs to reach target sites, is developing [3-9, 50, 52-54-215]. Some compounds that have demonstrated anticancer activities may be limited in their clinical development due to the need for high dosages. Success has also been seen with the drug quercetin using superparamagnetic magnetite NPs against breast cancer (MCF-7) cell lines [3-9, 50, 52-54].
- With **successful clinical trials drugs** being developed from plant origins are popular for clinical development[1-15-200]. Their non-toxic effects on normal cells and their cytotoxic effects on cancer cells put them in high demand [1-15-200].
- **In folk medicine**, turmeric has been used in therapeutic preparations over the centuries in different parts of the world [1-16-200]. In Ayurvedic and Chinese traditional medicine practices, turmeric is thought to have many medicinal properties including strengthening the overall energy of the body, relieving gas, dispelling worms, improving digestion, regulating menstruation, dissolving gallstones, and relieving arthritis [1-16-200]. *Curcuma longa*, also called as turmeric and contain curcumin as an ingredient, which is reported as potent anticancer agent and composed of the phenolic content [1-16-100].
- **Soursop** (*Annona muricata)* is a fruit found mainly in the rainforest of Southeast Asia, South America, and Africa [1-17, 18, 29, 30-100]. It is green with a prickly outer texture and a soft and creamy internal texture [1-17, 18-200]. The taste is commonly compared to a strawberry or pineapple. Research also showed that soursop has natural cytotoxicity effects [1-17, 18, 29, 30-70].
- ***Acorus calamus*** (Bauj) belongs to the *Acoraceae* family. A phytochemical study of *A. calamus* rhizomes resulted in separation of newer compounds like zingiberene and safrol [1-100].
- ***Ajuga parviflora*** (Neelkanthi) is a flowering plant belonging to *Lamiaceae* family. Conventionally being used as a medicine for curing malaria, oedema, fungal, and other microbes[1-100]. The cytotoxicity action of aqueous and methanol extracts from A. parviflora leaves was explored against leukaemia murine [L-1210] and human chronic myelogenous leukaemia [K-562] cell lines [1-100].
- ***Aloe vera*** belonging to *Asphodelaceae* family possesses wide range of pharmaceutical activities [1-26-55]. Other isolated compounds from A. vera leaves were examined against ovarian cancer [OVCAR-3], human colon cancer [HCT-116 and IGROV-1], and breast cancer [MCF-7] cell lines through MTT assay to assess in vitro cytotoxic activity[1-26-56]
- ***Asparagus racemosus*** (Satavari) belongs to Asparagus genus[1-100]. The kaempferol of *A. racemosus* displays encouraging actions in the experimental HT-29 and HCT-116 colon cancer cells along with regular immortalized intestinal cells [IEC-6 and INT-407] [1-100].
- ***Artemisia* herba-alba** (white wormwood) belongs to family *Asteraceae*, genus Artemisia[1-100]. The whole plant and specially leaf extract of *A. herba-alba* showed high anticancerous activity against 3 human tumour cell lines like human bladder carcinoma, human laryngeal carcinoma, human myelogenous leukaemia (K-562) cells [1-100].
- ***Boswellia serrata*** (Guggul) is a member of the family *Burseraceae* [1-100]. *B. serrata* is frequently used to cure inflammatory diseases i.e., viral, fungal, asthma, etc. The oleo gum resin extract of *B. serrata* had more anticancer activity against 3 human cancer cell lines like human laryngeal carcinoma, bladder carcinoma, human myelogenous leukaemia cells [1-100].
- ***Centella asiatica*** (Brahmi) belonging to *Apiaceae* family is a tradi- tional medicinal plant of India and China [1-141]. The ethyl acetate, aqueous, acetone and methanol extracts of *C. asiatica* leaves possesses alkaloids that were assessed for their cytotoxicity effect in human lung epithelial carcinoma (A-549) cell line with help of colorimetric MTT assay [1-141].
- ***Catharanthus roseus*** (Sadabahar) belongs to family *Apocynaceae* is native to India, China. Extracts from *C. roseus* are traditionally used to cure asthma, leukaemia, insomnia, cancer, and diabetes[1-200]. Vinblastine (VBL) was the very first alkaloid separated from the periwinkle plant of Madagascar in the 1950s. Vincristine (VCR) and its derivatives are hetero-dimeric (indoloid) alkaloids formed amid the biosynthesis of catharanthine and vindoline and are present in pink Catharanthus roseus [1-200].
- ***Curcuma longa*** (turmeric, Haldi) belonging to ginger family *Zingiberaceae*. Curcumin being the main constituent of *C. longa* is responsible for its beneficial activities [1-95, 203]. Curcumin displays anticancer, antidiabetic, and anti-inflammatory activities [1-95, 203].
- ***Dioscorea bulbifera*** (Air Potato) belonging to family *Dioscoreaceae* has 13 species globally[1-100]. It is mostly employed in India and China as traditional medicine for its anticancer and antidiabetic effects [1-100].
- ***Saussurea costus*** (kuth/ Indian costus) belonging to the family *Asteraceae*[1-100]. The leaves and root of *S. costus* are poteintially used traditionally in North Korea, Japan, China and India for cancer, diabetes, fungal, microbial, sore throat, inflammation, cough, and anti cancer agent [1-200].

- ***Taxus bacata*** (Thuner) belonging to family *Taxaceae* have anticancer, antimalarial, antiparasitic, antifungal, analgesic, antibacterial, anti-inflammatory, antimicrobial, anti-nocieptive, aphro- disiac, antipyretic, antirheumatic, anti-spasmodic, antioxidant, anticon- vulsance effects[1-200].
- ***Tinospora cordifolia*** (Amruthballi, Giloe or Guduchi) belonging to family *Menisermaceae* is found in China, Japan, India, Europe, and East Asia[1-100]. *T. cordifolia* extract is used in brain, intestine, breast, head, vaginal, prostate and neck cancer[1-100].
- ***Withanaia somnifera*** (Ashwagandha) belonging to family *Solanaceae* is grown in India, China, Japan, Europe and Asia and frequently used in cancer and diabetes [1-213].
- ***Andrographis paniculata*** is a robust chemoprotective drug showing effect against many viral and neoplastic agents as it can trigger both types of immune response [1-28, 135, 171, 182]. Andrographolide being cytotoxic to cancer cells like KB human epidermoid cancer cells, MCF-7 breast cancer cells, P388 lympho- cytic leukaemia cells, and HCT-116 colon cancer cells [1-28, 135, 171, 182].
- The oral intake of ***Phyllanthus amarus*** extract greatly improved life duration and decreased tumour size in Dalton's lymphoma ascites and Erlich ascites carcinoma affected mice [1-41, 51, 106, 71].
- **Viscotoxins (VT)** and lectins collected from the mistletoe plant (Viscum collection), constitute another group of phytocompounds with cytotoxic activity [1-100]. Viscotoxins are obtained from the extracts isolated from the common mistletoe plant [1-100].
- ***Punica granatum*** L. (Pomegranate) *(Lythraceae*, subfamily *Punicaceae*) is one of the important medicinal plant[1-43, 55-57]. Pomegranate components have antioxidant, anti-carcinogenic and anti-inflammatory components, which is effective on prevention and treatment of cancer and other chronic and infection diseases [1-43, 55-57].
- **Whole cell extracts** (ethanol extraction) from *Urtica membranacea* (Urticaceae), *Artemesia monosperma* (Asteraceae), and *Origanum dayi post* (Labiatae), plants indigenous to the coastal plain and desert areas of Israel, exhibited dose and time-dependent killing capabilities on various human derived hematological and solid tumor cell lines and primary cultures established from patients' biopsies [1-60-63, 212]. The killing activity was specific toward tumour cells, as the plant extracts had no effect on primary cultures of healthy human cells [1-60-63, 212].
- **One of the study** was carried out to evaluate the anticancer, antioxidant, and possible anti-inflammatory properties of diverse medicinal plants frequently used in Indian traditional medication [1-67]. The selected botanicals such as *Soymida fembrifuga* (Roxb.) A. Juss. (Miliaceae), *Tinospora cordifolia* (Willd.) Miers. (*Menispermaceae*), *Lavandula bipinnata* (L.) O. Ktze. (Lamiaceae), and *Helicteres isora* L. (Sterculiaceae) extracted in different solvents were evaluated for their *in vitro* anticancer and antioxidant activities [67].
- ***Annona muricata***: This is a scientific name of **Graviola**, which contains acetogenins having huge medicinal importance that hinder the production of ATP (adenosine triphosphate) in human cells, and will have a significant impact in the eradication of cancer drugs [29, 30, 80, 81, 142, 144, 157. 159, 160, 199, 202].
- The derivatives of **podophyllotoxin** (PTOX) etoposide , teniposide , and etoposide phosphate , are used for anticancer chemotherapy that is extracted from *Podophyllum peltatum* L. (*Berberidaceae*) and *Podophyllum emodi* Wall. (syn. *P. hexandrum*) [1-200]. The podophyllotoxin derivatives have antiproliferative activity against germ cell tumors and small cell and nonsmall cell lung cancers [1-200].
- **The first isolated compound** from *Taxus brevifolia* Nutt. (Taxaceae) bark was taxol or **Paclitaxel**. Various parts of Taxus species, such as *T. canadensis* Marshall, *T. baccata* L., and *T. brevifolia*, have been used for anticancer activity, for instance for the treatment of ovarian and breast cancers [1-100]. The effectiveness of the docetaxel anticancer agent was analyzed statistically by developing a clinical trial of more than one dozen taxanes analogues [1-200].
- **Camptothecin** Derivatives For the first time, In the early 1960's a phytochemical called camptothecin was extracted from a Chinese ornamental tree called *Camptotheca acuminata* Decne (*Nyssaceae*) species and used as an anticancer agent [1-100]. This shows the advancements in anticancer drug development. An extract camptothecin from ***Camptotheca acuminata*** species showed high anti-tumor and anticancer activity out of 1000 different plant extracts tested for the same activities [1-200].
- ***Annona squamosa*** or custard apple, a small green tree, 6–8 m tall, is found specifically in deciduous forests [80, 81, 142, 144, 157. 159, 160, 199, 202]. The medical applications are constipation, dysentery, antibacterial infection, epilepsy, dysuria, cardiac problems, hemorrhage, abortifacient properties, ulcers, fever, antifertility, antitumor, and worm infection treatments [80, 81, 142, 144, 157. 159, 160, 199, 202].
- **Phytochemicals** constituted in the *Arnebia euchroma* which have great importance in anti-immune deficiency, anti-microbial and anticancer activity are arnebin-7, acetyl-shikonin, isovaleryl-shikonin, shikonincoumarins, B-hydroxyisovaleryl- shikonin, deoxy-shikonin, β-β-di-methylacryl-shikonin, iso-butyryi-shikonin, stigma sterol, arnebinone, and isobutyl-shikonin [1-100].

- A plant species ***Asclepias curassavica*** constitutes a wide variety of biologically active compounds such as flavonol glycosides, carbohydrates, triterpenes flavonols, cardenolides, amino acids, etc [1-100]. A pronounced cytotoxicity activity against four different types of cancer cells was shown by cardenoliedes phytocompounds extracted from the aerial and root part of *Asclepias curassavica* [1-100].
- **Compounds having anticancer** activity include terpenoids, lignans, alkaloids, and flavonoids [1-90]. Terpenoids (steroids) are the major group and widely applicable in chemotherapy cancer treatment, e.g., Taxol can be mentioned . Steroidal saponin with few steroids and their glucosides, triterpenoids, alkaloids, and flavonoids exist in *Asaparagus racemosus* species [1-90].
- The plant ***Bacopa monnieri*** constitutes bacosides A and B, alkaloids, namely herpestine and brahmana, tetracyclic triterpenoid saponins, flavonoids, hersaponin, triterpenes such as bacosine, and sterols like bacostero [1-50, 198]. A natural product, phytoserols extracted from the aerial part of the plant species *Bacopa monnieri* have anticancer activity [1-55, 198].
- ***Cannabis sativa***: In the one of the study reported by Lukhele and Motadi, (2016) [249] cervical cancer cell lines (SiHa, HeLa, and ME-180) were exposed to different concentrations of ***Cannabis sativa*** extracts and that of its compound, cannabidiol, for the investigation of their anti-proliferative activity [175-177, 216-246, 249-261]. This study confirmed that *Cannabis sativa* extracts and Cannabidiol possess anti-proliferative effects using MTT assay [175-177, 216-246, 249-261-263, 309, 310]. The use of cannabinoids as anti-cancer agents is still under debate due to both cancer promoting and inhibiting effects shown in the last centuries [175-177, 216-246, 249-261-263]. Ligresti et al. (2003) demonstrated that the endocannabinoid system may play a role in cancer differentiation (by decreasing the levels of endogenous agonists in differentiated cells vs. undifferentiated ones), cell growth and cell migration leading to metastases[175-177, 216-246, 249-261-263, 309, 310].
- **Gallic acid** as the active component was purified from the fruit extract of *P. macrocarpa* and has demonstrated a role in the induction of apoptosis in lung cancer, leukemia, and colon adenocarcinoma cell lines [1-263].
- ***Artemisia annua*** (*Asteraceae*) also synthesize scopoletin and 1,8-cineole compounds. Similarly, semisynthetic derivatives of artemisinin are also generated such as arteether, artemether, and artesunate[1-263-264]. Artesunate has been studied to be a very effective anticancer compound [1-263-264].
- ***Fagonia indica***, locally known as "dhamasa" is a flowering plant and belongs to the family of caltrop, Zygophyllaceae[1-263-264]. The aqueous extracts of F. indica have been found very effective against different types of cancer specifically breast cancers. demonstrated significant activity against breast cancer cells line MCF-7 through an aqueous extract of F. indica [1-263-264].
- ***Garcinia oblongifolia*** (Lingnan *Garcinia*) belongs to the family of *Clusiaceae* and has a wide range of pharmaceutical activities[263-264]. They noted very high cytotoxic activities of these metabolites in the tested MCF-7 breast cancer cell line. However, they found the higher anti-cytotoxic activity of branch as compared to other plant parts [263-264].
- ***Garcinia indica***, commonly known as kokum, is also an important medicinal plant that belongs to the Garcinia genus[263-264]. The garcinol of G. indica shows positive activities in the experimental HT-29 and HCT-116 colon cancer cells along with normal immortalized intestinal cells (IEC-6 and INT-407) [263-264].
- ***Hedyotis difusa*** (*Rubiaceae*): Because of the recent advances in pharmacological practices, this herb received importance for having antitumor properties and showed effective results in treating cancers of the liver, colon, lungs, brain, and pancreas[263-264].
- ***Morus alba*** commonly called white **mulberry,** is native to China, Japan, India and is cultivated throughout the world where silkworm is raised[1-263-264]. Their leaves are the main source of food for silkworms. Extracts from M. alba are traditionally used to cure cough, edema, insomnia, bronchitis, asthma, nose bleeding, wound healing, eye infections, and diabetes[1-263-264].
- ***Paris polyphylla*** (called "Love Apple") belongs to family *Liliaceae* and contains 24 species throughout the world] [263-264]. P. polyphylla is mostly used by Indian and Chinese traditional medicine system for having potential anticancer properties. [263-264].
- ***Prunus armeniaca*** (Armenian plum) belongs to an important plant family Rosacea. Various parts of the plant are used as the major source of some important antioxidant substances and are commonly used against cancer and some other cardiovascular diseases [263-264].
- ***Scutellaria barbata***, the barbed skullcap is a key medicinal plant species of family Lamiaceae, used to treat inflammatory and cancer diseases[263-264].
- ***Tussilago farfara*** (commonly called coltsfoot) is one of the important medicinal plants, grown in Europe and various regions of western and central Asia, commonly used against cancer[263-264].
- ***Wedelia chinensis***, indigenous to India, South-East Asia, and China, is one of the important anticancer plants belonging to family Asteraceae which is rich in many important secondary metabolites like phenol, flavonoids, and tannin[263-264].

- **Secondary plant** metabolites have demonstrated crucial roles in the development of many conventional drugs currently available in the market. Notable drugs of plant origin approved for cancer therapy include **paclitaxel** (Taxol®) and docetaxel (Taxotere®) for breast cancer treatment, as well as vincristine (Oncovin®) and vinblastine (Velban®) for treating various forms of cancer [71-284].
- **Nanotechnology**-based cancer treatment products like Doxil® and Abraxane® have become commercially available [284]. The physical and chemical characteristics of nanoparticles endow them with unique features, facilitating easy absorption into cancer cells and interactions with cell components and cell membranes[284].
- Consequently, comprehensive **toxicity studies** are imperative to evaluate the safety of medicinal plant-synthesized nanoparticles for therapeutic use. While many studies have focused on the potency of medicinal plant-synthesized nanoparticles[284].
- **Colorectal cancer**, one of the leading causes of cancer-related deaths worldwide, may have just found an unlikely foe in a common weed. *Artemisia herba-alba*, a plant also commonly known as white wormwood or herba alba, has been used for medical purposes for thousands of years[285]. It was originally used in the Middle East and North Africa [285].
- **Damsin,** a natural compound isolated from the **South American** medicinal plant ***Ambrosia arborescens***, has been found to inhibit the growth of cancer stem cells, according to new research [294]. Professor Oredsson and her colleagues from Lund University in Sweden and the University Major of San Andrés in Bolivia studied the effect of damsin and its synthetic derivative called ambrosin on cancer stem cells in three different breast cancer cell lines. "Both damsin and ambrosin inhibit the growth and spread of cancer stem cells in breast cancer cell lines[294].

9. Causes of Cancer Development

The proximate cause of cancer (i.e. the event which is closest to, or immediately responsible for causing) is mutations of genes that keep normal cellular growth regulated [1-263-276]. **Mutations** in key regulatory genes alter the behaviour of cells and can potentially lead to the unregulated growth seen in cancer [1-263-276]. Proto-oncogenes are genes that, when mutated, may lead to unlimited cellular proliferation. It appears that a number of mutations are likely involved in cancer, and tumours rarely rely on one mutation alone [1-263-276]. It is the accumulation of such mutations that lead to the occurrence of cancer[1-263-276]. 1) **Lifestyle choices**: Smoking and alcohol are chemical teratogens (chemicals that cause mutations), while a diet high in fat and a sedentary lifestyle are thought to increase body fat, which stores teratogenic chemicals [1-263-276]. 2) **Environmental factors**: Radiation causes mutation directly by altering DNA. Chemicals work to disrupt transcription and translation processes or act as endocrine disrupters that can stimulate cell growth[1-263-276]. 3) **Infectious agents**: Some viruses act by inserting their own DNA into the nucleus, which can lead to oncogenic mutations. Furthermore, some bacterial infections may contribute to the proliferation of cancer cells [1-263-276]. Day to day, the anatomy undergoes many exogenous insults, such as ultraviolet (UV) rays, pollution, and tobacco smoke, that end in the assembly of reactive species, particularly oxidants and free radicals, liable for the onset of many diseases, together with cancer. There are various factors for the development of cancers in humans when epigenetics or genetic factors lead to the mutation of the normal cells . Epigenetics is the study of changes in heritable gene expression that lead to the proliferation of abnormal cells[1-263-276]. Th enzymes **cyclooxygenase-1 and 2** (COX-1 and COX-2) are the key enzymes involved in recruiting inflammation [1-263-266]. Nevertheless, the pro-inflammatory cytokines play a crucial role in the initiation and progression of various cancers [1-263-266].

10. Cancer Medications

There are many different types of cancer medications. These include alkylating agents, antimetabolites, nitrosoureas, and plant alkaloids [279]. **Nitrosoureas** are a subcategory of alkylating agents that can cross the blood-brain barrier [279]. This barrier protects the brain from many substances in the body [279]. Antimetabolites: Antimetabolites work by convincing cancer cells to consume them and then preventing their division into new cells [279]. Antitumor antibiotics: Antitumor antibiotics are chemicals that interfere with enzymes that support growth in cancer cells. Anthracyclines are a type of anti-tumor antibiotic[279]. Plant alkaloids: These are drugs that come from plants and have anti-tumor properties.Some examples of these drugs include taxanes and vinca alkaloids [1- 279]. Corticosteroids: These are synthetic versions of naturally occurring hormones that can reduce inflammation and treat cancer[279]. Some corticosteroids that are useful in cancer treatment include prednisone, methylprednisolone, and dexamethasone[279]. Their anti-inflammatory properties can reduce nausea, vomiting, and appetite problems from chemotherapy[279].

11. Anticancer Activity: Bioassays

The MTT/MTS in vitro cell proliferation assay is one of the most widely used assays for evaluating preliminary anticancer activity of both synthetic derivatives and natural products and natural product extracts [247]. The highly reliable, colorimetric based assay is readily performed on a wide range of cell lines [247]. This assay gives an indication of whole cell cytotoxicity [247]. However, to determine exact molecular target further assay needs to be performed[247]. Kinase inhibition assays are also one of the most widespread enzyme inhitition screeing assays performed [247]. Kineases are enzymes that play an important role in physiological processes and their inhibitors have been found to exhibit anticancer activity againist various human cancer cell lines [1-247-276]. According to the literature survey of some of the assays are, (1) **MTT Assay**, 2) "**Alamar Blue**" [1-247-276], 3) **SRB Assay** [1-247-276]. 4) **WST-1 Colorimetric Assay** [1-247-276, 311-313].

12. Conclusion

Cancer is a disease characterized by abnormal cell division and proliferation that result from disruption of molecular signals that control these processes. There are many strategies that aim to cure cancers, for instance, surgical operation on tumors, chemotherapy, cancer vaccinations, photodynamic therapy, radiotherapy, immunotherapy, stem cell alteration, or a combination. These are regularly observed to have extreme side effects. Such outcomes include constrained bioavailability, toxicity, non-specificity, rapid clearance, and limitation in metastasis. This shows that anticancer pills additionally affect dividing ordinary cells. Therefore, traditional medicine knowledge should be used to discover novel drug leads for cancer. Even though many plants are being used for treatment purposes, there is a lack of scientific evidence to support such use for several of these species. The anticancer medicinal plants that constitute phytocompounds to treat specific cancers can also be investigated for activities in other cancer cell lines and this could be decisive in present and future studies.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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