International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(REVIEW ARTICLE)

Check for updates

Role of Plant derived-medicine for controlling Cancer

Ravindra B. Malabadi [1,*], Sadiya MR [2], Kiran P. Kolkar [3], Simuzar S. Mammadova [4], Raju K. Chalannavar [1] and Himansu Baijnath [5]

[1] Department of Applied Botany, Mangalore University, Mangalagangotri-574199, Mangalore, Karnataka State, India/ Miller Blvd, NW, Edmonton, Alberta, Canada.
[2] Department of Biochemistry, JSS Medical College, Mysore- 570015, Karnataka State, India.
[3] Department of Botany, Karnatak Science College, Dharwad-580003, Karnataka State, India.
[4] Department of Business Management, Azerbaijan State Economy University (ASEU), 6 Istiglaliyyat Street, AZ 1001 Baku, Azerbaijan.
[5] Ward Herbarium, School of Life Sciences, University of KwaZulu-Natal, Westville Campus, Private Bag X54001, Durban 4000, South Africa.

International Journal of Science and Research Archive, 2024, 11(01), 2502–2539

Publication history: Received on 17 December 2023; revised on 20 February 2024; accepted on 22 February 2024

Article DOI: https://doi.org/10.30574/ijsra.2024.11.1.0315

Abstract

This review paper has highlighted a list of plants containing active phytochemicals with anticancer potential, as well as data supporting their use in cancer therapy, animal models, and their pharmacological properties. Cancer is among the leading causes of morbidity and mortality worldwide. Cancer is a disease characterized by abnormal cell division and proliferation that result from disruption of molecular signals that control these processes. 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. The spread of cancer from its cells or tissue of origin to another healthy part of tissues or organs is called metastasis**.** Some of the regular characteristics of cancers are apoptosis, angiogenesis, multiple replication, growth signal production, insensitivity to signals of anti-growth and metastasis. These features make cancer cells to have continuous growth, long time survival and the potential to invade normal cells. Moreover, if these activities are not blocked, cancer cells will continue to increase, overwhelm and finally kill the patient with 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. Today, despite considerable efforts, cancer still remains an aggressive killer worldwide. The success rate of these therapies is diminished by toxicities, drug resistance, recurrence and treatment failure. A significant challenge associated with cancer is that treatment is as much an art as it is a science. 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. Many cancer patients seek alternative and/or complementary treatments because of the high death rate linked with cancer and the adverse side effects of chemotherapy, radiation therapy, immunotherapy, surgery, and stem cell therapy. Medicinal plants could also possess effective anticancer compounds that may be used as adjuvants 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. Cell death is caused by the whole plant extracts via apoptosis. However, majority of plant extracts have been researched for cancer prevention rather than treatment, resulting in low efficacy and uptake in practice. Prevention is certainly an attractive cancer management strategy. Thus it might be possible to reduce the process of carcinogenesis with regular use of these plants along with a healthy lifestyle.

Keywords: Anticancer; Alkaloids; Ayurveda; Cannabis; Cancer; Chemotherapy; Drug; Prevention; Medicinal Plants; Oncology; Tumours of Malignant

* Corresponding author: Ravindra B. Malabadi

1. Introduction

Globally cancer is a disease which severely effects the human population. The cancer disease is characterised by cells in the human body continually multiplying with the inability to be controlled or stopped [1-265]. Cancer is a leading cause of death and a vital health care challenge in the world. Consequently, forming tumours of malignant cells with the potential to be metastatic. Cancer is the abnormal, uncontrolled division of cells in the body [1-200]. The cancer cells when malignant, invade various parts of the body through the bloodstream [1-200]. Cancer is a serious and significantly progressive disease [1-200]. Next to cardiovascular disease, cancer has become the most common cause of mortality in the entire 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 [1-200]. 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]. For many years, cancer was considered as a fatal disease and not curable and this creates a sense of fear and hopelessness in the patient's mind, and the pain and side effects during chemotherapeutic treatment [1-200]. The advancement of molecular and tumor biology changes the cancer treatment protocol that has been practiced for the past 15 years, based on histomorphology features and organ origin-based treatment [1-200].

A significant challenge associated with cancer is that treatment is as much an art as it is a science [1-263-276]. Even after the cell type, stage and grade (i.e. how aggressive the tumor is) have been determined, other variables such as the patient's general health, treatment history, preferences and support system, as well as the doctor's training, come into play to decide the appropriate treatment approach [1-263-276]. Initial treatment modality may include surgery, radiation, drug therapy, or some combination of these approaches, with variability seen by tumor type[1-263-276].

According to GLOBOCAN estimates, there will be 28.4 million new cases of cancer worldwide in 2040, a 47 percent increase over the average number of cases in the year 2020. A significant increase in the rate of transitioning is anticipated due to demographic shifts, from 65 to 95 percent vs. 32 to 56 percent transitioned, and this may further increase due to rapid economic expansion and globalization [1-200]. Cancer is one of the most life-threatening diseases, with more than 100 different types occurring due to some molecular changes within the cell [1-100-262]. It is the third leading cause of death worldwide following cardiovascular and infectious diseases [1-200]. The burden of cancer rose to 18.1 million new cases and 9.6 million deaths in 2018. 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]. Breast cancer is the most common form of cancer in women [1-200]. The incidence of breast cancer is the highest in India, USA, Canada, Pakistan, Bangladesh among the South-Central Asian countries [1-200-262]. 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]. In the Arabian world, carcinoma of the lung, liver, or bladder cancers are most common among men, and breast cancer is most common among women. The number of new cases is expected to rise by about 70% over the next two decades. Thus, there is a real need for new efficient anticancer drugs with reduced side effects, and plants are a promising source for such entities.

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. The field of oncology has 3 major areas based on treatments: medical oncology, radiation oncology, and surgical oncology. Gynecologic oncologists treat cancers in such reproductive organs as the cervix, fallopian tubes, ovaries, uterus, vagina, and vulva. Hematologist-oncologists treat blood cancers, such as leukemia, lymphoma, and myeloma. Neuro-oncologists treat cancers of the brain, spine, and nervous system. Cancer specialists, called Oncologists, have made remarkable advances in cancer diagnosis, prevention, and treatment [1-200]. Today, more people diagnosed with cancer and are living longer. However, some forms of the disease remain frustratingly difficult to treat [1-200]. Modern treatment can significantly improve the quality of life and may extend survival. According to the WHO, more than 80% of the population in the developing countries are dependent on traditional medicine for treating cancer [1-200]. According to statistics, 60% of the drugs for treating cancer derived from plants. More than 3000 plants have anticancer activity [1-200]. 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]. 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]. In India, China, Iran, Azerbaijan folklore, herbal medicines were prepared as teas, tinctures, poultices, powders, and other types of formulations [1-265]. The expertise to select the right plants, methods of drug concoction and their specific use has been first transferred orally from one generation to the next until set down [2-265-273]. It is estimated that 70–95% of the population in developing countries continues to use traditional medicines. Today medicinal herbs are defined as plants that contain valuable substances with therapeutic or beneficial effect in healing and prevention of various ailments in man and animals. Herbal products such as plant extracts, dry powders and parts of plants, fungi, and algae have been used as complementary treatments alongside conventional drugs [2-265-273].

Today, despite considerable efforts, cancer still remains an aggressive killer worldwide. Moreover, during the last decade, novel synthetic chemotherapeutic agents currently in use clinically have not succeeded in fulfilling expectations despite the considerable cost of their development [1-200-273]. 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]. Many cancer patients seek alternative and/or complementary treatments because of the high death rate linked with cancer and the adverse side effects of chemotherapy and radiation therapy. Traditional medicine has a long history that begins with the hunt for botanicals to heal various diseases, including cancer [1-200-273]. Phytochemicals are considered suitable candidates for anticancer drug development due to their pleiotropic actions on target events with multiple manners.

2. Cancer Treatment: Problems

Cancer treatment options include surgical interventions, chemotherapy and/or radiotherapy either alone or in combination, stem cell therapy, immunotherapy, target therapy, vaccination and chemically derived drugs [1-265]. However, they present several limitations including side effects or ineffectiveness. Even though these conventional treatment modalities have shown promise, the unwanted short and long terms side effects are vast [1-104, 143-160-200]. 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, 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 immunotherapies 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 pharmacodynamics 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]. Drugs are used to treat cancer. Most drugs available in the market are chemosynthetic drugs and have side effects on the patient during and after the treatment, in addition to cancer itself [1-200]. For instance, hair loss, loss of skin color and texture, loss of energy, nausea, infertility, etc [1-200]. To overcome these side effects, naturally obtained drugs from medicinal plants are preferred [1-200-273].

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. Certain types of cancer such as breast cancer, can be treated using biological drugs (Herceptin). However, the cost of these drugs is very high and their effectiveness is limited in most cases to certain kinds of tumors. In many cases, the tumor develops resistance to a particular drug and the patient is transferred to a different drug. In addition, many patients are treated with a combination of several drugs. Thus, there is no doubt that there is a

real need for new efficient anticancer drugs with reduced side effects, and plants are a promising source for such entities. Chemoprevention represents a different attitude in the battle against cancer. 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.

For the advancement of cancer treatment and control of progression, much research has been done by scientists [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]. Due to lack of effective drugs, cost of chemotherapeutic agents, and the side effects of anticancer drugs, cancer can be a cause of death [1-200]. Therefore, efforts are still being made to search for effective naturally occurring anticarcinogens that would prevent, slow, or reverse cancer development [1-100]. Indian cuisine often incorporates gruels, herbal drinks and spices made out of plants. These culinary preparations have enormous health benefits, including chemo-preventive properties, and are effective inhibitors of cancer. Prevention is certainly an attractive cancer management strategy. Thus it might be possible to reduce the process of carcinogenesis with regular use of these plants along with a healthy lifestyle [1-266].

3. Current Treatment Methods in Oncology

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 [1-283]. Targeted therapy possessed breakthrough potential inhibiting the growth and spread of specific cancer cells, causing less damage to healthy cells [277-283]. 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 [277-283]. Several new technologies are currently under research in clinical trials, and some of them have already been approved [277-283].

Current methods in oncology focus on the development of safe and efficient cancer nanomedicines [277-283]. Targeted medical care helped rising the bio-distribution of recent or already tested chemotherapeutical agents around the specific tissue to be treated; different methods, such as sequence medical care, siRNAs delivery, therapy, and inhibitor molecules, supply new potentialities to cancer patients [1-277]. Gene therapy acts by direct in situ insertion of exogenous genes into benign tumors. Stem cells can be used as regenerative medicine, therapeutic carriers, drug targeting, and generation of immune cells because of having unique biological actions on other cells [1-277]. On the opposite hand, thermal ablation and magnetic hyperthermia are promising alternatives to the growth surgical process [277]. Finally, radionics and pathomics approaches facilitate the management of huge knowledge sets from cancer patients to enhance prognosis and outcomes. Much progress has been made, but many others are likely to come soon, producing more and more ad hoc personalized therapies. Further development and refinement of drug delivery systems are essential for improving therapeutic outcomes [277-283].

4. Plant Derived 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]. In parallel, there is an increasing evidence for the potential of plant-derived compounds as inhibitors of various stages of tumorgenesis and associated inflammatory processes, underlining the importance of these products in cancer prevention and therapy [1-283]. Approximately 60% of drugs currently used for cancer treatment have been isolated from natural products. and the plant kingdom has been the most significant source [1-200-283]. These include *Vinca alkaloids, Taxus diterpenes, Camptotheca alkaloids*, and *Podophyllum lignans*. Currently, of 16 new plant-derived compounds being tested in clinical trials, 13 are in phase I or II and three are in phase III [1-200]. Among these compounds, *flavopiridol*, isolated from the Indian tree *Dysoxylum binectariferum*, and *meisoindigo*, isolated from the Chinese plant *Indigofera tinctoria*, have been shown to exhibit anticancer effects with

lesser toxicity than conventional drugs [1-283]. 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]. Globally, the incidence of plant-derived products for cancer treatment is from 10% to 40% with this rate reaching 50% in Asiatic patients. In Europe alone expenditure for anticancer herbal products is estimated to be 5 billion dollars per year [1-200].

A new trend, that involved the isolation of plant active compounds begun during the early nineteenth century. Discovery of plant-derived substances has evolved during the last 200 years due to the variety of experience and expertise needed in order to identify such compound. In 1950, the investigation of anticancer phytochemicals from medicinal plants to treat cancer began with the isolation of alkaloids (vincristine and vinblastine) from Madagascar periwinkle, and Catharanthus roseus G. Don. and podophyllotoxin from Podophyllum species [1-283]. Several other anticancer agents, such as campothecin derivatives, homoharringtonine, vinca alkaloids, podophyllotoxin derivatives, and taxanes have been isolated from medicinal plants [1-200]. Medicinal plants have a special place in the management of cancer. It is estimated that plant-derived compounds in one or the other way constitute more than 50% of anticancer agents [1-200]. Numerous cancer research studies have been conducted using traditional medicinal plants in an effort to discover new therapeutic agents that lack the toxic side effects associated with the present chemotherapeutic agents [1-200]. 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 utilized medicinal plants [1-283].

Bioactive plant-derived phytocompounds can be anticipated to play a more and more substantial function in the development of new drugs [1-200]. Therefore, there is a focus on using alternative treatments and therapies against cancer [1-200]. Many plant species are already being used to treat or prevent development of cancer [1-19]. Medicinal plants, through the diversity of their chemical constituents, are vital for the invention of novel substances with effectiveness against tumors and other malignant cells [1-283]. Drug development and discovery from medicinal plant-derived secondary metabolites has become an essential part of searching for anticancer therapies over the centuries [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 [1-283]. Herbal medication offers very reasonable alternate to modern medicine against cancer [1-270]. There is a constant demand for new therapies to treat and prevent this life-threatening disease. Scientific and research interest is drawing its attention towards naturally-derived compounds as they are considered to have less toxic side effects compared to current treatments such as chemotherapy [1-19-283].

With the success of these compounds that have been developed into staple drugs for cancer treatment new technologies are emerging to develop the area further [1-19-200]. 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 [1-19-283]. Three quarters of the prescribed anticancer drugs are plant-derived [1-200]. Classical examples include vinblastine, vincristine, taxol, camptothecin and podophyllotoxin [1-19-200]. However, only about 5–15% of the 300,000 higher plants have been screened for potential drugs [2-283]. Despite considerable efforts, clinical use of plant-based, semi-synthetic or synthetic chemotherapeutic agents have been found to be largely inadequate in fulfilling expectations of a safe and affordable cancer cure [1-19-283].

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. Researchers around the world are drawing their attention towards compounds of natural origin [1-200]. For decades, human beings have been using the flora of the world as a source of cancer chemotherapeutic agents [1-200]. Currently, clinically approved anticancer compounds are vincristine, vinblastine, taxanes, and podophyllotoxin, all of which come from natural sources [1-200]. 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]. 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]. Bioactive phytocompounds such as vinca alkaloids, taxanes, ellipticine, camptothecin, combretastatin, curcumin, podophyllotoxin, homoharringtonine and others, are acknowledged for their potential anticancer effects on various neoplastic diseases [1-200].

There are many forms of cancer amongst the human population but they share similar characteristics or genotypes such as insensitivity to signals which inhibit cell growth making their replication limitless [1-19-200]. Apoptosis is evaded

and never induced in cancer cells and angiogenesis is sustained within the tumor tissue allowing survival of cancer cells. Plant derived compounds have demonstrated properties to inhibit cancer cell activity such as inhibiting proliferation of cancer cells and inducing apoptotic cell death [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]. 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]. Also there are currently developments using new technologies such as nano-particles to be used in administration of anticancer compounds and therapies [1-19-270]. Their development could be applied to control sustained drug release and help in aims to create drugs that are tissue specific reducing severe side effects of treatments [1-19-200]. Plant-derived anticancer agents are effective inhibitors of cancer cells lines, making them in high demand. Exploitation of these agents needs to be managed to keep up with demands and be sustainable [1-20-220].

Cancer is a frightful disease and represents one of the biggest health-care issues for the human race and demands a proactive strategy for cure. Plants are reservoirs for novel chemical entities and provide a promising line for research on cancer. Cancer is a disorder that rigorously affects the human population worldwide. 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]. 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].

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 [1-280]. Clinical studies including phytochemicals are focusing on three crucial aspects of cancer research: improving cancer cell responses to standard chemo- and radiation, reducing the severe adverse effects of standard anticancer therapy, and looking for unwanted interactions with standard therapy. The preclinical studies showed numerous phytochemicals efficacy including lycopene, quercetin, resveratrol, curcumin, berberine, sulforaphane, and tea catechins like EGCG [1-280]. Plant-based isolated chemicals have been demonstrated to be less hazardous than laboratory manufactured compounds in previous studies and research [1-280].

5. Oncology Drug development and Marketing

Oncology drug development and marketing are governed globally by specialists and an advisory process mediated by regulatory organizations [1-274, 275]. The high cost involved in new drug development coupled with the threat of failure and adverse effects associated with cancer drug therapies poses to restrain the growth of oncology. The personalization of medicine has transformed the oncology treatment landscape. One of the biggest challenges, and a lookout for marketers and market researchers, is differentiation. Oncology marketing encompasses various elements, including product promotion, education, awareness, campaigns at health care professionals, patients and general public [274-275]. The primary goal is to raise awareness about cancer treatments, products, or services and drive their adoption. Cancer organizations must have a strong brand identity in today's highly competitive marketplace to stand out. But it is not just about creating a logo or a slogan [274, 275]. Branding also includes building your reputation and customer trust and sustaining your business. The matter of digital marketing in the field of oncology is increasing as technology advances [274-275]. It is an attractive way to reach multiple people quickly and can be tailored to target specific demographics. In addition, digital marketing allows marketing campaigns to be present and analyzed more effectively, helping to measure their effectiveness better. Regardless of the marketing method, medical practices and companies must create engagement [274-275]. So, custom content that inspires patients or potential patients to take action. The marketing efforts are intended to convert users to new patients for a cancer center or a new treatment. Recruit patients for upcoming clinical trials, or convert healthcare providers into prescribers for the treatment. The content created for these campaigns must be of high quality to outperform other companies [274-275]. With increased demand for novel therapies and personalized medicine in health care, Artificial Intelligence (AI) is revolutionizing pharmaceutical product development by accelerating drug discovery, streamlining lab operations, and personalizing biomanufacturing [274-276]. *In silico* techniques allowing for the design of biologics with optimized efficacy, toxicity, and drug properties helps to save time and resources and improve the success rates for biopharma [274-276].

Cancer is a class of chronic diseases that is characterized by the uncontrolled growth of cells. The most common cancer types are breast cancer, lung cancer, colorectal cancer, uterine cancer, and thyroid cancer. According to their mode of action, the three primary categories of medications used to treat cancer are cytotoxic medications, targeted medications,

and hormonal medications [274-275]. The market for oncology pharmaceuticals has experienced rapid expansion in recent years as a result of rising drug approval rates and the introduction of bio-similar cancer therapy products. In addition, rising research and development efforts for novel cancer medications that are extremely effective and have few adverse effects have been sparked by rising healthcare spending on cancer by the major players. The growth of the oncology drugs market is driven by an increase in the prevalence of cancer disease and the rise in the incidence of various cancer conditions, an increase in the popularity of advanced therapies, and a surge in the geriatric population worldwide [274-276].

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]. The biology of cancer is also very complex, leading to an abundance of treatment approaches. Incidence and prevalence rates differ globally, and treatment of the disease is managed by numerous physician specialties. In addition to these challenges, the continually evolving nature of understanding of the disease and treatment approaches makes it difficult to remain current [274-275]. Excluding any bio-similar or generics, there were 128 new approvals of cancer drugs across the US, EU4 + UK and Japan in 2021 (these include label extensions for existing agents). With this increase in cancer drug development and availability comes an increase in both cost and revenue from these products. One forecast predicts that the oncology market will generate $2.2 trillion in sales between 2023 and 2029, driven largely by US, highlighting the economic scale and importance of this ever-growing field [274-276]. In recent years, we have witnessed a continued increase in the use of immunotherapies, a treatment approach that uses the body's own immune system to fight disease, and this has now become one of the most used anticancer drug categories in a number of cancer types [274-276]. A significant proportion of new agents have been approved alongside new companion diagnostics tests, and continued to see an increased implementation of tumor agnostic biomarkers and liquid biopsies [274-276]. The novel approaches under development, including therapeutic vaccines, gene editing and blood-based early cancer detection, hold the promise of potentially revolutionizing treatment and diagnosis in the future, if they prove effective [274-276].

6. Herbal Medicine Treatment of Cancer: Problems

The majority of plant extracts have been researched for cancer prevention rather than treatment, resulting in low efficacy and uptake in practice [1-200]. 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]. Every proven medicine or its active ingredients (anticancer chemicals or isolated compounds) requires phase III clinical trials before it can be marketed [1-200]. The rules of the "Food and Drug Administration" (FDA) and the "European Medicines Agency" (EMA) need at least one controlled trial in phase III with statistically significant outcomes before they can be marketed [1-200]. For instance, the FDA has recently adopted the questions and answers guidelines of the International Council for Harmonization on the nonclinical evaluation of drugs intended to treat cancer. These guidelines include 41 questions and answers which provide additional information about anticancer drug development and are aimed at bringing harmonization in the process of anticancer drug development. The key difficulty with this technique is estimating the role of photochemicals other than active compounds seen in traditional therapy. Numerous challenging factors have created limitations in the development of natural anticancer bio-molecules 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 [1-280]. The development of these bioactive compounds is a complex and time-consuming process. Moreover, it is evident that plants of the same species grown in different areas vary in their profile of medicinal compounds. This calls for the need to focus on the production of uniform and high-quality plants with a uniform metabolite profile that once tested is declared safe or unsafe once and for all. This might be achieved through the help of in vitro growth and biotechnological and genetic studies on these anticancer plants [1-283].

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. Except for exceptional circumstances, all the drugs need to go through all the phases of trials according to the guidelines of international agencies such as the FDA and EMA [1-280]. However, it has been observed that pharmaceutical companies deviate from the standard protocol and start testing new compounds on human subjects earlier than the defined timeline [1-200]. The reason for such practices is to accelerate the approval of these compounds under the pressure of investors. This means that the drug is presented for approval with insufficient data on its quality, safety, and efficacy [1-200].

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 [1-280]. The

problem is that there is insufficient data available regarding the quality, safety, and efficacy of herbal drugs. *Fagonia indica*, for instance, has shown potent activity against breast cancer when tested in the MDA-MB-231 cell line. *Fagonia indica* is used traditionally to treat many disorders and people have even started the use of its herbal tea against breast cancer. However, the question remains that there are only a few reports available on the anticancer activity of the plant [1-200].

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[1-200]. 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 of the plant . The traditional belief that a single drug, "silver bullet" is sufficient to treat a single disease has been questioned [1-200]. This belief relies on the premise that human diseases have a uniform underlying genetic basis across patient's populations. However, recent advances in genomics demonstrated genetic diversity, i.e., polymorphism, implying that different patient populations may require different tailored drugs to their treatment, as personalized medicine [1-200]. Moreover, the shortage in successful new chemical entities together with a focus of the pharmaceutical industry is on such molecules to serve as "silver bullets". Furthermore, the shift of companies from unpredictable research to a more steady businesses and revenues had created a crisis and loss of faith of public opinion in "silver bullets [1-200-265].

Furthermore, adequate biopharmaceutical and clinical evidence is essential for delivering these biocompounds from the laboratory to the patient [1-200-265]. 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]. 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 [1-200-265]. The cytotoxicity of natural phytocompounds and their selectivity to cancer cells can be improved using extensive Structure Activity Relationship (SAR) analysis. For example, along with cytotoxicity, the selectivity of triterpene natural products to A431 and C6 glioma cell lines was found to be enhanced by the trivial modification of functional group substitutions as well as their stereochemistry [1-200]. The complexity of the extraction, purification, isolation and characterization of the natural compounds may be reduced by advanced analytical and computational technologies which enhance the treatment cost and result in an extra burden to patients[1-280]. However, as far as herbal compounds are considered as drugs, it is erroneously believed that they have no issues in terms of safety and side effects [1-200]. There are hundreds of species of plants that are toxic to health. In the same way, there are many compounds in otherwise friendly plants that cause cytotoxicity [1-200-265]. Based upon testing it has been proved that even anticancer plants result in cytotoxic effects. Moreover, nanotechnology along with site-directed drug delivery approaches has raised hopes for the non-toxic and successful development of anticancer therapy from natural sources [1-200-265].

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.

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]. Ironically, vast knowledge and experience in drug development is available in the pharmaceutical industry. Therefore, combining the benefits provided by both traditional and modern medicine has been previously suggested as a promising approach in order to reveal and bring to market new plant-derived substances. However, in the last centuries only several herbal medicines or botanical drugs have been approved by health authorities for human use [1-200-265]. Collaboration and coordination between World Health Organization (WHO), Federal Drug Administration (FDA), European and other regulatory agencies, and the pharmaceutical industry worldwide may lead to clear guidance for development of herbal medications while taking advantage of the huge potential held by traditional medicine for development of both anticancer and other health promoting drugs [1-200-265].

7. List of Anticancer Plants

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) [1-20-283].

8. Role of Plant Secondary Metabolites in Controlling Cancer

Cancer being a life treating ailment is the second reason of death universally. The growing threats of medication-resistant cancers indicates a crucial need for the improvement of more effective anticancer agents [1-20-200]. Cancer is amongst the main reasons of death leading to high health burden universally as it results to significant cost of management for individuals affected [1-20-280]. Some of the regular characteristics of cancers are apoptosis, angiogenesis, multiple replication, growth signal production, insensitivity to signals of anti-growth and metastasis [1-20-210]. These features make cancer cells to have continuous growth, long time survival and the potential to invade normal cells. Moreover, if these activities are not blocked, cancer cells will continue to increase, overwhelm and finally kill the patient with cancer [1-20-210]. Currently, different therapeutic strategies including chemotherapy agents, surgery and/or radiation are utilized for cancer treatment. Although, the chemotherapeutic agents used for cancer treatment can result to short time relief to patients with cancer and aid to elongate their life span, several of the anticancer agents showed adverse side effects [1-20-283]. Based on this, the search for alternative potential anticancer agents has been directed to natural products. Many studies have validated the anticancer efficacy of natural bioactive compounds [1-20-200]. Secondary metabolites are of special interest to scientists because of their unique pharmacophores and medicinal properties. Secondary metabolites like polyphenols, terpenes and alkaloids have been reported to possess antimutagenic and anticancer properties in many studies. 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 [1-20-265]. Other compounds such as fucoxanthin , cucumin, anthocyanin, genistein and others were reported to have anticancer actions [1-20-200]. Amongst the natural compounds with anticancer activity, phenolic molecules were reported to inhibit metastasis and invasion by cancer cell [1-20-280]. The rising burden of cancer worldwide calls for an alternative treatment solution. Herbal medicine provides a very feasible alternative to western medicine against cancer. The in vitro studies showed cancer cell inhibition through DNA damage and activation of apoptosis-inducing enzymes by the secondary metabolites in the plant extracts. Studies that reported in vivo activities of these plants showed remarkable results in the inhibition of cancer in animal models [1-20-265]. For instance, hepatocellular carcinomas (HCC) are considered as the fifth most common malignancy in the world with increasing incidence. Many studies have been performed on the treatment and prevention of using herbal medicine against HCC in which it is shown that all phases of HCC such as initiation, promotion, and progression could be a_ected by components of herbs [1-20-280].

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. Betulinic acid is a natural pentacyclic triterpenoid having cytotoxicity against many tumors cell types [1-20-280]. Betulinic acid causes apoptosis via activating the mitogen activated protein kinase cascade, inhibiting angiogenesis, and modulating pro-growth transcriptional activators and aminopeptidase-N activity [1-20-280]. It also induces apoptosis through a p53- and CD95-independent pathways efficiently killing cancer cells resistant to conventional chemotherapeutic drugs [1-20-283].

Camptothecin is a quinolone alkaloid derived from the Chinese tree *Camptotheca acuminata.* It attaches to type I DNA topoisomerase, stopping DNA cleavage, downgrading and thus producing DNA double strand break and cytotoxicity [1-

20-200]. Two FDA-permitted semi-synthetic camptothecin byproducts are irinotecan and topotecan are therapeutically active and lesser toxic [1-20-265-280]. Irinotecan is used to treat advanced large intestine and rectum cancers [1-20-200]. Topotecan can treat small cell lung, recurrent ovarian, and cervical cancer [1-20-280]. Podophyllotoxin is natural toxin found in *Podophyllum peltatum* and *Podophyllum emodi* of family *Berberidaceae*. It reversibly attaches to tubulin while its primary derivatives, etoposide as well as teniposide hinder topoisomerase II, ensuing in topoisomerase II-facilitated DNA cleavage [1-20-200]. Furthermore, podophyllotoxin may be effective against a range of drug-resistant tumor cells in terms of anti-multidrug resis tance [1-20-280].

Cancer has become one of the most fatal diseases in most countries. In spite of the medical care developing, cancer still remains a significant problem [1-20-200]. The majority of the cancers are resistant to treatment. Therefore, plant based cancer therapy is gaining importance [1-20-200]. 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]. It causes rapid cell death at high concentrations and triggers an inflammatory response at low concentrations [1-20-200]. Homoharringtonine is an alkaloid cephalotaxine from family Cephalotaxaceae *Cephalotaxus* genus [1-20-200]. These are accepted for treating chronic myeloid leukaemia. Homoharringtonine attaches to the Asite cleft of the big ribosomal subunit, stopping chain extension along with protein synthesis [1-20-200].

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]. Vinca alkaloids, camptothecin derivatives epipodophyllotoxin, and taxane diterpenoids are the four chief clinically effective plant- derivative anticancer agents [1-20-200]. Additional plant-derived anticancer medicines utilized in addition to these phytochemicals are combretastatins, ingenol mebutate, etc [1-20-270].

Since microtubules are involved in cell shape preservation, organelle transport, motility, like cell processes, Vinca alkaloids impact both malignant and non-malignant cells in non-mitotic cell cycle [1-20-200]. The semisynthetic equivalents of these two naturally isolated alkaloids, vinblastine and vincristine are used for 50 years for in vitro and in vivo actions [1-20-200]. The only two clinically approved semisynthetic counterparts are vinorelbine and vindesine to be used in conjunction with chemotherapy for treatment of leukaemia, Kaposi's sarcoma, breast and lung cancers, testicular carcinoma, Hodgkin and non-Hodgkin lymphomas [1-20-200]. Vinflunine is recently accepted for the second-line transitional cell carcinoma treament. Allicin (*Allium sativum*) of *Amaryllidaceae* family reduced human hepatic bile duct cancer growth in BALB/c nude mice [1-20-200]. The bicyclic diterpenoid lactone andrographolide is obtained from the plant *Andrographis paniculata* (family *Acanthaceae*) [1-20-200]. Andrographolide was discovered to constrain tumor growth by hindering hypoxia variation [1-20-200]. Apigenin (APG) is an anticancer flavonoid found naturally in fruits and vegetables. It has controlled the expression of Bcl-2 family proteins and triggered the caspase cascade, resulting in G2/M phase seizure and apoptosis [1-20-265]. It has suppressed NSCLC xenograft development and metastasis by inhibiting the dipeptidyl peptidase IV enzyme. Apigenin (APG's) efficacy is boosted when combined with other chemotherapeutic medicines or put in nanocarriers [1-20-220].

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 tumor formation and metastasis of 4T1Br4 mammary tumor cells to numerous lung, bone, and brain. Genistein is an oestrogen-like isoflavone found naturally in soy beans. By blocking unusual nuclear accretion of bcatenin and suppressing WNT signalling genes, genistein therapy reduced aberrant crypts in the azoxymethane- persuaded rat colon cancer [1-20-200]. Glycyrrhizin being the most abundant bioactive in roots of *Glycyrrhiza glabra* L condensed thromboxane synthase and multiplying cell nuclear antigen expression in athymic BALB/c nude mice xenografted with human lung adenocarcinoma [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 [252]. EGCG's anticancer efficacy is verified in numerous research using animal models and cell lines [1-20-200, 248]. Clinical trial data showed that a catechin mixture comprising EGCG is safe when given to high-grade prostatic intraepithelial neoplasia males. Polyphenon E (polyphenol formulation mainly EGCG) gathered in cancer tissue and reduced proliferation and apoptosis in a randomized, placebo-controlled phase II pilot study before surgery in bladder cancer [1-20-200, 252]. Both black and green tea are made from the leaves of the *Camellia sinensis* plant [248]. The key difference between the two is that black tea is oxidized and green tea is not [252]. Green tea should not be taken by patients suffering from heart conditions or major cardiovascular problems. Some studies revealed the capacity of tea plants to accumulate high levels of aluminum [252]. This aspect is important for patients with renal

failure because aluminum can be accumulated by the body, resulting in neurological diseases [252]. Another study found that higher intake of green tea might cause oxidative DNA damage of hamster pancreas and liver [252-273].

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 stabilizing 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]. Semisynthetic byproducts are created with augmented solubility, cytotoxicity in resistant tumors and reduced toxicity [1-200]. A docetaxel derivative of second-generation, Cabazitaxel shows cytotoxic activity against numerous docetaxel-resistant malignancies while having lesser general toxicity [1-200]. Unlike other taxanes, cabazitaxel passes the blood-brain barrier in vivo. Several paclitaxel analogues, including milataxel, tesetaxel, ortataxel, larotaxel, etc. are now in clinical trials [1-200-273]. A careful use of preclinical screening models in drug development process can result in probable lead compounds in anticancer drug progress with better initial efficacy, safety information, pharmacokinetic and toxicity data that aid in deciding if the molecule can be taken for further clinical trials [1-200]. Herbal medicine has become a very safe, non-toxic, and easily available source of cancer-treating compounds. Herbs are believed to neutralize the effects of diseases in a body because of various characteristics they possess.

All of the fundamental medicines are found in plants. Plant bioactive compounds have been shown to suppress cancer [1-200-273]. The chosen plants with anticancer properties showed essential role in battling oral, breast, colon, lung, stomach, cervical, hepatic, and blood cancer malignancies [1-200]. The secondary metabolites present in the plant extracts inhibited cancer cells by causing DNA damage and activating apoptosis-inducing enzymes in vitro. Also, in vivo studies of these plants and their phytochemical actions revealed significant outcomes in cancer suppression in animal models [1-220-263].

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-hydro-artemisinin 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 has been reported. 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].

With the advancement of information technology, artificial intelligence (AI) and bioinformatics, there is an increasing trend to build resources and databases that report herbal formulations, active components of the herb, and related information [1-263-264]. In addition, several researchers have developed strategies for In -silico- pharmacokinetic properties of molecules/drugs [1-263-264]. Such approaches are also applicable to photochemical and plant-based active drug components for their virtual screening, possible mode of action, and advanced drug discovery. 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 photochemicals other than active compounds and are present in the traditional medicine [263-264].

1) *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.] The leaves are employed to treat piles, ulcers and to expel the placenta, whereas the seeds are used to cure medical conditions in relation to cancer [1-200]. The medicinal value of the Glory lily is particularly due to the alkaloids especially colchicine, thiocolchicine and gloriosine as well as to the presence of 10 non-alkaloidal compounds viz. β-sitosterol, stigmasterol, chelidonic acid, luteolin, etc [1-200]. Colchicine is used as a mitosis-arresting agent and is used in cancer treatment and diabetics in addition to promoting polyploidy in agricultural crops. It is also used to treat cancer, rheumatism and cardiovascular diseases. Colchicine is found in significant quantities only in two plants viz [1], *Colchicum autumnale* and *Gloriosa* sp. In *G. superba*, colchicine yield ranges from 0.15% - 0.3% in the rhizomes, and 0.7% - 0.9% in the seeds[1]. The discovery of high colchicine content in this plant increased its demand in domestic and worldwide markets [1-280].

2) *Curcuma mutabilis* was collected from the Nilambur forest, Malappuram district of Kerala state, India [2-280]. 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]. Both the extract and the compound displayed superior anti-proliferative activity against several human cancer cell lines, without any display of cytotoxicity towards normal human cells such as peripheral blood derived lymphocytes and erythrocytes [2-280].

3) Polyphenolic compounds include flavonoids, tannins, curcumin, resveratrol and gallacatechins 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]. The cytotoxicity of polyphenols on a range of cancer cells has been demonstrated and their antioxidant properties determined [3]. Polyphenols are thought to have apoptosis inducing properties showing anticancer properties which can be utilized [3-200]. The mechanism in which polyphenols are thought to carry out apoptosis initiation is through regulating the mobilization of copper ions which are bound to chromatin inducing DNA fragmentation [3-200]. In the presence of Cu(II), resveratrol was seen to be capable of DNA degradation. Other properties plant polyphenols showed their ability to interfere with proteins which are present in cancer cells and promoting their growth [3-200]. Cancer agents may be altered through the polyphenol regulating acetylation, methylation or phosphorylation by direct bonding [3]. For example, curcumin treated cancer cells in various cells lines have shown suppression of the Tumour Necrosis Factor (TNF) expression through interaction with various stimuli [3-280].

4) 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 the seeds of plant [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]. The flavonoids extracted from *Erythrina suberosa* stem bark (4'-Methoxy licoflavanone (MLF) and *Alpinumi soflavone* (AIF)) were shown to have cytotoxic effects in HL-60 cells (human leukaemia) 12 [3-9-200]. MLF and AIF induced apoptosis through intrinsic and extrinsic signaling pathways. Other studies have looked at flavonoid extracts from fern species and found that even in low concentrations, they still demonstrated high percentage of anticancer activity [3-9-200]. Also, these flavonoids inhibit the expression of NF-κB which is needed for cancer cell survival and angiogenesis and proliferation [3-9-200].

5) Brassinosteroids (BRs) are naturally occurring compounds found in plants which play roles in hormone signaling 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. Two natural BRs have been used in investigations with cancerous cells to demonstrate the anticancer properties that these compounds possess [3-9-200]. 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]. A characteristic of cancer cells is that they do not naturally undergo apoptosis and proliferate indefinitely [3-9-200]. BRs can induce responses necessary for growth inhibition and induce apoptosis by interacting with the cell cycle [3-9-200]. Along with their anticancer properties, BRs generate different responses in normal and cancer cells [3-9-200].

6) 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 showed 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]. Taxanes such as paclitaxel and its analogue docetaxel are also microtubule disruptors. These compounds inhibit cell cycle phase transitions from metaphase to anaphase causing cell cycle arrest and apoptosis [3-9-200]. Replication of cancer cells is reduced by paclitaxel as it stabilizes or polymerizes microtubules in the cells [3-9-210]. Paclitaxel was one of the first drugs to have a huge impact on cancer treatment and vincristine and vinblastine were two of the initial drugs to be isolated [3-9-220]. Combinations of drugs derived from vinca alkaloids, Taxus diterpenes, Podiphyllum lignans and Camptotheca alkaloids in plant extracts may enhance their anticancer effects and improve their efficacy as therapeutic agents [3-9]. The investigation showed that the plant extracts with a combination of anticancer compounds were able to have killing activity which was specific to cancer cells and showed no effect on normal human lymphocytes and fibroblasts [3-9-200]. This makes plant extracts more desirable as therapeutic agents than those that are chemically derived which cause toxic complications in cancer treatment [3-9-218]. The plant extracts

induced apoptosis which was demonstrated by an increased sub-G1 phase population of cells with lower DNA content and condensation of chromatin. Also an increase in caspase 3 activation was seen after extract treatment which is a key stage in apoptotic cell death [3-9-217].

7) 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]. This research demonstrated enhanced activities of the NPs in cytotoxicity of MCF-7 cells compared to free or pure quercetin [3-10, 50, 52-54-200]. Nanoparticles (NPs), in their use for anticancer treatment are of growing interest and showed promise as a natural alternative to current treatments [3-9]. Jyoti *et al*., 2015 [1-10-200] investigated the noscapine analogue 9-bromo-noscapine in formulation with nanostructure lipid particles [10-200]. Here they showed enhanced cytotoxicity and apoptosis in lung cancer cell lines with increased uptake of drug into cancerous cells of the formulated noscapine analogue compared to the free drug [10-15, 50, 52-54-200].

8) 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]. There is a huge demand for medicinal plants in developing countries putting high pressure on the plant populations. Many medicinal plants are cultivated from wild populations for informal trade but this cultivation is not regulated [1-15-200]. Grape stem extracts have demonstrated to have antioxidant properties, prevent DNA damage from reactive oxygen species and shown anti-carcinogenic potential against an array of cancer cell lines from cervical cancer, thyroid cancer and many more [1-15-280].

9) 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]. The major active compound responsible for the pharmacodynamic action is the polyphenol curcumin [1-16-200]. Additionally, this natural polyphenol has been described as an anticancer agent, both in vitro and in vivo on a wide range of cancer types, such as colon, pancreatic, liver, cervical, pulmonary, thymic, brain, breast and bone cancer [1-16-100]. Curcumin, the main component of C. longa, plays an important role in the therapeutic activities of *C. longa*. Curcumin showed anticancer and anti-inflammatory activities as reported by many different studies. Cyclooxygenase (COX)-2 plays a vital role in the formation of colon cancer. Curcumin may thus play an important role in the prevention of colon cancer. Furthermore, the anticancer effects of curcumin on human breast cancer cell lines (MCF-7) were assessed through lactate dehydrogenase and 3-(4,5-dimethyl-2-thiazolyl)-2, 5-diphenyl-2H-tetrazolium bromide assays to assess cytotoxicity and cell viability, respectively. The results showed that curcumin induced cytotoxicity and inhibited cells in a time- and concentration-dependent manner [1-16-280].

10) 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, 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]. For cancer patients, chemotherapy and radiation therapy are cytotoxic therapies (meaning they kill cancer cells) [17, 18, 29, 30]. The fruit also has an ability to reduce the cell growth on a number of cancer cell lines, including breast, lung, pancreatic, prostate, ovarian, and colorectal [17, 18, 29, 30]. Ramphal (*Annona reticulata* L.) is one of the traditionally important plants used for the treatment of various ailments. including cancer [17, 18-200]. Ramphal may with other types of fruits in the *Annona* family, such as custard apple (*Annona sqamosa*) and sweetsop [17, 18, 29. 30-200]. Annonaceous acetogenins are a group of constituents obtained from plants belonging to *Annonaceae*, having potentials of anti-neoplastic agents [1-17, 18, 29, 30-200].

11) *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]. The cytotoxic action of these bioactive compounds was shown by 3-(4, 5-dimethylthiazol-2-yl)− 2, 5-diphenyltetrazolium bromide [MTT] assay in different human cancer cell lines [1-200].

12) *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].

13) *Aloe vera* belonging to *Asphodelaceae* family possesses wide range of pharmaceutical activities [1-26-55]. The leaves of *A. vera* showed the presence of secondary metabolites like doxorubicin, butyl-p-tolyl sulphide, lupeol isobarbaloin, 6- methyl-4-chromanone, barbaloin, lectin, emodin, aloe-emodin, aloesin, acemannan, anthrone-C-glycosides, sitasterol alexin-B, campesterol and butylated hydroxyanisole [1-200]. 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].

14) *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]. The root extract of *A. racemosus* helped in tyrosin, histone arginine and shatawarine isolation[1-100]. The chloroform, methanol, ethyl acetate, DMSO, and water extracts of *A. racemosus* tuber, root and leaves showed antitumor growth hangup of human colon cancer cells through MTT test [1-200].

15) *Artemisia* herba-alba (white wormwood) belongs to family *Asteraceae,* genus Artemisia [1-270]. The whole plant and specially leaf extract of *A. herba-alba* showed high anticancerous activity against 3 human tumor cell lines like human bladder carcinoma, human laryngeal carcinoma, human myelogenous leukaemia (K-562) cells. The phenol complexes perceived in Indian *A. herba-alba* are herbolide, torrentin, chlorogenic acid, dihydroreynosin, isophorone, rutin, schaftoside, isoschaftoside, vicenin-2, 11-epitaurin, vachanic acid, α,13-dihydrocostunolide, 3-Epi-erivanin, 1-b -hydroxy colartin, pinocarveol, artemisia ketone, deacetyl- torrentin, piperitone and herbalbin. The quercetin and apigenin administration in syngeneic mice repressed the development and metastatic budding of melanoma (B-16-BL-6) cells in vitro [1-100]. The chemopreventive activities of chlorogenic acid indicated possible role of microsomal glucose-6- phosphate translocase in the brain tumours growth [1-100].

16) *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 [1-200].

17) *Centella asiatica* (Brahmi) belonging to *Apiaceae* family is a traditional 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 [1-200]. *C. asiatica* leaf was physiologically active and had a significant cytotoxic impact. After 48 h of incubation, the leaf ethyl acetate extract of *C*. *asiatica* displayed the maximum cytotoxic activity, with an IC_{50} of 82 g/mL [1-141]. Some fractions of *C. asiatica* suppressed altered cell lines prolifeation like *Ehrlich ascites*, Dalton's lymphoma and ascites tumor cells dose-dependently. In long-term culture, partially purified fractions of *C. asiatica* greatly inhibited the propagation of mouse lung fibroblast cells. The direct inhibition of DNA synthesis after oral intake of *C. asiatica* extracts decelerated solid and ascites tumors development to improve life time of tumour mice [1-141].

18) *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]. The methanolic extracts of *C. roseus* exhibited note- worthy anticancer action on the (Hep-2) cell line. These extracts inhibited cells significantly, lowering viable cell count. The MTT assay was used to test the cytotoxicity effect of ethanolic extract of C. roseus flower in human epithelial cervical carcinoma cell line (HeLa). The Catharanthus alkaloids, also known as Vinca alkaloids (CAs or VAs) have covered approximately 130 terpenoid indole alkaloids [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]. This group is comprised of vinblastine, vincristine, anhydro-vinblastine, and the semisynthetic sub-ordinates vindesine (VDS), vinorelbine (VRL), and vinflunine (VFN) (the fluorinated analogue of vinorelbine). Since 2008, a novel synthetic vinca alkaloid known as vinflunine has been licensed for therapeutic use in Europe. Vinblastine and vincristine are now utilized for the treatment of different cancers in the US and other nations, whereas the semisynthetic vindesine is currently in phase II clinical trials for the treatment of hepatocellular cancers, leukemia and non-small cell lung cancer in South Africa [1-200]. The mechanism of the cytotoxic activity of the Catharanthus alkaloids is related to their impact on the microtubules. Vinca alkaloids (CAs or VAs) are frequently utilized as anticancer medications, either alone or in combination with other medicines, to treat a number of cancers, such as breast cancer, osteosarcoma, and acute lymphocytic leukem [1-200].

19) *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. Cyclooxygenase (C0X-2) has a vital role in initiation of colon cancer. The HT-29 colon cancer

cells treated with different concentrations of curcumin decreased expression of (COX-2) [1-95, 203]. Curcumin aiding in prevention of colon cancer and breast cancer cell lines (MCF-7) was assessed through SRB and MTT assays for cytotoxicity and cell viability, respectively which exhibited augmented caspase 3/9 activity and initiation of apoptosis indicating down- regulation of miR-21 the expression of miR-21 in MCF-7 cells by up-regulation of PTEN/Akt signalling pathway [1-95, 203]. Curcumin's anticancer potential seen through decrease growth in numerous tumor cell types. Curcumin down-regulate the expression lysyl oxidase (LOX), epidermal growth receptor 1 (EGR-1), activator protein 1 (AP-1), NF-kappa B, cycloxygenase 2 (COX2), matrix metallopeptidase 9 (MMP- (HER2), nitric oxide synthase (NOS) genes, etc[1-95, 203]. Turmeric suppresses c-Jun N-terminal kinase, protein tyrosine kinases, and protein serine/threonine kinases activities along with its gene expression impact. Turmeric limited tumor cell raid and metastasis by suppressing MMP-2 activity and HEp2 (epidermoid carcinoma cell line) cell raid in vitro[1-95, 203].

20) *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. *D. bulbifera* possesses significant secondary metabolites such as diosgenin, kaempferol-3, 5- dimethyl ether, lutein, zeaxanthin, neoxanthins, mono-arachidin, behenic acid, demethyl batatasin-IV, diosbulbin-B- d -F, docosyl ferulate, tristin, protocatechuic acid, adenosine, stigmasterol, azelaic acid and caryatin[1-280]. Aqueous, methanolic and ethanolic extracts of *D. bulbifera* exhibited likely anticancer effect against human gastric (BGC-823), human liver carcinoma (HepG-2 and SMMC-7721), human oesophagus adenocarcinoma (CaEs- 17) cell lines) and human colon adenocarcinoma (LoVo and SW-116) [1-200].

21) *Saussurea costus* (kuth/ Indian costus) belonging to the family *Asteraceae* [1-100]. The leaves and root of *S. costus* are potentially used traditionally in North Korea, Japan, China and India for cancer, diabetes, fungal, microbial, sore throat, inflammation, cough, etc [1-200]. *S. costus* possesses many biologically active isolated compounds like naringenin, vanillin, chlorogenic acid, kaempferol, ferulic acid, syringic acid, ellagic acid, taxifolin, methyl gallate, cinnamic acid, pyro-catechol, doconexent, butanedioic acid, etc [1-100]. The anticancer activity of *S. costus* reduced PKC improvement of matrix metal- lopeptidases (MmP-9 and MmP-2) causing death of HT-80 cells dose- dependently [1-100].

22) *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, and anticon- vulsance effects [1-200]. In vitro and in vivo researches exposed that oridonin persuades apoptosis in a wide range of cancer, including hepatocellular, cutaneous, colorectal, gallbladder, breast, gastric, and pancreatic malignancies [1-200]. The MTT test was used to assess the cytotoxicity of *T. bacata* aqueous and aqueous methanol extracts against human colon cancer (HCT-116) cell lines [1-200].

23) *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[1-280]. The methanolic, aqueous, and ethanolic extracts of stems caused programmed cell death inhibiting apoptosis. The in vitro cytotoxic effect of DMSO and ethanolic extract from *T. cordifolia* stems against murine monocyte/-macrophages (J-774-A-1), human melanoma (A-375) and human breast cancer (MCF-7) cell lines was determined by the colori metric MTT assay and TBE method [1-280].

24) *Withanaia somnifera* (Ashwagandha) belonging to family *Solanaceae* is grown in India, China, Japan, Europe and Asia and frequently used in cancer and diabetes [1-213-280]. The presence of these substances (withanolides, anahygrine, withananine, anaferine, withanine, β-sisterol, tropanol, chlorogenic acid, somniferiene, cysteine, scopoletin and somniferimine) contributes to anticancer and antidiabetic actions [1-213]. The hydroalcoholic extract has the highest scavenging activity when compared to the ethanolic extract [1-100]. The cytotoxicity of ethanolic, aqueous and hydro-alcoholic extracts of *W. somnifera* root, stem, and leaves on Hep-2 cells was examined with the MTT assay and the TBE method Hydro alcoholic (IC_{50} = 55 g/mL) and ethanolic (IC_{50} = 69 g/mL) extracts were determined to be the most active[1-213].

25) *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 [1-28-50-200]. Andrographolide inhibits colon cancer cell line HT 29 growth, promotes human peripheral blood lymphocytes proliferation as well as division along with pro-differentiative actions in M1 murine myeloid leukaemia cell line [28, 135, 171, 182]. *Andrographis paniculata* Wall (family *Acanthaceae*) is one of the most popular medicinal plants used traditionally for the treatment of array of diseases such as cancer, diabetes, high blood pressure, ulcer, leprosy, bronchitis, skin diseases, flatulence, colic, influenza, dysentery, dyspepsia and malaria for

centuries in Asia, America and Africa continents [1-28-60]. It possesses several photochemical constituents with unique and interesting biological properties [1-28, 135, 171, 182]. Ethanol extract of *A. paniculata* leaf has inhibition concentration (IC_{50}) for IMR-32 (M2 subtype mRNA) and human colorectal adenoma–carcinoma (HT-29 cell lines) at 200 /g/mL, whereas other extracts have 50% inhibition effect at 250/g/mL concentration for HT-29 cell lines. Anticancer activity of water, ethanol, and acetone extracts of *A. paniculata* leaves against HT-29 cancer cell lines had a 50% inhibition at 200 /g/mL concentration[1-28, 135, 171, 182-200].

26) The oral intake of *Phyllanthus amarus* extract greatly improved life duration and decreased tumor size in Dalton's lymphoma ascites and Erlich ascites carcinoma affected mice [1-41, 51, 106, 71]. This plant's chemoprotective qualities may be connected to its capacity to suppress carcinogenic chemical metabolic activation, and interfere with DNA repair [1-41, 51, 71, 216]. *Phyllanthus amarus* is an important plant of Indian *Ayurvedic* system of medicine which is used in the problems of cancer, stomach, genitourinary system, liver, kidney and spleen [1-41, 51, 71, 106-200]. It is bitter, astringent, stomachic, diuretic, febrifuge and antiseptic [1-200]. The whole plant is used in gonorrhea, menorrhagia and other genital affections. It is useful in gastropathy, diarrhoea, dysentery, intermittent fevers, ophthalmopathy, scabies, ulcers and wounds [1-41, 51, 71, 106-200].

27) 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. Viscotoxins are members of the thionin family type III and are characterized by three disulfide bridges [1-200]. They are cationic proteins, rich in cysteine, and comprising of 46 amino acid residues with six isomers, three of which are viscotoxin A2, A3 and B. Viscotoxins can be found inside the leaves and stems of the mistletoe plant. As viscotoxins are hydrophilic, they are present in the aqueous *Viscum album* L. extracts [1-200].

28) *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, treatment of cancer, other chronic and infection diseases [1-43, 55-57-200]. The use of the pomegranate juice, peel and oil has been indicated that pomegranate have anticancer activities, including interference with tumor cell proliferation, cell cycle, invasion and angiogenesis [1-43, 55-57-200]. These may be related to anti-inflammatory effects of pomegranate. The phytochemistry and pharmacological actions of pomegranate properties indicated a wide variety of clinical usage for the cancer prevention, treatment, and also other diseases where chronic inflammation is reliable to play a main etiologic role [1-43, 55-57-200]. The most components of the pomegranates are tannin and polyphenolics [1-43, 55-57]. Phytochemical analyses indicated that pomegranate peels possess active inhibitors, including phenolics and flavonoids. Pomegranate peel has ellagitannins, ellagic acid, gallic acid, hydroxybenzoic acids such as ellagic acid, gallagic acid, and ellagic acid glycosides [1-43, 55-57-200]. Punicalagin is the major bioactive component of pomegranate peel [1-43, 55-57-200]. Anthocyanidins are mainly contained cyanidin, pelargonidin and delphinidin and flavonoids such as kaempferol, luteolin, and quercetin [1-43, 55-57-273].

29) 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. These plants 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 tumor cells, as the plant extracts had no effect on primary cultures of healthy human cells [1-60-63, 212]. Cell death caused by the whole plant extracts was via apoptosis [1-60-63]. Plant extract from *Urtica membranacea* showed particularly strong anticancer capabilities since it inhibited actual tumor progression in a breast adeno-carcinoma mouse model [60-63, 212-273]. The results of this study confirmed that whole plant extracts are promising anticancer reagents [63, 212-280]. This study examined the effects of three whole plant extracts (ethanol extraction) on human tumor cells. The extracts were from *Urtica membranacea* (Urticaceae), *Artemesia monosperma* (Asteraceae), and *Origanum dayi post* (*Labiatae*) [1-63, 212-200]. All three plant extracts exhibited dose- and time-dependent killing capabilities in various human derived tumor cell lines and primary cultures established from patients' biopsies [63, 212-200]. The killing activity was specific toward tumor cells, as the plant extracts had no effect on primary cultures of healthy human cells. Cell death is caused by the whole plant extracts via apoptosis [1-63]. Plant extract (*Urtica membranacea*) showed particularly strong anticancer capabilities since it has inhibited actual tumor progression in a breast adenocarcinoma mouse model. Therefore, results of this study confirmed that whole plant extracts are promising anticancer reagents [1-63-273].

30) 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]. The results obtained indicated that *H. isora* has a potent cytotoxic activity toward the selected cancer cells such as HeLa-B75 (34.21 ± 0.24%), HL-60 (30.25 ± 1.36%), HEP-3B (25.36 ± 1.78%), and PN-15 (29.21 ± 0.52%) [67]. Interestingly, the selected botanicals selectively inhibited cyclooxygenase-2 (COX-2) more than (COX-1), which are the key enzymes implicated in inflammation. COX-2 inhibition was observed to be in the range of 19.66-49.52% as compared to COX-1 inhibition (3.93-19.61%) [67]. The results of the antioxidant study revealed that the selected plants were found to be effective 1,1-diphenyl-2-picrylhydrazyl (DPPH), hydroxyl (OH), and superoxide radical (SOR) scavenging agents [1-67]. High-performance thin layer chromatography (HPTLC) fingerprint of flavonoids was used as a measure of quality control of the selected plant samples [67]. The results of the present study findings strengthen the potentiality of the selected plants as a resource for the discovery of novel anticancer, anti-inflammatory, and antioxidant agents [1-67-200].

31) 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]. *Annona muricata* is extracted from the seeds, bark, fruit, and leaves. In addition, acetogenin has a chemotherapeutic ability against multiple drug-resistant cancers [29, 30, 80, 81, 142, 144, 157. 159, 160, 199, 202]. Some acetogenins are toxic for specific cancer cell lines, such as carcinoma tumors, prostatic adenocarcinoma, lung solid human breast cancer, human lymphoma, pancreatic carcinoma, multiple-drug resistant human breast adenocarcinoma, liver cancer, human lymphoma, and colonic adenocarcinoma. The ethanolic extract of *A. muricata* was tested for anticancer activity against MDA and SKBR3 breast cancer cell lines using the MTT assay method. The anticancer property of water and ethanolic extracts of *A. muricata* against EACC (Esophageal Adenoid Cystic Carcinoma) was tested using Trypan blue-exclusion assay [1-100]. An ethanolic leaves extract of *A. muricata* showed 32.9% inhibition of cell death at a concentration of 250 /g/mL and 100% maximum inhibition of cell death at a concentration of 750 /g/mL, even though the water– leaves extract of different concentrations had no inhibition effect on the cancer cell line. IC_{50} of ethanolic extracts was determined to be 335.85 /g/mL [29, 30, 80, 81, 142, 144, 157. 159, 160, 199, 202].

32) The derivatives of podophyllotoxin (PTOX) such as Etoposide, teniposide, and etoposide phosphate, are used for anticancer chemotherapy that is extracted from *Podophyllum peltatum* L. (Family-*Berberidaceae*) and *Podophyllum emodi* (syn. P. hexandrum) [1-200]. PTOX is an aryltetralin-lignan with strong cytotoxic activity. The podophyllotoxin derivatives have antiproliferative activity against germ cell tumors, small cell and non-small cell lung cancers [1-200]. The 4-aminoalkyl-40-O-demethyl-4-desoxypodophyllotoxin, TOP-53, is a podophyllotoxin derivative with antitumor activity, and anticancer activity against lung cancer and lung metastatic cancer. The cytotoxicity activity of TOP-53 was determined using IC_{50} and showed 0.016–0.37 /g/mL against murine tumors and 0.26–8.9 /g/mL against human non-small cell lung cancer (NSCLC) cell lines [1-200]. TOP-53 podophyllotoxin derivative is also potent in antitumor activity for lung localized tumors and metastatic tumors in the lungs [1-100]. These derivatives prevent the polymerization of tubulin and thereby, could induce cell cycle arrest at mitosis and inhibit the formation of the mitotic-spindles microtubules [1-280].

33) 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]. This has led to substantial demand for it. In the ancient Indian holistic and natural medicine called *Ayurveda*, the leaves of *T. baccata* were used in the treatment of cancer [1-260]. Taxanes from *T. wallichiana* plant species have anti-inflammatory, analgesic, antipyretic, antiallergic, immunomodulatory, anticonvulsant, anti-conceptive, anti-osteoporotic, antiplatelet, antifungal, antibacterial activities, as well as antispasmodic effects [1-100]. A Taxus species constituent, paclitaxel, is found in the leaves. Baccatins exist in high amounts and are converted to paclitaxel and active paclitaxel analogs such as docetaxel or Taxotere, which are a significant source and major category of the drugs, and are utilized to treat Kaposi sarcoma, lung cancer, ovarian and breast cancer [1-200]. Paclitaxel also has the potential to treat non-cancerous diseases, such as rheumatoid arthritis, psoriasis, and multiple sclerosis. Breast cancer is mainly treated using a semi-synthetic derivative of docetaxel. The effectiveness of the docetaxel anticancer agent was analyzed statistically by developing a clinical trial of more than one dozen taxanes analogues [1-200].

34) Camptothecin derivatives: 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]. This is considered as the unique character of the *Camptotheca acuminata* plant species. The active chemicals isolated from it were identified as camptothecin, declared in the 1970s by the NCI (National Cancer Institute) as a candidate for clinical trials. However, it displayed a flaw in bladder toxicity and was no longer in use [1-100]. SmithKline Beecham (now Glaxo SmithKline) develops Topotecan (Hycamtin) and effective camptothecin derivatives, and Japanese

company developed Irinotecan, Yakult Honsha, which are more effective than camptothecin. Irinotecan is utilized to treat colorectal cancers, whereas whereas lung and ovarian cancer are treated by topotecan [1-100]. A natural quinoline, camptothecin (CPT) has anticancer activity and inhibits Topoisomerases 1[1-250]. It is also used as a chemotherapeutic drug to treat tumors and metastatic colorectal cancer and is known as a bio-available derivative of irinotecan [1-200]. Topotecan is also a CPT derivative that treats ovarian cancer and small cell lung cancer [1-250].

35) *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. Constitutes a compound of acetogenins having anti-microbial, anti-neoplastic, pesticidal, parasiticidal, and parasiticidal effects. Squamostatin and squamocin extracted from *A. squamosa* seeds compounds of acetogenins showed a cytotoxic effect [80, 81, 142, 144, 157. 159, 160, 199, 202]. By the activation of caspase 3, squamocin prevents human leukemia cell line proliferation and leads to apoptosis. Another part of acetogenin called ascimicin can inhibit and is cytotoxic to 9KB, A549, HT-29, and 9ASK tumor cells [80, 81, 142, 144, 157. 159, 160, 199, 202]. To treat chronic diseases such as; skin complaints, insect bites, and cancerous tumors, all parts of A. squamosal were used in traditional medicine. The phytochemicals existing in the leaves are anti-ulcer, anti-diabetic, anti-fungal, anti-inflammatory, anti-depressant, and antimicrobial [80, 81, 142, 144, 157. 159, 160, 199, 202]. The chemical compounds constituted in *Annona squamosa* are phenolic compounds, terpenoids, alkaloids, flavonoids, glycoside, saponin, and steroids which are all-natural products. The alkaloids obtained from the aerial part showed anticancer activity in 0.01 to 100 /g/mL concentration ranges on liver, breast, and colon cancer cell lines [80, 81, 142, 144, 157. 159, 160, 199, 202]. Isoquinoline alkaloid extract possesses a high anticancer activity against colon cancer cells (HCT116) and human breast cancer cells (MCF-7) [1-250].

36) 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 secondary metabolite of *Arnebia euchroma* called shikonin, found mainly in the root, prevents a compound that malfunctions and deletes the process of action in the cell, rapidly causing carcinomas [1-180]. The phytochemicals existing in the *Arnebiaeu chroma* plant are utilized for treating carcinogenic diseases. The phytochemicals utilized for the treatment are acetyl-shikonin, teracryl-shikonin, and β-β, -dimethylacryl-shikonin. The roots of *Arnebia euchroma* also constitute a dimeric naphthoquinone compound called Shikometabolin H, epoxyarnebinol, and 2,3-secodiplopterol dioic acid helps to reduce the STAT3 transcriptions, the activators of human carcinogenic cells, and increase the antitumor immunity [1-170-250].

37) A plant species *Asclepias curassavica* constitutes a wide variety of biologically active compounds such as flavonol glycosides, carbohydrates, triterpenes flavonols, cardenolides, amino acids, etc. The chemical called cardenolides has the constituents calotropin, coroglaucigenin, calactinasclepin, asclepain CI, asclepiadin CII, curassavogenin, asclepogenin, calotropagenin, uzarin, uzarigenin, uscharidin, corotoxigenin, uscharidin, calotroposide, kidjolanin, clepogenin, and desglucouzarin, which are applicable for pharmacological purposes such as anticancer, antipyretic, analgesic, antimicrobial, cardiovascular, and many other pharmacological activities [1-100]. Calotropin (a cardiac glycoside), an alcoholic extract of *Asclepias curassavica* species, has a cytotoxic effect against nasopharynx carcinoma cells [1-270]. 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].

38) 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 [1-90-250]. Shatavarin I to X (shatavarins) are the major steroidal glucosides or saponins extracted from the root [1-90-250]. The non-polar and polar extracts from the total extracts and their formulation are capable of immune–pharmacological activity in cancer chemotherapy [1-90-250]. The 7,12-dimethylbenzanthracene (DMBA)-induced mammary carcinogenesis can be inhibited by the *Asparagus racemosus* plant species extract, as investigated in rats [1-90]. The compound shatavarin IV (84.69 %) with its fraction, codedAR-2B containing 5.05% shatavarin IV, is capable of cytotoxicity. Shatavarin IV from shatavarin's rich fraction has a tremendous anticancer effect in vivo and in vitro [1-100].

39) 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, 198-260]. The activity of stigmasterol tested on the growth of murine models of cancer, which becomes

transplantable by decreasing the viable cell count, a packed cell volume, tumor volume, inhibiting EAC (Ehrlich ascites carcinoma), was investigated in vivo and increases the life expectancy of the victim, protecting the liver of the EAC tumor-bearing mice [1-35,198]. The antitumor mechanism functioned by the initiation of PP2A by ceramide causing apoptosis, as is indicated by a structure analogous to phytosteroids. The main criteria to prove the value of the anticancer agent is increasing the age of the animals [1-50, 198-250].

40) 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 (CBD) possess anti-proliferative effects using MTT assay [175-177, 216-246, 249-261]. MTT assay determines IC_{50}, which represents the half maximal concentration that induces 50 % cell death [175-177, 216-246, 249- 261]. *Cannabis sativa* extracts were able to reduce cell viability and increase cell death in SiHa, HeLa, and ME-180 cells [175-177, 216-246, 249-261]. These results correlated with the earlier findings, whereby they reported reduced cell proliferation in colorectal cancer cell lines following treatment with *Cannabis sativa* [175-177, 216-246, 249-261]. Another study reported that *Cannabis sativa* extracts rich in cannabidiol (CBD) were able to induce cell death in prostate cancer cell lines LNCaP, DU145, and PC3 at low doses (20–70 μg/ml) [175-177, 216-246, 249-261]. It was suggested that cannabidiol (CBD) might be responsible for the reported activities. Therefore, cannabidiol (CBD) was included as a reference standard in order to determine whether the reported pharmacological activities displayed by *Cannabis sativa* extracts might have been due to the presence of this compound [175-177, 216-246, 249-261-263].

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]. The fact that cannabinoids play a role in cell fate decision, proliferation, and apoptosis might imply different effects under different conditions. 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]. On the other hand, their results imply that in the gastrointestinal system cannabinoid receptors are involved in inhibition of cell proliferation of colorectal carcinoma. In studies using cell lines, the anti-neoplastic effect of both natural and synthetic cannabinoids, cannabinoids agonist, and endocannabinoids have been shown for several cancer types including carcinomas (skin, lung, prostate, and uterine), neuroblastoma, gliomas, lymphomas, thyroid epithelioma, and breast cancer. Although the mode of action leading to these effect is not completely clear, cannabinoids receptors appear to mediate it [175-177, 216-246, 249-261-263].

41) 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]. It is a polyhydroxy phenolic compound and a natural antioxidant that can be obtained from a variety of natural products i.e., grapes, strawberries, bananas, green tea, and vegetables [263]. It also plays a critical role in preventing malignancy transformation and the development of cancer [263]. Similarly, other compounds such as Vinca alkaloids, podophyllotoxin, and camptothecin obtained from various plants are used for the treatment of cancer [1-263].

42) *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. Artesunate on 55 different cancer cell lines including leukemia, melanoma, lung cancer, colon cancer, renal cancer, ovarian cancer, and tumors of the central nervous system[1-263-264]. They suggested that artesunate was the most effective against leukemia and colon cancers. Furthermore, it was observed through these studies that the artesunate was more active than the drugs used for such cancers. The ethanolic extracts of leaves lead to growth inhibitions (57.24% and 67.07%) in HeLa and AGS cells, respectively at a concentration of 500 mg/mL[1-263-264].

43) *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. One of the study demonstrated significant activity against breast cancer cells line MCF-7 through an aqueous extract of *F. indica* [1-263-264].

44) *Garcinia oblongifolia* (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].

45) *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* showed 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].

46) *Hedyotis difusa* (*Rubiaceae*): Because of the recent advances in pharmacological practices, this herb has received importance for having antitumor properties and showed effective results in treating cancers of the liver, colon, lungs, brain, and pancreas [263-264]. *H. diffusa* contains important bioactive derivatives of polysaccharides, triterpenes, and anthraquinones. Methyl anthraquinonesare, one of the bioactive compounds in *H. diffusa*, is responsible for apoptosis of many cancers [263-264].

47) *Morus alba* commonly called as 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]. *M. alba* contains many pharmaceutically important compounds like kuwanol, hydroxymoricin, moranoline, morusin, calystegin, albafuran, and albanol. The leaves of *M. alba* contain some active compounds such as quercetin, rutin, apigenin, and 1-deoxynojirimycin [263-264].

48*) 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. *P. polyphylla* consists of important secondary metabolites such as polyphyllin D, formosanin C, β-ecdysterone, dioscin, daucosterol heptasaccharide, oligosaccharides, octasaccharide, protogracillin, trigofoenoside A, yunnanosides G-J, padelaoside B, pinnatasterone, and other saponins [263-264]. Steroidal saponins are the main active components because of its structural diversity and bio-activities such as antitumor, immune-stimulator, analgesic, and hemostatic properties. Aqueous and ethanol extracts of *P. polyphylla* showed potential antitumor activity against human liver carcinoma (HepG2 and SMMC-7721) cell line, human gastric (BGC-823) cell line, human colon adenocarcinoma (LoVo and SW-116) cell line, and human esophagus adenocarcinoma (CaEs-17) cell lines [263-264].

49) *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. The fruit part of *P. armeniaca* contains various important secondary metabolites like *β*-carotene, flavonoids, organic acids, thiamine, minerals, and oils. The seeds of *P. armeniaca* contains plenty of cyanogenic glycosides, used against different types of cancers [263-264].

50) *Scutellaria barbata*, the barbed skullcap is a key medicinal plant species of family *Lamiaceae*, used to treat inflammatory and cancer diseases [263-264]. It is rich in important secondary metabolites like alkaloids, flavones, steroids, and polysaccharides. *In vitro* studies showed positive activities against a vast range of cancers i.e., colon cancer, lung cancer, hepatoma, and skin cancer. The apigenin and luteolin isolated from *S. barbata* gave cytotoxic activity against both human breast cancer cell line MDA-MB-231 and non-transformed breast cell line (MCF10A) [263-264].

51) *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]. It possesses a high quantity of flavonoids and other phenolic compounds and some trace elements (Zn, Mg, and Se). The presence of these substances plays a key role in the anticancer activities of this plant [263-264].

52) *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 [263-264-280]. The essential oils of *W. chinensis* give a positive effect on lung cancer during the *in vitro* study. The GC-MS analysis recorded the presence of two important compounds carvacrol and trans-caryophyllene. High anti-scavenging activities were found at different levels of dose [263-266-280].

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 behavior 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 tumors rarely rely on one mutation alone [1-263-276]. It is the accumulation of such mutations that lead to the occurrence of cancer. The fact that cancer is caused by mutations has many implications for its treatment. However, mutations do not occur in a vacuum. Many factors can be involved in the mutation of genes, including[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 [1-263-276].

Our bodies constantly fight off cancer. If damaged DNA is detected, our DNA repair mechanism typically restores the cell's genetic material. If this mechanism fails and poorly differentiated cells are detected, our immune system typically destroys the damaged cells before they can multiply and spread [1-263-276]. However, increasing age has an impact on these processes. Some people also inherit genes that predispose them to developing cancer. Cancer is not inevitable, but it is much more likely to develop in people with so-called cancer genes than among the general population [1-263-276]. About 5-10% of cancers are thought to be hereditary. Hereditary cancer tends to occur at an earlier age than the sporadic form of the same cancer, so screening is recommended [1-263-276]. For example, mutations to tumor suppressor genes BRCA1 and BRCA2 predispose individuals who carry them to breast and ovarian cancers, in addition to a higher risk of other tumors as well [1-263-276]. Each type of cancer is unique – a disease within itself, with its own causes, symptoms, and methods of treatment. Leukaemias, lymphomas and myelomas are considered haematologic malignancies, while tumors affecting a specific organ are considered solid tumors. As with all groups of disease, some types of cancer are more common than others [1-263-276].

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]. Cancer is caused by the abnormal function of the genes and the manipulated pattern of gene expression, loss of the process of normal cell growth, development, and control; malfunctioning of apoptosis; initiation of angiogenesis, and metastasizing to other healthy tissue or organs [1-263-276]. Currently, one in six deaths are due to cancer worldwide and around 70% of deaths from cancer occur in low- and middle-income countries. This could be due to behavioral and dietary risks such as physical inactivity, smoking, use of alcohol and having an unhealthy diet low in fruit and vegetables. Additional factors contributing to the high incidence rate are an aging population, and exposure to certain chemicals, metals and infectious agents. Cancer is also due to the food and beverages adulterations with pesticide, insecticide chemicals and synthetic or artificial colorants in food. This makes cancer an important health problem which requires effective prevention and treatment measures [1-263-266].

Cancer is an extreme metabolic disorder that has seen significant advancement in treatment plans and preventative remedies. It is also called neoplastic disease, characterized by the uncontrolled proliferation followed by the constant multiplication of human cells. This leads to the development of tumors of harmful malignant cells with the capacity to be metastatic. Cancer is initiated by mutations of following genes; (a) oncogenes: RAS, Bcl-2, RAF, and MYC; (b) tumor suppressor genes: NF1, NF2, p53; and (c) DNA repair genes: p21, p22, p27, p51, p53, and tool box for DNA. These resultant genetic modifications can be triggered by an imbalance in hormones and in the immune system, and by exposure to external stimuli (e.g., radiation, pesticide, tobacco smoking, carcinogenic chemicals and metals, aflatoxin and several steroidal medications) [1-263-266]. A number of treatment approaches, such as chemotherapy, radiation therapy, thermal ablation, and resection have been developed as anticancer therapies. The success rate of these therapies is diminished by toxicities, drug resistance, recurrence and treatment failure [1-263-266]. Moreover, the cost of these therapies is out of reach for lower income populations. Thus, the current research has aimed to discovery of natural bio-molecules with potent anticancer activity as well as negligible side effects with a view to avail them from laboratory to bedside of patients at lower cost[1-263-266]. The spread of cancer from its cells or tissue of origin to another healthy part of tissues or organs is called metastasis [1-263-266]. According to the ancient Greeks, cancer was considered as constitutional melancholy and black bile. Various cancer research bodies give first attention to early diagnosis, prevention, and treatment of cancer [1-263-266].

Moreover, it is increasingly being realized that many of today's diseases are due to the "oxidative stress" that results from an imbalance between the formation and neutralization of poor oxidants [1-263-266]. Oxidative stress is initiated by free radicals, which seek stability through electron pairing with biological macromolecules such as proteins, lipids, and DNA in healthy human cells and cause protein and DNA damage along with lipid peroxidation [1-263-266]. These changes contribute to cancer, atherosclerosis, cardiovascular diseases, aging, and inflammatory diseases. All cells are exposed to oxidative stress, and thus, oxidation and free radicals may be important in carcinogenesis at multiple tumor sites [1-263-266].

The 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]. Besides the key role of COX in the initiation and progression of inflammation, over- expression of COX has been considered as one of the culprits in the formation of carcinogenic state in the body [1-263-266]. It is this molecular attribute of the COX up-regulation that has made it an attractive target for the design and development of anticancer agents [1-263-266]. Free radical induced oxidative stress and its relevance with inflammation and carcinogenesis is well established [1-263-266]. Therefore, inflammation, free radicals, and carcinogenesis are closely related with one another. The drug candidates having anti-inflammatory and free radical scavenging activities are more appreciated as anticancer agents [1-263-266].

10. Cancer Medications

There are many different types of cancer medications. These include alkylating agents, anti-metabolites, and plant alkaloids [279]. There can be side effects associated with cancer medications, including: anemia, hair loss, constipation, diarrhea, difficulty breathing, fatigue, nausea and vomiting [1-279]. The most common types of cancer medications include: alkylating agents, nitrosoureas, anti-metabolites, anti-tumor antibiotics, plant alkaloids, corticosteroids, and miscellaneous drugs that do not fall into any of these categories [279]. The alkylating agents were one of the earliest anticancer drugs and that they remain among the most common treatments today [1-279]. They work by damaging the DNA of cancer cells to prevent them from dividing. Some examples of alkylating agents include: altretamine, bendamustine, busulfan, carboplatin, chlorambucil, cisplatin, cyclophosphamide, dacarbazine, ifosfamide, mechlorethamine, melphalan, oxaliplatin, temozolomide, thiotepa and trabectedin [1-279]. Doctors primarily use alkylating agents to treat slow-growing cancers, as they are less effective against cells that divide quickly [279]. For example, doctors might use these medications to treat: breast cancer, Hodgkin disease, lung cancer, leukemia, lymphoma, multiple myeloma, ovarian cancer, and sarcoma [279]. The common side effects of alkylating agents may include: low blood pressure, fewer periods, blood disorders, seizures, hair loss and reduced sperm production. Alkylating agents damage DNA in cancer cells, but they may also affect bone marrow cells, which can cause leukemia. The risk of developing leukemia is small, but it increases with larger doses of alkylating agents. The risk of developing leukemia is highest around 5–10 years after treatment [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. However, getting through the blood-brain barrier is important for treating some cancers, including brain cancer. Nitrosoureas work by attaching themselves to DNA strands in cancer cells[279]. This prevents them from dividing. Some examples of nitrosoureas include: carmustine, lomustine and streptozoci [279].

Anti-metabolites: Antimetabolites work by convincing cancer cells to consume them and then preventing their division into new cells [279]. Some examples of antimetabolites include: azacitidine, 5-fluorouracil, 6-mercaptopurine, capecitabine, cladribine, clofarabine, floxuridine, fludarabine, gemcitabine, hydroxyurea, and methotrexate. Antimetabolites are usually effective for treating: breast cancer, leukemia, ovarian cancer, head and neck cancers, anal cancer, stomach cancer, colon cancer, and some skin cancers. Some side effects of anti-metabolites include: fatigue, fever, hair loss, kidney damage, liver failure, low white blood cell count, nausea, pancreatitis, loss of appetite, ulcers, and vomiting [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]. They bind with the DNA of fast-growing cancer cells to prevent them from reproducing. Some examples of anthracyclines include: daunorubicin, doxorubicin, doxorubicin liposomal, epirubicin, idarubicin, and valrubicin [279]. There are also several anti-tumor antibiotics that are not anthracyclines, including bleomycin, dactinomycin, and mitoxantrone [279]. Doctors might use antitumor antibiotics to treat: colorectal cancer, lung cancer, ovarian cancer, prostate cancer, One major side effect of anti-tumor antibiotics is an increased risk of heart damage. This side effect is rare, but it can occur with high doses of the drug [279]. For this reason, doctors typically limit how much of an anti-tumor antibiotic that someone can take [279].

Plant alkaloids: These are drugs that come from plants and have anti-tumor properties. They have different names depending on the enzyme that they act on. Mitotic inhibitors, for example, are a class of plant alkaloids that prevent cancer cells from replicating or stop enzymes from creating proteins to support reproduction in cancer cells. Some examples of these drugs include taxanes and vinca alkaloids [1- 279]. Topoisomerase inhibitors are a class of plant alkaloids that also have different names depending on which enzyme they work on [1-279]. Topoisomerase I inhibitors, for instance, interrupt DNA replication in cancer cells. One example is irinotecan. There are also topoisomerase II inhibitors, one example of which is etoposide [1- 279]. Plant alkaloids are useful for treating several cancers, including:

leukemia, lung cancer, ovarian cancer, gastrointestinal cancer, colorectal cancer, pancreatic cancer, Some possible side effects include: nausea, vomiting, abdominal pain, diarrhea, fatigue, allergic reactions, and hair loss [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]. Some possible side effects of corticosteroids include: an increased risk of infections, mood changes, difficulty sleeping, heartburn, blood sugar fluctuations, weight gain, headaches, and high blood pressure. Some examples of other medications used for cancer treatment include: all-trans-retinoic acid, arsenic trioxide, asparaginase, eribulin, hydroxyurea, ixabepilone, mitotane, omacetaxine, pegaspargase, procarbazine, romidepsin, and vorinostat. Cancer medications include a wide variety of drugs that use different mechanisms to fight the condition[279]. There are benefits and drawbacks to each type of medication, and doctors can advise on the best option for each individual case [279]. Treatment might involve cancer medications on their own or cancer medications alongside other treatment options. The duration and intensity of the treatment will depend on the severity of the cancer and the person's overall health [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]. Kinease inhibition assays are also one of the most widespread enzyme inhibition screening assays performed [247]. Kineases are enzymes that play an important role in physiological processes and their inhibitors have been found to exhibit anticancer activity against various human cancer cell lines [1-247-276].

11.1. MTT Assay

The MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay [247, 278], is a widely used colorimetric assay for evaluating the cytotoxic activity or cell viability in biological and pharmaceutical research [247, 278]. This assay measures the metabolic activity of cells, which is an indirect indicator of their viability. This assay was carried out to perform the comparative evaluation of curcumin, quercetin with its combination in the effect of MCF-7 cell line of breast cancer [247, 278]. This is a colorimetric assay that measures the reduction of yellow 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide by mitochondrial succinate dehydrogenase. The MTT gets reduced to an insoluble dark purple colored formazan product [247, 278]. The cells are then solubilized with an organic solvent such as DMSO and the absorbance is measured spectrometrically [247, 278]. Since the reduction of MTT can only occur in metabolically active cells, and the level of activity is a measure of the viability of the cells [278]. The MTT assay also measures the cell viability based on the generation of reducing equivalents in metabolic active cells. The higher the absorbance measured the higher is the cell viability [247, 278]. The [3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide] MTT colorimetric assay is the mostly used assay for anticancer activity [247, 278]. In this assay, the extracts were made to be dissolved in DMSO (Dimethylsulfoxide) along with diluted cell culture media. Initially, the cells taken from the cell lines were counted [247, 278]. The cells were diluted and seeded in 96 well microtiter plates. This was kept for incubation. The absorption was measured and the cell viability was calculated [1-247-276, 278].

11.2. "Alamar Blue" Resazurin Reduction Assay

In Resazurin reduction assay, the cells of cell lines were suspended in DMEM. This was seeded in 96-well plate at dilution. The plant extracts were made to be serially diluted along with the medium and supplied to the cells. This was kept for incubation. Following incubation, fresh media along with Resazurin was added and again incubated. The fluorescent intensity of dye was measured as a result of the cytotoxic activity of the cells [1-247-276].

11.3. SRB Assay

RPMI 1640 medium containing fetal bovine serum was selected, and the diluted cells were inoculated to 96 well plates. This was kept for incubation. The extract was then added and again incubated. The assay was then completed by the addition of TCA to the cells. Then the cells were finally added to the SRB solution. The absorbance was read [1-247-276].

11.4. WST-1 Colorimetric Assay

WST-1 (4- [3- (4-iodophenyl)-2 -(4-nitrophenyl) -2H-5-tetrazolio]-1, 3-benzene di-sulfonate) colorimetric assay was performed by incubating the inoculated cells to the 96 well plates along with the media. After incubation, appropriate concentrations of the extracts were made to be added. This was again incubated. The cells and the extract were solubilized in DMSO, and an appropriate quantity of WST-1 was added. The absorbance was calculated [1-247-276].

12. Conclusion

Cancer is a global burden. In low- and middle-income countries around 70% of deaths are due to cancer. For a number of years natural products have been a good source of agents for combating cancer and plants have played an important role in anti-cancer product development. 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. Treatment strategies of cancer rely on the cancer's type, stage and place. Chemotherapeutic operators include cytostatic and cytotoxic drugs that appear to be life-saving strategies alone or in combination with other cancer treatments. These chemotherapeutic agents contain topo-isomerase inhibitors, e.g., irinotecan (side effects include: neutropenia, sensory neuropathy, and diarrhoea); cyclophosphamide (undesired effects include: gastrointestinal toxicity, cardiovascular toxicity, pulmonary, nephrotoxicity and hematologictoxicity, and doxorubicin (side effects include cardiotoxicity); microtubules acting agent, e.g., vincristine, vinblastine, paclitaxel and docetaxel; and alkylating agents, e.g., oxaliplatin, carboplatin, melphalan, and cisplatin. These drugs are extraordinarily powerful in treating an extensive variety of cancers. However, these pills also have some disadvantages (side effects, cost, exceptional complexity, environmentally unfriendly, and harmful). Some cells in our frame multiply swiftly under ordinary physiological situations such as hair follicle cells, digestive tract cells and bone marrow cells, and to name a few. This shows that anticancer pills additionally affect dividing ordinary cells. This is a massive undertaking and cause dangerous side effects. These side effects may include diminished blood generation, immunosuppressant, hair falls, coronary heart diseases, GIT aggravation and apprehensive clutters. Another obstacle is that the most cancers cells resist remedies as they mutate; e.g., genes resistant to drug (abca4 and abca12) were over-expressed in most human mcf-7 breast cancer cells when docetaxel was administered. In any case, while phytochemical curcumin was applied in affiliation with docetaxel, over-expression of drug resistant genes were changed. Moreover, drug resistance to existing cancer treatments, which leads to the rapid buildup of CSCs, disease recurrence in treated tumors, and extensive metastasis in the late stages of cancer, necessitates fresh research into effective strategies to alleviate these burdens.

To totally eliminate drug-resistant cancer cells and CSCs, novel combination treatments targeting multiple elements of the tumor microenvironment are needed. According to a new study on Zebra fish embryos, silver nanoparticle toxicity is linked to accessible silver ions. Modern research demonstrated undetectable toxicity in healthy volunteers after the oral ingestion of commercially available silver nanoparticles. The biodegradability of silver nanoparticles (SNPs) is another important consideration. The renal clearance of glutathione-coated luminous gold nanoparticles was also recorded. According to a recent study, biogenic silver nanoparticles (SNPs) are generally less cyto-/genotoxic in vivo than chemically generated silver nanoparticles (SNPs).

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. Thus, it is very important that these plants/poly herbal formulae are evaluated in preclinical and clinical studies. Further, utilization of modern biotechnological approaches such as nanotechnology-based drug delivery systems will support the progression of medicinal plant research to its full potential and help to minimize side effects of the drugs developed from these plants. Medicinal plants could also possess effective anticancer compounds that may be used as adjuvants 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. The human clinical trials are warranted to verify the clinical utility of these medicinal plants in such treatment, since there could be positive as well as negative outcomes via pharmacodynamic and pharmacokinetic herb-drug interactions. Furthermore, research has suggested an inverse correlation between human cancers and various dietary constituents. The daily diet should be made up of nutrient rich plant foods, which includes vegetables, fresh fruits, beans, seeds, and whole grains. These foods or nutraceuticals construct a health-promoting, disease-preventing diet with protective substances.

Plants are used to produce medicine since various synthetic drugs showed side effects on the patient, and plant sources are easily accessible and cost-effective. Several active components of medicinal plant have been successfully isolated,

screened, and found to be effective in inhibiting or preventing various diseases and cancer. Since medicinal plant phytochemicals are utilized for the treatment of cancer, it is essential to further screen and investigate new plants for their phytochemicals, which are very strong and effective in the treatment of cancer. Medicinal plants are the only natural resource for developing effective, safe, and quality anticancer drugs, although some herbal remedies may cause serious health problems and may have side effects if used without the consultation of a professional or medical practitioner. Sometimes, the use of these medicinal plants may interact with regular or other drugs and lead to side effects, for instance, allergies. These medicinal plants are highlighted for their potential for anticancer activity. 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

Acknowledgments

We would like to thank and acknowledge, Karen Viviana Castaño Coronado MBA**,** Chief Communication Officer (CCO) and CO-Founder of LAIHA (Latin American Industrial Hemp Association), and CEO- CANNACONS, Bogota, D.C., Capital District, Colombia for thoughtful discussions, critical comments, supporting, promoting, encouraging and appreciating this research work. We also thank all the members of LAIHA for supporting and encouraging this research work.

Disclosure of conflict of interest: Nill

No conflict of interest to be disclosed.

References

[1] Pandey DK, Kaur P, Vijay Kumar, Banik RM, Malik T, Dey A. Screening the elite chemotypes of *Gloriosa superba* L. in India for the production of anticancer colchicine: Simultaneous microwave-assisted extraction and HPTLC studies. BMC Plant Biology. 2021; 21:77 https://doi.org/10.1186/s12870-021-02843-8.

[2] Soumya T, Lakshmipriya T, Klika KD, Jayasree PR, Manish Kumar PR. Anticancer potential of rhizome extract and a labdane diterpenoid from *Curcuma mutabilis* plant endemic to Western Ghats of India. Scientific Reports. 2021;11:552 | https://doi.org/10.1038/s41598-020-79414-8.

[3] Greenwell M, Rahman KSM. Medicinal Plants: Their Use in Anticancer Treatment. Int J Pharm Sci Res. 2015; 6(10): 4103–4112. doi:10.13040/IJPSR.0975-8232.6(10).4103-12.

[4] Steigerová J, Rárová L, Oklešťková J, Křížová K, Levková M, Šváchová M, Kolář Z, Strnad M. Mechanisms of natural brassinosteroid-induced apoptosis of prostate cancer cells. Food and Chemical Toxicology. 2012; 50:4068–4076.

[5] Malíková J, Swaczynová J, Kolář Z, Strnad M. Anticancer and antiproliferative activity of natural brassinosteroids. Phtyochemistry. 2008; 69:418–426.

[6] Unnati S, Ripal S, Sanjeev A, Niyati A. Novel anticancer agents from plant sources. Chinese Journal of Natural Medicines. 2013; 11(1):0016–0023.

[7] Amin A, Gali-Muhtasib H, Ocker M, Schneider-Stock R. Overview of Major Classes of Plant-Derived Anticancer Drugs. International Journal of Biomedical Science. 2009; 5(1):1–11.

[8] Cragg GM, Newman DJ. Plants as a source of anti-cancer agents. Journal of Enthnopharmacology. 2005; 100:72–79.

[9] Pezzuto JM. Plant-Derived Anticancer Agents. Biochemical Pharmacology. 1997; 53:121–133.

[10] Jyoti K, Kaur K, Pandey RS, Jain UK, Chandra R, Madan J. Inhalable nanostructured lipid particles of 9-bromo-noscapine, a tubulin-binding cytotoxic agent: *In vitro* and *in vivo* studies. Journal of Colloid and Interface Science. 2015; 445:219–230.

[11] Schnekenburger M, Dicato M, Diederich M. Plant-derived epigenetic modulators for cancer treatment and prevention. Biotechnology Advances. 2014; 32:1123–1132.

[12] Azmi AS, Bhat SH, Hanif S, Hadi SM. Plant polyphenols mobilize endogenous copper in human peripheral lymphocytes leading to oxidative DNA breakage: A putative mechanism for anticancer Properties. FEBS Letters. 2006; 580:533–538.

[13] Jordan MA, Wilson L. Microtubules as a target for anticancer drugs. Nature Reviews: Cancer. 2004; 4:253–266.

[14] Ahmad F, Ali M, Alam P. New phytoconstituents from the stem bark of *Tinospora cordifolia* Miers. Nat. Prod. Res. 2010; 24: 926– 934.

[15] Kumar S, Pathania AS, Saxena AK, Vishwakarma RA, Ali A, Bhunshan S. The anticancer potential of flavonoids isolated from the stem bark of *Erythrina suberosa* through induction of apoptosis and inhibition of STAT signalling pathway in human leukaemia HL-60 cells. Chemico-Biological Interactions. 2013; 205:128–137.

[16] Sivaraj R, Rahman PKSM, Rajiv P, Vanathi P, Venckatesh R. Biosynthesis and characterization of *Acalypha indica* mediated copper oxide nanoparticles and evaluation of its antimicrobial and anticancer activity. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2014; 129:255–258.

[17] Danciu et al., Evaluation of phenolic profile, antioxidant and anticancer potential of two main representants of *Zingiberacea*e family against B164A5 murine melanoma cells. Biological Research. 2015; 48: 1. doi:10.1186/0717-6287.

[18] Mishra ML, Shukla UN. RAMPHAL: AN ETHNO-MEDICINAL PLANT. Marumegh. 2018; 3(1): 20-24.

[19] Can Soursop (Graviola) Help Fight Cancer? (verywellhealth.com). 2023.

[20] **Sharma** AN, Dewangan HK, Upadhyay PK. Comprehensive Review on Herbal Medicine: Emphasis on Current Therapy and Role of Phytoconstituents for Cancer Treatment. Chem Biodivers. **2024.** e202301468. doi: 10.1002/cbdv.202301468.

[21] Subhash Chandra, Manoj Gahlot et al. Scientific evidences of anticancer potential of medicinal plants. Food Chemistry Advances. 2023; 2: 100239.

[22] Bisht VK, Negi JS, Bhandari AK, Sundriyal RC. (2011). Anti-cancer plants of Uttarakhand Himalaya: A Review. International journal of cancer research. *2011; 7* (3): 192– 208. 10.3923/ijcr2011.192.208.

[23] Revathi S, Lukmanul HF. Anti-microbial and anticancer activity of *Aegle marmelos* and gas chromatography coupled spectrometry analysis of their chemical constituents. International Journal of Pharma. Sciences and Research. 2019; 10 (1), 373–380.

[24] Verma, Shiv Prakash, Tripathi, Vikash Chandra, Das, Parimal. *Asparagus Race-mosus* Leaf Extract Inhibits Growth of UOK 146 Renal Cell Carcinoma Cell Line: Simultaneous Oncogenic PRCCTFE3 Fusion Transcript Inhibition and Apoptosis In-dependent Cell Death. Asian Pacific Journal of Cancer Prevention. 2014; 15 (5), 1937–1941. 10.7314/apjcp.2014.15.5.1937.

[25] **Pooja T**. Plants with Anticancer properties: A Review on traditional plants and herbs are used to evaluation for their anticancer potential. Journal of Pharmacy Re-search. 2017; 11 (s): 547–553.

[26] **Ankit S,** Robbie H, Sudeep C. Traditional herbal knowledge among the inhabitants: A case study in Urgam Valley of Chamoli Garhwal, Uttarakhand, India. Evidence-Based Complementary and Alternative Medicine. 2019; 1–21. 10.1155/2019/5656925.

[27] Karpagam T, Jannathul F, Revathy, Shanmuga P. Anti-Cancer Activity of *Aloe Vera* Ethanolic Leaves Extract against In vitro Cancer Cells. Research Journal of Pharmacy and Technology. 2019; 1*2* (5): 2167–2170.

[28] Avni G, Desai, GN, Qazi, Bhat HK. Medicinal plants and cancer chemoprevention. Current Drug Metabolism. 2008; 9 (7): 581–591 .

[29] Rajeshkumar S, Nagalingam M, Ponnanikajamideen M, Vanaja M. Anticancer activity of *Andrographis paniculata* leaves extract against neuroblastima (IMR-32) and human colon (HT-29) cancer cell line. World journal of Pharmacy and Pharmaceutical sciences. 2015; 4 (6): 1667–1675.

[30] Manoj K, Sushil C, Maharishi T, Prajapati U. Custard Apple (*Annona squamosa* L.) Leaves: Nutritional Composition, Phytochemical Pro-file, and Health-Promoting Biological Activities. Biomolecules. 2021; 11 (614): 1–22. 10.3390/biom11050614.

[31] Amudha P, Vanitha V. Phytochemical and Pharmacological Potential of Annona species: A review. Asian J Pharm Clinical Research. 2017; 10 (7): 68–75.

[32] Sun B, Lovell JF, Zhang Y. Current development of cabazitaxel drug delivery systems. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology. 2022: e1854.

[33] Shonia S, Kanga Rani S, Ammu KR. Bioactive Compounds: Natural Defense Against Cancer? Biomolecules. 2019; 9 : 758. 10.3390/biom9120758.

[34] Sultana N. Clinically useful anticancer, antitumor, and antiwrinkle agent, ursolic acid and related derivatives as medicinally important natural product. Journal of Enzyme Inhibition and Medicinal Chemistry. 2011; 26 :616–642.

[35] Tripti M, Rakesh A, Sanjeev M. Isolation, characterization and anticancer potential of Cytotoxic Triterpenes from *Betula utilis* Bark. PLoS ONE. 2016*;* 1–14. 10.1371.

[36] Parimalakrishnan S, Akalanka D, Anton S. Studies of anticancer and antipyretic activity of *Bidens pilosa* whole plant. African Health Sciences. 2006; 6 (1): 27–30.

[37] Sudhanshu M, Ram S, Bishnoi Rahul M, Deepti J. *Boswellia serrata R* oxb – A bioactive herb with various pharmacological activities. Asian Journal of Pharmaceutical and Clinical Research. 2020; 13 (11): 33–39.

[38] **Mazumder** K, Aktar A, Roy P, Biswas B, Hossain ME, Sarkar KK, Bachar SC, Ahmed F, Monjur-Al-Hossain ASM, Fukase K. A Review on Mechanistic Insight of Plant Derived Anticancer Bioactive Phytocompounds and Their Structure Activity Relationship. Molecules. 2022; 27: 3036. https://doi.org/10.3390/ molecules27093036.

[39] Wang Y, Zhong J, Bai J, Tong R, An F, Jiao P, et al. The application of natural products in cancer therapy by targeting apoptosis pathways. Current Drug Metabolism. 2018; 19 (9): 739–749.

[40] Kumar J, Sandal P, Singh A, Kumar A, Arya V, Devi R, et al., Conservation Status, Anticancer Compounds and Pharmacological Aspects of Royle: A Review Podophyllum hexandrum. Indian Journal of Ecology*.* 2022; 49 (3):1096–1102 .

[41] Patel PR, Akhil A, Nagar R, Patel C. In vitro anticancer activity of *Rubia cordifolia* against hela and HEP-2 cell lines. International journal of pharmacy and pharmaceutical sciences. 2011; 3 (2): 70–71.

[42] Rajeshkumar NV, Joy KL, Girija K. Antitumour and anticarcinogenic activity of *Phyllanthus amarus* extract. Journal of Ethnopharmacology. 2002; 81 (1):17–22.

[43] Hema MM, Jayachitra A. Anti cancer activity of ethanolic extract of *Plumbago zeylanica* against Dalton's Ascitic Lymphoma in mice. International Jour-nal of Applied Engineering Research. 2019; 14 (7): 1715–1721.

[44] Sharrif MM, Hamed HK. Chemical composition of the plant *Punica granatum* L. (Pomegranate) and its effect on heart and cancer. Journal of Medicinal Plants Research. 2012; 6 (40): 5306–5310.

[45] Ochwang'I DO, Kimwele CN, Oduma JA, Gathumbi PK, Mbaria JM, Kiama SG. Medicinal plants used in treatment and management of cancer in Kakamega County, Kenya. J. Ethnopharmacol. 2014; 151: 1040–1055.

[46] Khazir J, Mir BA, Pilcher L, Riley DL. Role of plants in anticancer drug discovery. Phytochem. Lett. 2014; 7: 173–181.

[47] Lichota A, Gwozdzinski K. Anticancer Activity of Natural Compounds from Plant and Marine Environment. Int. J. Mol. Sci. 2018; 19: 3533.

[48] Silvestri R. New Prospects for Vinblastine Analogues as Anticancer Agents. J. Med. Chem. 2013; 56: 625–627.

[49] Loef M, Walach H. Quality of life in cancer patients treated with mistletoe: A systematic review and meta-analysis. BMC Complement. Med. Ther. 2020; 20: 227.

[50] Kienle GS, Glockmann A, Schink M, Kiene H. *Viscum album* L. extracts in breast and gynaecological cancers: A systematic review of clinical and preclinical research. J. Exp. Clin. Cancer Res. 2009; 28: 79.

[51] Chaturvedi D, Goswami A, Saikia PP, Barua NC, Rao PG. Artemisinin and its derivatives: A novel class of anti-malarial and anti-cancer agents. Chem. Soc. Rev. 2009; 39: 435–454.

[52] Ghosh S, Dutta S, Sarkar A, Kundu M, Sil PC. Targeted delivery of curcumin in breast cancer cells via hyaluronic acid modified mesoporous silica nanoparticle to enhance anticancer efficiency. Colloids Surf. B Biointerfaces. 2021; 197: 111404.

[53] Patel JR, Tripathi P, Sharma V, Chauhan NS, Dixit VK. *Phyllanthus amarus*: ethnomedicinal uses, phytochemistry and pharmacology: A review. J Ethnopharmacol. 2011;138(2):286-313. doi: 10.1016/j.jep.2011.09.040.

[54] Malabadi RB, Lokare Naik S, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S. Synthesis of silver nanoparticles from in vitro derived plants and callus cultures of *Clitoria ternatea*; Evaluation of antimicrobial activity. Research in Biotechnology. 2012; 3(5): 26-38.

[55] Malabadi RB, Chalannavar RK, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S. Synthesis of antimicrobial silver nanoparticles by callus cultures and in vitro derived plants of *Catharanthus roseus*. Research in Pharmacy. 2012; 2(6):18- 31.

[56] Malabadi RB, Meti NT, Mulgund GS, Nataraja K, Vijayakumar S. Synthesis of silver anoparticles from in vitro derived plants and callus cultures of *Costus speciosus* (Koen.): Assessment of antibacterial activity. Research in Plant Biology. 2012; 2(4): 32-42.

[57] Bhatia D, Thoppil RJ, Mandal A, et al. Pomegranate bioactive constituents suppress cell proliferation and induce apoptosis in an experimental model of hepatocellular carcinoma role of Wnt/β-catenin signaling pathway. Evid Based Complement Alternat Med. 2013;2013:371813.

[58] Bishayee A, Bhatia D, Thoppil RJ, et al. Pomegranate-mediated chemoprevention of experimental hepatocarcinogenesis involves Nrf2-regulated antioxidant mechanisms. Carcinogenesis. 2011;32:888-9.

[59] Shahindokht Bassiri-Jahromi. *Punica granatum* (Pomegranate) activity in health promotion and cancer prevention. Oncology Reviews. 2018; 12:345: 1-7.

[60] Ravinder S, Chahal K, Nancy S. Chemical composition and Pharmacological activities of *Saussurea lappa* : A review. Journal of Pharmacognosy and Phytochemistry. 2017;6 (4): 1298–1308.

[61] Karna P, Chagani S, Gundala SR., et al., "Benefits of whole ginger extract in prostate cancer." British Journal of Nutrition. 2012; 107: 4: 473–484.

[62] Cassileth BR, and G. Deng G. "Complementary and alternative therapies for cancer," Oncologist. 2004; 9: 1: 80–89.

[63] Coseri S. "Natural products and their analogues as efficient anticancer drugs," Mini-Reviews in Medicinal Chemistry. 2009; 9:5: 560–571, 2009.

[64] Bora KS, Sharma A. "The genus Artemisia: A comprehensive review." Pharmaceutical Biology. 2011; 49: 1:101–109.

[65] Solowey E, Lichtenstein M. et al., Evaluating Medicinal Plants for Anticancer Activity. Thee Scientific World Journal. 2014; Volume 2014, Article ID 721402, 12 pages. Hindawi Publishing Corporation.

[66] Kathiresan K, Boopathy NS, Kavitha S. Coastal vegetation-an underexplored source of anticancer drugs. Nat Prod Radiol. 2006;5:115-9.

[67] Rao KV, Schwartz SA, Nair HK, Aalinkeel R, Mahajan S, Chawda R, *et al*. Plant derived products as a source of cellular growth inhibitory phytochemicals on PC-3M, DU-145 and LNCaP prostate cancer cell lines. Curr Sci. 2004;87:1585-8.

[68] Kelloff GJ. Perspectives on cancer chemoprevention research and drug development. Adv Cancer Res. 2008;78:199-334.

[69] Shaikh R, Pund M, Dawane A, Iliyas S. Evaluation of Anticancer, Antioxidant, and Possible Anti‐inflammatory Properties of Selected Medicinal Plants Used in Indian Traditional Medication. Journal of Traditional and Complementary Medicine. 2014; 4: 4: 253-257.

[70] Rahman AHMM: A review of medicinal plants with anticancer activity in Bangladesh. Modern Applications in Pharmacy & Pharmacology. 2018; 1(4): 000516.

[71] Chavan SS, Damale MG, Shamkumar PB, Pawar DP. Traditional medicinal plants for anticancer activity. International Journal of Current Pharmaceutical Research. 2013; 5(4): 50-54.

[72] Manivel G, Kandasamy CS, Hariprasad R, Baskar K, Jegadeesh S, Venkatanarayanan R. Review on anticancer activity of medicinal plants. International Journal of Advance and Ideas and Innovations in Technology. 2017; 3(3): 1024-28.

[73] Singh N, Mathur C, Sase NA, Rai S, Abraham J: Pharmaceutical properties of *Emblica officinalis* and *Phyllanthus Emblica* extracts. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2015; 6(1): 1007-16.

[74] Merina N, Chandra KJ and Jibon K: Medicinal plants with potential anticancer activity: A review. International Research Journal of Pharmacy. 2012; 3(6): 26-30.

[75] Garg A, Darokar MP, Sundaresan V, Faridi U, Luqman S, Rajkumar S. Anticancer activity of some medicinal plants from high altitude evergreen elements of Indian Western Ghats. The Journal of Research and Education in Indian Medicine. 2007; 13: 1-6.

[76] Umadevi M, Sampath Kumar KP, Debjit B and Duraivel S. Traditionally used anticancer herbs in India. Journal of Medicinal Plants Studies. 2013; 1(3): 56-74.

[77] Muniyandi K, George E, Mudidli V, Kalagatur NK, Anthuvan AJ, Krishna K. Antioxidant and anticancer activities of *P. stocksii* Hook. f. leaf and stem extracts. Agriculture and Natural Resources. 2017; 51: 63-73.

[78] Alzeer J, Vummidi BR, Arafeh R, Rimawi W, Saleem H, Luedtke NW. The influence of extraction solvents on the anticancer activities of Palestinian medicinal plants. Journal of Medicinal Plant Research. 2014; 8(8): 408-15.

[79] Gavhane DS, Moreganokar SD, Mhase AK. Cytotoxic and anticancer activity of *F. racemosa* fruit extracton MCF7 human breast cancer cell line by SRB method. Journal of Animal Research. 2016; 6(1): 43-7.

[80] Lowe HIC, Toyang NJ, Watson C, Badal S, Bahado-Singh P, Bryant J. *In-vitro* anticancer activity of the crude extract and two dicinnamate isolates from the Jamaican Ball Moss (*Tillandsia recurvata* L.) .2013; 3(1): 93-6.

[81] Shalabi M, Khilo K, Zakira MM, Elsebaei MG, Abdo W, Awadin W. Anticancer activity of *Aloe vera* and *Calligonum comosum* extracts separately on hepatocellular carcinoma cells. Asian Pacific Journal of Tropical Biomedicine. 2015; 5(5): 375-81.

[82] Gavamukulya Y, Abou-Elella F, Wamunyokoli F, AEI-Shemy H. Phytochemical screening, anti-oxidant activity and *in-vitro* anticancer potential of ethanolic and water leaves extracts of *Annona muricata*. Asian Pacific Journal of Tropical Medicine. 2014; 7(1): S355-S363.

[83] Sumithra P, Gricilda Shoba F, Vimala G, Sathya J, Sankar V, Saraswathi R. Anti-cancer activity of *Annona squamosa* and *Manilkara zapota* flower extract against MCF-7 cell line. 2014; 5(6): 98-104.

[84] Abu-rish EY, Kasabri VN, Hudaib MM, Mashalla SH, Al-Alawi LH, Tawaha KA. Evaluation of antiproliferative activity of some traditional anticancer herbal remedies from Jordan. Tropical Journal of Pharmaceutical Research. 2016; 15(3): 469-74.

[85] Daoudi A, Amal EL, Youbi HEL, Bagrel D, Aarab L. *In-vitro* anticancer activity of some plants used in Moroccan traditional medicine. Journal of Medicinal Plants Research 2013; 7(17): 1182-89.

[86] Akindele AJ, Wani Z, Mahajan G, Sharma S, Aigbe FR and Sati N: Anticancer activity of *Aristolochia ringens* Vahl. (Aristolochiaceae). Journal of Traditional and Complementary Medicine. 2015; 5(1): 35-41.

[87] Jarial R, Thakur S, Sakinah M, Zularisam AW, Sharad A, Kanwar SS. Potent anticancer, antioxidant and antibacterial activities of isolated flavonoids from *Asplenium nidus*. Journal of King Saud University- Science. 2018; 30: 185-92.

[88] Nair MS, Soren K, Singh V, Boro B. Anticancer activity of fruit and leaf extracts of *Averrhoa bilimbi* on MCF-7 Human breast cancer cell lines: A preliminary study. Austin Journal of Pharmacology and Therapeutics. 2016; 4(2): 1082.

[89] Saha S, Ghosh S. Tinospora cordifolia: One plant, many roles. Ancient Science of Life. 2012;31(4):151–157.

[90] Manglani N, Vaishnava S, Dhamodaran P, Sawarkar H. *In-vitro* and *in-vivo* anti-cancer activity of leaf extract of *B. grandiflora*. International Journal of Pharmaceutical Sciences. 2014; 6(3): 70-2.

[91] Gaidhani SN, Singh A, Kumari S, Lavekar GS, Juekar AS, Sen S. Evaluation of some plant extracts for standardization and anticancer activity. Indian Journal of Traditional Knowledge. 2013; 12(4): 682-87.

[92] Serasanambati M, Chilakapati SR, Manikonda PK, Kanala JR. Anticancer activity of methanolic extract of *Berberis aristata* in MCF-7 human breast cancer cell lines. International Journal of Life Sciences Biotechnology and Pharma Research. 2015; 4(1): 31-5.

[93] Bukke AN, Hadi FN, Babu KS, Shankar PC. *In-vitro* studies data on the anticancer activity of *Caesalpinia sappan* L. heartwood and leaf extracts on MCF7 and A549 cell lines. Data in Brief. 2018; 19: 868-77.

[94] Artun FT, Karagoz A, Ozcan G, Melikoglu G, Anil S, Kultur S. *In-vitro* anticancer and cytotoxic activities of some plant extracts on HeLa and Vero cell lines. Journal of the Balkan Union of Oncology. 2016; 21(3): 720-5.

[95] Thakkar KN, Prasad AK, Nayak J, Iyer SV, Kumar S. Antioxidant and *in-vitro* cytotoxic activity of extracts of aerial parts of *Cocculus hirsutus* (L) using cell line cultures (breast cell line). The J of Phytopharmacology. 2014; 3(6): 395-9.

[96] Rahman MA, Sahabjada, Akhtar J. Evaluation of anticancer activity of *Cordia dichotoma* leaves against a human prostate carcinoma cell line, PC3. Journal of Traditional and Complementary Medicine. 2017; 7(3): 315-21.

[97] Rosangkima G, Jagetia GC. *In-vitro* anticancer screening of medicinal plants of Mizoram state, India, against Dalton's lymphoma, MCF-7 and HeLa cells. International Journal of Recent Scientific Research. 2015; 6(8): 5648-53.

[98] Srivatsava P, Srivatsava A. *In-vitro* anti-cancer activity of ethanolic extract of *Cucurmin longa* (turmeric) in Hep-2 cell lines. International Journal of Engineering Research and General Science. 2015; 3(5): 495-08.

[99] Munro B, Vuong Q, Chalmers AC, Goldsmith CD, Bowyer MC, Scarlett CJ. Phytochemical, antioxidant and anti-cancer properties of *Euphorbia tirucalli* methanolic and aqueous extracts. Antioxidants. 2015; 4: 647-61.

[100] Yen GC, Chen CS, Chang WT, Wu MF, Cheng FT, Shiau DK. Antioxidant activity and anticancer effect of ethanolic and aqueous extracts of the roots of *Ficus beecheyana* and their phenolic components. Journal of Food and Drug Analysis. 2018; 26(1): 182-92.

[101] Alam P, Al-Yousef HM, Sidiqui NA, Alhowiriny TA, Alqasoumi SI, Aminal M.Anticancer activity and concurrent analysis of ursolic acid, β- sitosterol and lupeol in three different *Hibiscus species* (aerial parts) by validated HPTLC method. Saudi Pharmaceutical Journal. 2018; 26(7): 1060-67.

[102] Shaikh R, Pund M, Dawane A, Iliyas S. Evaluation of anticancer, antioxidant, and possible anti-inflammatory properties of selected medicinal plants used in Indian traditional medication. Journal of Traditional and Complementary Medicine. 2014; 4(4): 253-7.

[103] Talib WH, Mahasneh AM. Antiproliferative activity of plant extracts used against cancer in traditional medicine. Scientia Pharmaceutica. 2010; 78: 33-45.

[104] Ghagane SC, Puranik SI, Kumbar VM, Nerli RB, Jalalpure SS, Hiremath MB. *In-vitro* antioxidant and anticancer activity of *Leea indica* leaf extracts on human prostate cancer cell lines. Integrative Medicine Research. 2017; 6(1): 79-87.

[105] Medini F, Bourgou S, Lalancette KG, Snoussi M, Mkadmini K, Cote I. phytochemical analysis, anti-oxidant, anti-inflammatory and anticancer activities of the halophyte *Limonium densiflorum* extracts on human cell lines and murine macrophages. South African Journal of Botany. 2015; 99: 158-64.

[106] Qadir MI, Ali M and Ibrahim Z: Anticancer activity of *Morus nigra* leaves extract. A Journal of the Bangladesh Pharmacological Society. 2014; 9: 496-7.

[107] Karthikeyan K, Gunasekaran P, Ramamurthy N, Govindasamy S. Anticancer activity of *Ocimum sanctum*. Pharmaceutical Biology. 1999; 37(4): 285-90.

[108] Pandey K, Sharma PK, Dudhe R. Anticancer activity of *Parthenium hysterophorus* Linn. and *Oldenlandia corymbosa* Lam. by Srb method. Open Access Scientific Reports. 2012; 1(6): 1-3.

[109] Sumalatha D. Antioxidant and antitumor activity of *Phyllanthus emblica* in colon cancer cell lines. International Journal of Current Microbiology and Applied Sciences. 2013; 2(5): 189-95.

[110] Balasubramanian K, Padma PR. Anticancer activity of *Zea mays* leaf extracts on oxidative stree-induced Hep2 cells. Journal of Aquaculture and Meridian Studies. 2013; 6(3): 149-58.

[111] Robinson JP, Suriya K, Subbaiya R, Ponmurugan P: Antioxidant and cytotoxic activity of *Tecoma stans* against lung cancer cell line (A549). Brazilian Journal of Pharmaceutical Sciences. 2017; 53(3): 6.

[112] Dantu AS, Shankarguru P, Ramya Devi D, Vedha Hari BN. Evaluation of *in-vitro* anticancer activity of hydroalcoholic extract of *Tabernaemontana divaricate*. Asian Journal of Pharmaceutical and Clinical Research. 2012; 5(3): 59-61.

[113] Yadav SS, Meshram GA, Shinde D, Patil RC, Manohar SM, Upadhye MV. Antibacterial and anticancer activity of a bioactive fraction of *Syzygium cumini* L. seeds. HAYATI Journal of Biosciences. 2011; 18(3): 118-22.

[114] Alaklabi A, Arif IA, Ahamed A, Kumar RS, Idhayadhulla A. Evaluation of antioxidant and anticancer activities of chemical constituents of the *Saururus Chinensis* root extracts. Saudi Journal of Biological Sciences. 2017.

[115] Saranya K, Manivasagan V, Kanakadurga R, Babu VPM, Babu NGR. A survey on anticancer properties of Indian medicinal plants - A broad spectrum analysis. International Journal of Pharmaceutical Sciences and Research. 2019; 10(8): 3635-40. doi: 10.13040/IJPSR.0975-8232.10(8).3635-40.

[116] Regassa H, Sourirajan A, Kumar V, Pandey S, Kumar D, Dev K. A Review of Medicinal Plants of the Himalayas with Anti-Proliferative Activity for the Treatment of Various Cancers. Cancers. **2022**; 14, 3898. https:// doi.org/10.3390/cancers14163898.

[117] Aqil F, Munagala R, Agrawal AK, Gupta R. Anticancer phytocompounds: Experimental and clinical updates. New Look Phytomed. **2019**; 1: 237–272.

[118] Stavri M, Ford CHJ, Bucar F. et al., "Bioactive constituents of Artemisia monosperma." Phytochemistry. 2005; 66: 2: 233–239.

[119] Jones PA, Baylin SB. The epigenomics of cancer. Cell. **2007**; 128: 683–692.

[120] Folkman J, Kalluri R. Cancer without disease. Nature. **2004**; 427: 787.

[121] Sahai E. Mechanisms of cancer cell invasion. Curr. Opin. Genet. Dev. **2005**; 15: 87–96.

[122] Varmus H, Kumar HS. Addressing the growing international challenge of cancer: A multinational perspective. Sci. Transl. Med. **2013**; 5: 175cm.

[123] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA A Cancer J. Clin. **2021**; 71: 209–249.

[124] Hussain M, Khera RA, Iqbal J, Khalid M, Hanif MA. Phytochemicals: Key to effective anticancer drugs. Mini-Rev. Org. Chem. **2019**; 16: 141–158.

[125] Sudhakar A. History of cancer, ancient and modern treatment methods. J. Cancer Sci. Ther. **2009**; 1:1.

[126] Kumar A, Sharipov M, Turaev A, Azizov S, Azizov I, Makhado E, Rahdar A, Kumar D, Pandey S. Polymer-Based Hybrid Nanoarchitectures for Cancer Therapy Applications. Polymers. **2022**; 14: 3027.

[127] Kumar S, Sharma AK, Lalhlenmawia H, Kumar D. Natural Compounds Targeting Major Signaling Pathways in Lung Cancer. Target. Cell. Signal. Pathw. Lung Dis. **2021**; 1: 821–846.

[128] Patil S, Ashi H, Hosmani, J et al., Tinospora cordifolia (Thunb.) Miers (Giloy) inhibits oral cancer cells in a dose-dependent manner by inducing apoptosis and attenuating epithelial-mesenchymal transition. Saudi J. Biol. Sci. 2021; 28;4553–4559.

[129] Muthu C, Ayyanar M, Raja N, Ignacimuthu S. Medicinal plants used by traditional healers in Kancheepuram District of Tamil Nadu, India. J. Ethnobiol. Ethnomedicine. **2006**; 2, 43.

[130] Yadav R, Das J, Lalhlenmawia H, Tonk RK, Singh L, Kumar D. Targeting cancer using phytoconstituents-based drug delivery. In Advanced Drug Delivery Systems in the Management of Cancer; Academic Press: Cambridge, MA, USA, 2021; 499–508.

[131] Cragg GM, Newman DJ. Plants as a source of anti-cancer agents. J. Ethnopharmacol. **2005**; 100: 72–79.

[132] Kuruppu AI, Paranagama P, Goonasekara CL. Medicinal plants commonly used against cancer in traditional medicine formulae in Sri Lanka. Saudi Pharm. J. **2019**; 27: 565–573.

[133] Lichota A, Gwozdzinski K. Anticancer activity of natural compounds from plant and marine environment. Int. J. Mol. Sci. **2018**; 19, 3533.

[134] Gezici S, Sekero glu N. Current perspectives in the application of medicinal plants against cancer: Novel therapeutic agents. Anti-Cancer Agents Med. Chem. (Former. Curr. Med. Chem. Anti-Cancer Agents). **2019**; 19: 101–111.

[135] Esghaei M, Ghaffari H, Esboei BR, Tapeh ZE, Salim FB, Motevalian M. Evaluation of anticancer activity of Camellia sinensis in the Caco-2 colorectal cancer cell line. Asian Pac. J. Cancer Prev. APJCP. **2018**; 19: 1697.

[136] Sharangi, A.B. Medicinal and therapeutic potentialities of tea (Camellia sinensis L.)—A review. Food Res. Int. **2009**; 42: 529–535.

[137] Subbarayan PR, Sarkar M, Impellizzeri S, Raymo F, Lokeshwar BL, Kumar P, Ardalan B. Anti-proliferative and anti-cancer properties of Achyranthes aspera: Specific inhibitory activity against pancreatic cancer cells. J. Ethnopharmacol. **2010**; 131: 78–82.

[138] Chakraborty A, Brantner A, Mukainaka T, Nobukuni Y, Kuchide M, Konoshima T, Nishino H. Cancer chemopreventive activity of Achyranthes aspera leaves on Epstein–Barr virus activation and two-stage mouse skin carcinogenesis. Cancer Lett. **2002**; 177: 1–5.

[139] Kumar RA, Sridevi K, Kumar NV, Nanduri S, Rajagopal S. Anticancer and immunostimulatory compounds from Andrographis paniculata. J. Ethnopharmacol. **2004**;92, 291–295.

[140] Kumar A, Shashni S, Kumar P, Pant D, Singh A, Verma RK. Phytochemical constituents, distributions and traditional usages of Arnebia euchroma: A review. J. Ethnopharmacol. **2021**; 271: 113896.

[141] Pal HC, Sehar I, Bhushan S, Gupta BD, Saxena AK. Activation of caspases and poly (ADP-ribose) polymerase cleavage to induce apoptosis in leukemia HL-60 cells by Inula racemosa. Toxicol. Vitr. **2010**; 24: 1599–1609.

[142] Kumari P, Misra K, Sisodia BS, Faridi U, Srivastava S, Luqman S, Kumar JK. A promising anticancer and antimalarial component from the leaves of Bidens pilosa. Planta Med. **2009**; 75: 59–61.

[143] Sundararajan P, Dey A, Smith A, Doss AG, Rajappan M, Natarajan S. Studies of anticancer and antipyretic activity of Bidens pilosa whole plant. Afr. Health Sci. **2006**; 6: 27–30.

[144] Kanipandian N, Li D, Kannan S. Induction of intrinsic apoptotic signaling pathway in A549 lung cancer cells using silver nanoparticles from Gossypium hirsutum and evaluation of in vivo toxicity. Biotechnol. Rep. **2019**; 23: e00339.

[145] Roy DC, Barman SK, Shaik MM. Current updates on Centella asiatica: Phytochemistry, pharmacology and traditional uses. Med. Plant Res. **2013**; 3: 777–780.

[146] Chen Y, Chen Y, Shi Y, Ma C, Wang X, Li Y, Li X. Antitumor activity of Annona squamosa seed oil. J. Ethnopharmacol. **2016**; 193: 362–367.

[147] Chen X, Guo J, Bao J, Lu J, Wang Y. The anticancer properties of Salvia miltiorrhiza Bunge (Danshen): A systematic review. Med. Res. Rev. **2014**; 34: 768–794.

[148] Rady I, Bloch MB, Chamcheu RCN, Banang Mbeumi S, Anwar MR, Mohamed H, Chamcheu JC. Anticancer properties of graviola (*Annona muricata*): A comprehensive mechanistic review. Oxidative Med. Cell. Longev. **2018**; 2018: 1826170.

[149] Gavamukulya Y, Abou-Elella F, Wamunyokoli F, AEl-Shemy H. Phytochemical screening, anti-oxidant activity and in vitro anticancer potential of ethanolic and water leaves extracts of Annona muricata (Graviola). Asian Pac. J. Trop. Med. **2014**; 7: S355–S363.

[150] Soni D, Grover A. "Picrosides" from Picrorhiza kurroa as potential anti-carcinogenic agents. Biomed. Pharmacother. **2019**; 109: 1680–1687.

[151] Ganogpichayagrai A, Palanuvej C, Ruangrungsi N. Antidiabetic and anticancer activities of Mangifera indica cv. Okrong leaves. J. Adv. Pharm. Technol. Res. **2017**;8:19.

[152] Bijauliya RK, Alok S, Singh M, Mishra SB. A comprehensive review on cancer and anticancer herbal drugs. Int. J. Pharm. Sci. Res. **2017**; 8: 2740–2761.

[153] Patel PR, Raval BP, Karanth HA, Patel VR. Potent antitumor activity of Rubia cordifolia. Int. J. Phytomedicine. **2010**; 2: 44–46.

[154] Son JK, Jung SJ, Jung JH, Fang Z, Lee CS, Seo CS, Woo MH. Anticancer Constituents from the Roots of Rubia cordifolia L. Chem. Pharm. Bull. **2008**; 56: 213–216.

[155] Ghosh S, Das S, M, Patra A, Hazra B. Anti-inflammatory and anticancer compounds isolated from Ventilago madraspatana Gaertn., Rubia cordifolia Linn. and Lantana camara Linn. J. Pharm. Pharmacol. **2010**; 62: 1158–1166.

[156] Singh S, Mehta A, Baweja S, Ahirwal L, Mehta P. Anticancer activity of Andrographis paniculata and Silybum marianum on five human cancer cell lines. J. Pharmacol. Toxicol. **2013**; 8: 42–48.

[157] Sagar SM. Future directions for research on Silybum marianum for cancer patients. Integr. Cancer Ther. **2007**; 6: 166–173.

[158] Kumar DR, George VC, Suresh PK, Kumar RA. Cytotoxicity, apoptosis induction and anti-metastatic potential of Oroxylum indicum in human breast cancer cells. Asian Pac. J. Cancer Prev. **2012**; 13: 2729–2734.

[159] Wang L, Xu J, Yan Y, Liu H, Karunakaran T, Li F. Green synthesis of gold nanoparticles from *Scutellaria barbata* and its anticancer activity in pancreatic cancer cell (PANC-1). Artif. Cells Nanomed. Biotechnol. **2019**; 47: 1617–1627.

[160] Nair PR, Melnick SJ, Wnuk SF, Rapp M, Escalon E, Ramachandran C. Isolation and characterization of an anticancer catechol compound from Semecarpus anacardium. J. Ethnopharmacol. **2009**; 122: 450–456.

[161] Jagtap UB, Bapat VA. Antioxidant activities of various solvent extracts of custard apple (*Annona squamosa* L.) fruit pulp. Nutrafoods. **2012**; 11: 137–144.

[162] Kadali VN, Pola SR, Sandeep BV. Anti cancer properties of plants present in west Godavari district of Andhra Pradesh, India-a mini review. Indian J. Tradit. Knowl. **2010**;3: 211–217.

[163] Soni VK, Pathak M, Yadav DK, Maurya R, Sahai M, Jain SK, Misra-Bhattacharya S. Immunomodulatory constituents from Annona squamosa twigs provoke differential immune response in BALB/c mice. Curr. Sci. **2013**; 104: 1224–1230.

[164] Pandey N, Barve D. Phytochemical and pharmacological review on Annona squamosa Linn. Int. J. Res. Pharm. Biomed. Sci. **2011**; 2: 1404–1412.

[165] Yang CS, Maliakal P, Meng X. Inhibition of carcinogenesis by tea. Annu. Rev. Pharmacol. Toxicol. **2002**; 42: 25–54.

[166] Rao AR. Inhibitory action of Asparagus racemosus on DMBA-induced mammary carcinogenesis in rats. Int. J. Cancer. **1981**; 28: 607–610.

[167] Rumjuankiat K, Sonhom N, Showpanish K, Somsri A, Pilasombut K. In vitro antioxidant activities and volatile compounds from Karanda (Carissa carandas L) fruit wine. Int. J. Agric. Res. **2018**; 14: 1843–1860.

[168] Shameem N, Kamili AN, Parray JA, Hamid R, Bandh SA. Antimicrobial and antioxidant activity of methanol extracts of Arnebia benthamii (Wall ex. G. Don) Johnston—A critically endangered medicinal plant of North western Himalaya. J. Anal. Sci. Technol. **2015**; 6: 36.

[169] Diwanay S, Chitre D, Patwardhan B. Immunoprotection by botanical drugs in cancer chemotherapy. J. Ethnopharmacol. **2004**; 90: 49–55.

[170] Gupta M, Mazumder UK, Kumar RS, Gomathi P, Rajeshwar Y, Kakoti BB, Selven VT. Anti-inflammatory, analgesic and antipyretic effects of methanol extract from Bauhinia racemosa stem bark in animal models. J. Ethnopharmacol. **2005**; 98: 267–273.

[171] Patil CD, Borase HP, Salunkhe RB, Suryawanshi RK, Narkhade CP, Salunke BK, Patil SV. Mosquito larvicidal potential of Gossypium hirsutum (Bt cotton) leaves extracts against Aedes aegypti and Anopheles stephensi larvae. J. Arthropod-Borne Dis. **2014**; 8:91.

[172] Hajiaghaalipour F, Kanthimathi MS, Sanusi J, Rajarajeswaran J. White tea (*Camellia sinensis*) inhibits proliferation of the colon cancer cell line, HT-29, activates caspases and protects DNA of normal cells against oxidative damage. Food Chem. **2015**; 169: 401–410.

[173] Kupchan SM, Baxter RL. Mezerein: Antileukemic principle isolated from Daphne mezereum L. Science. **1975**; 187: 652–653.

[174] Tundis R, Loizzo MR, Bonesi M, Peruzzi L, Efferth T, Daphne ST, Mezereum L. A study of anti-proliferative activity towards human cancer cells and antioxidant properties. Nat. Prod. Res. **2019**; 33: 1809–1812.

[175] Rajeshkumar S, Nagalingam M, Ponnanikajamideen M, Vanaja M, Malarkodi C. Anticancer activity of andrographis paniculata leaves extract against neuroblastima (IMR-32) and human colon (HT-29) cancer cell line. World J. Pharm. Pharm. Sci. **2015**; 4: 1667–1675.

[176] Kumar D, Harshavardhan SJ, Chirumarry S, Poornachandra Y, Jang K, Kumar CG, Yoon Y-J, Zhao B-X, Miao J-Y, Shin D-S. Design, synthesis in vitro anticancer activity and docking studies of (-)-catechin derivatives. Bull. Kor. Chem. Soc. **2015**; 36: 564–570.

[177] Bushman JL. Green tea and cancer in humans: A review of the literature. Nutr. Cancer. **1998**; 31: 151–159.

[178] Alper M, Güne SH. The anticancer and anti-inflammatory effects of Centaurea solstitialis extract on human cancer cell lines. Turk. J. Pharm. Sci. **2019**; 16: 273.

[179] Guzman M. Cannabinoids: Potential anticancer agents. Nat. Rev. Cancer. **2003**; 3: 745–755.

[180] Janatová A, Doskocil I, Božik M, Franková A, Tlustoš P, Kloucek P. The chemical composition of ethanolic extracts from six genotypes of medical cannabis (Cannabis sativa L.) and their selective cytotoxic activity. Chem. Biol. Interact. **2022**; 353: 109800.

[181] Bala A, Mukherjee PK, Braga FC, Matsabisa MG. Comparative inhibition of MCF-7 breast cancer cell growth, invasion and angiogenesis by Cannabis sativa L. sourced from sixteen different geographic locations. S. Afr. J. Bot. **2018**; 119: 154–162.

[182] Muriel JM. Herbs or natural products that decrease cancer growth. Oncol. Nurs. Forum. **2004**; 31: 75.

[183] Singh G, Pathania R, Khan M, Tonk RK, Kumar D, Dash AK. Identification and quantification of some natural compounds of *Pinus gerardiana* leaf extract and its antimicrobial and antioxidant activities. Pharmacologyonline. **2021**; 2: 333–351.

[184] Bhoomika R, Ramesh KG, Anita AM. Phyto-pharmacology of Achyranthes aspera: A Review. Pharmacogn. Rev. **2007**; 1: 143.

[185] Arora S, Tandon S. *Achyranthes aspera* root extracts induce human colon cancer cell (COLO-205) death by triggering the mitochondrial apoptosis pathway and S phase cell cycle arrest. Sci. World J. **2014**; 2014: 129697.

[186] Geethangili M, Rao YK, Fang SH, Tzeng YM. Cytotoxic constituents from *Andrographis paniculata* induce cell cycle arrest in jurkat cells. Phytother. Res. Int. J. Devoted Pharmacol. Toxicol. Eval. Nat. Prod. Deriv. **2008**; 22: 1336–1341.

[187] Thomson M, Ali M. Garlic [Allium sativum]: A review of its potential use as an anti-cancer agent. Curr. Cancer Drug Targets. **2003**; 3: 67–81.

[188] Balasenthil S, Ramachandran CR, Nagini S. Prevention of 4-nitroquinoline 1-oxide-induced rat tongue carcinogenesis by garlic. Fitoterapia. **2001**; 72: 524–531.

[189] Lawania RD, Mishra A. Anticancer potential of plants and natural products: A review. J. Diagn. Tech. Biomed. Anal. **2013**; 1: 104–115.

[190] David M, Karekalammanavar G. Spectrographic analysis and in vitro study of antibacterial anticancer activity of aqueous ethanolic fruit extract of Carissa carandas. J. Adv. Sci. Res. **2015**; 6: 10–13.

[191] Sharma N, Samarakoon KW, Gyawali R, Park YH, Lee SJ, Oh SJ, Jeong DK. Evaluation of the antioxidant, antiinflammatory, and anticancer activities of Euphorbia hirta ethanolic extract. Molecules. **2014**; 19: 14567–14581.

[192] Pereira DM, Valentao P, Correia-da-Silva G, Teixeira N, Andrade PB. Plant secondary metabolites in cancer chemotherapy: Where are we? Curr. Pharm. Biotechnol. **2012**; 13: 632–650.

[193] Oberlies NH, Kroll DJ. Camptothecin and taxol: Historic achievements in natural products research. J. Nat. Prod. **2004**; 67: 129–135.

[194] Joshi BC, Verma P, Juyal V, Sah AN. A Review of Himalayan Medicinal Plants against Cancer. Curr. Tradit. Med. **2021**; 8: 31–47.

[195] Karunakar H, Satyanarayana D, Joshi AB. Phytochemical investigation of root extract of the plant Carissa spinarum. Rajiv Gandhi Univ. Health Sci. J. Pharm. Sci. **2012**; 2: 55–59.

[196] Mitra SK, Prakash NS, Sundaram R. Shatavarins (containing Shatavarin IV) with anticancer activity from the roots of *Asparagus racemosus*. Indian J. Pharmacol. **2012**; 44: 732.

[197] Rahman MA, Akhtar J, Arshad M. Evaluation of cytotoxic potential and apoptotic effect of a methanolic extract of Bauhinia racemosa Lam. against a human cancer cell line, HeLa. Eur. J. Integr. Med. **2016**; 8: 513–518.

[198] Gueritte F, Fahy J. Anticancer Agents from Natural Products; CRC Press: Boca Raton, FL, USA, 2005; 123–135.

[199] Esposito S, Bianco A, Russo R, Di Maro A, Isernia C, Pedone PV. Therapeutic perspectives of molecules from Urtica dioica extracts for cancer treatment. Molecules. **2019**; 24: 2753.

[200] Gurav S, Gurav N. A Comprehensive review: Bergenia ligulata—A controversial clinical candidate. Int. J. Pharm. Sci. Rev. Res. **2014**; 5: 1630–1642.

[201] Singh SK, Shanmugavel M, Kampasi H, Singh R, Mondhe DM, Rao JM, Qazi GN. Chemically standardized isolates from Cedrus deodara stem wood having anticancer activity. Planta Med. **2007**; 73: 519–526.

[202] Ghosh T, Maity TK, Singh J. Evaluation of antitumor activity of stigmasterol, a constituent isolated from *Bacopa monnieri* Linn aerial parts against Ehrlich Ascites Carcinoma in mice. Orient. Pharm. Exp. Med. **2011**; 11: 41–49.

[203] Biba VS, Amily A, Sangeetha S, Remani P. Anticancer, antioxidant and antimicrobial activity of *Annonaceae* family. World J. Pharm. Pharm. Sci. **2014**; 3: 1595–1604.

[204] Desai TH, Joshi SV. Anticancer activity of saponin isolated from Albizia lebbeck using various in vitro models. J. Ethnopharmacol. **2019**; 231: 494–502.

[205] Karia P, Patel KV, Rathod SS. Breast cancer amelioration by Butea monosperma in-vitro and in-vivo. J. Ethnopharmacol. **2018**; 217: 54–62.

[206] Yadav DK, Singh N, Dev K, Sharma R, Sahai M, Palit G, Maurya R. Anti-ulcer constituents of *Annona squamosa* twigs. Fitoterapia. **2011**; 82: 666–675.

[207] Kuttan R, Bhanumathy P, Nirmala K, George MC. Potential anticancer activity of turmeric (*Curcuma longa*). Cancer Lett. **1985** ;29: 197–202.

[208] Das PK, Goswami S, Chinniah A, Panda N, Banerjee S, Sahu NP, Achari B. *Woodfordia fruticosa*: Traditional uses and recent findings. J. Ethnopharmacol. **2007**; 110: 189–199.

[209] Chitra V, Sharma S, Kayande N. Evaluation of anticancer activity of *Vitex negundo* in experimental animals: An in vitro and in vivo study. Int. J. Pharm. Tech. Res. **2009**; 1: 1485–1489.

[210] Kumar A, Patil M, Kumar P, Bhatti RC, Kaur R, Sharma NK, Singh A. *Mallotus philippensis* (Lam.) Müll. Arg.: A review on its pharmacology and phytochemistry. J. Herbmed Pharmacol. **2020**; 10: 31–50.

[211] Joshi RK. GC-MS Analysis of Volatile Organic Constituents of Traditionally Used Medicinal Plants from theWestern Ghats of India: Blumea lanceolaria (Roxb.) Druce., Heliotropium indicum L. and Triumfetta rhomboidea Jacq. J. Mex. Chem. Soc. **2020**; 64: 74–82.

[212] Vyas M. A short review on anticancer investigations of *Strychnos nuxvomica*. Int. J. Green Pharm. (IJGP). **2016**; 10: 87–90.

[213] Khan M, Garg A, Srivastava SK, Darokar MP. A cytotoxic agent from *Strychnos nuxvomica* and biological evaluation of its modified analogues. Med. Chem. Res. **2012**; 21: 2975–2980.

[214] Rao PS, Ramanadham M, Prasad MNV. Anti-proliferative and cytotoxic effects of *Strychnos nuxvomica* root extract on human multiple myeloma cell line–RPMI 8226. Food Chem. Toxicol. **2009**; 47: 283–288.

[215] Ansari JA, Ahmad MK, Khan AR, Fatima N, Khan HJ, Rastogi N, Mahdi AA. Anticancer and Antioxidant Activity of *Zingiber officinale* Roscoe Rhizome; NISCAIR-CSIR: New Delhi, India, 2016.

[216] Bisht D, Kumar D, Kumar D, Dua K, Chellappan DK. Phytochemistry and pharmacological activity of the genus artemisia. Arch. Pharm. Res. **2021**; 44: 439–474.

[217] Rai M, Jogee PS, Agarkar G, Santos CA.D. Anticancer activities of *Withania somnifera*: Current research, formulations, and future perspectives. Pharm. Biol. **2016**; 54: 189–197.

[218] Bupesh G, Manikandan E, Thanigaiarul K, Magesh S, Senthilkumar V. Enhanced antibacterial, anticancer activity from *Terminalia chebula*. Med. Plant Rapid Extr. Phytosynthesis Silver Nanoparticles Core-Shell Struct. J. Nanomed. Nanotechnol. **2016**;7: 355.

[219] Wani K, Shah N, Prabhune A, Jadhav A, Ranjekar P, Kaul-Ghanekar R. Evaluating the anticancer activity and nanoparticulate nature of homeopathic preparations of Terminalia chebula. Homeopathy. **2016**; 105: 318–326.

[220] Malabadi RB, Kolkar KP, Chalannavar RK. *Cannabis sativa*: Ethnobotany and phytochemistry. International Journal of Innovation Scientific Research and Review. 2023; 5(2): 3990-3998.

[221] Malabadi RB, Kolkar KP, Acharya M, Chalannavar RK. *Cannabis sativa*: Medicinal plant with 1000 molecules of pharmaceutical interest. International Journal of Innovation Scientific Research and Review. 2023; 5(2):3999-4005.

[222] Malabadi RB, Kolkar KP, Chalannavar RK. *Cannabis sativa*: Industrial hemp (fiber type)- An Ayurvedic traditional herbal medicine. International Journal of Innovation Scientific Research and Review. 2023; 5 (2): 4040-4046.

[223] Malabadi RB, Kolkar KP, Chalannavar RK. Medical *Cannabis sativa* (Marijuana or Drug type); The story of discovery of Δ9-Tetrahydrocannabinol (THC). International Journal of Innovation Scientific Research and Review. 2023; 5 (3):4134-4143.

[224] Malabadi RB, Kolkar KP, Chalannavar RK. Δ9-Tetrahydrocannabinol (THC): The major psychoactive component is of botanical origin. International Journal of Innovation Scientific Research and Review. 2023; 5(3): 4177-4184.

[225] Malabadi RB, Kolkar KP, Chalannavar RK. *Cannabis sativa*: Industrial Hemp (fibre-type)- An emerging opportunity for India. International Journal of Research and Scientific Innovations (IJRSI). 2023; X (3):01-9.

[226] Malabadi RB, Kolkar KP, Chalannavar RK. Industrial *Cannabis sativa* (Hemp fiber type):Hempcrete-A plant based eco-friendly building construction material. International Journal of Research and Innovations in Applied Sciences (IJRIAS). 2023; 8(3): 67-78.

[227] Malabadi RB, Kolkar KP, Chalannavar RK, Lavanya L, Abdi G. *Cannabis sativa*: The difference between Δ8-THC and Δ9-Tetrahydrocannabinol (THC). International Journal of Innovation Scientific Research and Review. 2023; 5(4): 4315-4318.

[228] Malabadi RB, Kolkar KP, Chalannavar RK, Lavanya L, Abdi G. Hemp Helps Human Health: Role of phytocannabinoids. International Journal of Innovation Scientific Research and Review. 2023; 5 (4): 4340-4349.

[229] Malabadi RB, Kolkar KP, Chalannavar RK, Lavanya L, Abdi G. *Cannabis sativa*: Botany, cross pollination and plant breeding problems. International Journal of Research and Innovations in Applied Science (IJRIAS). 2023; 8 (4): 174-190.

[230] Malabadi RB, Kolkar KP, Chalannavar RK, Lavanya L, Abdi G, Baijnath H. Cannabis products contamination problem: A major quality issue. International Journal of Innovation Scientific Research and Review. 2023;5(4): 4402-4405.

[231] Malabadi RB, Kolkar KP, Chalannavar RK, Lavanya L, Abdi G. Medical *Cannabis sativa* (Marijuana or drug type): Psychoactive molecule, Δ9-Tetrahydrocannabinol (Δ9-THC). International Journal of Research and Innovations in Applied Science. 2023; 8(4): 236-249.

[232] Malabadi RB, Kolkar KP, Chalannavar RK, Mondal M, Lavanya L, Abdi G, Baijnath H. *Cannabis sativa*: Release of volatile organic compounds (VOCs) affecting air quality. International Journal of Research and Innovations in Applied Science (IJRIAS). 2023; 8(5): 23-35.

[233] Malabadi RB, Nethravathi TL, Kolkar KP, Chalannavar RK, Mudigoudra BS, Lavanya L, Abdi G, Baijnath H. *Cannabis sativa*: Applications of Artificial Intelligence and Plant Tissue Culture for Micropropagation. International Journal of Research and Innovations in Applied Science (IJRIAS). 2023; 8(6): 117-142.

[234] Malabadi RB, Nethravathi TL, Kolkar KP, Chalannavar RK, Mudigoudra BS, Abdi G, Baijnath H. *Cannabis sativa*: Applications of Artificial intelligence (AI) in Cannabis industries: In Vitro plant tissue culture. International Journal of Research and Innovations in Applied Science (IJRIAS). 2023; 8 (7): 21-40.

[235] Malabadi RB, Kolkar KP, Brindha C, Chalannavar RK, Abdi G, Baijnath H, Munhoz ANR, Mudigoudra BS. *Cannabis sativa*: Autoflowering and Hybrid Strains. International Journal of Innovation Scientific Research and Review. 2023; 5(7): 4874-4877.

[236] Malabadi RB, Kolkar KP, Chalannavar RK, Munhoz ANR, Abdi G, Baijnath H. *Cannabis sativa*: Dioecious into Monoecious Plants influencing Sex Determination. International Journal of Research and Innovations in Applied Science (IJRIAS). 2023; 8(7): 82-91.

[237] Malabadi RB, Kolkar KP, Chalannavar RK, Abdi G, Munhoz ANR, Baijnath H *Cannabis sativa*: Dengue viral disease-Vector control measures. International Journal of Innovation Scientific Research and Review. 2023; 5(8): 5013-5016.

[238] Malabadi RB, Nethravathi TL, Kolkar KP, Chalannavar RK, Mudigoudra BS, Abdi G, Munhoz ANR, Baijnath H. *Cannabis sativa*: One Plant-One-Medicine for many diseases-Therapeutic Applications. International Journal of Research and Innovations in Applied Science (IJRIAS). 2023; 8(8): 132-174.

[239] Malabadi RB, Nethravathi TL, Kolkar KP, Chalannavar RK, Mudigoudra BS, Abdi G, Munhoz ANR, Baijnath H. Fungal Infection Diseases- Nightmare for Cannabis Industries: Artificial Intelligence Applications International Journal of Research and Innovations in Applied Science (IJRIAS). 2023; 8(8):111-131.

[240] Malabadi RB, Kolkar KP, Chalannavar RK, Baijnath H. *Cannabis sativa*: Difference between Medical Cannabis (marijuana or drug) and Industrial hemp. GSC Biological and Pharmaceutical Sciences. 2023; 377-381.

[241] Malabadi RB, Kolkar KP,Chalannavar RK, Acharya M, Mudigoudra BS. *Cannabis sativa*: 2023-Outbreak and Re-emergence of Nipah virus (NiV) in India: Role of Hemp oil. GSC Biological and Pharmaceutical Sciences. 2023; 25(01):063–077.

[242] Malabadi RB, Kolkar KP, Chalannavar RK, Acharya M, Mudigoudra BS. Industrial *Cannabis sativa*: Hemp-Biochar-Applications and Disadvantages. World Journal of Advanced Research and Reviews. 2023; 20(01): 371–383.

[243] Malabadi RB, Kolkar KP, Chalannavar RK, Vassanthini R, Mudigoudra BS. Industrial *Cannabis sativa*: Hemp plastic-Updates. World Journal of Advanced Research and Reviews. 2023; 20 (01): 715-725.

[244] Malabadi RB, Kolkar KP, Chalannavar RK. Industrial *Cannabis sativa*: Hemp oil for biodiesel production. Magna Scientia Advanced Research and Reviews. 2023; 09(02): 022–035.

[245] Malabadi RB, **Sadiya MR**, Kolkar KP, Chalannavar RK. Biodiesel production via transesterification reaction. Open Access Research Journal of Science and Technology. 2023; 09(02): 010–021.

[246] Malabadi RB, **Sadiya MR**, Kolkar KP, Chalannavar RK. Biodiesel production: An updated review of evidence. International Journal of Biological and Pharmaceutical Sciences Archive. 2023; 06(02): 110–133.

[247] Malabadi RB, Kolkar KP, Chalannavar RK. Industrial *Cannabis sativa*: Hemp oil for biodiesel production. Magna Scientia Advanced Research and Reviews. 2023; 09(02): 022–035.

[248] Malabadi RB, **Sadiya MR**, Kolkar KP, Lavanya L, Chalannavar RK. Quantification of THC levels in different varieties of *Cannabis sativa*. International Journal of Science and Research Archive. 2023; 10(02): 860–873.

[249] Malabadi RB, **Sadiya MR**, Kolkar KP, Chalannavar RK. Pathogenic *Escherichia coli* (*E. coli*) food borne outbreak: Detection methods and controlling measures. Magna Scientia Advanced Research and Reviews, 2024; 10(01): 052–085.

[250] Malabadi RB, **Mammadova SS**, Kolkar KP, Sadiya MR, Chalannavar RK, Castaño Coronado KV. *Cannabis sativa*: A therapeutic medicinal plant-global marketing updates. World Journal of Biology, Pharmacy and Health Sciences. 2024; 17(02): 170–183.

[251] McCauley J, Zivanovic A, Skropeta D. Bioassays for Anticancer Activities. In: Roessner, U., Dias, D. (eds) Metabolomics Tools for Natural Product Discovery. Methods in Molecular Biology, vol 1055. Humana Press, Totowa, NJ. 2013; https://doi.org/10.1007/978-1-62703-577-4-1.

[252] **Malabadi RB,** Kolkar KP, Acharya M, Chalannavar RK. Tea (*Camellia sinensis*): Phytochemistry and Health Benefits- Tea Cup that Cheers has Tears. International Journal of Innovation Scientific Research and Review. 2022; 4(4): **2**620- 2633.

[253] Lukhele ST, Motadi LR. Cannabidiol rather than Cannabis sativa extracts inhibit cell growth and induce apoptosis in cervical cancer cells. BMC Complement Altern Med. 2016; 16:335.

[254] **Cherkasova V**, Wang B, .;Gerasymchuk M, Fiselier A, Kovalchuk O, Kovalchuk I. Use of Cannabis and Cannabinoids for Treatment of Cancer. Cancers **2022**; 14: 5142. https://doi.org/10.3390/ cancers14205142.

[255] Razlog R, Kruger CA, Abrahamse H. Enhancement of conventional and Photodynamic therapy for Treatment of Cervical Cancer with Cannabidiol**.** Integrative Cancer Therapies 2022; 21: 1–11.

[256] **Hinz B, Ramer** R. Cannabinoids as anticancer drugs: Current status of preclinical research. British Journal of Cancer. 2022; 127:1–13. https://doi.org/10.1038/s41416-022-01727-4.

[257] Ligresti A, Moriello AS, Matias I, et al. Anti-tumor activity of plant cannabinoids with the emphasis on the effect of cannabidiol on human breast cancer. J Pharmacol Exp Ther. 2006;318(3):1375–87.

[258] Alexander A, Smith PF, Rosengren RJ. Cannabinoids in the treatment of cancer. Cancer Lett. 2009;285:6–12.

[259] Shrivastava A, Kuzontkoski PM, Groopman JE, Prasad A. Cannabidiol induces programmed cell death by coordinating the cross-talk between apoptosis and autophagy. Mol Cancer Ther. 2011;10(7):1161–72.

[260] Yamaori S, Kushihara M, Yamamoto I, Watanabe K. Characterization of major phytocannabinoids, cannabidiol and cannabinol, as isoform-selective and potent inhibitors of human CYP1 enzymes. Biochem Pharmacol. 2010;79:1691–8.

[261] Safaraz S, Adhami VM, Syed DN, Afaq, Mukhtar H. Cannabinoids for cancer treatment: Progress and promise. Cancer Res. 2008;68(2):339–44.

[262] Sharma M, Hudson JB, Adomat H, Guns E, Cox ME. In Vitro Anticancer Activity of Plant-Derived Cannabidiol on Prostate Cancer Cell Line. Pharmacol Pharm. 2014;5:806–20.

[263] Caffarel MM, Andradas C, Perez-Gomez E, Guzman M, Sanchez C. Cannabinoids: A new hope for breast cancer therapy? Cancer Treat Rev. 2012;38:911–8.

[264] Romano B, Borrelli F, Pagano E, Cascio MG, Pertwee RG, Izzo AA. Inhibition of colon carcinogenesis by a standardized Cannabis sativa extract with high content of cannabidiol. Phytomedicine. 2014;21(5):631–9.

[265] Seltzer ES, Watters AK, MacKenzie D Jr, Granat LM, Zhang D. Cannabidiol (CBD) as a promising anti-cancer drug. Cancers. 2020;12:3203.

[266] Nejhad AA, Behbahani BA, Hojjati M, Vasiee A, Mehrnia MA. Identification of phytochemical, antioxidant, anticancer and antimicrobial potential of *Calotropis procera* leaf aqueous extract. **Scientific Reports.** 2023; 13:14716 | https://doi.org/10.1038/s41598-023-42086-1.

[267] Khan T, Ali M, Khan A. Anticancer Plants: A Review of the Active Phytochemicals, Applications in Animal Models, and Regulatory Aspects. Biomolecules.. **2020**; 10, 47; doi:10.3390/biom10010047.

[268] Calixto J. Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). Braz. J. Med. Biol. Res. **2000**; 33: 179–189.

[269] Fridlender M, Kapulnik Y and Koltai H. Plant derived substances with anti-cancer activity: from folklore to practice. Front. Plant Sci. 2015; 6:799. doi: 10.3389/fpls.2015.00799.

[270] Kuruppu AI, Paranagama P, Goonasekara CL. Medicinal plants commonly used against cancer in traditional medicine formulae in Sri Lanka. Saudi Pharmaceutical Journal. 2019; 27: 565–573.

[271] Mukavi JW, Mayeku PW. In vitro anti-cancer efficacy and phyto-chemical screening of solvent extracts of Kigelia africana (Lam.) Benth. Heliyon. 2020; 6 : e04481.

[272] Khanna G, Mishra AK. Analytical Studies of Anticancer Medicinal Plant of North East India. International Journal of Biotechnology and Biomedical Sciences. 2019; 5:1: 24-29.

[273] Morris CC, Ramyashree CS, Kruthika P, Pap-puswamy M, Chaudhary A, Meyyazhagan A, Anand A V, Balasubramanian B. A review on anti-cancer plants of India. Plant Science To-day (Early Access). https://doi.org/10.14719/ pst.2372.

[274] Kumar G, Gupta R et al., Anticancer activity of plant leaves extract collected from a tribal region of India. 3 Biotech. 2019; 9:399 https://doi.org/10.1007/s13205-019-1927-x.

[275] Begum I, Sharma R, Sharma HK. A REVIEW ON PLANTS HAVING ANTI-CANCER ACTIVITY. Curr Trends Pharm Res, 2017; 4(2):39-62.

[276] Kalita S, Sarma A, Hazarika A et al., A Review on Medicinal Plants Having Anticancer Properties of Northeast India and Associated Endophytic Microbes and their Future in Medicinal Science. Pure Appl Microbiol. 2022;16(3):1608-1621. doi: 10.22207/JPAM.16.3.57.

[277] Abu-Darwish MS and Efferth T. Medicinal Plants from Near East for Cancer Therapy. Front. Pharmacol. 2018; 9:56. doi: 10.3389/fphar.2018.00056.

[278] Oncology: The disease, dynamics & challenges of Global market research (ipsos.com). 2023.

[279] North America Oncology Drugs Market Analysis Report 2022 to 2030 (insights10.com). 2023.

[280] Accelerate Pharmaceutical Product Development with Artificial Intelligence (medidata.com). 2024.

[281] Debela DT, Muzazu SGY et al., New approaches and procedures for cancer treatment: Current perspectives. SAGE Open Medicine. 2021; 9: 1–10. https://doi.org/10.1177/2050312121103436.

[282] Senthil D, Velliyagounder V, Kanakaraj L Cytotoxic evaluation of curcumin and quercetin in MCF-7 cell lines. World Journal of Biology Pharmacy and Health Sciences. 2024; 17(02): 149–154.

[283] Common cancer medications | Medical News Today. 2024