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A Comprehensive Review on Medicinal Plants against Lung Cancer

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ABSTRACT

Lung cancer is a disease with a high probability of occurrence as well as a high mortality rate. Despite the fact that numerous therapies are available, a huge number of patients die each year as a result of cancer. The rising research direction in health care pharmacy paves the way for the development of an effective and side effect-free anticancer medicine. Chemical entities found in plants are extremely useful in cancer studies. Most notary bioactive phytochemicals are preferred because they act differently only on cancer cells exclusively and not normal cells. Carcinogenesis is a multi-step process that involves numerous signaling events. Phytochemicals have a pleiotropic activity which can target these events in a variety of ways, making them an excellent choice for anticancer medication therapy. Efforts are underway to create lead candidates derived from phytochemicals that can reduce the progression of cancer without inducing any side effects. The purpose of this review is to provide information on medicinal plants that have anticancer effect against lung cancer.

Keywords: Medicinal plant, Secondary metabolites, Antitumor activity, Lung cancer and Phytochemicals.

INTRODUCTION

Cancer is a deadly disease characterized by aberrant cell proliferation. It is the leading cause of death and morbidity worldwide, with the number of cases increasing over time[1]. This disease is the second biggest cause of death in affluent countries, after cardiovascular disease[2,3]. Uncontrolled proliferation and dedifferentiation of a normal cell characterize the cancer phenomena[4]. Changes in various cellular signaling pathways link cancer to a category of hereditary illnesses[5]. The illusion of uncontrollable cell expansion reductions in apoptosis is one of the main alterations that determine malignant development[6]. The lifestyle changes are the most common cause of cancer, there is an urgent need to find a better cure for the condition. Because of the high mortality and occurrence, it has become

significant public health and economic issue that needs comprehensive prevention[7].

Lung cancer is often diagnosed malignancies in the world. Lung cancer, like all malignancies, has the best chance of being cured if diagnosed early in the disease's progression[8].The most recurrent cancer in the world is lung cancer, with 6.3 percent of people developing lung or bronchial cancer at some point in their lives[9]. Dynamic tobacco smoking, secondhand tobacco smoke outflow (aloof smoking), line and stogie smoking, indoor and outside air contamination, atomic openness, nickel, chromium, and arsenic have been considered as the causing agents for huge cases[10]. Tobacco use is the leading cause of lung cancer, and males are more likely than women to develop the disease[11]. Non-small cell lung carcinoma (NSCLC), which includes Squamous Cell Lung Carcinoma (SCLC), Adenocarcinoma, and Large Cell Carcinoma, for 80% of lung cancer cases, while Small Cell Lung Carcinoma accounts for 20%[12]. In addition, there has been an upsurge in research into tumor-associated biomarkers, with the goal of lowering lung cancer mortality rates through early identification and prognosis[13]. A cancer underdeveloped cell model has also been considered, as it provides new insights into the limitations of current cancer treatments[14]. The discovery of multiple sub-atomic pathways that influence the formation, mobility, and visibility of lung cancer is leading to the creation of new therapeutic techniques[15]. Clinical evidence supports selective suppression of the Vascular Endothelial Growth Factor (VEGF) or Epidermal Growth Factor (EGF) signaling pathways in the treatment of advanced Non-Small Cell Lung Carcinoma (NSCLC)[16].

Plant-derived chemicals are more tolerant and non-toxic to normal human cells; hence medicinal plants have a number of advantages over artificial products[17]. Radiotherapy and chemotherapy, which are now used to treat cancer, have a variety of side effects such as neurological, cardiac, renal, and pulmonary toxicity, which can have a major impact on an individual's health[18]. As a result, an alternate technique must be developed that includes a less toxic and more potent anticancer medicine than which is available on the market. Several research have been conducted on naturally occurring chemicals that have been shown to exhibit cytotoxicity effects, indicating that they have the potential to kill cancer cells[19]. Because of these benefits, medicinal plants are in high demand, and various species have been studied and selected for use in the creation of cancer treatments[20] as shown in the Fig. 1. Medicinal plants contain wide spread varieties of secondary metabolites which contain flavonoids, flavones, anthocyanins, lignans, coumarins, isocatechins and catechins[21]. These bioactive antioxidant and anticancer compounds of medicinal plants are mainly responsible to reduce the cancer effects. The cumulative side effects and high-cost medication has its impact on the focus of research for herbal medicines[22]. The review also focused on bioactive compounds in plant parts responsible for anticancer activity with their pharmacological potential.

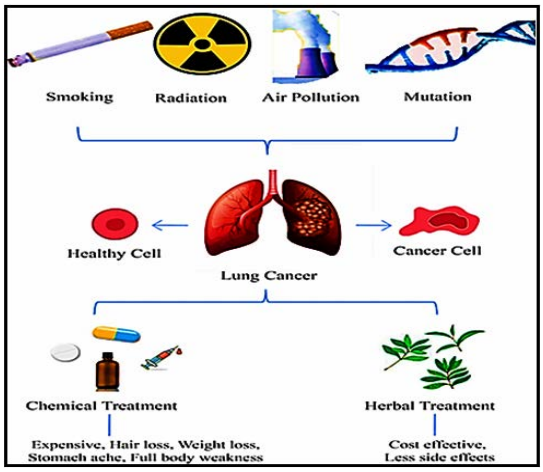


Fig. 1. Pictorial Representation of both healthy Lung cell and Lung cancer cell along with its Causes and Treatment Effects of Lung Cancer

Natural Lead Molecules towards Treatment of Cancer

Despite the availability of numerous drugs for cancer treatment, Cancer is still the second biggest cause of mortality worldwide[23]. Chemotherapy and newer cancer treatments have been linked to a slew of side effects in patients. Millions of people are diagnosed with cancer each year and die as a result of their sickness[24]. Cancer affects over 3500 million people worldwide each year, accounting for more than 2-3 percent of all fatalities[25]. Though Chemo preventive medicines are particularly effective in the treatment of cancer, due to their toxicity, their usage is limited[26]. Because of the negative side effects of chemotherapy and nuclear cancer treatment, new and improved treatments are urgently needed[27]. Cancers can be avoided by following a healthy

lifestyle, refraining from smoking, successfully treating inflammatory conditions, and taking vitamin supplements to promote immune function, as the old adage says[28]. Chemotherapy sole major treatment option for advanced-stage malignancies is extremely hazardous to normal tissues[29]. The discovery of Podophyllotoxin in the late 1960s started a search for natural cancer treatments, and lead to the discovery of anticancer drugs like vincristine, vinblastine, campthothecin and taxol[30].

Nature's disease-fighting qualities can be found in over a thousand plants. The effect of a synthetic variation of the chemotherapy medicine, Etoposide has been discovered in small cell lung and testicular malignancies. It is possible to develop a modern cancer prevention medicine based on medicinally active herbs and their mechanisms of action that were previously unknown. Potent chemicals extracted from medicinal plants have been used to make a variety of medicines over the years[31]. For the medication development and manufacturing process, the following three testing procedures are used:

(1) Isolation and characterization of active molecules based on bioactivity,
(2) Rational drug design-based alteration and
(3) Synthesis of analogues and mechanism of action studies 32.

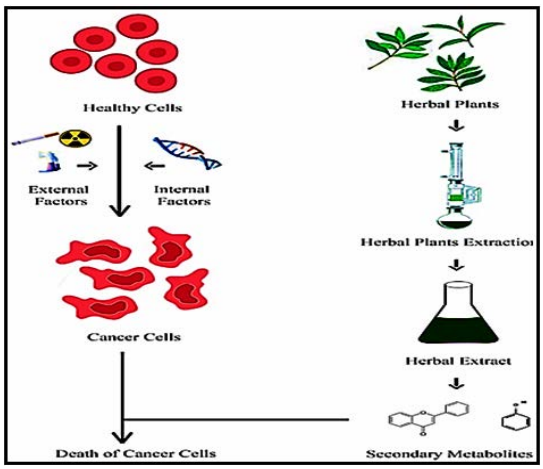


Fig. 2. Flow chart representing the Herbal Treatment on Cancer Cells

Traditional medicine and Ayurvedic knowledge aid in the discovery of new cancer therapy options with high efficacy and minimal toxicity[33]. The discovery of bioactive lead compounds, chemical modulation, and the enhancement of other pharmacological profiles are the primary goals in the drug invention[34]. Traditional medicine for illness prevention is still practiced throughout the Indian subcontinent, which offers a variety of botanical diversity[35]. According to ethno historic sources, medicinal plants have been utilized as a remedy for a variety of human diseases; the reason for this is because they are reservoirs of potent chemical compounds that act as a curative medication with fewer side effects[36]. The healthcare sector has become increasingly focused on herbal medicine over the last decade which in turn treats the lung cancer patients increasing its positivity towards herbal treatment as shown in the Fig. 2, has a global impact on both global health and foreign exchange. In addition to their cultural and moral relevance, herbal medicines are more acceptable in these countries. Cancer is the most frequent genetic disease for which medicinal plants can be utilised for the treatment[37].

So, for several phytochemicals have been stated to reduce the development of cancer cells. Vincristine affects causes spiral aggregation through tubulin self-microtuble assemblies[38]. Docetaxel has the ability to inhibit topoisomerase; however, it also damages DNA[39].Synthetic chemistry involves the use of technical combinatorial chemistry in the generation of novel leads, as well as drugs derived from natural ingredients[40]. Nature is an enticing source of potential therapeutic candidate chemicals due to the vast chemical complexity present in millions of species of plants. Many plant-derived chemicals are currently being employed in cancer therapy with great effectiveness[41].

Plant Compounds with Anticancer Properties

While folk medicine has been practiced for thousands of years in Asian and African tribes, the use of medicinal plants is fast spreading throughout the rest of the world[42]. Certain countries, according to the World Health Organization (WHO), rely on plant-based medicine as their primary supply of pharmaceuticals, while industrialized countries benefit from the medical benefits of naturally produced compounds[43]. Fig. 3 illustrates the anticancer chemicals and its structure isolated from terrestrial plants includes Polyphenols, Flavonoids and Brassinosteroids[44].

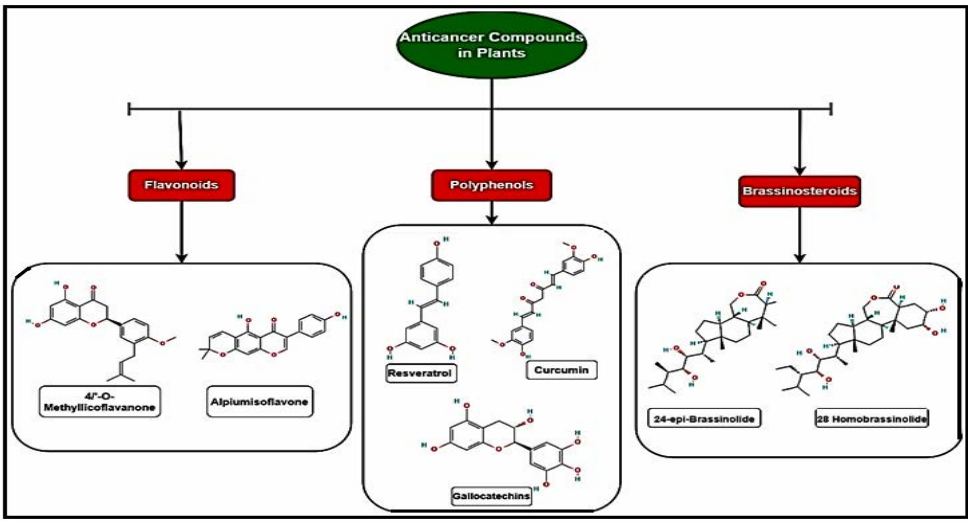


Fig. 3. The above figure portrays the Plants' compounds with chemical structure related to Anticancer Properties

Polyphenols

Polyphenols, which are natural antioxidants, are included in a person's diet, they are thought to increase protection and reduce cancer risk[45]. Polyphenols are thought to cause apoptosis, which means they have anticancer properties. Polyphenols are understood to trigger apoptosis by inhibiting the mobilization of copper ions bound to chromatin, resulting in DNA breakage[46]. Plant polyphenols have the ability to stop cancer cells from growing by interfering with proteins prevalent in cancer cells. The food sources including almonds, grapes, and red wine have been reported to contain polyphonic named resveratrol and[47] Gallocatechins, which are antioxidants, are found in green tea[48]. These polyphenols may control acetylation, methylation, or phosphorylation by directly interacting with cancer agents. Curcumin has been shown to cure tumor cells in various cells, including the suppression of Tumor Necrosis Factor (TNF) production when subjected to diverse stimuli[49].

Flavonoids

Flavonoids are polyphenolic chemicals that make up a diverse range of plant-derived metabolites, over 10,000 structures identified[50]. Flavonoids are phenol-like active agents in plants that are garnering interest in research due to their possible health advantages[51]. Radicals have been shown to scavenge radicals, and flavonoids have been proven to have cytotoxicity[52]. Flavonoids have anticancer properties in persons with Hepatitis-2, which causes hepatoma (H-G), and in women with breast cancer (MCF-7)[53]. MLF(4'-Methoxy licoflavanone) found to be cytotoxic in HL-60 cells (human leukemia) via the intrinsic and extrinsic death pathways of apoptosis[54]. When apoptotic proteins are triggered, mitochondrial membranes lose their potential, and cancer cells' mitochondria become unable to function[55]. Flavonoids from ferns have also been demonstrated to have anticancer properties at very low doses in other investigations[56]. Polyphenols, as earlier stated, may alter the impact of proteins substances that may be employed to enhance cellular survival[57]. STAT proteins (Signal Transducers and Activators of Transcription) support both cell survival and development[58]. Members of this protein family are dephosphorylated by MLF (4'-Methoxy licoflavanone) and AIF (Alpinumi soflavone) which decreases cancer cell survival. This inhibitory mechanism, which prevents the formation of new blood vessels and cell development, normally limits Nuclear factor-B (NF-B) production and survival[59].

Brassinosteroids

Plant brassinosteroids control cell

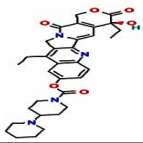
development and differentiation, as well as the elongation of stem cells and root cells[60]. Plant senescence is also monitored using brassinosteroids. They are necessary for plant development and production [61]. Another naturally occurring substance with medical relevance in the fight against cancer is brassinosteroids[62]. Two natural brassinosteroids have been employed in cancer cell research to demonstrate their anticancer effects. In laboratory trials, a mixture of anticancer chemicals known as 28-homobrassinolide (or 28-hómoCS) and 24-epibrassinolide (or 24-epiBL) was found to be effective against a wide spectrum of cancer cell types at low doses[63,64]. Cancer cells lack the ability to undergo apoptosis and hence exist in a permanent state of proliferation, whereas brassinosteroids can cause reactions that inhibit cell development and accelerate cell death[65]. T-phastictumourlines, multiple myeloma MLC, and osteosarcoma HAG have all received brassinosteroids. It also studied against the breast cancer cell lines consisting estrogen and human epidermal growth factor 2 (HER2) proteins.[66]

Although most research has focused on the Androgen receptor, which is prevalent in breast cancer cells, it appears to have a structure comparable to the estrogen receptor in prostate cancer (LNCaP and DU-145 cell lines)[67]. All hormone-responsive and hormone-responsive cancer cells are inhibited by Brainers. Brassinosteroids has the potential to be cytotoxic, producing DNA damage and halting the cell cycle. G1 cell cycle protein participation was considerably reduced in 28-homoCS and 24-epiBL-treated breast cancer cells. At this point in the cell cycle, cells go through either repair or apoptosis; brassinosteroids cause cells to go into apoptosis[68]. In the case of brassinosteroids, the combination of apoptotic proteins that promote survival and those that destroy cells is essential in prostate cancer cell lines[69]. Bax becomes hyper proliferative after radiation treatment, but Bcl-2 is inversely controlled[70]. In addition to their anticancer capabilities, brassinosteroids cause a variety of reactions in both normal and cancer cells[71]. Brassinosteroids derived agents are of concern for therapeutic qualities since they are not cytotoxic to human cells and are cancer cell selective, which is a critical criterion in anticancer treatment[72].

Plants Used for Lung Cancer and Other Cancer Treatment

Cancer affects more than 4 million people and Lung cancer affects 2.1 million in the country each year[73]. Continual research is being carried out over the world to identify effective cancer treatments, such as chemotherapy, which entails high-risk quantities of chemical drugs that can lead to high toxic events[74]. Medicinal plants use antioxidant and anticancer chemicals that are thought to reduce or destroy cancerous cells to treat and cure cancer. Certain plants may also contain constants that can be employed in nature to prevent the spread of cancer or reduce the risk of getting various types of cancer[75]. Any descriptions of plants that may be utilised to treat cancer, as well as their respective developments, are listed in Table 1 and Table 2.

Table 1: Plants Secondary Metabolites Contains Anti-lung Cancer Capacity

Name of Secondary metabolites	Chemical structure	Plant source and its family	Treatment of cancer and type	Mode of function and action	References
Irinotecan		*Camptotheca acuminate* (Nyssaceae)	To treat Colorectal and lung tumors.	During reticence of DNA genetic material topoisomerase I	[76]

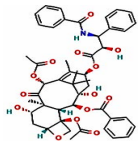
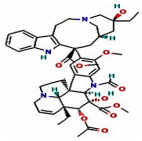
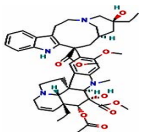
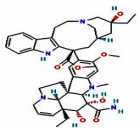
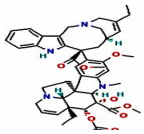
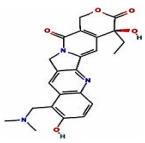
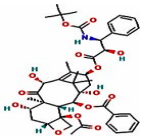
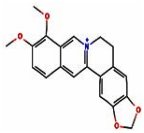
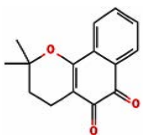
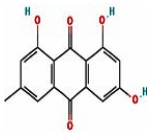
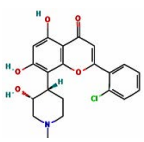
Taxol		Taxus brevifolia and *Taxus baccata* (Taxaceae)	Lung cancer	Act as Anti-mitotic agent	[77]
Vincristine		*Catharanthus roseus* (Apocynaceae)	Blood Leukemia, lymphomas, breast carcinoma, lung tumor and pediatric solid tumors.	Inhibit cells accumulation by process in mitotic block.	[78]
Vinblastine		*Catharanthus roseus* (Apocynaceae)	Used to treat renal cancer, breast, lung, and lymphoma.	During mitotic block, it can inhibit cell proliferation.	[79]
Vindesine		*Catharanthus roseus* (Apocynaceae)	Lung, kaposi's sarcoma, leukemias, lymphomas, breast and Advanced testicular cancer.	Blocking mitosis.	[80]
Vinorelbine		*Catharanthus roseus* (Apocynaceae)	Lung, kaposi's sarcoma, leukemias, lymphomas, breast and Advanced. testicular cancer	Blocking mitosis.	[81]
Topotecan		*Camptotheca acuminate* (Nyssaceae)	Extra Ovarian carcinoma, lung carcinoma and pediatric tumors.	For the period of impede of DNA Over winding that enzymes' name as topoisomerase I.	[82]
Docetaxel (Paclitaxel's semi-synthetic derivative)		Taxus brevifolia, *Taxus baccata* (Taxaceae)	Cancer for Breast and lung cancer	Prevent or avert cell mitosis through binding toward microtubules.	[83]
Berberine		*Arcungelisia flava* (Menispermaceae) and *Hvdrastis canadensis* L. (Ranunculaceae)	Breast, osteosarcoma, prostate, lung, and liver cancer	Inhibits cell proliferation through mitochondria apoptotic pathway	[84]
Betalapachone		*Tabebuia avellanedae* (Bignoniaceae)	Pancreatic, breast, prostate cancer, promyelocytic leukemia and lung cancer	Topoisomerase I and II inhibition	[85]
Emodin		*Rheum rhabarbarum* (Polygonaceae)	Leukemia, lung, ovarian and liver cancer	Apoptosis induction	[86]
Flavopiridol		*Amoora rohituka* and *Dysoxylum binectariferum* (Meliaceae)	Non-Hodgkin's lymphoma,non-small cell lung, renal cell carcinoma, chronic lymphocytic leukemia &colorectal cancer	Inhibits the advancement of the cell cycle in the G1 or G2 phases.	[87]

Table 2: List of Natural Medicinally Significant Plants towardsLung Cancer and Other Cancer Therapy

Name of plant	Name of Species	Common nameof plant	Name of Compound	Function and Mechanism of action	References
Pink-wheel flower	*Catharanthus roseus*	Pink Periwinkle, Rose Periwinkle and Madagascar periwinkle.	Vincaleukoblastine, Vincristine, Eldisine or Vindesine, Navelbine or Vinorelbine.	Blood Leukemia, lymphomas, breast carcinoma, lung tumor, pediatric solid cancers and others	[88].
Pink trumpet Tree	*Handroanthus impetiginosa*	Pink Lapacho and iperoxo.	Lapachone, Lapachic acid	It be promote like a cure and used for a numeral of human being ailment, as well as cancer.	[89].
Yew plant	*Taxus baccata* var.	Common yew and European yew.	Taxotere or Docetaxel, Pacilitaxel or Taxol.	Lung and breast cancer.	[90].
Marijuana	*Cannabis sativa*	Ganja, Cannabisand Hemp.	Delta,Tetra-hydrocannabino, cannabinoids	Modulates tumor growth	[91].
Evergreen timber tree	*Taxus brevifolia*	Pacific yew or Western yew	Taxol	Lung cancer, Pancreatic cancer, and Breast cancer are all treated.	[92].
Ground lemon	*Podophyllum Peltatum*	Mayapple, American mandrake and Indian apple.	Podophyllotoxin or Podofilox, trans- Etoposide, Podophyllic Acid and	Teniposidum Treatment of lung and testicular tumor.	[93].
Stinking Tree	*Nothapodytes foetida*	Nothapodytes Tree.	Acetylcamptothecin or camptothecin acetate, Camptothecine and Scopolectol	In that tree is used into the production of anti-leukemia and anti-tumoral drugs.	[94].

CONCLUSION

The natural world is a one-of-a-kind source of structures with high phytochemical diversity, many of which have fascinating biological functions and medicinal capabilities. In light of the global rise in various malignancies, an intensive search for innovative lead compounds aimed at expanding curative remedial is crucial. It is difficult to find out the novel functionality as well as composition concerning the possessions of phytochemicals. This is mostly due to the occurrence of a large number of phyto-chemicals, which causes biological responses to become more complicated. Medicinal herbs have been intensively explored for cancer treatment all around the world. Human experimentation with numerous plant species has also taken place. Despite the fact that numbers of studies have looked at potential mechanisms of action for these compounds, the vast majority of them has just offered preliminary screening results and so has not defined any mechanism of action. Furthermore, new research findings suggest that extracts could be employed as a phytotherapeutic adjuvant in the treatment of various stages of lung cancer. This may lead to increased public safety, easier access to health services and as a result in increasing survival of lung cancer patients. Several countries have investigated medicinal plants with antitumor potential, including those used to treat lung cancer. This review focus on many medicinal herbs investigated for anti-cancer activity in lungs and in turns its use in cancer treatment. This could lead in advancement and improved access to health care which could possibly a higher quality of life for lung cancer patients.

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Conflict of Interest

We wish to confirm that there is no conflict of interest associated with the present publication.

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