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A Brief Description of Different Types of Cancers and Role of Some Herbs & Bioactive Compounds in Lung Cancer Management

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ABSTRACT

Cancer immunotherapy has considerably raised patient survival rates and significantly improved patients' quality of life in comparison to the gold standard of care, which includes chemotherapy, radiation therapy, and surgery. Immunotherapy has firmly established itself as a novel pillar of cancer care across the board, from the metastatic stage all the way through adjuvant and neoadjuvant treatment in a wide variety of cancer types. In this overview, the primary emphasis will be placed on the seminal moments in the history of cancer immunotherapy that prepared the way for the cutting-edge treatments that are available today. Cancer treatment that makes use of medicinal herbs and the phytocompounds that can be obtained from those herbs is becoming an increasingly attractive option. It has been demonstrated in a number of clinical studies that the use of herbal medicines in conjunction with conventional therapy can increase survival rates, immunological modulation, and quality of life (QOL) in patients who have cancer. In addition to this, we highlight the challenges and restrictions currently faced by cancer checkpoint immunotherapy as well as the cutting-edge research being conducted in the fields of individualized cancer vaccines, autoimmunity, the microbiome, the microenvironment of tumors, and metabolomics to find solutions to these problems. For hundreds of years, practitioners of traditional medicine have depended on treatments derived from plants. Many studies on their use have been carried out all over the world, and some of the findings have led to the development of medicines that are derived from plants. The global market for medicinal plant products is estimated to be worth more than one hundred billion dollars each year. This research investigates the role, contributions, and utility of medicinal plants in the context of the current strategic methods to disease prevention, notably lung cancer, which is a public health concern. The focus of this research is on the current strategic approaches to disease prevention.

Keywords- Cancer, Lung cancer, Bioactive compounds, Herbs.

I. INTRODUCTION

According to the first recognized characteristics of cancer, there are six primary capabilities that might lead to the development and spread of cancer[1]. According to recent developments in our conceptual understanding of cancer biology that have occurred over the course of the previous decade, the reprogramming of metabolism and the avoidance of destruction by the immune system have lately been proposed as additional hallmarks of cancer. In this paper, we believe that epigenetic alteration should be recognized as a defining

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feature of cancer and a focus for future research into the development of treatments for cancer[2].

Cancer can be identified by its telltale symptoms, which include unchecked cell proliferation and the spread of metastases. The activation of oncogenes and/or the downregulation of tumour suppressor genes are the primary factors responsible for the inactivation of apoptotic mechanisms and the uncontrolled progression of the cell cycle [3]. This holds true in the overwhelming majority of circumstances. In contrast to noncancerous tumours, malignant ones have the potential to spread throughout the body through a process known as metastasis [4]. During this process, the receptors that are responsible for cell adhesion are down-regulated, which is necessary for tissue-specific cell-cell attachment. On the other hand, the receptors that promote cell mobility are up-regulated.

In addition, when membrane metalloproteases are active, cancer cells that have metastatic potential are able to spread physically [5]. This route is supplied by the spread of cancer. There are a variety of different methods that might bring about these changes to DNA as well as the structure of cells. The most common factors that lead to the development of cancer are mutations, chromosomal translocations and deletions, and changes in the expression or activity of signaling pathways[6]. These alterations could cause the activation of genes that inhibit apoptotic pathways or that promote dysregulated cell cycle. The current body of research contains a great number of evaluations that are all-encompassing and cover all of these different procedures[7].

The process of carcinogenesis is one that is not well understood, and the function of epigenetics is also unknown. Recent research has demonstrated that epigenetic alteration plays a crucial role in both the beginning stages of the development of cancer progenitor cells as well as their maturity [8].

This characteristic, which is another hallmark of cancer, can be construed as a factor that contributes to the development of cancer. DNA bases and histones are susceptible to change when subjected to covalent alterations[9]. Recent work done by our research team resulted in the creation of an innovative model for the progression of cancer. According to this model, epigenetic changes play an essential part in the development of therapeutically important cellular features. Epigenetic changes can cause the formation of malignant characteristics in cells even when there are no mutations present[10].

Cancer is still the most common and difficult disease to treat in the modern era[11], despite the best efforts put forth for prevention and the cure attained in a large percentage of malignancies by surgery, radiotherapy, or chemotherapy, especially when discovered early on. The majority of cancer patients still lose their battle with the disease each year, and we are a long way from being able to completely eradicate cancer. Despite enormous investments, oncologists and other medical professionals continue to encounter challenges[12].

Radiotherapy is an increasingly popular form of cancer treatment because to the fact that it spares healthy tissue and has only modest effects on the body as a whole. However, in certain circumstances, cancers that have been treated with radiation might return with radioresistance, which ultimately results in the treatment not working[13]. Even the most cutting-edge treatment has not been able to generate a complete remission, and patients frequently have tumor recurrence and/or distant metastases after radiation therapy. This is despite the fact that there has been substantial advancement and development in the technology of radiation therapy in recent years[14]. Chromosomal rearrangements and genomic instability are known to be caused by radiation; many of these changes are similar to those that are observed in human cancers. Irradiation with sub-lethal doses of photons has also been shown to boost the migratory and invasion capabilities of cancer cells, which in turn promotes the spread of the disease to other organs[15].

Hadron therapy is a relatively recent method of treating cancer that involves irradiating tumors with light nuclei (such as alphas and carbon ions) in addition to protons (which is known as proton therapy). Two of its primary advantages over traditional radiation are precision ballistics, which have a finite range and maximal dose deposition at the end of the ions' path (also known as the Bragg peak).

Additionally, greater biological efficiency can be found in the area surrounding the Bragg peak[16]. This permits more exact targeting of the tumor, resulting in little damage to the surrounding healthy tissue. Even though hadron therapy seems to have more promise, particularly in the fight against radio-resistant cancers, more research is still required to assess its long-term implications in terms of recurrence and/or other symptoms[17].

Cytotoxic medications are the foundation of chemotherapy, despite the fact that they frequently induce incapacitating side effects and a decrease in quality of life for patients. A growing number of anticancer treatments are currently in the research and development stage. Each of these medicines will target a distinct group of molecules that are known to contribute to the beginning, advancement, and spread of cancer[18].

As a result, researchers and medical professionals are now focusing their efforts on developing personalized cancer treatments for individual patients. On the other hand, due to the dynamic nature of cancer cells, it may be challenging to develop universally applicable personalized treatments that can be administered to such a large number of patients. The high cost of this method of treatment presents yet another possible obstacle associated with it[19].

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II. TYPES OF CANCER

a. Lung Cancer

In the year 2020, breast cancer in women will be the sole cause of death due to cancer. This prediction is based on current trends. Lung cancer, often known as lung ca, has been the most dangerous and widespread form of the disease for a good number of years. Mortality and morbidity due to Lca are more likely to afflict men than they are women in general. Men are also more likely to be affected by Lca. On the other hand, this ratio could shift quite a bit depending on where you are. [20] Lung cancer continues to be the leading cause of mortality due to cancer and is the most common type of the disease to be identified in men. Although it is the third most common form of cancer in women, lung cancer is the second leading cause of mortality due to the disease, ranking behind only breast cancer and colon cancer respectively. It is anticipated that by the year 2020, there would be over 2.2 million newly diagnosed cases of lung cancer, representing a jump of 36.6% from the number of cases diagnosed in 2008. It is projected that lung cancer would be the cause of death for 1.8 million persons in the year 2020[21], representing a jump of 30.4% from 2008. In 2018, we project that the ASRw for Lca will be 13.1, and in 2020, we project it will be 13.3. This is lower than the ASRw that was recorded in 2012, which was 14.0, and in 2008, which was 15.2, which was the highest on record. In spite of the fact that the overall number of Lca cases has grown over the course of time, this has not been the case [22].

It is now a well-established fact that the development of Lca cancers can be contributed to by both inherited and environmental factors. The primary reason for the rise in the number of people diagnosed with lung cancer all over the world is the continued use of tobacco products. The incidence of lung cancer, both in terms of newly diagnosed cases and fatalities, varies substantially across the globe's various areas. In developing and transitioning regions (such as Africa), they are substantially lower, whereas in established regions (such as North America and Europe), they are three to four times higher [23]. They are a representation of the temporal patterns that are formed by the pandemic of cigarette smoking, with a lag time of around 20 years between changes in smoking prevalence and changes in the rates of lung cancer incidence and death. This lag time is due to the fact that there is a correlation between smoking and lung cancer. Since radon is the second leading cause of lung cancer in North America, the International Agency for Research on Cancer (IARC) has classified human exposure to radon as carcinogenic (IARC Group 1) since 1988. Radon is the second leading cause of lung cancer in North America. According to a report published by the International Agency for Research on Cancer (IARC) in 2013, particulate matter (PM) in outdoor air pollution is a factor in the development of lung cancer in humans and is carcinogenic. There is a correlation between arsenic poisoning in drinking water and food sources and an increased risk of developing lung cancer.

According to the International Agency for Research on Cancer and the World Health Organisation, the incidence of lung cancer among women in the MENA region in 2018 was lower than the incidence globally[26]. This information was gathered from both organisations. Between Yemen and Lebanon, the prevalence of lung cancer among women ranged anywhere from 4.2% to 23.0%. Lebanon is a growing nation in the Middle East with a population of approximately 6 million people as of the year 2016. According to the HDI cutoff for high-population nations in 2017, Lebanon's health index for the time period covered by the data in this book was on par with that of the developed world. The Human Development Index (HDI) is a metric that provides an all-encompassing evaluation of a nation's performance with regard to the enhancement of life expectancy, educational attainment, and economic prosperity. The vast majority of Lebanon's inhabitants calls one of the country's several urban hubs their permanent home. [25] Research found that lung cancer was the second most prevalent form of cancer in men (ASRw: 28.3), second only to prostate cancer (ASRw: 28.5), and the third most common form of cancer in women (ASRw: 11.87), second only to colorectal cancer (ASRw: 11.90). These statistics were taken from the 2004 Cancer Statistics Review published by the American Cancer Society.

b. Colorectal Cancer

It is estimated that over 550,000 individuals lose their lives to colorectal cancer (CRC) each year, making it the sixth greatest cause of death due to cancer worldwide. The diagnosis of CRC accounts for 10% of all new cases of cancer. Even if 25%-50% of CRC patients present at an early stage but subsequently have recurrence or metastasis, only 14% of patients will still be alive after five years if they are diagnosed with CRC at an advanced stage. This is despite the fact that CRC patients can initially present at an early stage[27].

Changes to the normal colonic epithelium, such as the production of adenomatous polyps that can expand in number and size, contribute to the onset of colorectal cancer by accumulating mutations at both the molecular and epigenetic levels. This is how colorectal cancer is initiated.

Even while a polyp with malignant features does not necessarily progress to an invasive cancer, it nevertheless has the potential to metastasize. The polyps develop uncontrollably, allowing them to infect neighbouring tissues like the digestive tract wall and then spread across the body's lymphatic and circulatory systems[28].

Factors that increase the risk of developing colorectal cancer (CRC) include age, a personal or family history of the disease, physical inactivity, obesity, a poor diet, smoking, and alcohol use. Colorectal cancer rates

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are on the rise in industrialised countries due to a number of factors, including an ageing population, poor modern dietary habits, and an increase in the number of people engaging in dangerous behaviours like smoking, not getting enough exercise, and being overweight[29].

The early diagnosis and effective treatment of colorectal cancer still face considerable clinical hurdles. This highlights the critical need to discover novel chemicals linked to tumours that can be utilised to create game-changing clinical diagnostics and therapeutic targets for a wide range of cancers[30].

Screening for colorectal cancer is performed with the goal of locating and treating SSLs and adenomas at an earlier stage of the disease. Stool-based testing, colonoscopy, sigmoidoscopy, and computed tomographic colonography (CTC) are some of the screening approaches that can detect advanced adenomatous polyps[31]. However, colonoscopy is the most effective screening method for finding SSLs. After endoscopic polyp ectomy, there is a decreased risk of developing colorectal cancer as well as a decreased risk of dying from CRC. The "ideal" screening test would have good sensitivity and specificity, be fully non-invasive, risk-free, practicable, and affordable, and would be able to detect the presence of the condition in question[32].

Tests for colorectal cancer (also known as CRC) can be divided into two categories: those that can be utilized on their own (such as colonoscopy), and those that, if they are positive, require further testing in the form of a colonoscopy. The colonoscopy is the only screening technique that does not consist of two parts. If you get a positive result from any of the other methods of CRC screening, you will need to have a follow-up colonoscopy. This is one of the significant drawbacks of these other methods[33]. These tests include FS, CTC, and CCE that are based on stool samples. Organized screening makes more effective use of this two-step testing approach, although it does call for substantial support from the underlying system in order to be fully implemented. The vast majority of screens only involve a single procedure, and in the United States (US), only a handful of healthcare institutions conduct integrated, systematic screening. People who are unable to have a colonoscopy or a faecal immunochemical test (FIT), or who have incomplete colonoscopies, require additional two-step procedures. These procedures include the FS, a multitarget stool DNA test (mts-DNA), colonoscopy tissue culture evaluation (CTC), or colonic culture and evaluation (CCE). Comparative research on the two has been conducted by a relatively small number of researchers. [34] This article contains a description of many screening procedures as well as an overall summary of them.

The American Cancer Society (ACS) recommends that people age 45 and older who have an average risk of colorectal cancer get screened using either a high-sensitivity stool-based test or a visual examination. Both of these screening methods can be performed at home. This recommendation is contingent on the patient's willingness to undergo testing as well as the accessibility of the relevant diagnostic tools. If a screening test that does not involve a colonoscopy produces positive results, a colonoscopy should be done as soon as it is practically possible.

The restriction that screening should begin at age 45 is a guideline that should be taken very seriously. Adults older than 50 years old are strongly advised to take part in tests on a regular basis[35].

c. Bladder Cancer

The tenth most prevalent form of the disease found all over the world is bladder cancer, which is also referred to as urinary bladder cancer. This form of cancer is seen more frequently in a variety of areas across the globe, particularly in the industrialised Northern hemisphere. The cancer of the urinary system remains the most common type of cancer in the population as a whole. Urine is collected and stored in the urinary bladder, which is a sac-like structure located in the lower abdomen. Urine is stored in the urinary bladder. Urine is eliminated from a person's body when they urinate [36]. Urine is flushed out of the system. In order for the body to have adequate space for the urine that it generates, the urothelial cells that line the urinary bladder and the urinary tract must undergo a process that causes them to become flatter. The smooth muscular lining of the bladder is capable of dilation for the purpose of accommodating a bigger volume and contraction for the purpose of forcing urine through the urethra. The cells that line the urinary tract and the bladder are called urothelial cells. These cells are continually exposed to environmental substances that have the potential to cause mutations in the cells.

These poisons are eliminated from the body through the urine, where they are filtered out by the kidneys. It should not come as a surprise that the vast majority of cancer cases, particularly in industrialized countries, are caused by urothelial cells, which are mostly situated in the bladder. There is a significant correlation between exposure to secondhand smoke from tobacco products and various types of environmental and occupational contaminants. There is a fourfold difference in the rates of bladder cancer between men and women, and it is possible that this disparity is attributable to men's larger exposure to cigarette smoke and occupational hazards. For smokers, the chance of developing bladder cancer is second only to the risk of developing lung cancer[37]. It is one of the less common cancers to be found by accident during an autopsy, and bladder cancer is one of those malignancies. Patients who have just been diagnosed with bladder cancer have an asymptomatic gross hematuria in 85% of cases, and nearly all patients have microscopic hematuria. The use of the Valsalva maneuver is frequently associated with brief episodes of blood in the urine. For this reason, a comprehensive evaluation of hematuria for bladder cancer requires the

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use of diagnostic modalities such as cystoscopies of the bladder, imaging of the upper tract, and cultures of the urine[38].

Despite recent advancements in treatment, such as improved detection, robotic surgery, and immunotherapy, bladder cancer continues to be one of the major causes of mortality from cancer worldwide, particularly in industrialized countries. The overall medical expenses associated with treating a patient who has bladder cancer are the most expensive of any malignancy. The expense of providing medical attention to a single patient is from $129,000 and $251,000 on average. In the European Union (EU), it is expected that yearly directed medical expenses will reach €4.9 billion, whereas in the United States, it is projected that annual directed medical expenses would exceed $4 billion. Therefore, a better understanding of the epidemiology of bladder cancer and the factors that put people at risk is necessary for cancer prevention and burden reduction[39].

d. Melanoma

Melanocytes, which create the UV-blocking pigment melanin, reside in the epidermis' basal layer. With only about 1500 melanocytes per mm2 in the epidermis and a division rate of less than twice yearly, melanocytes are a small but significant fraction of skin cells. Keratinocytes release beta-melanocyte stimulating hormone (-MSH) in response to ultraviolet (UV) irradiation. After binding to the melanocortin 1 receptor (MC1R), this hormone triggers melanin production in melanocytes. The cytoplasm of neighbouring keratinocytes is accessible via extensions on melanocytes that resemble fingers[40]. This is the mechanism by which melanin is communicated between different cell types.2 Sunlight triggers the production of melanin in keratinocytes, which protects the cell nucleus from the sun's cancer-causing ultraviolet (UV) rays. Maturation of keratinocytes involves keratinization, followed by anucleation (the removal of the cell's nucleus), and lastly cell death. This is why the dead keratinocytes and the melanin pigment in keratinocytes work together to shield the living cells just beneath the skin's surface[41].

Both eumelanin (which gives skin its black or brown colour) and pheomelanin (which gives hair and eyes their red or yellow hue) are produced by melanocytes. Although the total number of melanocytes in the skin is essentially constant across different skin tones[42], the ratio of eumelanin to pheomelanin in the skin is what ultimately defines skin colour. Having darker eumelanin, which provides a more effective UV barrier, lowers the risk of developing skin cancer in people with darker skin tones. This explains why those with darker complexion tend to have a lower risk overall. Not only does pheomelanin not provide enough defence against UV rays, but its production results in the creation of carcinogens[43]. UVA radiation has been shown to promote DNA damage by damaging pheomelanin, which in turn increases the production of reactive oxidative species (ROS)[44]. Those with naturally fair skin that does not tan, blond or red hair, and light eyes have a substantially higher risk of developing melanoma than the average person. This danger is well above typical levels[45].

The MC1R gene is involved in the process of controlling pigmentation in the skin, hair, and eyes. Individual differences in MC1R activity are due to polymorphisms in the MC1R gene[46]. Pheomelanin production that is mostly reddish-yellow, combined with non-tanning fair skin, blue eyes, and blonde hair, are the most common symptoms of reduced MC1R function, which is caused by gene variations. When MC1R is active, the production of the pigment eumelanin takes place, which is responsible for dark and brown skin.1 Those who have variants of MC1R that function less effectively are more likely to acquire mutations because they are subjected to more UV damage[47]. The accumulation of mutations in particularly sensitive areas of the genome is what leads to the development of malignant skin conditions[48].

Only 22.1% out of every 100,000 Americans will develop melanoma, according to data published by the Centres for Disease Control and Prevention (CDC). This cancerous growth begins in cells called melanocytes[49]. Although it accounts for only 4% of all cases of skin cancer, it is the leading cause of death from the disease in 75% of all cases[50]. According to projections made by the American Cancer Society, there will be 96,480 newly diagnosed instances of melanoma in 2019, with 7,230 people succumbing to the disease[51].

e. Prostate cancer

On average, a guy is 67 years old when he receives the diagnosis that he has prostate cancer. Prostate cancer can frequently be cured if it is detected at an early stage; however, even after the cancer has spread, it frequently responds to treatment[52]. Depending on how slowly or swiftly the tumour grows, some patients may live for a very long time even after the cancer has migrated to distant areas like the bone. Among American men diagnosed with prostate cancer between 2012 and 2018, those with local or regional disease had a 5-year relative survival rate of better than 99%, whereas those with distant disease had a rate of 32%[53]. The overall survival rate was 97%. The treatment technique is mostly determined by the patient's age as well as any prior diseases. When choosing on a course of therapy, it is essential to make a risk-benefit analysis and take into account any potential adverse effects.

Even in cases when the disease is treated with a conservative approach and no attempt is made to cure the condition, many people, particularly those whose tumors are circumscribed, may pass away from other conditions without ever being debilitated by prostate cancer.

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Positive results can almost certainly be attributed to screening with the prostate-specific antigen (PSA) test[54]. Patients with asymptomatic tumours that are unlikely to be lethal can be identified using this test. It is estimated that between 30 and 70 percent of men older than 60 have these clinically indolent tumors, and this estimation is based on autopsy data collected from individuals who passed away from causes other than prostate cancer.

Any examination of survival following therapy for prostate cancer, as well as any comparison of the various treatment modalities, is made more difficult by the fact that there is evidence suggesting an increase in the discovery of tumors that are not fatal. Comparisons of treatments that are not based on random sampling can be clouded by the presence of biases in patient selection as well as temporal trends[55].

Long-term relative survival rates after a diagnosis of prostate cancer, for example, improved dramatically as more sensitive means of diagnosis were developed. These are the findings of a population-based study that was carried out in Sweden between the years 1960 and the late 1980s, long before the use of PSA for the purposes of screening. The study was carried out before the use of PSA for screening purposes. This investigation covers the period of time beginning in the early 1960s and continuing through the late 1980s. In spite of the fact that careful waiting, active surveillance, and palliative hormonal treatment were the standard for the treatment of localised prostate cancer during the rest of the timeframe, approximately 150 radical prostatectomies were performed annually in Sweden in the late 1980s [56]. In spite of the fact that patient waiting is the standard practise, this was actually the situation. If all cases of prostate cancer detected between 1960 and 1964 were fatal, then according to the estimates of the study, at least 33 percent of tumours diagnosed between 1980 and 1984 are projected to be non-fatal. [57] This assumption is based on the assumption that all cases of prostate cancer diagnosed between 1960 and 1964 were fatal. Their assumption was founded on the fact that between the years 1960-1964, all of the instances resulted in a fatal outcome. Since PSA screening has become the primary method for diagnosing prostate cancer in the United States, there has been a significant increase in the ability to detect low-risk kinds of prostate cancer [58].

f. Pancreatic cancer

Adenocarcinoma of the pancreas is a type of cancer that spreads quickly and has a poor outlook for patients. The most recent data on pancreatic adenocarcinoma, including its prevalence, risk factors, pathogenesis, diagnostics, potential biomarkers, and treatment approaches [59]. It is safe to infer that most references to "pancreatic cancer" relate to ductal adenocarcinomas, even though this study focuses exclusively on pancreatic adenocarcinoma as its primary area of investigation. This is the situation as a consequence of the high incidence of pancreatic ductal adenocarcinomas. In terms of the overall incidence of cancer, pancreatic cancer ranks only fifteenth, despite the fact that it is responsible for the seventh-highest number of cancer-related deaths globally [61]. According to projections made by the organisation Globocan, there will be 45,8918 newly diagnosed cases of pancreatic cancer in 2018, which will ultimately result in the deaths of 43,2242 persons all over the world [62]. The incidence is at its maximum in Africa and South Central Asia among older adults, whereas it is at its lowest in Europe and North America among young adults.

This lends validity to the view that the developed world has a higher overall incidence rate than the developing world. Wong et al. observed that in countries with a higher human development index, both male and female pancreatic cancer occurrences were higher[63]. This lends credence to the observation that the developed world has a higher human development index**.**

g. Uterine cancer

This year, nearly 60,000 new cases of uterine corpus cancer will be discovered in American women, and the disease will be responsible for more than 11,000 deaths. As the most common type of gynecologic malignancy in women, this makes it the most concerning[64]. Endometrial carcinomas are responsible for the vast majority of these occurrences, whereas sarcomas are responsible for fewer than ten percent of all uterine corpus cancers[65]. Endometrioid carcinomas are responsible for roughly 83 percent of all cases of malignancy that occur in the uterine corpus[66]. About one to two percent of endometrial carcinomas are clear cell carcinomas, while four to six percent of endometrial carcinomas are the more aggressive serous and papillary serous carcinomas[67]. If endometrioid carcinomas of type 1 are to be effectively understood, controlled, and possibly prevented, they must be differentiated from type 2 serous endometrial carcinomas and other very aggressive non-endometrioid carcinoma histotypes. This is necessary in order to distinguish between the three[68].

Endometrial hyperplasia (EH) is a condition that is characterised by uncontrolled endometrial development that is driven by endogenous or exogenous oestrogen and is not challenged by progesterone or progestins. The prevalent view believes that the majority of instances of endometrial endometrioid cancer begin with some kind of endometrial hyperplasia (EH). Endometrioid cancer can be identified by its hallmark characteristics, which include microsatellite instability caused by mistakes in mismatch repair (MMR) and a virtually diploid karyotype [69]. Endometrioid carcinoma is a subtype of endometrial cancer that develops from atypical premalignant lesions known as endometrial intraepithelial neoplasia (EIN). Endometrial intraepithelial neoplasia (EIN) is another name for

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endometrioid carcinoma. Both endometrioid intraepithelial neoplasia and uterine endometrioid carcinomas, which are caused by hormones, generally exhibit ER and PR. Ongoing research is being conducted to investigate the elements that lead to endometrial cancer; however, new factors, such as insulin resistance and hyperandrogenemia, are being investigated as possible contributors [70].

h. Thyroid cancer

After undergoing histological analysis, the FNA specimens revealed the presence of four distinct types of thyroid cancer. Papillary thyroid carcinoma accounts for around seventy to eighty percent of all cases of thyroid cancer. Patients are regarded to benefit the most from having papillary thyroid carcinoma as opposed to other types of thyroid cancer due to the fact that it grows and spreads slowly [71]. Due to the presence of several papillary and follicular components, this location is ideally suited to support the growth of adenocarcinomas.

Although it is more prevalent than papillary thyroid carcinoma and may be connected to iodine deficiency, only about 14% of thyroid tumours are follicular thyroid carcinoma. This is despite the fact that it is more common than papillary thyroid carcinoma. The treatment for Hurthle-cell carcinoma is the same as that for follicular carcinoma [72], as Hurthle-cell carcinoma is a subtype of follicular carcinoma.

About three percent of all thyroid malignancies are caused by what is known as medullary thyroid carcinoma. These cancerous growths, which usually manifest in the thyroid gland, originate in cells that are not part of the thyroid gland. They have been related in certain cases to a condition known as multiple endocrine neoplasia type 2, which affects a number of different endocrine glands. Because cancers like medullary carcinoma cause an excessive amount of calcitonin to be produced, this hormone might be utilised as a diagnostic tool. Although it only accounts for approximately 2% of all thyroid tumours, anaplastic thyroid carcinoma is the most lethal form of thyroid cancer because of its rapid spread to lymph nodes and other organs. This is despite the fact that it only accounts for around 2% of all thyroid tumours. Malignancies of the thyroid include not only the aforementioned four types of thyroid cancer but also lymphomas and variants of these diseases. Cancers of the papillary and follicular cells of the thyroid are examples of well-differentiated thyroid cancers. On the other hand, medullary and anaplastic malignancies of the thyroid are examples of poorly differentiated thyroid cancers.

It is possible that preoperative staging and imaging will be of significant help in improving both the prognosis and the treatment plan for a patient who has thyroid cancer. There is a correlation between the size of the primary tumour and the likelihood of lymph node involvement in the cervical region, although in other cases, the likelihood of lymph node involvement is independent of the size of the underlying tumour. To assist in the identification of possible metastases, preoperative neck ultrasound for the contralateral lobe and cervical lymph nodes is recommended for all patients undergoing thyroidectomy for cancer; however, neck ultrasounds only identify fifty percent of the lymph nodes that are discovered during surgery [73].

In the event that it is essential for the treatment of the disease, it is possible to confirm lymph node metastases with the use of ultrasound-guided fine-needle aspiration cytology (FNA) on the suspicious lymph nodes and/or measurement of thyroglobulin in the needle washout. You are free to choose either of these two paths. The next step is to determine the present stage of the development of the cancer using the information gathered.

i. Oral and Oropharyngeal cancer

In Eastern Europe, France, and numerous regions of South America (including Brazil and Uruguay), high rates of cigarette usage and alcohol consumption are related with the highest prevalence of oral cancer [74]. Betel quid, which can be chewed with or without tobacco or areca nuts, is commonly used in India, Papua New Guinea, and Taiwan, China. These three countries all have among the worst rates of oral cancer incidence and mortality in the world. Betel quid can be chewed with or without tobacco or areca nuts. When age is taken into account, the incidence rate among men is approximately twice as high as that among women [75]. There is no discernable trend in incidence rates from low and middle income countries (LMICs) to high income countries (HICs), when nations are classed by their level of economic development [76]. The gender discrepancy between male and female cancer incidence rates is greater than fivefold in nations that have relatively complete data on cancer registration, with India having the highest and Belarus having the lowest incidence rates respectively. Estimates of the age-adjusted incidence rate of oral cancer could have significant variations across regions and countries. Oral cancer is most usually seen on the tongue, whereas the buccal (cheek) mucosa is the most commonly affected area in South and Southeast Asia. The most common site for oral cancer is the tongue. In Western countries, the most significant factors are alcohol and tobacco, while in South and Southeast Asian countries, the most significant contributors are betel quid and tobacco [77]. The fundamental factors can be somewhat different from one nation to the next. Death rates due to oral cancer range from 1 to 15 per 100,000 people per year around the globe; however, death rates in Eastern European nations such as the Czech Republic, Hungary, and the Slovak Republic are over 10 per 100,000 people each year. The mortality rate associated with oral cancer is influenced by a number of factors, including the prevalence of the disease, the availability of various treatment options, and regional variations in the frequency of the disease [78].

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There is a substantial association between the rising rates of cigarette and alcohol consumption, which are evident among both men and women, and the rising rates of death. This correlation is very high. In Karachi, Pakistan, and Taiwan, China, an increase in the number of cases has been attributed, respectively, to higher rates of cigarette and areca nut use, as well as higher rates of alcohol use. Oral cancer incidence has been gradually declining over the past two decades due to a reduction in both the number of persons who smoke and the amount of alcohol they consume. On the other hand, white men in the United States have recently exhibited an increase in malignancies near the base of the tongue. This trend may be driven by the human papillomavirus, which is abbreviated as HPV[79].

Incidence and mortality rates for oral cancer have been progressively decreasing across Europe over the past two decades, with the exception of a few nations in Central Europe where they have been on the rise due to shifts in alcohol and tobacco use. In these countries, the decline in incidence and mortality rates has been caused by a combination of factors[80]. Since the early 1990s, when they reached their highest point, death rates from oral cancer have been gradually declining in France. This trend has coincided with a decline in the amount of alcohol that individuals consume on an individual level[81]. Both the frequency of the disease and its fatality rate have stayed essentially unchanged in nations such as the Nordic countries, Russia, and the United Kingdom. While death rates have been on the down in Australia, Hong Kong Special Administrative Region of China, and China overall, they have been on the rise in Japan and the Republic of Korea.

j. Breast Cancer

Carcinogenesis refers to the process through which normal cells, tissues, or organs undergo malignant transformations that can lead to the development of a wide variety of cancers. This process can take place in any cell, tissue, or organ[82]. Among them are the capabilities of evading death by apoptosis, dividing without limit, boosting angiogenesis, ignoring signals that inhibit growth, inducing its own growth signals, metastasizing, and rejecting signals that inhibit growth[83]. The onset of cancer can be attributed to a variety of causes, including predispositions that are passed down via families as well as environmental influences. Cancer now ranks among the main causes of death around the world due to the worrisome annual growth in the number of people who lose their lives to the disease[84]. Most cancers do not always cause death, but they might reduce one's quality of life and add to the expense of treatment.

According to GLOBOCAN 2020, there will be 2.3 million new cases of breast cancer detected over the world this year[85], making it the sixth leading cause of cancer death this year. In transitioning countries (Melanesia, Western Africa, Micronesia/Polynesia, and the Caribbean), breast cancer deaths are reported at a higher prevalence (an incidence rate approximately 88% higher) than in transitioned countries (Australia/New Zealand, Western Europe, Northern America, and Northern Europe). Reason being, the incidence of breast cancer is greater in developing nations than in developed ones[86]. Breast cancer rates can be lessened and the disease can be treated more effectively if a number of preventative activities are taken, such as engaging in generally healthy behaviours and participating in screening programmes. Currently, the task of developing efficient strategies for the worldwide management of breast cancer falls on the shoulders of the Breast Health Global Initiative (BHGI)[87].

Breast cancer accounts for 19.6 million of the estimated 107.8 million DALYs (days adjusted for life) lost worldwide due to malignant neoplasms in women, as reported by the World Health Organisation (WHO). The number of new cases of breast cancer diagnosed worldwide in 2020 is projected to be 2.26 million [95% UI, 2.24-2.79 million]. It is projected that 29% of all female cancer diagnoses in the United States will be due to breast cancer[88]. Using newly available data from GLOBOCAN 2018, researchers found a significant positive relationship between the HDI and ASIR of breast cancer. Based on statistics from 2020, countries with a high HDI had the highest ASIR (75.8 per 100,000), while those with a medium or low HDI had the lowest (27.8 and 36.1, respectively).

Among females, breast cancer is the most prevalent form, and it is the leading cause of cancer-related deaths worldwide. In 2012, the death rate from breast cancer was 13.6 for every 100,000 persons around the world after adjusting for age. This amounts to 684,996 fatalities (95% uncertainty interval: 675,493-694,633). Despite the fact that the incidence rates are highest in industrialized nations, it is expected that by the year 2020, Asia and Africa will be responsible for 63% of all deaths. Survival rates for women diagnosed with breast cancer are lowest in countries with low per capita incomes and a large number of countries with middle-incomes, while they are highest in countries with high per capita incomes[89].

0.30 was the mortality-to-incidence ratio (MIR) for breast cancer in the year 2020. This ratio is a measure of the percentage of patients who survive for five years after their diagnosis[90]. When the clinical stage of breast cancer is taken into consideration, the five-year survival rate for localized cancer is 89.6%, while the survival rate for regional cancer is 75.4% in highly developed healthcare systems such as those found in Hong Kong, Singapore, and Turkey. Survival rates for both localised and regional breast cancer were 76.3% and 47.4% in developing nations such Costa Rica, India, the Philippines, Saudi Arabia, and Thailand, respectively[91].

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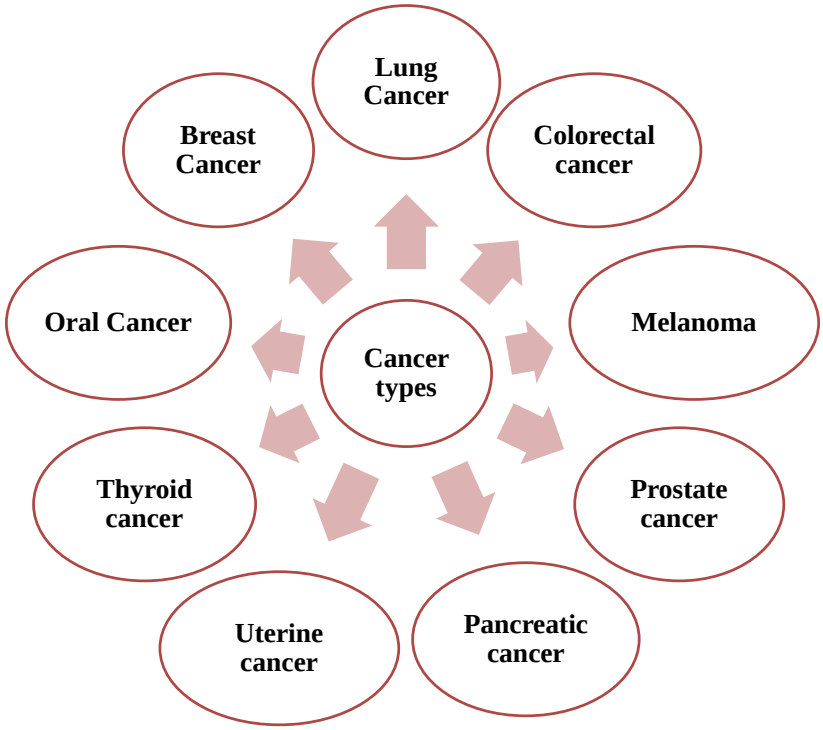

Fig 1: Types of Cancer

III. HERBS USED IN LUNG CANCER

The most popular preparations of plants that are used for therapeutic purposes are beverages like tea and infusions of herbs [92]. In recent years, there has been an increase in the use of these compounds in an effort to reduce the risks of cardiovascular disease and cancer. Because of this, it is even more important to characterise the effect that these substances have. Numerous herbal teas and infusions have been found to prevent the growth of human lung cancer cells, and a significant number of these are used on a consistent basis in Hong Kong, Macau, Taiwan, and Mainland China [93]. Although these medications are frequently prescribed to cancer patients, very little is known about the impact they have on the cells of the body. In both preclinical and clinical investigations, herbal extracts have demonstrated potential as anticancer medications, with the treatment of lung cancer showing the greatest promise as a potential application of this potential. According to the findings of the research, the principal mechanism of action demonstrated by these extracts is that of inducing apoptosis in the target cells. The majority of the content focuses on the achievements of herbal treatments originating in China [94]. A number of these studies came to the conclusion that apoptosis, which occurs in lung cancer cells, may have been associated to the mode of action of the extracts. This one is fairly good in terms of the response when compared to the one observed with more typical forms of chemotherapy treatment [95]. Several different medicinal herbs that have an anticancer effect especially target the cells that make up lung cancer. In cell culture and animal models of lung cancer, the traditional Chinese herb selaginella tamariscina was proven to suppress the growth of cancerous lung cells and prevent their spread. Crocus sativus L. is a flowering plant that is most well known as saffron. Its aqueous extract is widely utilised in a variety of culinary applications as well as complementary and alternative cancer treatments. According to the findings of research into the effect that it had on cancer cells, the ability to inhibit the progression of lung cancer was linked to the induction of apoptosis. The leaves of Toona sinensis contain a bioactive component that has been found to delay the progression of H441 xenograft tumours in experimental models of both treatment and prevention. This effect was seen in both types. During the in vitro testing of the natural product, there was evidence of cell death. It was shown that the methanolic fraction of Sesbania grandiflora had very powerful antiproliferative effects in human lung cancer cell lines. It was shown that cells that had high levels of reactive oxygen species (ROS) intermediates were more likely to undergo apoptosis [96]. The investigation on Prunella's active components discovered that total triterpenes and total phenols, both of which were found to have antilung cancer action, had synergistic effects when combined, according to the findings of the study. Both of these compounds were found to have antilung cancer action individually. This demonstrated that the anti-lung cancer activities of the chemical were the consequence of a variety of elements interacting synergistically with one another. The Descurainia sophia plant is revered for its medicinal qualities in Korea, where locals have used it

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for treatment for hundreds of years. Studies using gene expression profiling have indicated that the anticancer action of D. sophia seed ethanol extract against lung cancer is linked to the change of metabolic and signalling pathways. Patients with lung cancer who took a butanol extract of mountain ginseng experienced a reduction in the amount of cell proliferation that was occurring in their bodies. These techniques were employed to increase the activity of p53 while simultaneously lowering the activity of NF-B [97].

In addition, a substantial amount of study has been conducted on the potential anticancer effect of compounds that have been derived from a diverse array of medicinal plants. [6] Gingerol, a potent component of ginger (Zingiber officinale), was given to mice that had been injected with B16F10 melanoma cells before to the experiment. As a direct consequence of this, the mice exhibited a marked reduction in the quantity of lung metastases [98]. Embelin, which can be found in the fruits of the Embelia ribes plant, has been demonstrated to contain anticancer potential against lung cancer cells. This is in addition to its great array of other medicinal capabilities. Embelin can be found in the fruits of the Embelia ribes plant. Recent studies suggest that the p38 and JNK pathways are involved in the partial mediation of embelin's induction of apoptosis in cells. Salvia miltiorrhiza Traditional Chinese medicine has made use of the medicinal plant bunge, sometimes commonly referred to as danshen, for over a thousand years. It has been found that the diterpene tanshinone I, which is only found in this particular species, can slow down the development of lung cancer [99]. An animal model did not develop lung tumours as a result of exposure to the chemical because it has the potential to inhibit cell proliferation in the S and G2/M stages of the cell cycle.

This ability is what led researchers to conclude that the chemical is responsible for the absence of the disease. It was discovered that the carbazole alkaloid girinimbine, which was derived from Murraya koenigii Spreng, might inhibit the growth of lung cancer cells by triggering apoptosis via both the intrinsic and the extrinsic pathways. Non-small cell lung cancer cells were induced to self-destruct when treated with capilliposide, which was produced from the Lysimachia capillipes herb used in traditional Chinese medicine. After the patient received treatment in vivo, the growth of the tumour in the xenografts was greatly inhibited. In vitro studies showed that capilliposide caused mitochondria to undergo apoptosis, which was demonstrated by an increase in the formation of intracellular reactive oxygen species (ROS). In China, a supplement made from an extract taken from the root of the Scutellaria baicalensis plant is frequently given to people suffering from lung cancer. Recent investigations[100] have established a connection between its function and the substances baicalin, baicalein, and wogonin. In the laboratory, subamolide A extracted from Cinnamomum subavenium was found to be effective at eliminating lung cancer cells. These cells underwent apoptosis as a direct result of mitotic catastrophe, which was triggered by reactive oxygen species (ROS). It has been demonstrated that the monoterpene terpinen-4-ol, which is found in the oils of many aromatic plants, has an anticancer impact on non-small cell lung cancer (NSCLC) cells by triggering death through the mitochondrial apoptotic pathway [101]. In Taiwanese traditional medicine, the Davallia divaricata plant has a long legacy of usage in the treatment of lung cancer. Because this plant contains davallic acid, extracts of it have the potential to be used in medicinal treatment. Recent research[102] has indicated that this molecule is responsible for oxidative stress, which ultimately leads to the death of lung cancer cells. The total flavonoids found in Daphne genkwa were able to limit the formation of tumours and the spread of metastasis by protecting the host immunocytes and their potential for proliferation while selectively reducing the growth of cancer cells. In this subfraction, Daphnodorin B was the predominant species [103].

In addition, a number of studies have shown that the adverse effects of chemotherapy can be lessened by using it in conjunction with alternative treatments or herbal remedies. When combined, the traditional Chinese medicine Xiao-Ai-Ping and the cancer-fighting agent cisplatin produce a synergistic growth-suppressing impact in LLC xenografts. Infiltration and activation of CD8+ T cells are encouraged as a means of accomplishing this goal [104]. In traditional Chinese medicine, marsdenia tenacisima has a long history of use as a cancer treatment. In patients who had non-small cell lung cancer (NSCLC), it boosted the efficacy of the tyrosine kinase inhibitor gefitinib. This effect occurred regardless of the patients' EGFR status. When plant extracts such as doxorubicin or cisplatin were combined with plant extracts such as Phyllanthus emblica and Terminalia bellerica, there was a synergistic influence, and there was the potential to use lower doses of the chemotherapy drugs. [105] Additionally, there was the potential to use lower doses of the plant extracts. The cancer-fighting properties of the traditional Chinese medicine known as Fuzheng Fangai tablet (FZFA) have been demonstrated. Recent studies have demonstrated that FZFA and cyclophosphamide (CTX) suppress the SOCS/JAK-STAT pathway and inflammatory cytokine responses, which dramatically slows the growth and spread of LLC. It was also discovered that the combination formulation was more effective than CTX on its own [106]. Osthole, a chemical that has the potential to be used in medicine, can be produced from a diverse array of plant materials. When cisplatin, one of the most powerful chemotherapeutic medications used in the treatment of lung cancer, was combined with osthole, the results revealed that growth suppression and activation of apoptosis were increased. This was the case even though both of these processes were already taking place. A combination of platinum-based chemotherapy

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and traditional Chinese medicine including astragalus may increase the effectiveness of both treatments, according to the findings of a meta-analysis of randomised clinical trials. Fig 2. According to the findings of a clinical research, the use of conventional chemotherapy in conjunction with traditional Chinese medicine for the treatment of non-small cell lung cancer improved short-term therapeutic efficacy and increased median survival, but it had no detectable influence on the median time to disease progression [107].

There have been a great deal of investigations done, and a number of anticancer medicines that are derived from natural components have been developed into effective chemotherapeutic cancer medications. The potential for chemotherapy to have adverse results and repercussions includes, among other things, the development of toxic side effects and drug resistance. Therefore, additional research is required to uncover naturally occurring chemicals that are equally as useful while having less side effects that are undesirable [108]. Evidence from clinical trials designed to combat cancer has demonstrated that certain plants native to Thailand show potential in this regard [109]. We evaluated the cytotoxic activity and apoptotic induction of ethyl acetate and 50% ethanolic extracts from three different plant species using a human lung cancer A549 cell line and primary cancer cells produced from human lung cancer tissues [110]. It was discovered that the extracts of all three plant species possessed cytotoxic effects. Bridelia ovata Decne, Croton oblongifolius Roxb., and Erythrophleum succirubrum Gagnep were the three plant species that were utilised in this investigation[111].

The species known as B. ovata and C. oblongifolius are both classified as belonging to the genus Euphorbia [112]. In traditional Thai medicine, the B. ovata plant, also known as Ma-Ga, is used as an expectorant, a laxative, and a medicinal astringent. B. ovata has been used to extract a number of phytochemicals, including triterpenes and phytosterols [113]. Recent research[114] indicates that an ethanolic crude extract of B. ovata can inhibit the invasion and migration of human hepatocellular carcinoma HepG2 cells. This finding was made possible by the fact that an ethanolic crude extract of B. ovata was used.

To treat disorders such as dysmenorrhea, diarrhoea, dyspepsia, and chronic liver enlargement, C. oblongifolius, which is also known as Plao-Yai in Thai, is used as a purgative and tonic. Plao-Yai is the name of the plant in Thai. Plao-Yai is the name given to this plant in the Thai language [115]. In addition, C. oblongifolius and C. sublyratus are utilised in the treatment of stomach ulcers and gastric cancer within the framework of Thai traditional medicine[116]. C. oblongifolius has been linked to the production of a wide variety of phytochemicals, including but not limited to megastigmane glycosides, labdanes, clerodanes, halimane, and cembranes. In numerous different types of human cancer cell lines, the clerodane compound croblongifolin has been shown to be capable of causing cell death. [117] Research has been conducted on a variety of human cancer cell lines, including but not limited to HepG2, SW620, CHAGO, KATO3, and BT474.

[118] The E. succirubrum plant is classified as a member of the botanical family known as Leguminosae-Caesalpinioideae. In Thai medicine, it is referred to as "Phan-Saat," and it is used to treat a wide range of conditions, including fever and issues with the skin [119]. After being exposed to cassaine diterpenoid dimers, which were extracted from the bark of the E. succirubrum plant, human gastric cancer cells were shown to go through the process of apoptosis [120]. In addition, human hepatocellular carcinoma cells (HepG2) are more susceptible to the cytotoxic effects of the crude ethanolic extract of E. succirubrum than other cell types. The specific process by which a cell passes away, on the other hand, is still not well understood [121].

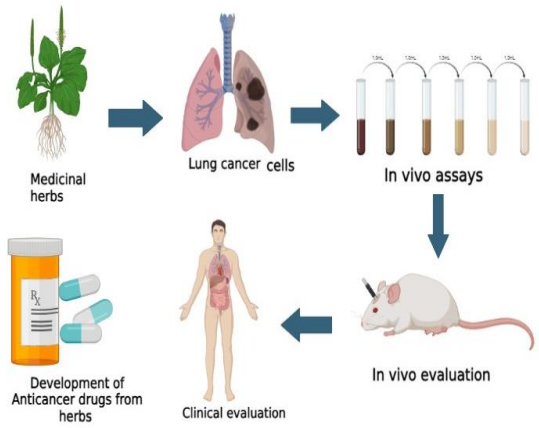

Fig 2: Medicinal herbs used in Development of Anticancer drugs and role in Lung cancer

IV. CONCLUSION

The most recent findings from research on a variety of malignancies are compiled here. In this article, we discuss a wide variety of cancers, including those that affect the lung, colon, bladder, skin, mouth, breast, thyroid, womb, pancreas, and prostate, amongst other organs and tissues. Numerous nations have conducted research on medicinal plants that have the ability to prevent or treat cancer, with a particular focus on those that show promise in the treatment of lung cancer. Natural substances derived from plants continue to be a major source of herbal therapies and chemicals with physiologically active qualities since many different plant species are active in a wide variety of experimental situations. There is a need for additional research to discover the most effective approach of chemically characterizing or standardizing the extracts that are used. Mice have been used in almost all of the pharmaceutical industry's studies. On the other hand, human study was

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also carried out on a variety of plant species. Inhibiting the growth of lung cancer cells has been studied using a number of medicinal herbs, as this study shows. These research have yielded important data that suggest medicinal herbs may be useful in cancer treatment. Preliminary screening results are all that have been published so far in the great majority of investigations, with no description of the underlying mechanism of action, despite the fact that numerous studies indicate that analysis of putative mechanisms of action of these drugs has been conducted. The only classification that can accurately describe them in relation to these investigations is "active."

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