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Review

Nutraceutical Management Of Lung Cancer

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	Abstract
Published on: 14 Sep 2024	<p>Cancer is a chronic disease in which cells in the body grow out of control. Lung cancer is the most often cancer in both men and women. Worldwide lung cancer kills over 1 million people a year. The major risk factor for lung cancer is smoking, which accounts for 75-85% of lung cancer related deaths. Extensive prospective epidemiologic data clearly established cigarettes smoking has the major causes of lung cancer. Because cigarette consists of chemicals including nicotine, hydrogen cyanide, formaldehyde, arsenic, ammonia, benzene. Thus, nicotine is the primary chemical causing the lung cancer. Lung cancer can be broadly classify into two forms such as Small Cell Lung Cancer(SCLC) and Non-small Cell Lung Cancer(NSLC). Smoking cause cancer heart diseases, stroke, lung cancer and chronic obstructive pulmonary disease. Metastatic lung cancer is the fourth stage of cancer spread widely around your body like brain, bones or liver. However, early diagnosis and treatment can save life. CT scan imaging is best imaging technic but it is difficult to interpret and identified cancer from CT scan images. In spite of surgical interventions, chemotherapy, radiation therapy and targeted therapy. Some patients are considering alternative therapies with herbal or natural products. Chemotherapy is to main option but do not have increase success rate.</p>
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	<p>Keywords: Small and non small lung cancer, Tobacco smoking, shortness of breath, Ganoderma, Green Tea, Onion, Curcumin.</p>

INTRODUCTION

Cancer is a disease in which cells in the body grow out of control. Lung cancer is a type of a cancer that starts when abnormal cells grow in an uncontrolled way in the lungs. It is a serious health issue that can cause severe harm and death. Lung cancer is one of the main reason for death in the world among both men and women. World wide lung cancer kills over 1 million people a year. Extensive prospective epidemiologic data clearly established cigarette smoking as the major cause of lung cancer. Lung cancer also caused by exposure to other people's smoke (called second hand smoke), radon, air pollution, a family history of lung cancer and asbestos. It estimate that 75-80% of lung cancer deaths due to the disease[2]. In 1878, malignant lung tumors represent only 1% of all cancer seen at autopsy. In 1918, the percentage had risen to almost 10% and by 1924 to more than 14%.

It was also noted that while most lung tumor occurred in men, there seemed to be a steady increase in women. The illness typically took between six months and two years to diagnose and, in almost every case, chronic bronchitis had been present for a long time. The extraordinary rising tobacco use was the single most important cause of rising incidence of lung cancer.[1,3]

Classification

Lung cancer are classified as,

1. Small cell lung cancer
2. Non-small cell lung cancer

Small cell lung cancer

Small cell lung cancer is the type of cancer is a poorly differentiated and high grade neuro-endocrine tumor accounting for 10-15% of all lung cancer. Small cell lung cancer usually starts in the bronchi and then affects the whole lung. These cancer cells are small and are considered to be quite aggressive in nature and they have a large growth factor. Genomic profiling of small cell lung cancer reveals extensive chromosomal rearrangement and a high mutation burden and almost always including functional in activation of the tumor genes. Small cell lung cancer is characterized by short tumor doubling time and metastasis at an early stage, with more than half of the patients diagnosed advanced stage[3,4]. Because of the reason at the time of diagnosis, these tumors have often metastasis to other part of the body like liver, brain and bone marrow. Small cell lung cancer accounts for 20-25% of all lung cancer. Therefore, screening and early diagnosis could lead to better prognosis. The standard treatment of small cell lung cancer patient comprises chemotherapy combined with chest radiotherapy (Fig:1).[4]

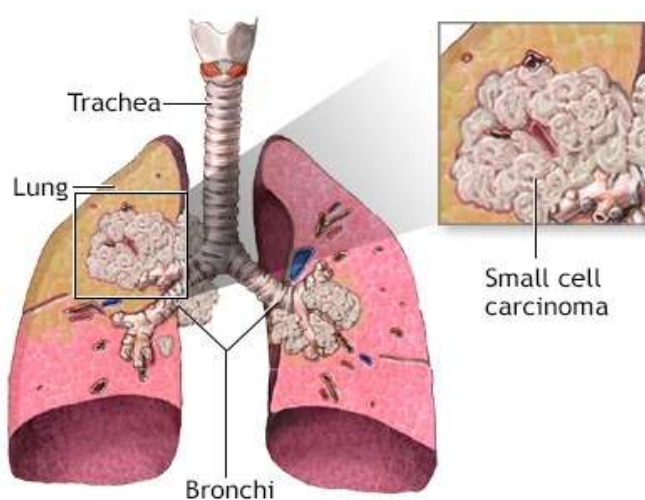


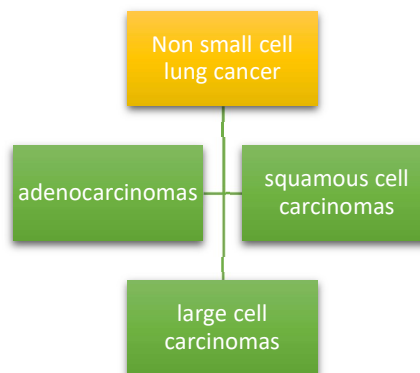
Fig 1: Small cell lung cancer

Non-small cell lung cancer

Non-small cell lung cancer usually grows and spreads more slowly than small cell lung cancer (Fig:2).



Fig 2: Non-small cell lung cancer



Type of non-small cell lung cancer

- **Squamous cell carcinomas:** It usually arise centrally in large bronchi. Squamous cell carcinomas has unknown metastasis that is slow effects the liver, adrenal gland and lymph nodes and it is not easily visualized on x-ray (Fig:2.1).[2,4]

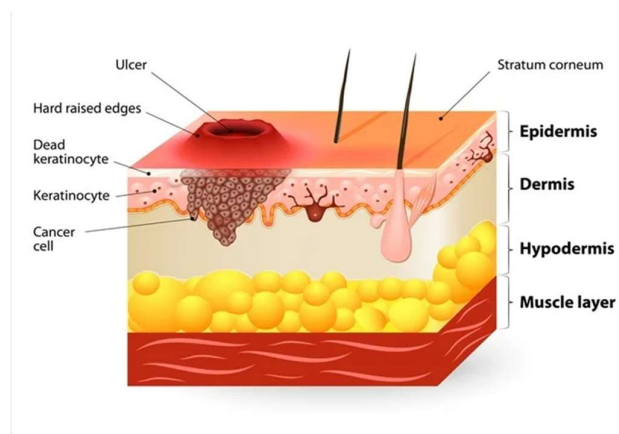


Fig 2.1: Squamous cell carcinomas

- **Adenocarcinoma:** Adenocarcinoma is formed from granular structure in epithelial tissue are often found in the periphery of the lungs. It is clearly defined peripheral lesion and easily seen on CXR. It is slow

metastatic in nature which is present with or develop brain, liver, adrenal or bone metastasis (Fig:2.2).[2,4]

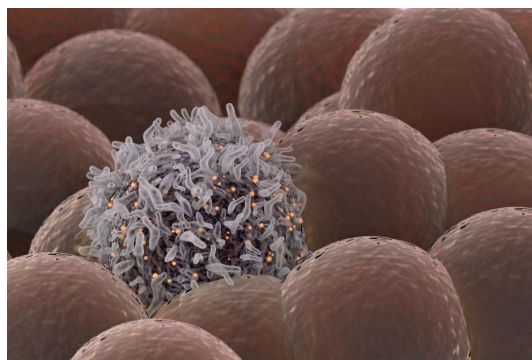


Fig 2.2: Adenocarcinoma

- **Large cell carcinomas:** It can occur in any part of the lung and tend to grow and spread faster than the other two types. These are tends to occur in the periphery of lung invading sub-segmental bronchi or larger airways. Metastasis is slow but early metastasis occurs to kidney, liver, organs as well as the adrenal gland (Fig:2.3).[4]

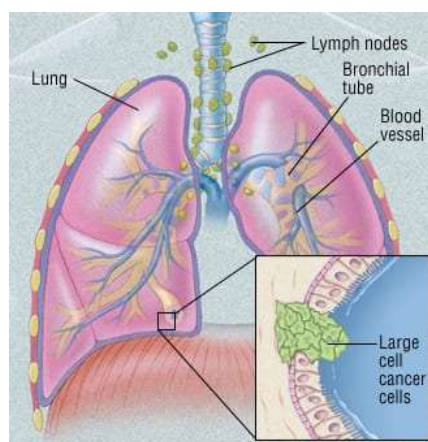


Fig 2.3: Large cell carcinomas

Symptoms

Lung cancer cause severe symptoms are pain, dyspnea and anorexia. The person aged sixty four and under had increase the incidence of early fatigue, taste changes and sleep problems men over sixty four had increase the incidence of cough and less than 10% weight loss. Although there was a general increase in the number of symptoms as the performance status worsened those with poorest performance status reported the fever symptoms[5,6]. (Fig:3)

Lung cancer symptoms are;

- Cough
- Dyspnea
- Hoarseness
- Chest pain
- Wheezing
- Hemoptysis
- Nausea/vomiting

- Swelling of face and arms
- Anorexia
- Weight loss
- Fatigue
- Bone pain
- Clubbing
- Headache
- seizures

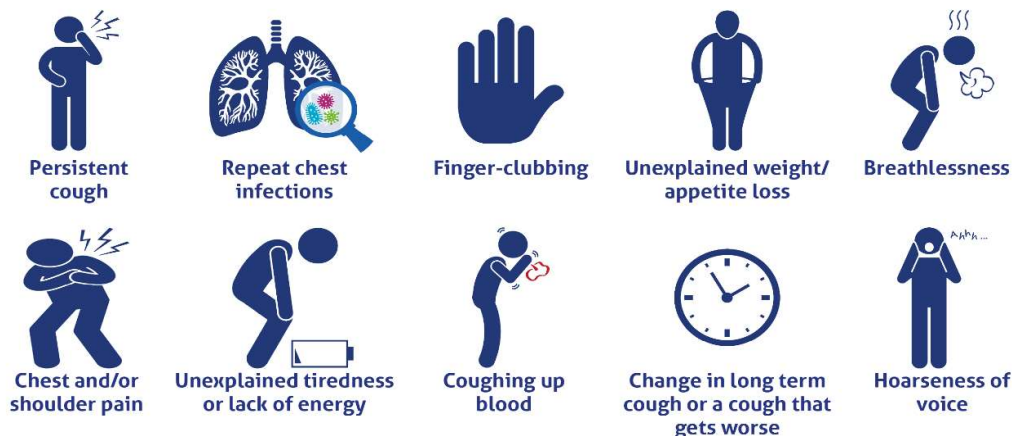


Fig 3: Symptoms of lung cancer

Evaluation

Initial evaluation for lung cancer realize on patient history and physical examination, laboratory test, chest computed, tomography, positron emission tomography. Smoking cessation remains the critical component of preventive primary care. The earliest diagnosis of lung cancer is crucial especially in screening high risk population. For example; smokers, exposure to fumes, oil fields, toxic occupational places etc...with an urgent need to identified novel biomarkers[10,9].

- **Physical examination:** most early lung cancer patients have no obvious related positive signs. Patients present extra pulmonary signs such as clubbing fingers (toes), non-wandering joint pain, male breast hyperplasia, skin darkness or dermatomyositis, ataxia and phlebitis. In patients with highly suspected lung cancer, vocal cord paralysis, superior vena cava obstruction syndrome, Horner's syndrome and pan coast syndrome may be found by physical examination, suggesting the possibility of local invasion and metastasis[10].
- **Laboratory examination**
 - ✓ routine blood test
 - ✓ liver and kidney function and other necessary biochemical and immunological tests
 - ✓ coagulation function test
- **Imaging examination:** imaging examination method of lung cancer mainly include chest x-ray, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, radionuclide imaging, positron emission tomography-CT (PET-CT) and other methods. Imaging examination is the best method for non-invasive detection and evaluation of tumors. In the diagnosis and treatment of lung cancer, one or more imaging examination method should be selected reasonably and effectively according to different examination purposes[9].
- **Chest x-ray:** Chest radiography is often the basic image examination method for the discovery of lung diseases in primary hospitals, which has limited value in the diagnosis of early lung cancer. Once lung cancer was suspected in the chest radiography, CT scan should be timely executed[10,11].

Diagnosis

The diagnostic evaluation of patients with suspected lung cancer includes tissue diagnosis a complete staging workup, including evaluation of metastasis and a functional patient evaluation. histologic diagnosis may be obtained with sputum cytology, the paracentesis, accessible lymph node biopsy, bronchoscopy, transthoracic needle aspiration, video assisted thoracoscopy or thoracotomy. Further more, accurate diagnosis is vital for the most suitable treatment of individual patient with lung cancer[7,8].

Causes and risk factors

Smoking causes the majority of lung cancers both in smokers and in people exposed to second hand smoke. But lung cancer also occurs in people who never smoked and in those who never had prolonged exposure to second hand smoke. In these cases, there may be no clear cause of lung cancer[10,3].

General risk factors

- Family history and high penetrance genes
- Tobacco smoking
- Diet and alcohol
- Chronic inflammation from infections and other medical conditions
- Ionizing radiation
- Occupational exposures
- Air pollution
- Other risk factors

Family history and high penetrance gene

A positive family history of lung cancer has been found to be a risk factor in several registry based studies that have reported a high familial risk for early onset lung cancer. Increased relative risk were found even after careful adjustment for smoking. A linkage analysis of high risk pedigrees in identified a major susceptibility locus to chromosome.

Tobacco smoking

Tobacco smoking is the major causes of all major histological type of lung cancer. A carcinogenic effect of tobacco smoke on the lung was demonstrated in epidemiological studies conducted. The risk among continues smoker relative to that among never smokers in the order of 20-50 fold. Duration of smoking should be considered the strongest determinant of lung cancer risk among smokers. Newer, low yield cigarettes caused a shift in the site of disease (from trachea and bronchus to peripheral lung), and hence in the histology of lung cancer, from predominantly squamous cell to adenocarcinoma the risk decreases in ex-smokers and a favourable effect of stopping is apparent event for cessation later in life. Although cigarettes are the main tobacco product smoked and an exposure- response relationship with lung cancer risk has also been shown for cigars, cigarillos and pipes, indicating a carcinogenic effect of these products.

An increased risk of lung cancer has also been shown following consumption of local tobacco products such as bidi and hookah. A causal relationship between second hand smoke exposure and lung cancer risk in non-smokers is supported by epidemiological evidence and biological credibility; the excess risk is estimated to be between 20-30% for non-smokers who are married smokers.

Diet and alcohol

Evidence from case control studies suggests that eating a diet high in fruits and vegetables, particularly cruciferous vegetables, may help prevent lung cancer. Result from prospective trials that provide comprehensive data on dietary intake, however, are less consistent in demonstrating a similar effect. Consuming a lot of meat, in especially fried are well done red meat, may rise your chance of developing lung cancer. These is because cooking releases nitrosamines into the air. Estimated intake of saturated fat did not appear to be associated with an elevated risk of lung cancer, according to a pooled analyses of eight cohort studies.

Chronic inflammation from infection and other medical conditions

Patients with chronic pulmonary diseases are at increased risk for lung cancer, and a number of studies have suggested that these is independent of smoking. Patients with pulmonary tuberculosis have been found to be at increased risk of lung cancer.

Ionizing radiation

Exposure to ionizing radiation increase the risk of lung cancer. These increased risk has been reported in atomic bomb survivors as well as patient treated with radiotherapy. Underground mines exposed to radioactive radon and its decay products, which emit alpha particles, have been consistently found to be at increased risk of lung cancer.

Occupational exposures

Occupational exposures play a significant role in lung cancer aetiology and the risk of lung cancer is increased among workers employed in a number of industries and occupations. The most important occupational lung carcinogens are reported to be asbestos, silica, radon, heavy metals and polycyclic aromatic hydrocarbons.

- **Asbestos:** All different forms of asbestos (chrysotile and amphiboles, including crocidolite, amosite and tremolite) are carcinogenic to the human lung are the potency of chrysotile is lower than that of other type of probably due to its earlier clearance.
- **Metals and mixed occupation exposures:** chromium compounds increase the risk of lung cancer among chromate production workers, chromate pigment manufacturers, chromium platers and ferrochromium producers. No such risk has been detected among workers exposed only to chromium compounds. Studies of nickel miners, smelters, electrolysis workers and high nickel alloy manufacturers showed an increased risk of lung cancers. An increased risk of lung cancer has also been reported among workers in cadmium based battery manufacture, copper cadmium alloy workers and cadmium smelters, but the evidence is not as strong as for other agencies. An increased risk of lung cancer has also been reported among people exposed to high level of arsenic in drinking water.
- **Silica:** An increased risk of lung cancer has been consistently reported in cohorts of silicotic patients. Many studies investigated crystalline silica-exposed workers in foundries, pottery making, ceramics, brickmaking and stone cutting, some of whom might have developed silicosis.
- **Polycyclic aromatic hydrocarbons:** polycyclic aromatic hydrocarbon are a complex and important group of chemicals formed during combustion of organic materials. An increased risk of lung cancer has been reported in several industries and occupations involving exposure to poly cyclic aromatic hydrocarbon such as aluminum production, coke production, iron and steel founding, tar distillation roofing and chimney sweeping.

Air pollution

Indoor air pollution is thought that to be a significant risk factor for lung cancer in both men and women who have never smoked it also consist of cold burning in poorly ventilated houses, burning of wood and other solid fuels, as well as fuels from high temperature cooking using and refined vegetable oil such as rapeseed oil. Environmental measurements are fine particles are suggested of a small increase in risk among people classified as most highly air pollution.

Other risk factors

Estrogen and progesterone receptor are expressed in the normal lung and in lung cancer cell lines, and estradiol has a proliferative effect on the later type of cells. There is some evidence that a reduced body mass index is associated with an increased risk of lung cancer[3].

Complications

Lung cancer can cause complications such as

- Shortness of breath
- Coughing up blood
- Pain
- Fluid in the chest (pleural effusion)
- Cancer that spread to other parts of the body (metastasis)
- Superior vena cava syndrome
- Blood clots
- hypercalcemia

Shortness of breath

Breathlessness may occur in lung cancer patients if the malignancy spreads to the point where it blocks the main airways. Additionally, fluid buildup around the lungs from lung cancer can hinder the affected lung's ability to

fully inflate during inhalation.

Coughing up blood

Lung cancer can cause bleeding in the air way, which can cause you to cough up to blood (hemoptysis). Sometimes bleeding can become severe. Treatment are available to control bleeding.

Pain

Pain can result from advanced lung cancer that has progressed to the lung lining are to another part of the body, including the bone. Inform your physician if you are in pain, as there are numerous way to manage it.

Fluid in the chest (pleural effusion)

Lung cancer can cause fluid to accumulate in the space that surround the affected lung in the chest cavity (pleural space) fluid accumulate in the chest can cause shortness of breath. Treatments are available to drain the fluid from your chest and reduce the risk that pleural effusion will occur again.

Cancer that spread to other parts of the body (metastasis)

Lung cancer often spreads (metastasizes) to other part of the body, such as the brain and the bones. Cancer that spreads can cause pain, nausea, headache or other science and symptoms depending on what organ is affected once lung cancer has spread beyond the lungs, it's generally not curable. Treatments are available to decrease signs an symptoms and to help to you live longer.

Superior vena cava syndrome

Sometimes the cancerous tumor in your lung can grow into, press against or block one of the large veins in the chest called superior vena cava syndrome and happens to about 2-4% of people with lung cancers. Its more common in peoples with a type of lung cancer called small cell lung cancer. The blockage may cause blood to back up in other veins around it, in the chest wall, and in the upper body. Because of the blockage, veins may get larger, which can lead to swelling in your chest, neck and face. These can be pain full and make you feel short of breath or flushed pressure on the vein may cause shortness of breath, headache, blurry vision, dizziness and drowsiness. In rare cases, these syndrome can be life threatening.

Blood clot

When you have lung cancer, its common to have blood clots. If you develop thrombocytosis, your body would make too many platelets, a type of blood cell that helps you stop bleeding by forming a clot. It can be risky to have too many platelets. It can lead to clots in the blood vessel that can cause stroke or heart attack. Usually, thrombocytosis happens in people with late-stage lung cancer. But like many people with cancer, its common to have blood that clots more easily, which rise your changes for dangerous blood clots.

Hypercalcemia

Hypercalcemia is the calcium level in the blood may be higher than normal. If you have lung cancer, you may be more likely to get the conditions. Hypercalcemia may happen when the cancer in lungs spread to bone. The bones may leak calcium in blood may cause bones to become weak and easy to break. It may also cause back or hip pain. usually, hypercalcemia happens in people who have stage 3 or stage 4 lung cancer. It can also rarely happen when cancer make hormones that may cause calcium to build up in blood[11].

Pathophysiology

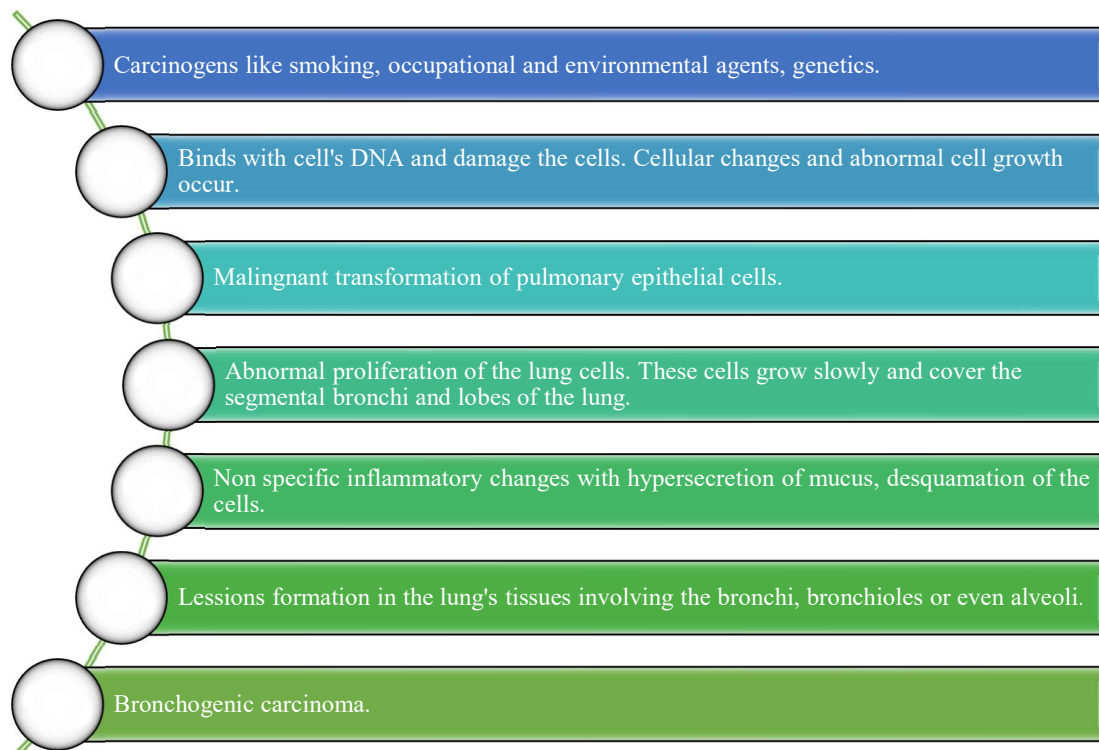
Lung cancer's pathogenesis is extremely intricate and poorly understood. It is postulated that continuous exposure occur. It leads to genetic mutation and affect protein synthesis. These in turn, disturbs the cell cycle and promote carcinogenesis. Cellular and molecular subtypes are the basis for the histopathological classification of lung cancer, which is crucial for both diagnosis and treatment. The 2021 world health organization classification system of lung tumors divide in the lung cancer as follow:

- Precursor glandular lesions
- Adenocarcinomas
- Adenosquamous carcinomas

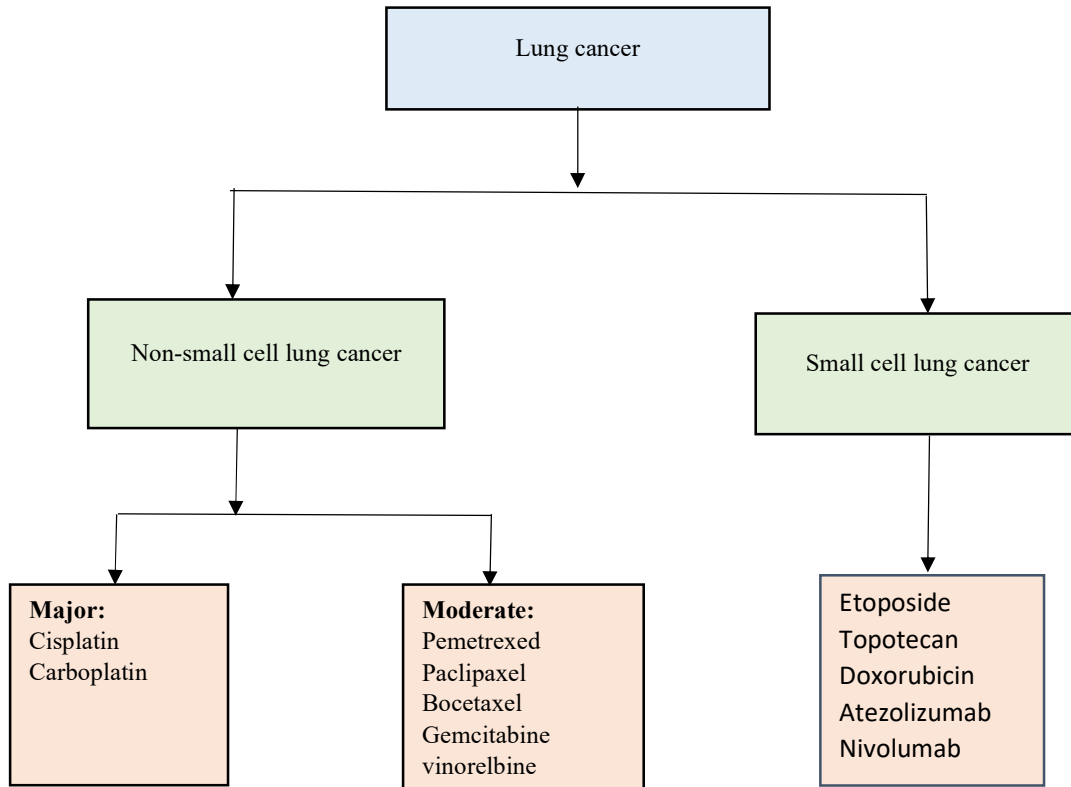
- Squamous precursor lesion
- Squamous cell carcinomas
- Large cell carcinomas
- Lung neuro endocrine neoplasm
- Salivary gland- type tumors
- Neuroendocrine tumors
- Neuroendocrine carcinomas
- And other epithelial tumors

The world health organization state that prognostic value can obtained by identifying histological characteristics that measure invasion depth and made of speed. For instance, they claim that cancers that disseminate through the atmosphere should be reported on pathological evaluation since they are linked to a greater recurrence rate following restricted resection. Also, the previously clear cell, signet ring subtype have been discontinued by the most recent world health organization classification as they appear to be cytological features that can occur in any adenocarcinomas. The world health organization classification places significant emphasis on immune histochemical staining to classify cancers that may not have typical cytologic features on light microscopy[12].

Process



Allopathy medicine Classification



Mechanism of action

The drug interfere with structures in a cell called microtubules that help more chromosomes during mitosis. Then it stops the growth of cancer cells and other dividing cells by blocking cell division.[14].

Adverse drug effect

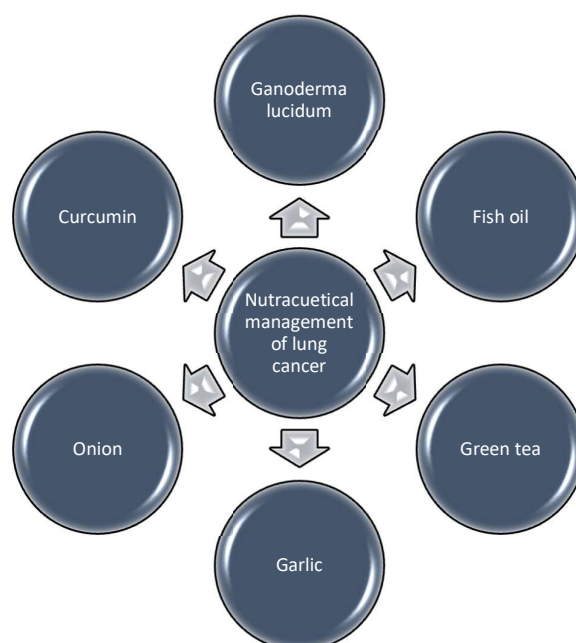
- Constipation
- Hair loss
- Vomiting
- Bleeding
- Diarrhea
- Feeling sick
- Blurred vision
- Fatigue
- Rashes
- Dizziness
- Low blood pressure
- Urine and renal problems
- Shortness of breath
- Hearing changes
- Headache
- Pain during urination
- Loss of appetite
- Numbness
- Nausea
- Swollen legs

- Cough
- Drowsiness
- Mouthsores
- Muscles or joint pain[15]

Nutraceutical management

Nutraceuticals is a combination of the words “nutrition” and “pharmaceuticals”. Nutraceuticals are food are part of foods that have a substantial role in changing and sustaining normal physiological activity in humans. Their ability to reduce cancer incidence in these studies is slightly related to apoptosis. Dietary fiber, prebiotics, probiotics, polyunsaturated fatty acids, antioxidants and other herbal foods are example of food products utilized as nutraceuticals. Most of the nutraceuticals are derived from plants and animals origin and act as biochemical metabolites either by direct intermediary metabolism or regulating immunity[16].

Nutraceutical management of lung cancer are,



Ganoderma lucidum

Ganoderma lucidum (GL) commonly known as “lingzhi” or “reishi”, is a well-known medicinal mushroom with antioxidant and anti-cancer activity belonging to the family: Ganodermataceae. The chemical constituents of ganoderma lucidum is lingzhi8 (LZ8) (Fig:4) is the 1st protein isolated from GL, which function as immune modulatory protein in lung cancer cells. Ganoderma, a genus of more than 300 species of wood-decaying fungi in the order polyporales. Reishi mushroom is a bitter tasting fungus with no proven health benefits. It is thought to have some effects on the immune system. These study examined the effect of a commercial GL product (GLSF) containing the spore and fruiting body in a 30:8 ratios on tobacco smoke carcinogen-induced lung toxicity and carcinogenesis. The potential chemo-preventive effect of GLSF was evaluated in-vivo and in-vitro. The non-tumorous human bronchial epithelial cells were treated with GLSF extract, which significantly blocked malignant transformation induced by benzo pyrene diol epoxide (BPDE) in a dose-dependent manner. GNSF treatment also the expression of inflammatory, angiogenic and apoptotic markers in lung tumor. Therefore, GLSF may be used for ameliorating tobacco smoke carcinogens-induced lung toxicity and carcinogenesis[16].

Preparation

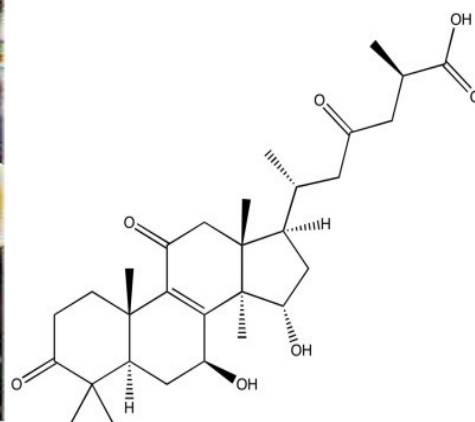
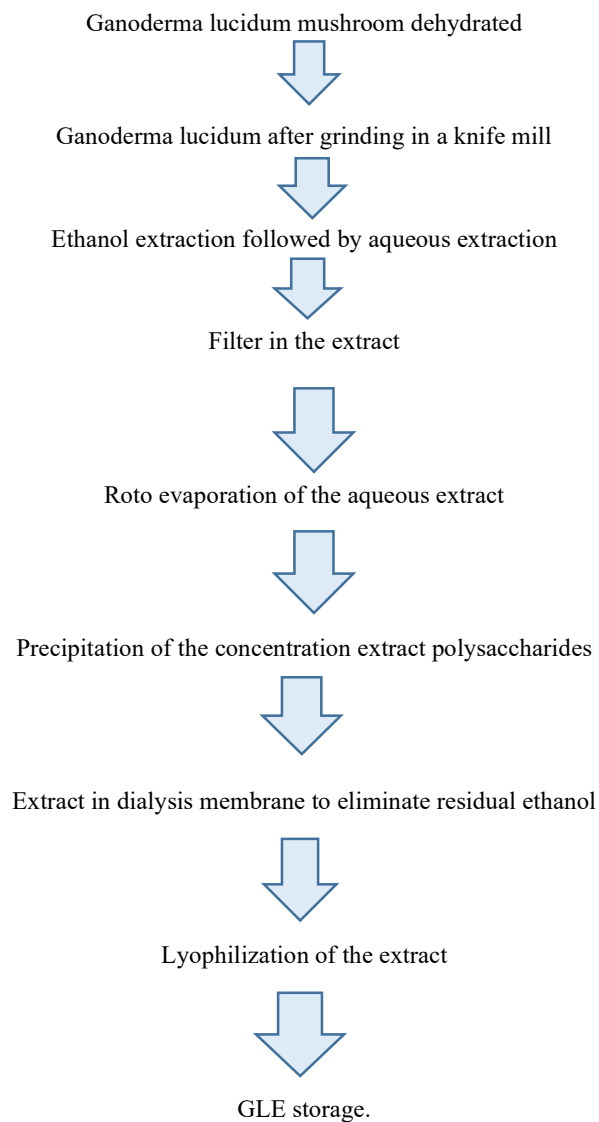


Fig4: Ganoderma lucidum and chemical structure of lingzhi8

Fish oil

Fish oil is a dietary supplement that contains omega-3 fatty acids particularly eicopentaenoic acid, and decosahexaenomic acid through in doses that vary widely among brands. Omega-3 fatty acids are the components of cell membrane phospholipid, can provide energy and are also used to produce eicosanoids, which are important signaling molecules. fish oil is very popular supplement, with its estimated among 7.8% of adults and 1.7% of a children in the united states during a given 30 day period. Research has evaluated the roles of fish oil to reduce cancer incidence and improve cancer outcome by preventing toxicity or treating cancer-or treatment –associated side effects[15]. (Fig:5)



Fig5: Fish oil capsules

Green tea

Green tea is a beverage widely used by lung cancer patients and the public for its alleged anticancer properties. Green tea applied topically may improve the healing time of radiation burns[17]. (Fig:6)



Fig6: Green tea

Garlic

Productive effect of garlic on the development of cancer. Garlic contains bioactive substantial anti-carcinogenic effect via a number of pathway, including cell cycle arrest, apoptosis and stimulation of the angio-genic cascade. Traditionally, garlic and its related compounds have been stated to have several biological activities including anti-carcinogenic, antioxidant, antidiabetic, reno-protective, anti-atherosclerotic, anti-bacterial, anti-fungal and anti-hypertensive activities. They are mostly used for treating respiratory diseases such as bronchitis and asthma[18]. (Fig:7)



Fig 7: Garlic

Onion

Onion (*allium cepa*) is the member of the family: Amaryllidaceae and one of the most widely cultivated species of the genus *Allium*. Onion has plentiful chemical compounds such as allicin, quercetin, fisetin, other sulphur compounds: diallyldisulphide and diallyltrisulphide. The onion extract also found to inhibit the growth of these type of cancer cells. Motivated by the onion flavonoid's ability to combat cancer. Onion possesses numerous pharmacological properties, including anti-cancer, anti-diabetic and anti-platelet properties as well as effect on respiratory system[18]. (Fig:8)



Fig 8: Onion

Curcumin

Turmeric is the product of *curcuma longa* a rhizomatous herbaceous perennial plant belonging to the ginger family: Zingiberaceae. Ingredients that are active the dietary spice turmeric. Curcumin has the potential anti-oxidant and anti-tumor effects[18]. (Fig:9)

Caution: Inhibition of cytochrome p450.

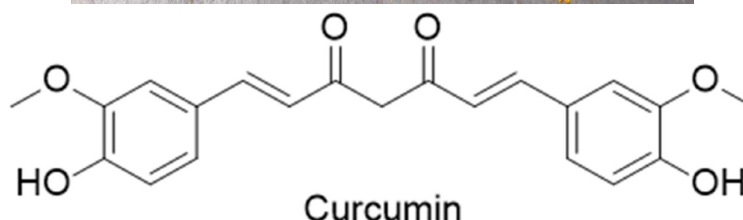


Fig 9: Curcumin and its chemical structure

CONCLUSION

In summary, our findings clearly show that dietary supplements containing GLSF may protect against lung damage and tumor formation caused by tobacco smoke, which may be partially explained by GLSF's ability to modify the pathways involved in inflammation and apoptosis. Given that GLSF is a naturally occurring substance that has been used for many years, the result of the studies suggests that a retrospective clinical trial be created to see if smoker who take GLSF see a decrease in lung cancer cases compared to those who do not. Lung cancer can also be prevented by the usage of nutraceuticals such as, fish oil, green tea, garlic, onion and curcumin. Ganoderma lucidum has been used to treat a variety of chronic diseases such as cancer, bronchitis, asthma and diabetes. It has also been recognized as an adjective and alternative therapy against cancer and diabetes.

REFERENCES

1. Hanspeter Witschi. A Short History of Lung Cancer. *Toxicological Sciences*, 2021;64(1):4–6. <https://doi.org/10.1093/toxsci/64.1.4>
2. Johnson TE, Kassie F, O'Sullivan MG, Negia M, Hanson TE, Upadhyaya P, Ruvoilo PP, Hecht SS, Xing C. Chemopreventive effect of kava on 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone plus benzo[a]pyrene-induced lung tumorigenesis in A/J mice. *Cancer Prev Res (Phila)*. 2008 Nov;1(6):430-8. doi: <https://doi.org/10.1158/1940-6207.CAPR-08-0027>
3. Peto R, Darby S, Deo H, Silcocks P, Whitley E, Doll R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. *Bmj*. 2000 Aug 5;321(7257):323-9. doi: <https://doi.org/10.1136/bmj.321.7257.323>
4. Gamandeep. Lung cancer. 2018 Oct 23; Available link: <https://www.slideshare.net/GAMANDEEP/lung-cancer-120398117>
5. Krech RL, Davis J, Walsh D, Curtis EB. Symptoms of lung cancer. *Palliative Medicine*. 1992 Oct;6(4):309-15. <https://journals.sagepub.com/doi/abs/10.1177/026921639200600406>
6. Collins LG, Haines C, Perkel R, Enck RE. Lung cancer: diagnosis and management. *Am Fam Physician*. 2007 Jan 1;75(1):56-63. PMID: 17225705. <https://pubmed.ncbi.nlm.nih.gov/17225705/>

7. Nooreldeen R, Bach H. Current and future development in lung cancer diagnosis. International journal of molecular sciences. 2021 Aug 12;22(16):8661.<https://www.mdpi.com/1422-0067/22/16/8661>
8. Division of Infectious Diseases, Faculty of Medicine, The University of British Columbia, Vancouver, BC V6H 3Z6, Canada Author to whom correspondence should be addressed. Int. J. Mol. Sci. 2021; 22(16): 8661; <https://doi.org/10.3390/ijms22168661>
9. Health Commission Of The People's Republic Of China N. National guidelines for diagnosis and treatment of lung cancer 2022 in China (English version). Chin J Cancer Res. 2022 Jun 30;34(3):176-206.doi: 10.21147/j.issn.1000-9604.2022.03.03
10. Lung cancer.<https://www.mayoclinic.org/diseases-conditions/lung-cancer/symptoms-causes/syc-20374620>
11. Melinda Ratini, DO. When Cancer Spreads to the Lungs. August 24, 2022. Available from: <https://www.webmd.com/bio/melinda-ratini>
12. Sonia Amin Thomas. U.S. Pharmacist. Lung Cancer Overview: Focus on Newer Therapies. Feb 18, 2015.<https://www.uspharmacist.com/article/lung-cancer-overview-focus-on-newer-therapies>
13. Sharon Reynolds. National Cancer Centre. Manipulating an Immune Cell May Make Radiation Therapy More Effective, Study Suggests. February 12, 2024.<https://www.cancer.gov/news-events/cancer-currents-blog/2024/radiation-cancer-bambi-immune-response>
14. Shahid A, Chen M, Yeung S, Parsa C, Orlando R, Huang Y. The medicinal mushroom *Ganoderma lucidum* prevents lung tumorigenesis induced by tobacco smoke carcinogens. Front Pharmacol. 2023 Sep 6;14:1244150.doi: 10.3389/fphar.2023.1244150
15. Andrea S. Blevins Primeau. Fish Oil and Cancer. September 29, 2017.<https://www.cancertherapyadvisor.com/factsheets/fish-oil-and-cancer/>
16. Fritz H, Seely D, Kennedy DA, Fernandes R, Cooley K, Fergusson D. Green tea and lung cancer: a systematic review. Integrative Cancer Therapies. 2013 Jan;12(1):7-24.<https://doi.org/10.1177/1534735412442378>
17. Hsu PP. Natural medicines comprehensive database. Journal of the Medical Library Association. 2002 Jan;90(1):114.<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC64772/>