Cancer is one of the leading cause of death worldwide, it shares highest mortality rate among other disease worldwide, around 14.1 million incidences and 8.2 million deaths reported in 2012 globally (Figure 1). Due to high incidence (1.8 million, 12.9% of total) and death (1.6 million deaths, 19.4%) rate lung cancer remains the most common cancer in the world, whereas breast cancer which is the second most common cancer (1.7 million cases, 11.9%), and ranks as the fifth most death causing cancer globally (0.52 million death, 6.4%), because of relatively favourable prognosis these are followed in terms of incidences; colorectal cancer, prostate
cancer, stomach cancer and liver cancer, these six cancers represented 55% of total cancer burden in 2102. In developed countries only four cancers including breast, lung, colorectal and prostate cancer represent the half of the cancer burden, whereas in less developed countries lung, breast, stomach, colorectal, liver and cervical cancer represent half of the cancer incidence burden. Lung cancer was the most common cancer worldwide among men, it ranks second in developed counties (4,90,000 cases) after prostate cancer (7,59,000). Lung, liver and stomach are the prominent cancers in males in under developed countries both in the terms of incidence and death. These cancers represent 40% of total incidences and 48% of total deaths. Breast cancer in women is the most common cancer both in underdeveloped and developed countries, whereas more cases are taking place in underdeveloped countries (8,83,000) than developed countries (7,94,000). Most cancer cases (4.1 million, 29.4% of the total) and deaths (2.75 million, 33.6%) took place in Eastern Asia and North America ranks second in term of new cases and third in term of cancer deaths.

Lung cancer has remained as one of the most common cancer globally for decades, there was an estimate of 6,60,000 incidences in 1980 and 1.8 million new cases (12.9% of total) were estimated in 2012, out of which 58% occurred in less developing countries. Lung cancer is the most common cancer in men with highest rate in Central and Eastern Europe and Eastern Asia (Ferlay J et al 2015).

Incidences of cancer are increasing continuously in developing countries (Figure 2), because of acquisition of several cancer promoting lifestyle like western diet, smoking, alcohol, pollution

**Figure 1:** Incidence and death rate globally in 2012, (Ferlay J et al 2015)
etc. Several treatment such as surgery, chemotherapy, radiotherapy, targeted therapy are available to decrease the burden of cancer. Despite intensive efforts and substantial advances in research of treatment, cancer still is one of the most death causing disease worldwide.

Figure 2: Incidences in more develop and less developed regions (Ferlay J et al 2015)

In India, lung cancer comprises 6.9% of all new cases and 9.3% of cancer related deaths in both sexes. The incidence and pattern of lung cancer varies with geography, ethnicity, pollution level and tobacco consuming populations. One million incidences and 0.68 million deaths (Figure 3) were reported in India in 2012 (Ferlay J et al 2015).
Despite of several available therapies, lung cancer mortality is high with 15% survival rate after diagnosis. Lung cancer histological classified into two forms including small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC). Here, classification of the cells is based on the size of the nucleus of the cancer cells, small nucleus containing cells are classified as SCLC and NSCLC has bigger nucleus. Nuclear size of small and non-small cells reflects the amount DNA content present inside the cells, the small nucleus have less DNA content and are found in hypodiploid forms, on the other hand non-small bigger nucleus cells contain high DNA contain and are usually found in hyperdiploid form. NSCLC contributes the 80-85% of lung cancer. The NSCLC is further sub-classified into the large cell carcinoma, squamous carcinoma and adenocarcinoma (Forgacs E 2001; Mateen S et al 2010). The squamous carcinoma is a kind of lung cancer, which arises from the squamous epithelial cells, they are not found at lung epithelial, but glandular and secretary cells can be converted into the squamous cell carcinoma by mutations or by other means including tobacco consumption, alcohol consumption and radiation exposure. Adenocarcinoma is epithelial cancer which arise in the cells with glandular or secretary properties.

In small cell lung cancer, for more than 90% of cases, deletion in the short arm of the chromosome 3 (3p deletions) is found. In non-small carcinoma, 50% deletion is found on the 17p13 chromosome and 15 to 30% on 13q14 chromosome. The deletion at 17p13 and 13q14 results in the down-regulation of tumour suppressor genes, p53 and Rb as a consequence of which, there is loss of cell cycle regulation leading to cancer initiation (Petersen I et al 2009; Petersen I 2011).

Lung cancer development includes has three stages initiation, promotion and progression stages. There are several risk factors associated with lung cancer development including smoking tobacco, alcohol consumption, air pollution, westernized life style, prior lung diseases, genetic and hormonal effects and ionization radiations. Active and passive smoking of tobacco are the major risk factors for lung cancer development (Kubík A and Reissigová J 1990). Several
environmental exposures including asbestos, beryllium, arsenic, silicon compounds and the compounds like herbicides, pesticides and insecticides are risk factors for promotion of lung cancer (Sun S et al 2007). It has been reported that people with higher Body Mass Index (BMI) have higher probability to develop lung cancer. History of non-cancerous disease can also promote lung cancer development such as chronic bronchitis, tuberculosis, pneumonia and emphysema asbestosis. Synergetic effect of several risk factors increases the aggressiveness of tumour growth (Takezaki T et al 2001; Wang X R et al 2009).

Several efforts are being taken to decrease the burden of lung cancer worldwide including chemotherapy, radiotherapy, surgery and targeted therapy. Many undesirable side effects have been reported after using these approaches, such as chemotherapy adversely affect dividing cells, blood cells and digestive tract cells. People with defective blood cells easily become more prone to infections. Chemotherapy includes many other side effects such as hair loss, diarrhea, vomiting, mouth sores and loss of appetite. Fatigue is also a common side effect of chemotherapy. Some people lose their ability to think and learn, the overall life becomes poor. In women chemotherapy may cause the ovary damage and menopause. It may cause result in long term side effects like infertility and kidney damage (Azzoli C G et al 2003). There are several drugs available in the market but reported to have undesirable side effects. Thus there is need to make the best possible strategies, with easy availability in market, less side effects and affordable pricing.

Chemoprevention of cancer has emerged as one of the most promising approach against lung cancer. Chemoprevention is explained as the use of dietary or pharmalogical agents which are capable to reverse or inhibit the phenomena of carcinogenesis. These agents are being used against many cancers. Chemoprevention has been validated as effective against many cancers. The term chemoprevention was given by Sporn and coworkers in 1976 to explain the pharmacologic or dietary intervention to the phenomena of carcinogenesis that results into the decrease in cancer growth. Sporn discussed the potential of retinoid for lung cancer, which later underwent clinical trials with null adverse effects in the patients (Keith R L and Miller Y E 2013). Chemoprevention can be divided into primary, secondary and tertiary groups. Here primary chemoprevention deals with the cancer growth among high risk population, secondary deals with the cancer development in the population with precursor lesions (severe dysplasia), tertiary chemoprevention studies cancer development in people with previous cancer (Keith R L
There are three approaches for selecting most promising chemopreventive agents for lung cancer observational studies, including determining the effect of drug or targeted agent on tumour or dysplastic cancer cells, pre-clinical animal models for lung tumorigenesis, end point trial in humans.

There are many ways of chemoprevention, the use of phytochemicals is considered as the safest approach. Phytochemicals are the secondary metabolites found in the plants products such as roots, stem, bark, fruits, vegetables, leaves, flowers and seeds. Plants and their various formulations are in medical use since ancient time, several herbal preparations from ancient philosophies and old cultural origin are being used in folk medicine to treat many diseases. Ayurveda and ancient literature is a great source for science of good health and wellbeing. It is estimated that plant kingdom comprises 2,50,000 species and only 10% have been evaluated for pharmacological applications. Phytochemicals are natural compounds and are mostly non-toxic to normal human body cells, they are known to possess several biological activities including antibacterial, antiviral, anti-proliferative and anti/protozoans. Several phytochemicals have been reported to show anti-cancer potential against many cancer like liver, colon, brain, lung, cervical and pancreatic. Phytochemicals are not primarily essential for survival of plants, but are required mainly for defense purpose of plants from insects, herbivores, pathogens, bacteria and viruses (Singh S et al 2016). Alkaloids, phenolics, glycosides, flavonoids, gums, phenols, dibenzofurans and polyphenols are group of secondary metabolites, the elements or their altered forms like taxol, etoposide acestin, evodiamine, fisetin, silibinin and usnic acid etc are the phytochemicals in this regard.

Usnic acid (UA) a dibenzofuran derivative secondary metabolite reported abundantly and exclusively in lichens. It is a yellow colored phytochemical found at outer cortex surface of lichens. Lichens are the symbiotic consortium between fungi (mycobiont) and algae (photobiont). Algae provides carbohydrate through photosynthesis for itself and fungal partner and fungi provides water, mineral and structural support. Lichens are naturally found on rocks, tree’s bark, bare land, metal, glass and leaves. Lichens produce hundreds of secondary metabolites including aliphatic, cycloaliphatic, aromatics and terpene compounds. Many of them have been utilized as potential anti-cancer agents pharmacologically, but still several groups are yet to be investigated.
Usnic acid is found in several species of the Ramalina (Ramalinaceae), Cladonia (Cladoniaceae), Lecanora (Lecanoraceae), Usnea (Usneaceae), Evernia, Parmelia (Parmeliaceae) and several in other genera. Usnic acid has shown many biological activities like anti-inflammatory, anti-viral, anti-bacterial, chelating agent, anti-proliferative, analgesic and anti-pyretic (Guo L et al 2008). It has shown anticancer potential against many cancer cell lines such as liver, cervical, brain, lung, colon, stomach and pancreases but details of the mechanism remains to be explored. In many cancers Usnic acid has shown cytotoxic effects, accompanied with induction of apoptosis and cell cycle arrest. Usnic acid has been shown to inhibit many mitogenic signaling pathways like Akt and Erk and also found to inhibit invasion and migration of cancer cells, detailed mechanisms against lung cancer has not been explained so far. Use of Usnic acid could be a good approach to make strategies against lung cancer (Singh N et al 2013; Yang Y et al 2016).