



## Functional Foods for Lung Cancer Prevention

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### Abstract

Worldwide lung cancer is one of the most important research areas. Basically, Lung cancer is diagnosed in later stages where the distal metastasis and local invasion prevails. Therefore, the rate of death due to lung cancer is high as compare to other cancers. The preventive effect of functional food against lung cancer is creating a new opportunity in the field of research. Recent research has made significant claims that the interaction of functional ingredients of food with tumours help in inhibiting the metastasis process. Clinical studies must be conducted in order to shed more focus on the possible use of functional components over the inhibition of lung cancer. This mini review emphasizes on exploring the virtues and current knowledge related to lung cancer and the potential of some functional components on reducing the incidences of cancer metastasis.

**Keywords:** Bioactive Compound; Functional Foods; Lung Cancer; Metastasis; Non-Small Cell

### Abbreviations

ADP: Adenosine Di-Phosphate; Akt: Protein Kinase B; APO1: Apo-Lipoprotein A1; BAD: Bcl Associated Death Promotor; BAX: Apoptosis Regulator; Bcl: B-Cell Lymphoma; CAM: Cell Adhesion Molecule; Cdc: Cyclin-Dependent Kinase; Cdk-4: Cyclin dependent Kinase-4; Fas: Apoptosis Antigen 1; IL: Inter Leukin; MMP: Matrix Metalloproteinase; NPAT: Nuclear Protein; p-53: Tumour Protein; P-21/WAF1: Cyclin Dependent kinase inhibitor 1; Tyr: Tyrosine; Thr: Threonine; VEGF: Vascular Endothelial Growth Factor.

### Introduction

Cancer is a complex disease involving an unusual growth of the cells known as tumour. These cells are having the ability to invade or move to other body parts through blood and lymphatic vessels [1]. A general set of genes are mainly identified in many tumours [2]. The sure sign of cancer cells include continuity of cell proliferation signal, uncontrolled normal cell cycles, and reduce apoptosis process [3]. Cancer is one of the major causes of death globally [1].

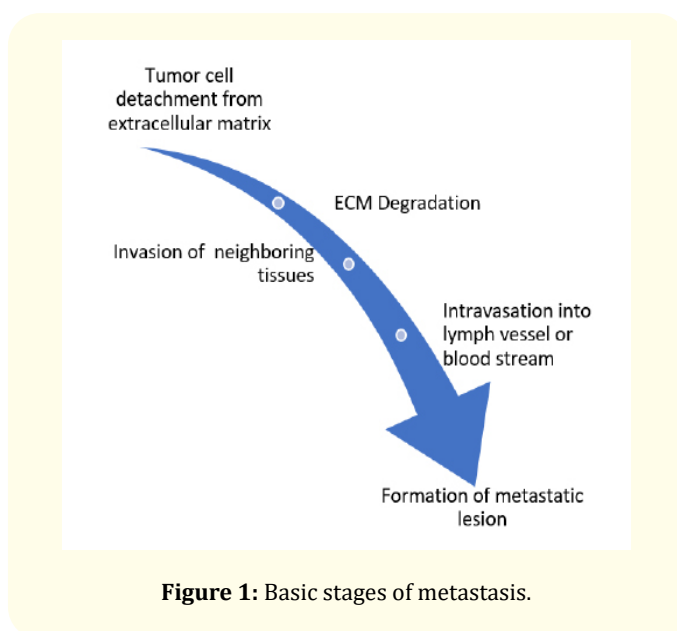
Of the all cancers, lung cancer is the most common disease that causes death [4]. Worldwide 2.1 million (11.6 % of all cancers) people are suffered from lung cancer. Number of deaths caused by lung cancer is 1.8 million (18.4 % of all cancers) [5]. It is reported that lung cancer was the first leading cause of death for males and

second for female [5]. There are many factors responsible for the outbreak of lung cancer. These factors include smoking, consumption of toxic heavy metals, transport pollution [6], respiratory diseases, exposure to toxic dusts such as silica, asbestos etc. [7]. Moreover, Smoking is found to be the major cause (80-90%) among all the cases of lung cancer [8,9].

Lung cancers are mainly classified as NSCLC (Non-Small Cell Lung Cancer) and SCLC (Small Cell Lung Cancer). The two types differ from each other in terms of their growth and the ability to spread [10]. 85-95% of lung cancers are NSCLC. Based upon the type of lung cells, their microscopic morphology and the manner of cancer initiation, it is further divided into 3 types [11]. They are slightly different from one another but possess same outlook (prognosis) and are mostly treated in the similar way. The most commonly occurring NSCLC is Adenocarcinoma. It is frequently found in smokers and also in former smokers. It grows on the outer edges of lungs. The growth of this type of cancer is slower than the other types [12]. Squamous cell carcinoma (epidermoid carcinoma) is another type of NSCLC. Mostly the smoker as well as the former smoker suffers from this type of cancer. It originates in the middle of the lungs near the bronchi (the main airways) [12]. Large cell carcinoma is the least common type of NSCLC; it grows and spread quickly to other organs, making it very difficult to treat [13].

Small cell lung cancer (SCLC), also called oat cell cancer. A small group consisting of 10% to 15% people suffers from this type. The rate of growth and spreading is very quick and even at the early stage; it spreads to the other body parts [14]. Most of the time, the early symptoms of lung cancer are not seen or are ignored, so generally, it is diagnosed in later stages where the distal metastasis and local invasion have been already prevailing.

The basic stages of metastasis (Figure 1) consist of tumour cell detachment from the extracellular matrix, surrounding tissues and basal lamina. The tumour intravasates into the blood stream and migrates to other locations. Extravasation takes place at the lateral site causing lesion. The above steps require functions like cell disruption, adhesion of cell matrix, angiogenesis etc [15].



**Figure 1:** Basic stages of metastasis.

Despite availability of several advanced treatments, overall survival rate of the lungs cancer patient is reported to be 5 years (limited to 15 % men and 21% for women) [16].

Therefore, novel and innovative approaches are required in order to prevent and treat lung cancer [17]. World Cancer Research Fund and the American Institute for Cancer Research reported that body composition, physical activity, food and nutrition plays a crucial central role in the cancer prevention [18] (WCRF/AICR, 2007).

Number of bioactive compounds from natural plant sources contains anticancer properties. These bioactive compounds are secondary metabolites of plant such as flavonoid, polyphenols, glycosides, possess anti-allergic, antiviral, antibacterial, anticancer and anti-oxidative properties. *In-vitro* and *in-vivo* study showed that these metabolites activate apoptosis, and delay metastasis [19].

### Functional foods and lungs

The Institute of Medicine's Food and Nutrition Board defined functional foods as "any food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains [20]. "Numerous scientific evidences explain the preventive effect of functional properties against different types of cancer [1,21,22]. The mechanisms behind preventive effect of functional foods against the different type of cancers are antioxidant, antibacterial, anti-inflammatory, detoxifying of enzymes, inhibiting the cell proliferation, immune- modulatory, inducing apoptosis, scavenging the free radicals and so on [21]. Basically, plants are the major source of naturally occurring health beneficial compounds. These secondary metabolites of plants are responsible to inhibit the lung ailments and help to maintain the health of lung. Table 1 demonstrated the *in-vitro*, *in-vivo* and clinical experimental trial of these metabolites against cancer cell. Several aromatic and pungent compounds in succulent plants trigger the mucous membrane of respiratory tract to eliminate undesirable agents and help to fight against harmful microbes. These aromatic components act as anti-tussive, antimicrobial and expectorants agents. The bioactive compounds improve the secretion of mucous membrane, decrease the inflammatory effect and destroy the pathogenic microbial cells by impairing the hydrogen bonds in the mucous membrane. Some plant metabolites help to fight against lung cancer by quenching angiogenesis, inducing apoptosis and repressing inflammatory pathways.

Thymol and menthol can behave as antimicrobial, anti-inflammatory and antioxidants agents. Also, they have an ability to impair hydrogen bonds and reduce the viscosity of mucous membrane; moreover, the air flow into the lungs is enhanced. Citrus fruits have antioxidant and antimicrobial properties that help to halt the occurrence of cancer. Limonoids and D-limonene of citrus peel protects the lung tissues. In patients of chronic obstructive pulmonary disease, pinene and eucalyptol were reported to be very helpful to clear and reduce the decongestive mucous [23]. Isoflavones (in Soyfoods), some phenolic compounds such as Epi- gallo- catechin gallate (in tea), curcumin (in turmeric) exhibit anticancer effects. It has investigated that Soybeans are able to provide protection against lung, prostate, colorectal, breast, uterine cancers [24]. Tannins possess anti-carcinogenic effect by scavenging free radicals and detoxifying carcinogens. Among these tannins, ellagic acid has been widely used as a natural medicine for prevention and treatment of cancers [25]. In various studies, it has been found that Malabaricone B (mal B), which is a phenolic compound present in spices, shows toxic effects on human lung cancer and T leukemia cell lines. However, they are nontoxic to human normal cells [26]. Antioxidants such as PEG-SOD and N-acetyl cysteine have the abil-

Bioactive component	Mechanism	Ref.
Berberine	Arrest the G1 phase, Preventive effect against telomerase and topo-isomerase Reduction of cyclin B1 levels.	[35]
Dihydroartemisinin	Activation of p38 and enhancement of Ca <sup>2+</sup>	[36]
Lignan and Arctigenin	Activation of Akt, arrest at G0/G1 phase through down regulation of NPAT.	[10]
Female Ginseng extract	Activation of caspase 3 and 9 which is mediated by the suppression of bcl-2 and cdk-4 expression. Cell reduction in S phase.	[37]
Saiko-saponin D	Increase in p53 and p21/WAF1, Induce Fas/APO1, Increase in caspase- 8 activity.	[38]
Polysaccharopeptide	Activation of T and B lymphocytes, monocytes, IL-2 and 6.	[39]
Adlay millet extract	Retardation of expression in cyclin A. Activation caspase cascade, Downgrading of poly [ADP- ribose] polymerase	[40]
Curcumin	Decrease in p53, BCL-2 BCL-XL, Repression of VEGF, MMP-2, MMP-9.	[41]
β-elemene	Arrest G2/M phase Increase the phospho-Cdc2 (Tyr15) and p27/Kip1, Decrease the phospho-Cdc2 (Thr161)and cyclin B1, Reduction of Cdc25C, Activation of Cdc2 IncreaseChk2	[42]
Antofine	Inhibition of protein synthesis.	[43]
Ganoderic acid X	Arrest of G1 phase, Reduction of mitochondrial potential, Release of cytochrome c, Decrease the ratio of BCL-2/BAX.	[44]
Stilbenoids; 3,4,5-trimethoxy-4'-bromo-sis-stilbene	Possess apoptosis via p53 and 21 Pathway Arrest of the G2/M phase.	[45]
Cheddar cheese peptide Extract	Induce apoptosis Arrest cell cycle	[46]
Ursolic acid	Inhibition of DNA synthesis.	[47]
Ponicidin	Down regulation of BCL-2 and survivin, Up regulation of BAX.	[48]
Gallic acid	Arrest G2/M phase, Production of intracellular Ca <sup>2+</sup> , Reduction of mitochondrial membrane potential, Activation of capase-3 and cytochrome c, Increase the BAX and BAD, Decrease BCL-2 and Bcl-XL.	[49]
8-epi-xanthatin	Inhibition of microtubule interfering	[50]
Dihydroactinidiolide, sterols (stigmasterol, campesterol and B-sitosterol), -Tocopherol, phytol	Cytotoxic effect	[51]
Resveratrol	Changes in expression of many genes	[52]

**Table 1:** Bioactive components and their role in preventing lung cancer.

ity to permeate through the cell. It was reported that because of the presence of these antioxidants in mal B, it strongly induces apoptotic effect [26]. The study also suggested that mal B (100 mg/kg) retards the tumor growth. A functional food colorant, Phycocyanin has anticancer effect against Non-small cell lung cancer (NSCLC). The results suggested that Phycocyanin promotes cell cycle arrest, apoptosis and suppress cell migration, proliferation [27]. Acai fruit seeds have well-fortified antioxidant properties. The Acai seed extracts exhibit the strong cytotoxic effect on human lung cancer cell line [28]. Study shows that lycopene has anti-carcinogenic effect and play an important role to prevent cancers in mammary gland, skin, liver and lungs [29]. Some studies showed that beta-carotene delay the formation of pre-neoplastic enzyme altered lesions but long term dosage enhanced the tumor formation in rats [30]. However, wide range of clinical trials suggest that cancer was not prevented by  $\beta$ -carotene, N-acetylcysteine,  $\alpha$ -tocopherol, retinol, retinyl palmitate, or isotretinoin for heavy smokers [31-34]. The available data also suggested that beta carotene supplements for smokers increases the chances of lung cancer. Thus, smoker must avoid beta carotene supplements [33].

## Conclusion

The major cause of mortality and morbidity are lung related disorders. Presently, the conventional therapeutics is not able to solve the entire problems. However, various traditional foods are available in the market and graded as dietary supplement for the lung health. These foods are effective up to a confined range. Moreover, an attention is required for standardization of different bioactive compounds in terms of bioaccessibility, bioavailability and dosage. Hindrance in Metastasis can help in spreading the tumour in other parts of body. Still, there is no any international regulation and legislation available related to the standardizing parameters of crude extracts obtained from different sources. No actual human trials and the subset of data is limited to cell line studies or mice studies hence there is a huge potential of exploring the anti-metastatic components that could help in preventing the metastasis of tumour and hence localize it to a particular location so that it can be removed surgically.

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