

A Comprehensive Review of Ethnobotanical Studies on Traditional Indian Herbal Plants for Lung Cancer Management

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Abstract

Lung cancer is a leading cause of cancer-related deaths in the world. Current therapies for lung cancer are often limited by many side effects. This review compiles and evaluates ethnobotanical evidence and modern scientific findings of Indian herbal plants traditionally used for respiratory and tumor-related disorders, with a focus on their relevance to lung cancer management. Herbal phytochemicals and how they show their potent activities were also listed in this study. Traditional Indian plants can manage lung cancer via various mechanisms such as induction of apoptosis, inhibition of PI3K/Akt and STAT3 pathways, suppression of metastasis-related genes, modulation of oxidative stress, and enhancement of host immune responses. Quercetin, kaempferol, apigenin, vincristine, vinblastine, matrine, ursolic acid, betulinic acid, paclitaxel, caffeic acid, etc. are the major phytochemicals which are responsible for the management of lung cancer. Plants, like Curcuma longa, Withania somnifera, Tinospora cordifolia, Ocimum sanctum, Azadirachta indica, Andrographis paniculata, Phyllanthus amarus, Boerhavia diffusa, Glycyrrhiza glabra, & Zingiber officinale, are the few Indian plants has various derivatives of phytochemicals utilize to manage cancers in respiratory system. These plants exhibit anticancer activity in the control of lung cancer via different pathways like apoptosis (programmed cell death), arrest in cell division, angiogenesis inhibition & metastasis, alteration of oxidative stress and disruption of signaling pathways. This review study mainly focusing on various Indian plants utilizing in the management of lung cancer and their diverse pathways to induce the cancer cells. Also included artificial intelligence data in the diagnosis and monitoring. By bridging traditional knowledge and contemporary biomedical research, this review aims to accelerate development of plant-derived interventions that are safe, effective, and culturally appropriate for lung cancer management.

Keywords: Ethnobotanical distribution, herbal plants, lung cancer, phytochemicals, traditional medicines

INTRODUCTION

Lung cancer is considered as one of the major cancer-related mortality causes globally. Early detection of

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cancer is very crucial for the treatment; however, it is often diagnosed in the advanced stages. Smokers, prolonged exposure to fumes, occupational hazardous exposure, and labor in oil fields are at high risk [1]. Continuous screening in high-risk people and modifications can improve the survival in lung cancer patients. Drug resistance, metastasis, and continuous recurrence affect the quality of life (QoL) [2]. There are two types of lung cancer: (1) small-cell lung cancer (SCLC) and (2) non-small-cell lung cancer (NSCLC). In these, 85% of cases are NSCLC, large-cell carcinoma, adenocarcinoma, and squamous-cell carcinoma. SCLC is a very highly aggressive lung cancer having rapid proliferation, high mortality rate, early metastasis, and frequent early relapses [3]. In the

brain, active neuronal activity influences glioma growth via paracrine mechanisms, and these glioma cells integrate with neuronal circuits for their own growth. Like this, lung cancer cells can grow near neurons and influence the neurons to release acetylcholine and norepinephrine. It could increase the growth of cancerous cells and activate tumor cell growth [4].

Traditional medications or herbals could induce cell death (apoptosis by stimulating mitochondria to release cytochrome C), inhibits cell proliferation (cell division, cyclins, and CDKs), inhibition of oxidative stress and inflammation in chronic inflammations (inhibits NF- κ B, COX-2, inflammatory cytokines and ROS), DNA fragmentations and by modulating cell signaling like PI3K/Activation of Protein Kinase B (Akt)/STAT3/p53 activation (tumor protein 53)/ERK/MAPK/mTOR [5].

Phytochemicals, like alkaloids, phenols, flavonoids, glycosides, proteins, carbohydrates, and fixed oils, revealed significant role in lung cancer. These phytochemicals may possess antioxidant, anti-inflammatory, enzyme inhibition, antibacterial, and anticancer effects (Figures 1 & 2) [6].

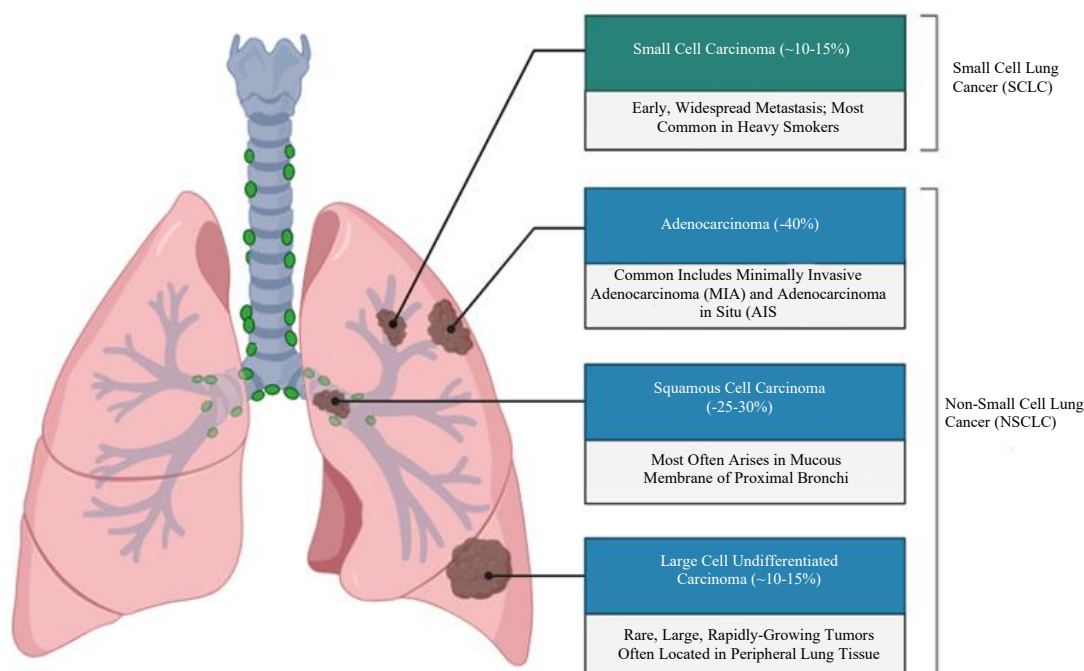


Figure 1. Lung cancers based on the appearance of the cells.

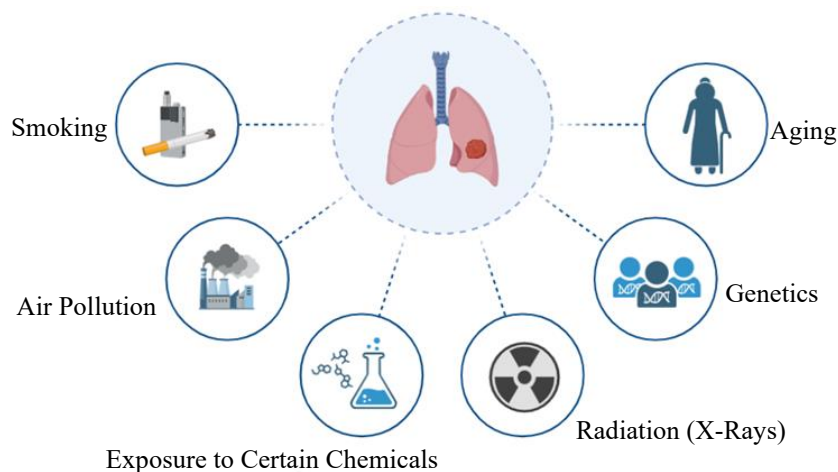


Figure 2. Factors influencing lung cancer.

Various types of phytochemicals are available and can target cancer cells via different mechanisms. Catenin beta 1 (CTNNB1), Signal Transducer & Activator of Transcription 3 (STAT3), hypoxia-inducible factor 1 subunit alpha (HIF1A), heat shock protein 90 alpha family class A member 1 (HSP90AA1), and erb-b2 receptor tyrosine kinase 2 (ERBB2) are cancer genes which integrates various cellular processes and have major role in cancer genesis. The affinity between 6-alpha-diol and HIF1A has potential as therapeutic agents for lung cancer [6, 7].

COLLECTION OF DATA

For this review study research and reports were collected from various e-databases like PubMed, Web of Science, Springer Link, Science Direct, Wiley Blackwell and google scholars. Together we made this data from gathered all the data together. Peer reviewed data and e-books also included. Keyword related data included to know the research gap of this study conducted and reviewed yet.

PHYTOCHEMICALS IN LUNG CANCER

Traditional Indian medicinal systems identified diverse plants to treat lung cancer, and they show very minimal adverse side effects [8]. The lung tumor immune microenvironment is given in Figure 3 and Mechanisms of Phytochemicals are given in (Figure 3 and Table 1).

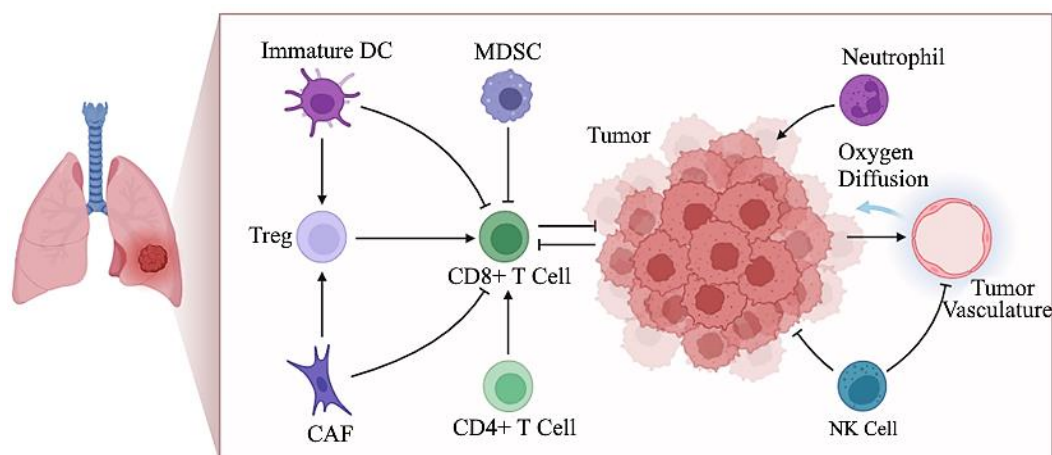


Figure 3. The lung tumor immune microenvironment.

Table 1. Mechanisms of phytochemicals.

| Plant name (scientific name) | Phytochemical constituents | Mechanisms of phytochemicals |
|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Curcuma longa</i> (Turmeric) | Diferuloylmethane, Demethoxycurcumin, Bidemethoxycurcumin, Tumerone, Atlantone, Zingiberone | Phytochemicals revealed potent anti-inflammatory activity and antioxidant [9]. Phytochemicals on A549 cells exhibited induce of apoptosis, intracellular RoS, and MMP [10]. TPE-1, turmeric derived polysaccharides improved cytotoxic effects of NK cells and T cells against tumor cells [11]. Lung cancer cells (A549 & H460) treated curcuminoid extracts and nano-emulsions inhibited G2/M, stimulate release of cytochrome C, and reduce in CDK1 expression [12]. |
| <i>Withania somnifera</i> (Ashwagandha) | Withaferin A Withanone [15] | <i>Withania somnifera</i> , ethanolic extract reported anti angiogenic, potent apoptotic, and anti-mitigated activity [13]. Major phytochemical constituent, Withaferin A (WA) had shown anti-neoplastic activities in in-vitro and in-vivo significantly [14]. WA has potent cytostatic effect and could stimulate apoptosis in CRC cells via Reactive oxygen species mediated mitochondrial impairment and c-Jun N-terminal Kinas's inhibition [15]. |
| <i>Andrographis paniculata</i> | Wogonin, 14-deoxy-11-oxo-andrographolide, Mono-O-methylwightin, Deoxycamptothecine, Quercetin tetramethyl (3',4',5,7) ether, 14-deoxy-andrographolide, & Andrographolide-19-β-D-glucoside | Key targets, like AKT1, NCOA1, RELA, and MAPK14, were identified [16]. Ethanolic extract of <i>Andrographis paniculata</i> could decrease the telomerase enzyme, enhance apoptosis and expression of caspase-3 [17]. AD, Andrographolide significantly reduces NSCLC via suppressing JAK2 (or) STAT3 signalling pathway [18]. Flower extract (aqueous) induces the secretion of apoptotic proteins (IL-2, TNF α, and IFN-γ) in A549 cells [19]. |

| | | |
|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Azadirachta indica</i> | Desacetylnimbin, Nimbandiol, Nimbin, Nimbinene, Nimbolide, Salannin, Vepinin, Diterpenoids [20, 21] | Target genes as EGFR, BRAF and PIK3CA against NSCLC by the active components of <i>A. indica</i> [20]. Phytochemicals possess free radical scavenging and other pharmaceutical properties via the regulation of proinflammatory enzymes (COX & TOX) [21]. <i>A. indica</i> inhibit induce apoptosis, oxidative stress, inhibit invasion and proliferation, antimetastatic. And antiangiogenesis [22]. |
| <i>Ocimum sanctum</i> (Tulsi) | Eugenol, Rosmarinic acid, Quercetin, Rutin, Carvacrol, Thymol, β -Caryophyllene | OC has ability to control enzymatic activity (GSH, GST, GSH-Px, SOD and CAT). OC induce apoptotic signalling, cell cycle arrest, and disrupt membrane receptors [23]. Ethanol extract may suppress PI3K/Akt, COX-2, uPA, uPAR, MMP-9, VEGF and EGFR in OPN treated NCI-H460 cells [24]. |
| <i>Centella asiatica</i> | Asiaticoside, Asiatic Acid, Madecassoside, Madecassic Acid | Asiatic acid (AA), increased microtubule-associated protein 1 light chain 3 (LC3) and decreased the expression of p62. In vivo study shown enhanced apoptosis and mitochondrial cell damage [25]. Phytochemicals can inhibit ionizing radiation-induced migration & invasion of A549 lung cells [26]. Triterpenoids exhibit high anti-angiogenic [27]. |
| <i>Camellia sinensis</i> | Epigallocatechin-3-gallate (EGCG), Epigallocatechin (EGC), Epicatechin-3-gallate (ECG), Epicatechin (EC) | EGCG triggers induction of apoptosis, modulation of Bax/bcl-2 ratio and by triggering G2/M cell cycle arrest [28]. Exhibited apoptotic cell death A549 cells [29]. EGCG, induce stabilization of HIF-1 α & oxygen-dependent degradation [30]. |
| <i>Lawsonia inermis</i> | Lawson, Luteolin, Apigenin, Quercetin, β -Sitosterol, Gallic Acid, Coumarins | Extract can induce cytotoxic properties against A549, DLD1, HepG2 [31]. Oral feeding of leaf powder with water, decrease tumor growth and topical application decreased metastasis of tumor cells [32]. Leaf extracts in various extracts shown potent cytotoxic activity [33, 34]. |
| <i>Tabernaemontana divaricata</i> | Coronarine, Voacangine, Voacamine, Catharanthine, Dregamine | Plant extract shown high potent cytotoxic activity on COR L23 lung cancer cell lines [35]. Monoterpene indole alkaloids, such as 3 α -hydroxymethyl-ibogamine, 3 α -acetatemethoxyl-ibogamine, and 16 α -hydroxyl-ibogamine, have shown least cytotoxic against A-549 lung cancer cell lines (IC ₅₀ > 20 μ M) [36]. |
| <i>Moringa oleifera</i> | Benzy Isothiocyanate, Niaziminin, Kaempferol, Quercetin, Chlorogenic Acid, Ferulic Acid, β -Sitosterol, Glucosinolates | Leaf extracts (MLE) in urethane-induced lung cancer in adult male albino rats has shown significant anti-cancer activity via improving collagen and inducing apoptosis [37]. 80 targeted proteins identified and caffeic acid shown potent anticancer activity (EGFR-mediated oncogenic signalling inhibitor) [38]. |
| <i>Terminalia chebula</i> | Chebularic Acid, Chebulinic Acid, Gallic Acid, Ellagic Acid, Chebulanin, Quercetin, Kaempferol, Luteolin | Fruit extract against A549 and MCF-7 cells reported it exhibit potent anti-inflammatory and anticancer activity [39]. Ethyl acetate fruit extract has ability to stimulate the apoptotic factors, like cytochrome-C, which can induce cell death [40]. Photothermal/photodynamic therapies of extract could inhibit the growth of cancerous cells [41]. |
| <i>Bacopa monnieri</i> | Bacosides, Brahmine, Nicotine Alkaloids, Betulinic Acid, Stigmasterol, β -Sitosterol, Luteolin, Apigenin | Methanol extracts identified triterpenoid glycosides, bacopasaponin K, bacopasaponin L, bacopaside IV & VII, bacopasaponin E, bacoside A ₃ , bacopasaponin F, bacopasaponin C, bacopaside I, and bacopaside II. Which results high cytotoxic effects against PC9 [42]. |

AI IN LUNG CANCERS

AI is advancing in all fields nowadays. AI in oncology can effectively diagnose, treat, evaluate prognosis, and provide advanced treatment to lower the lung cancer related mortality [43]. Promising approach of AI in lung cancer able to monitor, screen, and detect cancerous cells. It can noticeably improve the ability to detect lung nodules early, lower the number of unnecessary false alarms, and help in distinguishing different types of nodules with better accuracy [44]. Recent AI advances and machine learning offers significant potential to overcome many of the existing limitations in lung cancer screening and to promote greater fairness and accessibility in patient care [45].

PRE-CLINICAL AND CLINICAL STUDIES

Various parts of *Withania somnifera* (Ashwagandha), have been studied on animals and it showed potent anticancer and immunomodulatory activity [46]. Oral administration of *Moringa oleifera* leaf extract showed potent anticancer activity (apoptosis) in mice (F1 to F15) and the study conducted by comparing with 5-fluorouracil treated animals [47].

CONCLUSION

This review study concluded, various Indian herbals, their phytochemicals and their mechanisms. Data which identified from the articles reports that all study available on in vitro cell lines A549, H1299, and

H460. Very least studies are reported in vivo and human studies. PI3K/Akt, MAPK, STAT3, p53, RoS pathways are still needed to be studied. Nanotechnology can enhance the absorption and metabolism of target-based delivery. Precise treatments and combinational therapy have limited data.

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