Decoding Lung Cancer Targets Using Solanum Trilobatum: An *In Silico* Approach

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ABSTRACT

Background:

Lung cancer is a major global health burden, characterized by high mortality rates and limited effectiveness of existing therapeutic strategies. The search for novel, targeted and less toxic anticancer agents has led to increased in medicinal plants. *Solanum trilobatum*, a well- known medicinal plant in traditional medicine possesses a wide range of bioactive phytochemicals with reported pharmacological properties including anticancer activity. This study explores the potential of *Solanum trilobatum* phytocompounds against lung cancer- associated molecular targets using *In silico* approaches.

Objective:

To identify and characterize the key phytoconstituents present in *Solanum trilobatum* extract with potential anticancer activity. To perform *In silico* molecular docking studies of selected phytoconstituents against lung cancer-related target proteins (EGFR, VEGF, ALK, ROS1, c-MET) to predict binding affinity and interaction mechanism.

Key findings:

Key molecular targets involved in lung cancer progression such as epidermal growth factor receptor (EGFR), Vascular endothelial growth factor (VEGF), Anplastic lymphoma kinase (ALK), ROS proto oncogene (ROS1), Mesechymla epithelilal transition factor (c-MET) signalling proteins were reviwed for computational analysis. Results of Molecular docking studies were revealed strong binding affinities and stable interactions, suggesting the potential inhibitory effects of the phytocompounds of *Solanum trilobatum* on critical cancer related pathways.

Conclusion:

The study revealed that phytoconstituents of *Solanum trilobatum* could be considered as the promising inhibitor against lung cancer.

Keywords: Lung cancer, Molecular targets, *Solanum trilobatum*, Phytochemistry, *Insilico*screening, Anticancer activity.

1. INTRODUCTION

Lung cancer is a type of malignancy that begins in the tissues of the lungs, most commonly in the cells lining the air passages. It is the **leading cause of cancer-related deaths worldwide**, both in men and women. Lung cancer primarily occurs in people who smoke, although non- smokers can also develop the disease due to environmental and genetic factors.(Khuder, 2001) The global burden of lung cancer is significant. According to the **GLOBOCAN 2022** estimates, lung cancer accounted for **11.4% of all new cancer cases and 18% of all cancer deaths**, making it the most lethal form of cancer globally. In India, lung cancer ranks among the top cancers affecting males and is increasingly being reported in urban populations due to tobacco use, air pollution, and occupational exposures.

Solanum trilobatum Linn (Family:Solanaceae) commonly known as purple fruited pea eggplant or thoothuvalai a medicinal herb traditionally used in Ayurvedic and Siddha system for treating asthma, bronchitis and other respiratory disorders. Investigation of phytochemical constituents have revealed the presence of steroidal alkaloid, flavonoids, phenolic compounds and saponin exhibit wide pharmacological activities such as antioxidant, anti-inflammatory, antimicrobial, anticancer etc. Given its importance to respiratory relevance, *S.trilobatum* presence a rationale potential candidate for lung cancer research.

The integration of *Insilico* techniques in herbal products (phytoconstituents) research enables systematic screening of phytoconstituents against cancer specific molecular targets. This chapter focuses on decoding of lung cancer associated targets using *Solanum trilobatum* phytoconstituents through computational approach.

2. REVIEW

2.1 Types of lung cancer

Majorly there are two types of lung cancer namely Non-small cell lung cancer and Small cell lung cancer.

2.1.1. Non-small cell lung cancer:

More than 80% of lung cancer cases are non-small cell lung cancer (NSCLC). It encompasses squamous cell carcinoma and adenocarcinoma. The other two less prevalent forms of NSCLC are sarcomatoid carcinoma and adenosquamous carcinoma.

- Adenocarcinoma, which begins in cells that line the alveoli and make mucus.
- Squamous cell carcinoma, which begins in the thin, flat cells that line the inside of the lungs.

Other less common types of NSCLC include the following.

- Sarcomatoid carcinoma: This type of lung cancer has features of carcinoma (cancer that starts in the skin or in the lining or covering of organs) and sarcoma (cancer of the supportive or connective tissue, such as bone, cartilage, fat, muscle or blood vessels).(*Cancer.Gov/Publications/Dictionaries/Cancer-Terms/Def/Sarcomatoid- Carcinoma*, n.d.)
- Adenosquamous carcinoma: This type of cancer affects both squamous cells and cells of glandular tissue.
- Pancoast: This is a rare tumor that grows in the top part of the lungs and may affect the surrounding structures.

2.1.2. Small cell lung cancer

- **Small cell lung cancer**, also known as SCLC, makes up about 10% to 15% of all lung cancers. It tends to grow and spread quickly. There are two main types of SCLC, which derive their names from how the cancer cells look under a microscope.

- Small cell carcinoma: Also known as "oat cell" cancer, this is the most common type of SCLC. It is fast-growing and may spread quickly to other parts of the body.
- Combined small cell carcinoma: This rare type of lung cancer has features of both SCLC and NSCLC contained within the same tumor.

2.1.3. Other Types of Lung Tumors

Besides NSCLC and SCLC, there are other types of lung tumors that are less common. These include the following.

- **Lung carcinoid tumors**: Also known as lung carcinoids or neuroendocrine tumors, these are slow-growing tumors that make up less than 5% of all lung cancers.
- **Salivary gland-type lung carcinoma**: This is a slow-growing tumor of the central airway that starts in the mucus-secreting (submucosal) glands.
- **Large cell neuroendocrine carcinoma**: This is a rare, fast-growing tumor with features of SCLC and NSCLC.
- **Mediastinal tumors**: These are rare and begin growing in the space between the lungs. They may be slow-growing or aggressive, depending on the organs involved.
- **Mesothelioma**: This is a rare, fast-growing tumor that may start in the lining around the lungs. Most cases are caused by exposure to asbestos. (*Definition of Mesothelioma - NCI Dictionary of Cancer Terms - NCI*, 2011)

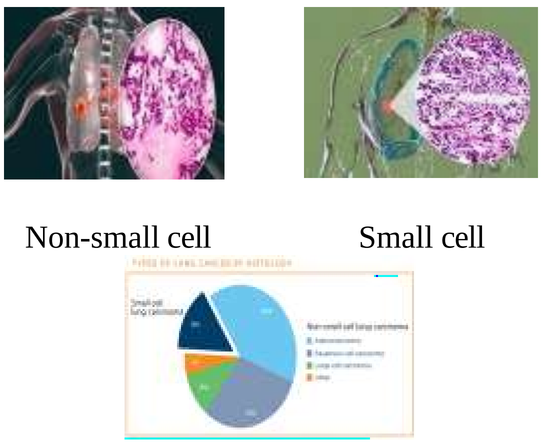


Figure 1: Types of lung cancer (2,4,6)

2.2. Stages of lung cancer:

Cancer is usually staged based on the size of the initial tumour. Each stage has several combinations of size and spread that can fall into this category.

2.2.1. Stage 0: Cancer is in the top lining of the lung or bronchus. It hasn't spread to other parts of the lungs or outside of the lungs.This is called "in situ" disease, meaning that the cancer is "in place" and has not spread from where it first developed.

2.2.2. Stage 1: Cancer is spread inside the lung

Stage I lung cancer tumors are small primary tumors that are in one lung only. Stage I lung cancer has not spread to any lymph nodes and has not metastasized. Stage I lung cancer is divided into two substages, stage IA and stage IB, based mainly on the size of the tumor. Smaller tumors, those no more than 3 centimeters (cm) in the greatest dimension, are stage IA, while slightly larger ones—more than 3 cm but no more than 4 cm in the greatest dimension— are stage IB. Stage IB tumors may or may not have grown into the main bronchus or the lung's inner lining or have caused lung collapse or swelling

2.2.3. Stage 2: Cancer is larger than Stage I, has spread to lymph nodes inside the lung, or there's more than one tumour in the same lobe of the lung. They have grown into the lung's outer lining or nearby sites including the chest wall, phrenic nerve, or the heart's lining, or there are primary and secondary tumors in the same lobe.

2.2.4. Stage 3: Cancer is larger than Stage II, has spread to nearby lymph nodes or structures or there's more than one tumour in a different lobe of the same lung.

2.2.5. Stage 4: Cancer has spread to the other lung, the fluid around the lung, the fluid around the heart or distant organs.

Unlike the earlier stages of lung cancer, stage IV lung cancer has metastasized to distant parts of the body. The tumors may be of any size and may or may not have spread to lymph nodes.

Stage IV lung cancer is divided into two stages: stage IVA and stage IVB.[4,5,6,7,8,10] Stage IVA tumors may be of any size, may or may not have spread to any lymph nodes, and have metastasized, either from one lung into the other lung, into the lung's lining (and have formed secondary nodules), into the heart's lining (and have formed secondary nodules), or into the fluid around the lungs or the heart; and/or tumors have spead to one site outside the chest area (e.g., adrenal gland or bones)

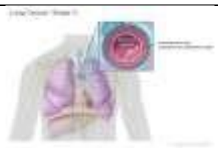
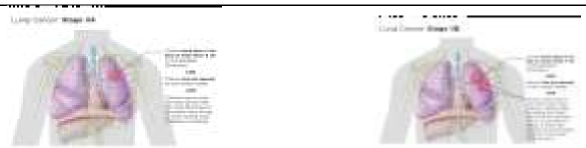
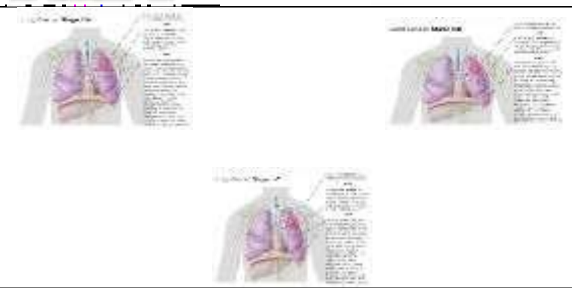
Stage 0	
Stage 1	
Stage 2	
Stage 3	
Stage 4	

Figure 2: Stages of lung cancer (*Cancer.Gov/Publications/Dictionaries/Cancer-*

***Terms/Def/Sarcomatoid-Carcinoma*, n.d.)**

2.3. *Insilico* approach – Lung cancer drug discovery

Molecular docking, ADMET, Drug likeness prediction, Network pharmacology and Molecular dynamic simulation are considered as essential tool in predicting binding affinity, interaction pattern, evaluation of absorption, distribution, metabolism, excretion and toxicity profiles of

phytoconstituents of medicinal herb molecular target therapy is an emerging technique to stop the development, progression, and tumor metastasis,(Sanchez-Cespedes et al., 2002) and causes high effectiveness and less toxicity than traditional treatment.

Recent studies have revealed that molecular target therapy has led to significant clinical success in the treatment of numerous cancers like chronic myelogenous leukemia, colon cancer, breast cancer, and lung cancer(Carretero et al., 2010). The use of molecular target therapy has improved the survival rates of lung cancer patients(Sanchez-Cespedes et al., 2002). Research findings revealed that drugs that are used in molecular target therapy, block important signaling pathways such as EGFR, ALK, VEGF, and KRAS resulted in improving survival outcomes, minimizing systemic toxicity and enabling personalized treatment strategies.

Figure 3: Statistics of Pathways of lung cancer

2.3.1. Epidermal growth factor receptor tyrosine kinase

EGFR is encoded by the EGFR gene(Liu et al., 2013) and is widely expressed in normal tissues originating from epithelial, mesenchymal, and neural cells(Mitsudomi et al., 2000). EGFR is a kind of transmembrane protein that has cytoplasmic kinase activity. EGFR activates downstream signaling pathways such as RAS-MAPK, PI3K-AKT, STAT, and binding of growth factors (epidermal growth factor) stimulates these signaling pathways, whose most important obligation is transferring important growth factor signaling from the extracellular environment to the cell (12). Activation and regulation of EGFR and downstream genes lead to apoptosis, proliferation, and angiogenesis (Delmore et al., 2011). Mutations in EGFR activate the abnormal signaling pathway and cause an increase in cell survival, proliferation, angiogenesis, and a tendency to metastasize (Beroukhim et al., 2010). It is observed that EGFR is expressed almost in 93% of NSCLC patients, of which about 45% are overexpressed and mostly found in patients who are not smokers (Brock et al., 2008).

EGFR acts as a tumor marker and becomes an attractive tool in molecular lung cancer target therapy(Li et al., 2013). High expression of this gene has been attributed to treatment resistance and poor diagnosis(Beroukhim et al., 2010). However, lung cancer patients, who have mutations in the EGFR gene, are sensitive to tyrosine kinase inhibitors (TKIs) drugs(Peifer et al., 2012).

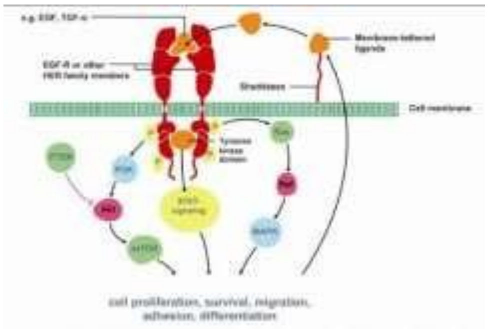


Figure 4: EGFR pathway(“Targeted Therapies in Lung Cancer and Biomarkers,” n.d.)

2.3.2. Vascular endothelial growth factor

VEGF binds to VEGF receptors on vascular endothelial cells which regulate vascular endothelial cell proliferation and migration, stimulate angiogenesis in embryonic growth, and heal adult wounds(Sini & Devi, 2004). The effects of VEGF on cells through several signaling pathways including the PI3K pathway, MAPK / ERK pathway, and others(Ranjith et al., 2010). Tumor cells in order to keep growing and survive, need the formation of new blood vessels. This process is provided through the angiogenesis process, and for this reason, angiogenesis becomes a hallmark of cancers(Sivakumar et al., 2024). Tumor tissue vessels are aberrant, twisting, fragile, and leaky.

Due to the detachment of perivascular cells, tumor vessels are incoherent, immature, dysfunctional, and less integrated, and this feature increases tumor spread and metastasis (22). VEGF is a major mediator of tumor angiogenesis that causes stimulation of the growth of new blood vessels and provides tumor cells oxygen and nutrients(Sini & Devi, 2004). Moreover, recent data have shown that VEGF is involved in tumor metastasis.

This suggests that VEGF and its signaling pathways appear as attractive targets for the treatment of various types of cancer, including lung cancer. There are reports that revealed serum levels of VEGF are high in both types of lung cancer. VEGF through activation of MEK/ERK and PI3K/AKT signaling pathways induces lung cancer cell proliferation(Ganesan et al., 2013). In lung cancer treatment, targeting VEGF with antibodies and VEGF receptors with small molecules has been studied(Beroukhim et al., 2010).

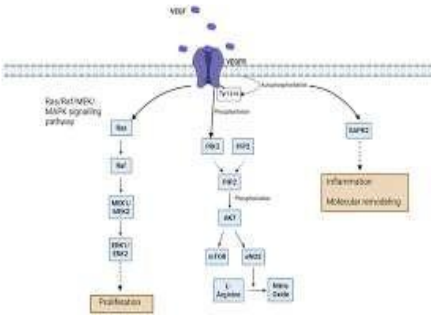


Figure 5: VEGF pathway(*VEGF and VEGFR Signaling Pathways Involved in Lung Cancer Development* .... , n.d.)

2.3.3. Anaplastic lymphoma kinase

ALK gene encodes ALK, which is a receptor tyrosine kinase, involved in the development of the nervous system during embryogenesis. In adult persons, only specific neurons express ALK. RAS–MAPK, PI3K –AKT, and JAK-STAT pathways are regulated by ALK (Roskoski, 2017). Mutation, gene amplification, and chromosomal rearrangement are the reasons that abnormally activate ALK(Roskoski, 2017). The most usual abnormality of ALK that occurs in lung cancer is ALK rearrangement so 3% to 5% of lung cancer patients have ALK rearrangement. Translocation between the N-terminal of echinoderm microtubule-associated protein-like 4 (EML4) and ALK gene leads to EML4-ALK formation (Solomon et al., 2009)which has carcinogenic and malignant features and occurs in 80% of ALK positives in lung cancer. ALK translocation increases tyrosine kinase activity, which increases cell proliferation, survival, and tumorigenesis. Also, ALK fusion is used as a therapeutic target that responds well to ALK TKI which leads to inhibiting the ALK downstream signaling pathway and induces apoptosis(Holla et al., 2017)

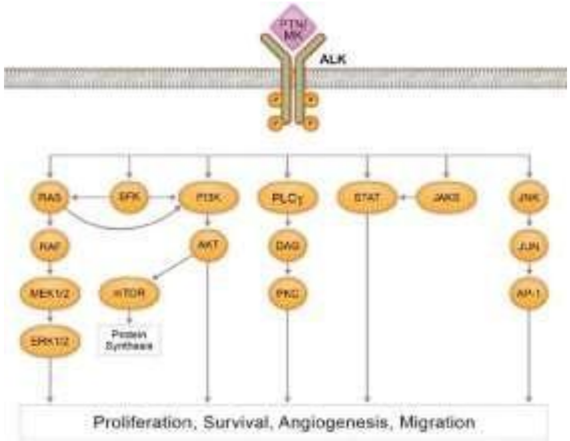


Figure 6: ALK pathway(*Figure 1. Anaplastic Lymphoma Kinase (ALK) Signaling*, n.d.)

2.3.4. KRAS (Kirsten rat sarcoma virus)

KRAS proto-oncogene gene encodes the KRAS protein, a guanine triphosphatase (GTPase), which has a major role in the regulation of several cell functions and acts as signal transduction for EGFR, MET, and ALK. KRAS activity is controlled by the GTP/GDP ratio(Kim et al., 2021). The most common mutation in KRAS is point mutation (Brock et al., 2008)which inhibits KRAS ability in the hydrolysis of GTP and activates KRAS downstream signaling cascades, leading to uncontrolled cell proliferation and survival.

Deregulation of the KRAS pathway is found in 25% of NSCLC cases. The G12C mutation, which is present in 16% of all lung adenocarcinomas, is the most frequent change in KRAS in lung cancer. The KRAS G12C mutation has been identified as a possible target for new therapeutics(Cucurull et al., 2022).

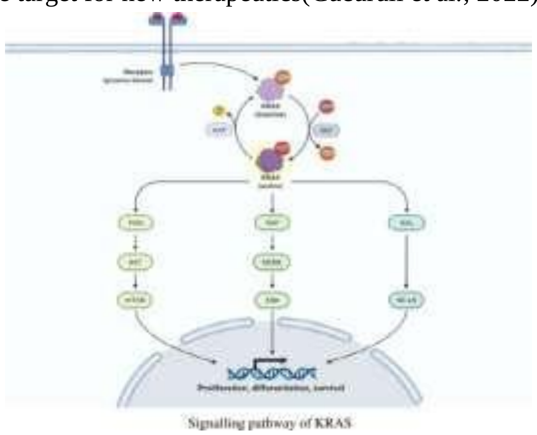


Figure 7: KRAS pathway(*An Updated Review on KRAS Mutation in Lung Cancer (NSCLC) and Its Effects on Human Health | Applied Biochemistry and Biotechnology | Springer Nature Link*, n.d.)

2.3.5. HER2 gene

HER2 gene encodes the tyrosine kinase receptor of the ERBB family which directly adjusts the EGFR signaling pathway that leads to activation of MAPK, JAK-STAT, and P3K/Akt signaling pathways. In several malignancies like bladder, breast, ovarian, stomach, pancreatic, and lung cancers, the HER2 signaling pathway is hyper-activated which results in uncontrolled cell development(*Introductory Chapter: HER2 – A Key Player in Cancer Biology | IntechOpen*, n.d.). Overexpression, amplification, and mutation are three types of HER2 gene aberration observed in NSCLC. Based on several recent studies, in NSCLC patients HER2 overexpression is linked to poor outcomes while the predictive importance of HER2 mutation and amplification is unknown (*Introductory Chapter: HER2 – A Key Player in Cancer Biology | IntechOpen*, n.d.).

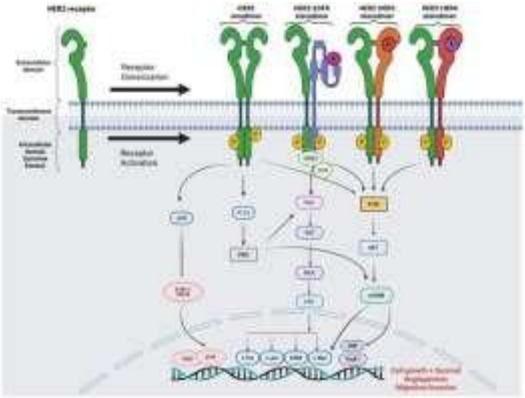


Figure 8: HER 2 gene(Aliaga et al., 2025)

2.3.6. BRaf murine sarcoma viral oncogene homolog B

The BRAF gene encodes a serine/threonine-protein kinase and belongs to the Raf kinase family that regulates cell development, differentiation, and proliferation through the MAPK signaling pathway. Mutations in the BRAF gene will result in the development and progression of cancer.

BRAF mutations, mostly as a V600E mutation, have been discovered in 50% of all melanomas. BRAF is one of the most critical genes linked to the development of NSCLC and is found in 1.5-3.5% of NSCLC patients(*BRAF Mutation and Cancer | Johns Hopkins Medicine*, n.d.).

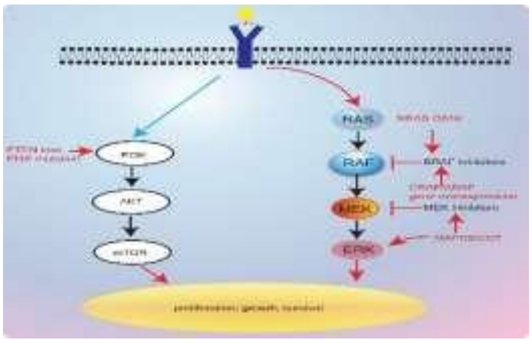


Figure 9: BRAF pathway(Yan et al., 2022)

2.3.7. C-ros oncogene

ROS proto-oncogene encodes a membrane protein with tyrosine kinase activity. ROS1 has a critical role in the activation of JAK/STAT, RAS/RAF/MEK/ MAPK, and PI3K/AKT/mTOR pathways activation of which causes cell development, proliferation, and cell differentiation. Any alteration in the ROS1 gene contributes to tumor formation and progression. In numerous types of cancers such as ovarian and colorectal cancer ROS1 gene rearrangement has been found. ROS1 rearrangements are seen in about 1–2% of NSCLC patients who are young, female, and have never smoked. ROS1 is currently recognized as a unique molecular target in NSCLC(*ROS1 (ROS Proto-Oncogene 1 , Receptor Tyrosine Kinase),* n.d.).

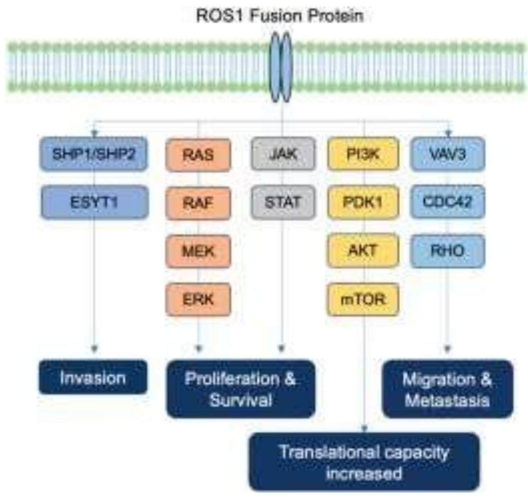


Figure 10: ROS1 pathway(Yang et al., 2023)

2.3.8. C-mesenchymal-epithelial transition factor

c-MET gene produces a tyrosine receptor kinase that has an essential role in vital biological functions including cell development, cell cycle, cell differentiation, repair of injured tissues, liver regeneration, and embryogenesis(Viticchiè & Muller, 2015). c-MET and its ligand hepatocyte growth factor (HGF) activate MAPK and PI3K/AKT/mTOR signaling pathways. In numerous malignancies, including NSCLC, up-regulation, amplification, or mutation of the c-MET receptor causes carcinogenesis, poor prognosis, and metastasis. As a result, it has been considered an interesting therapeutic anti-cancer target. According to several studies, c-MET overexpression was identified in 60% of NSCLC patients(Faiella et al., 2022).

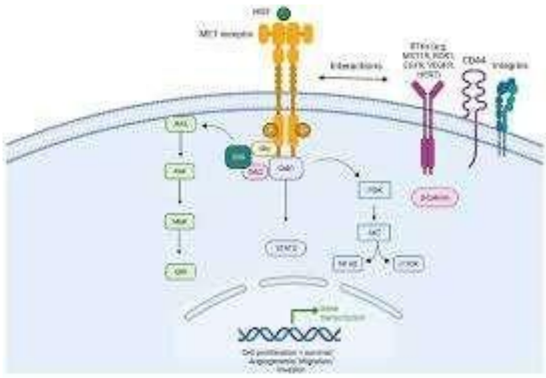


Figure 11: c-MET pathway(Spitaleri et al., 2023)

2.4. Synthetic and botanical description of *Solanum trilobatum*

Solanum trilobatum i a member of the Solanaceae family and the order Solanales. It includes a huge number of plants, with about 102 genera and 2500 species. It is a perennial herb that is spiky and spread out, has a bright green hue, and has a woody base. This herbaceous plant grows to be 2 to 3 meters tall and can be found all throughout India, but it grows best in dry areas, where it often grows as a weed along roads and in barren areas. *Solanum trilobatum* has a growth habit that is very branching and spiky. Its leaves are deltoid or triangular in shape and have uneven lobes. The blooms of this plant are purple-blue and grow in cymes.

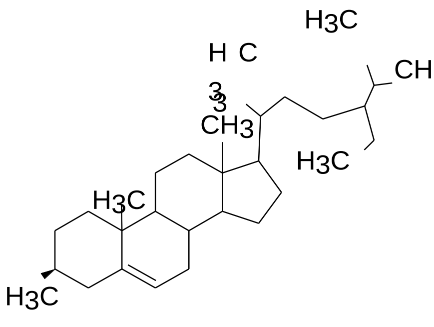
The berries, on the other hand, are round and usually red or scarlet in color(Anirudhan & Nair, 2009).

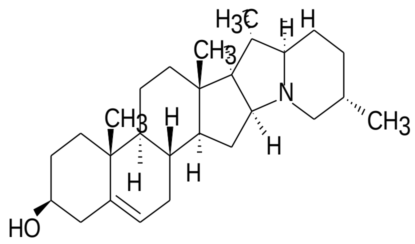
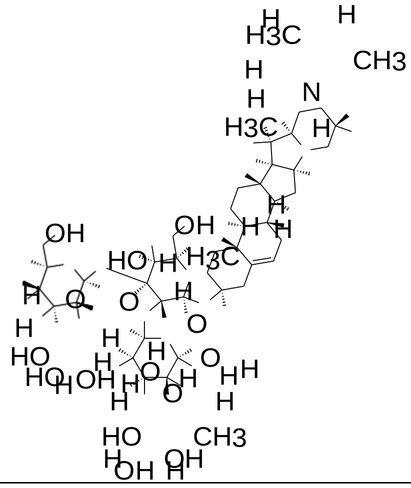
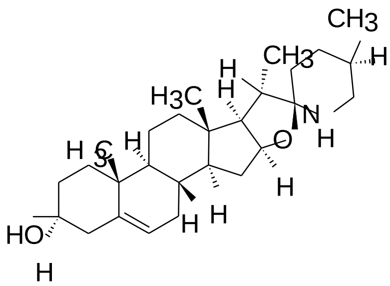
1.	Kingdom	Plantae
2.	Division	Tracheophyte
3.	Class	Magnoliopsida
4.	Order	Solanales
5.	Family	Solanaceae
6.	Genus	Solanum
7.	Species	Trilobatum

Figure 12: *Solanum trilobatum*- Description

Solanum trilobatum possess a variety of secondary metabolites including alkaloids, flavonoids, glycosides, triterpenoids, steroids, phenols, tannins, anthraquinones,amino acids, and saponins. Dried leaves demonstrated the presence of saponins, phytosterols, carbohydrates and tannins. In contrast, the stem part showed that it has carbohydrates, saponins, phytosterols, tannins, flavonoids, and cardiac glycosides(Sahu et al., 2013). *Solanum trilobatum* shows the presence of various chemical components such as sobatum, β- solamarine, solasodine, solanine, solanidine, tomatidine and diosgenin etc

Table 1: Structure and Pharmacological activity of *Solanum trilobatum*(Sivakumar et al., 2024)

Sl.No	Phytoconstituents	Structure	Pharmacological activity
1	Sobatum		Anticancer/cytotoxic activity Anti-inflammatory action Antioxidant activity

2	Solanidine		Anticancer/cytotoxic activity Anti-inflammatory activity Antioxidant activity Antimicrobial Antidiabetic Antiviral activity
3	Solanine		Anticancer activity Antimicrobial and antifungal activity Anti-inflammatory activity Antioxidant activity Hepatoprotective
4	Solasodine		Anticancer /cytotoxic activity Anticonvulsant effect Anti-inflammatory activity Antioxidant activity Antimicrobial activity Immunomodulatory properties

2.5. Decoding lung cancer targets – Phytoconstituents of Solanum trilobatum – Insilico approach

Decoding of lung cancer targets involves identifying protein that play essential role in tumor initiation, progression and metastasis.The targets are retrieved from publicly available database (PDB). The interaction between lung cancer related protein and predicted phytoconstituents of *Solanum trilobatum* provides a rationale for therapeutic activity.The screening of lung cancer targets with bioactive molecules of *Solanum trilobatum* are validated using molecular docking technique.

The primary purpose of molecular docking is to determine the binding affinity between the ligands (phytoconstituents) with the biological target in concern. The AutoDock Vina technique has been utilized to conduct docking research on the suggested compounds, which resulted in the expected conclusions.The phytoconstituents (Betastilbosterol, Solanidine, Solanine, Solasodine) were docked into the grid box that have been constructed to encapsulate the active surface of the protein.

2.5.1. Analysis of the interaction of Epidermal growth factor receptor (EGFR) (PDB: 6JXO) with Phytoconstituents of Solanum trilobatum

With Epidermal growth factor receptor, the binding energies of the 4 phytoconstituents ranges of from -10.2 to -8.5 kcal/mol. Solanidine and Solasodine shows highest binding energy. Solanine shows 1 conventional hydrogen bond with SER A: 720. Betastilboterol shows least binding energy when compared with others phytoconstituents (table 2)

2.5.2. Analysis of the Vascular endothelial growth factor receptor (VEGF) (PDB: 4ASE) with Phytoconstituents of *Solanum trilobatum*

In the molecular docking study the binding energies of the 4 phytoconstituents with vascular endothelial growth factor receptor ranges of from -9.6 to -9 kcal/mol. Solanidine and Solasodine shows highest binding energy as -9.6 kcal/mol. Solanine shows 5 conventional hydrogen bond with ARG A:842, ALA A:1050,ASP A:1062,ASP A:1056, ASN A:923.
Betastilboterol shows least binding energy when compared with others phytoconstituents (table 3)

2.5.3. Analysis of the interaction of Anaplastic lymphoma kinase (ALK) (PDB: 6CDT) with Phytoconstituents of *Solanum trilobatum*

The binding energies of phytoconstituents (Betastilbosterol, Solanidine, Solanine, Solasodine) ranged from -9.3 to -7.2 kcal/mol against ALK shown in the table 1. Among the selected four phytoconstituents, Solasodine shows highest binding energy when compared with others. In addition Solanine showed 6 conventional hydrogen bonds where Betastilbosterol and Solanidine shows 1 conventional hydrogen bond with ALA A:1274 (table 4)

2.5.4. Analysis of the interaction of ROS proto oncogene 1 (ROS1) (PDB: 4UXL) with Phytoconstituents of *Solanum trilobatum*

In this study, the binding energies of the 4 phytoconstituents with ROS proto oncogene 1 ranges of from -10 to -8.3 kcal/mol. Solasodine shows highest binding energy as -10 kcal/mol. Solanine shows 4 conventional hydrogen bond with LEU A:1951, SER A:1953, ARG A:2083, ASP A:2102. Betastilboterol shows least binding energy when compared with others phytoconstituents (table 5)

2.5.5. Analysis of the interaction of Mesenchymal epithelial transition factor (c-MET) (PDB: 3ZZE) with Phytoconstituents of *Solanum trilobatum*

The results of molecular docking study revealed the binding energies of the 4 phytoconstituents with c-MET factor ranges of from -10.8 to -8.7 kcal/mol. Among them Solasodine showed highest binding energy as -10.8kcal/mol. Solanine shows 4 conventional hydrogen bond with LEU A: 1951, SER A: 1953, ARG A: 2083, ASP A:2102. Betastilboterol shows least binding energy when compared with others phytoconstituents (table 6)

In accordance with the results the binding energies of the four phytoconstituents with Epidermal growth factor receptor (PDB ID: 6JX0) , Vascular endothelial growth factor receptor (PDB ID: 4ASE) , Anaplastic lymphoma kinase (PDB ID: 6CDT) and ROS proto oncogene 1 (PDB ID: 4UXL), c-Mesenchymal epithelial transition factor (PDB:3ZZE) were ranged from
-10.2 to -8.5 kcal/mol, -9.6 to -9kcal/mol, -9.3 to -7.2 kcal/mol, -10 to -8.3 kcal/mol, -10.8 to -
8.7 respectively. Based on the findings, it was observed that all the four phytoconstituents bind more effectively with the target proteins. In the BIOVIA Discovery Studio Visualizer, the binding interaction concerning the active site of the target protein including amino acid residues have been observed.

Table 2: Docking studies of phytoconstituents with epidermal growth factor receptor (EGFR)

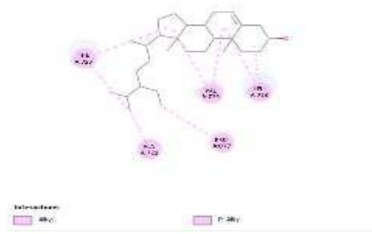
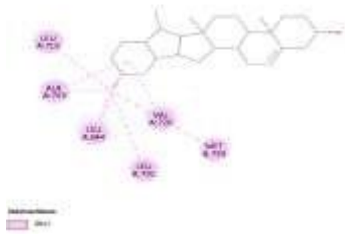
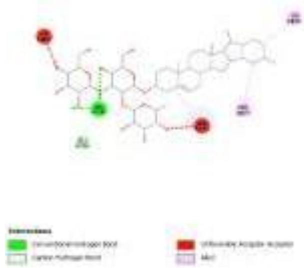
Ligand	Binding energy	No.of Hydroge n Bonding	Hydroge n bond distance	Amino acids	2D Binding interation image
Betastilbosterol	-8.5	0	0	-	
Solanidine	-10.2	0	0	-	
Solanine	-9	1	2.78	SERA:72 0	
Solasodine	-10.2	0	0	-	

Table 3: Docking studies of phytoconstituents with vascular endothelial growth factor receptor (VEGF)

Ligand	Binding energy	No.of Hydrogen Bonding	Hydrogen bond distance	Amino acids	2D Binding interation

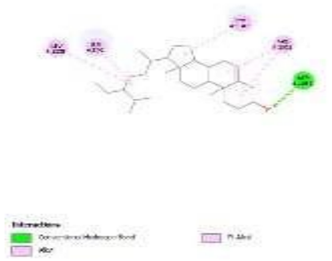
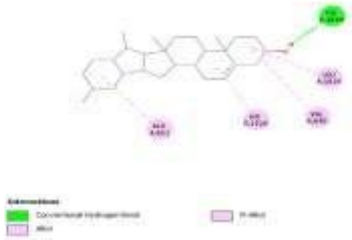
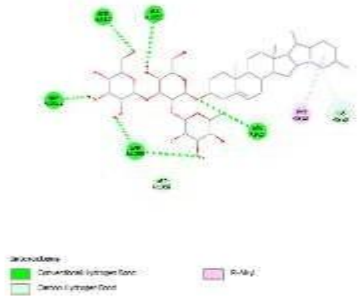
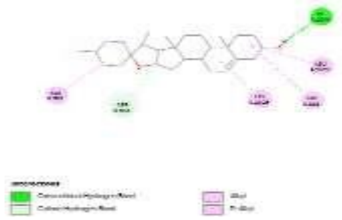
Betastilbosterol	-9	1	1.88	ASP A:1052	
Solanidine	-9.6	1	2.87	ILE A:1044	
Solanine	-9.2	5	3.06 3.10 2 3.07 2.88	ARG A:842 ALA A:1050 ASP A:1062 ASP A:1056 ASN A:923	
Solasodine	-9.6	1	2.70	ILE A:1044	

Table 4: Docking studies of phytoconstituents with Anaplastic lymphoma kinase (ALK)

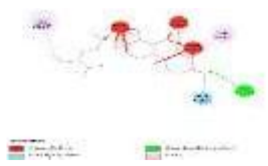
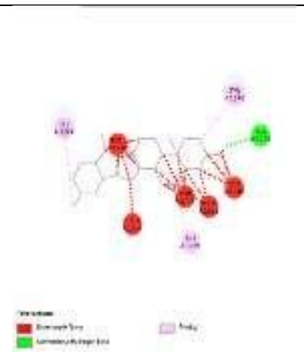
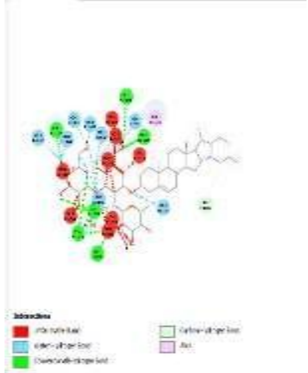
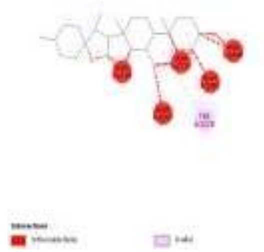
Ligand	**Binding energy**	**No.of Hydroge n Bonding**	**Hydroge n bond distance**	**Amino acids**	**2D Binding interation image**
Betastilbosterol	-7.2	1	2.73	ALA A:1274	
Solanidine	-9.2	1	2.08	ALA A:1274	
Solanine	-8.7	6	2.45 2.86 3.26 2.73 2.76 2.40 3.06	PHE 1127 ASN 1249 ASN 1254 ASP 1270 ARG 1275	
Solasodine	-9.3	0	-	-	

Table 5: Docking studies of phytoconstituents with ROS proto oncogene (ROS1)

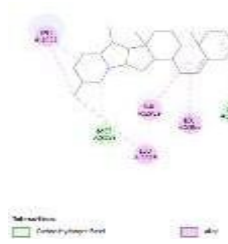
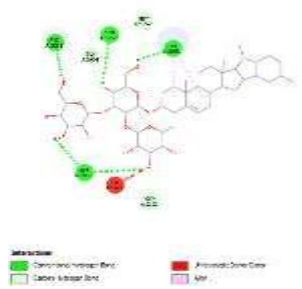
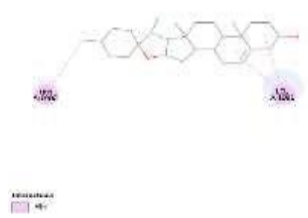
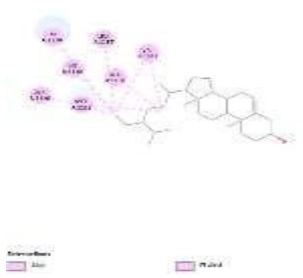
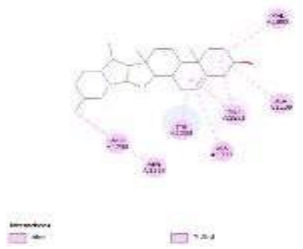
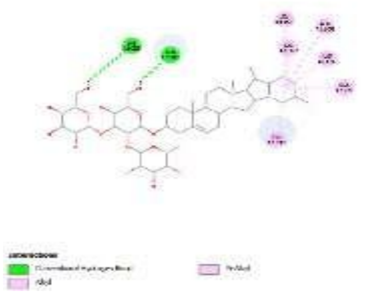
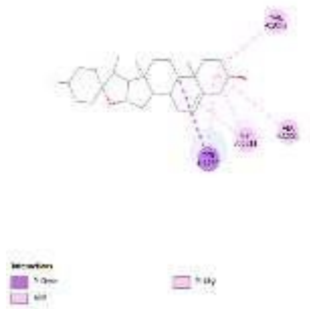
Ligand	**Binding energy**	**No.of Hydrogen Bonding**	**Hydrogen bond distance**	**Amino acids**	**2D Binding interation image**
Betastilbosterol	-8.3	0	-	-	
Solanidine	-9.8	0	-	-	
Solanine	-8.9	4	2.07 2.85 2.76 2.87	ARG A:2083 SER A:1953 LEU A:1951 ASP A:2102	
Solasodine	-10	0	-	-	

Table 6: Docking studies of phytoconstituents with Mesenchymal epithelial transition factor (c-MET)

Ligand	**Binding energy**	**No. of Hydrogen Bonding**	**Hydrogen bond distance**	**Amino acids**	**2D Binding interation image**
Betastilbosterol	-9.5	0	-	-	
Solanidine	-10.8	0	-	-	
Solanine	-8.7	2	2.26 2.93	ARG A:1086 VAL A:1083	
Solasodine	-10.5	0	-	-	

Docking score interaction profile and ADMET results where integrated to identify potential lead phytoconstituents. Compounds with strong binding affinity, favourable pharmacokinetic parameters and stable interaction patterns with lung cancer targets proposed a promising candidate.

3. DISCUSSION AND FUTURE PERSPECTIVE:

Lung cancer remains one of the leading causes of cancer related to mortality worldwide, primarily due to late diagnosis, high metastatic potential and resistance to conventional chemotherapeutic agents. Medicinal plants have gained increasing attention as potential sourced of anticancer agents and *Solanum trilobatum* a traditional medicinal plants widely used in South Asian systems of medicine has emerged as promising candidate.shows significant role respiratory disorders earlier. *Solanum trilobatum* possess bioactive phytochemicals such as Solasodine, Solanine, Solanidine and Betastilbosterol exhibit various activity such as anticancer, antioxidant etc. In the context of lung cancer molecular targets such as epidermal growth factor receptor (EGFR), Vascular endothelial growth factor (VEGF), Anaplastic lymphoma kinase (ALK), ROS proto oncogence (ROS 1), Mesenchymal epithelial transition factor (c-MET) play significant role in tumour growth, angiogenesis and apoptosis evasion.

Insilico studies provide a cost effective and efficient approach to evaluate the interaction between phytocompounds of Solanum trilobatum and lung cancer-related molecular targets. Molecular docking analyses have demonstrated strong binding affinities of selected compounds with key oncogenic proteins suggesting their potential to inhibit tumor-promoting pathways. Overall, the integration of *Insilico* approaches with phytochemical research highlights the therapeutic potential of *Solanum trilobatum* in lung cancer. These findings lay a foundation for further *In vitro* and *In vivo* studies to validate the anticancer efficacy and molecular mechanisms of these compounds, potentially contributing to the development of plant-based targeted therapies for lung cancer.

4. CONCLUSION:

As cancer is a heterogeneous disease involving genetic, architectural, metabolic, pathophysiological, and immunological complexities many attempts have been made to identify biomarkers associated with innate and acquired radioresistance. In both types of lung cancer, early diagnosis and treatment in the early stages of the sickness are basic and the most important condition for effective therapy, therefore it is important to focus on increasing early detection of lung cancer. Monotherapy is not particularly effective in treating cancers, and there have been significant efforts to develop optimal combination methods to improve the efficacy and therapeutic effects of anticancer therapy.

Overall, the integration of molecular targeted therapy with in *Insilico* methodologies provides a robust platform for precision oncology. The updated review reinforce the significance for targeted phytoconstituents as essential components of modern lung cancer therapy and highlight the growing role of Insilico tools in bridging the gap between molecular biology and clinical application.

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