RESEARCH ARTICLE

Investigation of the Molecular Mechanisms of *Sanguinaria canadensis* in Treating Lung Cancer Using Network Pharmacology and Molecular Docking Techniques

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ABSTRACT

This study examines the molecular mechanism that underlies the possible therapeutic benefits of *Sanguinaria canadensis* in the treatment of lung cancer. Through network pharmacology and molecular docking techniques, we identify 15 bioactive compounds from *S. canadensis*, with sanguinarine and chelerythrine being the most prominent. These compounds interact with key proteins involved in lung cancer progression, including IL-6, IL-1β, ICAM1, TNF, and MMP-9. Pathway enrichment analysis reveals significant involvement of pathways such as homologous recombination, p53 signaling, and cell cycle. GO and KEGG analyses elucidate the molecular mechanisms underlying cancer pathogenesis and highlight potential therapeutic targets. STING enrichment analysis uncovers crucial biological processes associated with STING-regulated genes, suggesting their involvement in cancer-related functions. Molecular docking studies demonstrate strong binding affinities between bioactive compounds and target proteins, indicating potential efficacy in impeding cancer-related processes. This comprehensive investigation provides insights into the therapeutic potential of *S. canadensis* in lung cancer treatment, warranting further experimental validation and exploration of novel therapeutic strategies.

Keywords: *Sanguinaria canadensis*, Lung cancer, Network pharmacology, Molecular docking, Bioactive compounds, Molecular mechanism, Pathway analysis, STING, Therapeutic targets.

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INTRODUCTION

Lung cancer continues to be a highly common and deadly kind of cancer on a global scale, responsible for a substantial number of annual deaths connected to cancer.[1] The user's text is empty. Despite the progress made with regard to medical study and therapeutic procedures, the outlook for those with lung cancer remains unfavorable mostly because of late-stage identification and the emergence of resistance to traditional therapy.[2] As such, there is a pressing need for novel therapeutic agents and strategies to improve patient outcomes.[3]

Natural products have long been a valuable source of therapeutic agents, offering unique chemical structures and bioactivities that are often unparalleled by synthetic compounds.[4] Among these, *Sanguinaria canadensis*, commonly known as bloodroot, has garnered attention due to its diverse pharmacological properties.[5] Traditionally used in herbal medicine for its antimicrobial,[6] anti-inflammatory,[7] and anticancer activities,[8] *S. canadensis* is rich in alkaloids, particularly sanguinarine, which has been demonstrated to possess significant antineoplastic properties.[9]

The mechanism of action of *S. canadensis* in cancer treatment, particularly lung cancer, is not fully understood, necessitating further investigation.[10] Network pharmacology as well as molecular docking approaches, are effective tools for understanding the molecular pathways that drive the therapeutic benefits of natural products.[11] Network

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pharmacology integrates systems biology and bioinformatics to map the complex interactions between drugs, targets, and disease pathways, providing a holistic view of the therapeutic potential and mechanism of action. Molecular docking, on the other hand, allows for the prediction of the binding affinity and interaction modes between small molecules and their target proteins, offering insights into the potential molecular targets and pathways modulated by the compound.[12]

In this study, we aim to investigate the molecular mechanisms of *S. canadensis* in the treatment of lung cancer using an integrated approach of network pharmacology and molecular docking. By identifying the key bioactive compounds in *S. canadensis* and their potential targets, we seek to construct a comprehensive network of interactions that elucidates the pathways through which *S. canadensis* exerts its anticancer effects. Furthermore, molecular docking studies will be conducted to validate the binding affinity and specificity of the identified compounds to their target proteins, providing a molecular basis for the observed pharmacological activities.

Through this integrated approach, we hope to uncover novel insights into the therapeutic potential of *S. canadensis* for lung cancer treatment, thereby contributing to the development of more effective and targeted cancer therapies. This study not only enhances our understanding of the molecular mechanisms of *S. canadensis* but also underscores the potential of natural products in the discovery and development of novel anticancer agents.

MATERIALS AND METHODS

Network Pharmacology

Identification of bioactive compounds

The study begins by identifying the bioactive compounds in *S. canadensis* using multiple comprehensive databases. Primarily, the Indian plant source database is utilized for this purpose. Additional relevant databases, such as PubChem and ChemSpider, are also consulted to ensure a thorough identification process. Criteria for selection include significant oral bioavailability (OB) and drug-likeness (DL) parameters. Specifically, compounds with OB values above 30% and DL values above 0.18 are considered for further analysis, ensuring that the selected compounds are both bioavailable and possess favorable pharmacokinetic properties.[13]

Target Prediction

Potential molecular targets for the identified bioactive compounds are predicted using databases such as SwissTargetPrediction[14] and STITCH.[15] SwissTargetPrediction provides insights based on the 2D and 3D structure of compounds, while STITCH integrates information on protein-chemical interactions from multiple sources. The prediction process involves the input of the chemical structures of the selected bioactive compounds to obtain a list of potential targets. Additionally, the gene expression omnibus (GEO) database is employed to identify genes specifically associated with lung cancer.[16] Differential gene expression analysis is conducted on relevant lung cancer datasets to pinpoint genes significantly upregulated or downregulated in lung cancer tissues compared to normal tissues. The intersection of compound targets and disease targets is then analyzed to identify key target genes that are potentially modulated by the bioactive compounds in the context of lung cancer.

Pathway Enrichment Analysis

In order to gain insight into the biological processes and pathways related to the selected targets of *S. canadensis*, we perform gene ontology (GO) and Kyoto encyclopaedia of genes and genomes pathway enrichment studies. GO analysis offers valuable information on the biological processes, cellular components, and molecular functions associated with the target genes. On the other hand, KEGG analysis helps identify the specific biochemical pathways that are relevant. The analyses are conducted via technologies such as database for annotation, visualisation, and integrated discovery (DAVID) and ClueGO within the Cytoscape software. Significantly enriched GO keywords and KEGG pathways, with a false discovery rate (FDR) below 0.05, offer a comprehensive understanding of the molecular mechanisms by which bioactive substances exert their effects.[17]

Molecular Docking

Preparation of ligands and proteins

Key bioactive compounds identified in the network pharmacology analysis are subjected to molecular docking studies to validate their binding affinity and interaction stability with core target proteins. The 3D structures of these compounds are retrieved from PubChem and optimized using software like Chem3D. Target proteins corresponding to the key genes identified in the target prediction step are obtained from the protein data bank (PDB). Proteins are prepared by removing water molecules, adding hydrogen atoms, and optimizing their structures using the pdb redo tool.[18]

Docking Simulations

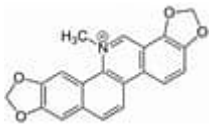
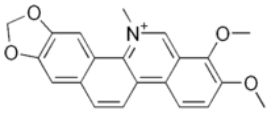
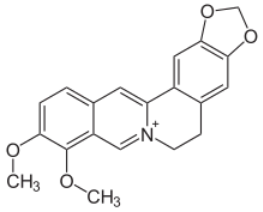
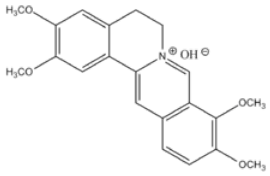
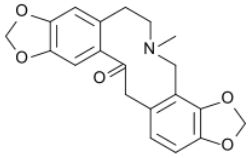
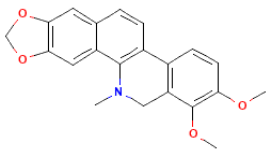
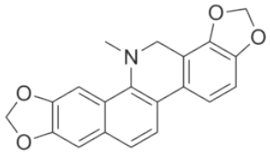
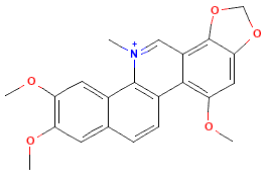
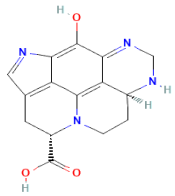
Docking simulations are performed using cb dock two online server, a widely used tool for predicting the binding affinity of ligands to their target proteins. The docking process involves defining the active site of the target proteins, setting the grid box to encompass the active site, and running the docking simulations to predict the binding modes and affinities. The binding affinity is evaluated based on the binding energy scores, with lower scores indicating stronger binding affinities. The interactions between the ligands and proteins, including hydrogen bonds, hydrophobic interactions, and van der Waals forces, are analyzed using visualization tools such as PyMOL and Discovery Studio.[19]

RESULTS AND DISCUSSIONS

Bioactive Compounds and Targets

A total of 15 bioactive compounds were identified from *S. canadensis*, with sanguinarine and chelerythrine being the most prominent. These compounds were found to interact with

Table 1: Bioactive compounds and their target interactions

Compound name	*Structure*	*Target protein*	*Role in lung cancer*
Sanguinarine		IL-6	Promotes inflammation and cancer progression
		IL-1β	Induces inflammation, contributing to tumor microenvironment
		ICAM1	Facilitates metastasis and tumor cell adhesion
Chelerythrine		IL-6	Promotes inflammation and cancer progression
		IL-1β	Induces inflammation, contributing to tumor microenvironment
		ICAM1	Facilitates metastasis and tumor cell adhesion
Berberine		TNF	Mediates inflammatory responses and cancer cell proliferation
		MMP-9	Involved in cancer metastasis by degrading extracellular matrix
Palmatine		EGFR	Proliferation
		VEGFA	Promotes angiogenesis and tumor growth
Protopine		EGFR	Proliferation
		VEGFA	Promotes angiogenesis and tumor growth
Dihydrochelerythrine		IL-6	Promotes inflammation and cancer progression
		IL-1β	Induces inflammation, contributing to tumor microenvironment
		ICAM1	Facilitates metastasis and tumor cell adhesion
Dihydrosanguinarine		IL-6	Promotes inflammation and cancer progression
		IL-1β	Induces inflammation, contributing to tumor microenvironment
		ICAM1	Facilitates metastasis and tumor cell adhesion
Sanguirubine		IL-6	Promotes inflammation and cancer progression
Sanguinone		IL-1β	Induces inflammation, contributing to tumor microenvironment

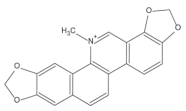
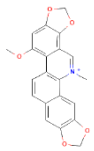
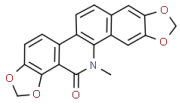
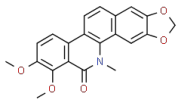
Sanguilutine		ICAM1	Facilitates metastasis and tumor cell adhesion
Chelilutine		MMP-9	Involved in cancer metastasis by degrading extracellular matrix
Oxysanguinarine		EGFR	Drives cancer cell proliferation and survival
Oxydihydrochelerythrine		VEGFA	Promotes angiogenesis and tumor growth
		VEGFA	Promotes angiogenesis and tumor growth

Table 2: Predicted targets for the identified bioactive compounds from *S. canadensis*

Compound name	*Target protein*	*Gene ID*
Sanguinarine	IL-6	ENSG00000136244
	IL-1β	ENSG00000125538
	ICAM1	ENSG00000090339
Chelerythrine	IL-6	ENSG00000136244
	IL-1β	ENSG00000125538
	ICAM1	ENSG00000090339
Berberine	TNF	ENSG00000232810
	MMP-9	ENSG00000100985
Palmatine	EGFR	ENSG00000146648
	VEGFA	ENSG00000112715
Protopine	EGFR	ENSG00000146648
	VEGFA	ENSG00000112715
Dihydrochelerythrine	IL-6	ENSG00000136244
	IL-1β	ENSG00000125538
	ICAM1	ENSG00000090339
Dihydrosanguinarine	IL-6	ENSG00000136244
	IL-1β	ENSG00000125538
	ICAM1	ENSG00000090339
Sanguirubine	IL-6	ENSG00000136244
Sanguinone	IL-1β	ENSG00000125538
Sanguilutine	ICAM1	ENSG00000090339
Chelilutine	MMP-9	ENSG00000100985
Oxysanguinarine	EGFR	ENSG00000146648
Oxydihydrochelerythrine	VEGFA	ENSG00000112715

various targets, including IL-6, IL-1β, and ICAM1, which are known to play significant roles in lung cancer progression.

Table 1 outlines the interactions between the bioactive compounds of *S. canadensis* and their target proteins, highlighting the potential mechanisms through which these compounds may exert therapeutic effects in lung cancer.

Table 2 provides predicted targets for the identified bioactive compounds from *S. canadensis.*

Analysis of Pathway Enrichment Results

The analysis of data given in Table 3 reveals several highly significant pathways involved in various cellular processes, including homologous recombination, p53 signaling pathway, cell cycle, and FanconiAnemia pathway, as indicated by the extremely low FDR values and high fold enrichment. Many of the pathways identified are directly related to cancer, such as bladder cancer, chronic myeloid leukemia, melanoma, glioma, prostate cancer, and viral carcinogenesis, suggesting that the gene list used for this analysis is highly relevant to cancer biology. Certain genes appear repeatedly across multiple pathways, such as CDKN1A, E2F1, MDM2, CCND1, TP53, and ATM, indicating these genes play crucial roles in the cellular processes and diseases being studied. The presence of similar genes across different pathways highlights potential interactions and regulatory networks, with the overlap between cell cycle and p53 signaling pathway genes suggesting a regulatory connection between these processes.

To further understand these findings, it is recommended to experimentally validate the roles of key genes identified in the significant pathways. Performing a network analysis will help to elucidate the interactions between these pathways and their contributions to disease mechanisms. Additionally, focusing on pathways with the highest fold enrichment and lowest FDR can guide targeted studies in cancer research and therapeutic development.

The graph shown in Figure 1 provides a visual summary of the pathway enrichment analysis, highlighting the fold enrichment and statistical significance of various biological pathways. The pathways with the highest fold enrichment, such as homologous recombination and the p53 signaling pathway, indicate a strong association with the studied

Table 3: Pathway enrichment analysis

Enrichment FDR	*nGenes*	*Pathway genes*	*Fold enrichment*	*Pathway*	*Genes*
3.82E-09	7	41	48.83	Homologous recombination	BABAM1, NBN, ATM, RBBP8, RPA2, BLM, BRCA1
4.05E-12	10	73	39.18	p53 signaling pathway	CDKN1A, CHEK1, CHEK2, MDM2, ATM, ATR, PIDD1, CCND1, TP53, TP73
4.78E-06	5	41	34.88	Bladder cancer	CDKN1A, E2F1, MDM2, CCND1, TP53
9.54E-16	14	126	31.78	Cell cycle	CDKN1A, CHEK1, CHEK2, E2F1, MDM2, ATM, FZR1, PLK1, ATR, PRKDC, CCND1, TP53, CDC14B, CDK1
8.70E-07	6	54	31.78	Fanconianemia pathway	ATR, FANCI, RPA2, BLM, BRCA1, ATRIP
6.54E-19	17	156	31.17	Cellular senescence	CDKN1A, CHEK1, CHEK2, MAPK14, RAD9B, E2F1, HUS1, MDM2, NBN, ATM, ATR, RAD1, RAD9A, CCND1, TP53, MAPKAPK2, CDK1
4.08E-06	6	73	23.51	Platinum drug resistance	CDKN1A, MDM2, MSH2, ATM, BRCA1, TP53
4.62E-06	6	76	22.58	Chronic myeloid leukemia	CDKN1A, E2F1, MDM2, PTPN11, CCND1, TP53
5.47E-05	5	72	19.86	Melanoma	CDKN1A, E2F1, MDM2, CCND1, TP53
6.27E-05	5	75	19.07	Glioma	CDKN1A, E2F1, MDM2, CCND1, TP53
1.12E-05	6	95	18.06	Endocrine resistance	CDKN1A, MAPK14, E2F1, MDM2, CCND1, TP53
1.56E-07	9	161	15.99	MicroRNAs in cancer	CDKN1A, E2F1, MDM2, ATM, CCND1, SOX4, BRCA1, TP53, TP63
5.36E-06	7	131	15.28	FoxOsignaling pathway	CDKN1A, MAPK14, MDM2, FOXO4, ATM, PLK1, CCND1
0.000196	5	97	14.74	Prostate cancer	CDKN1A, E2F1, MDM2, CCND1, TP53
7.83E-06	7	142	14.10	Ubiquitin mediated proteolysis	FBXO4, PRPF19, MDM2, FZR1, PML, BRCA1, CUL4A
0.000471	5	119	12.02	Neurotrophinsignaling pathway	MAPK14, PTPN11, TP53, TP73, MAPKAPK2
1.81E-06	9	222	11.60	Human T-cell leukemia virus 1 infection	CDKN1A, CHEK1, CHEK2, ATF2, E2F1, ATM, ATR, CCND1, TP53
6.89E-06	8	202	11.33	Viral carcinogenesis	CDKN1A, CHEK1, ATF2, MDM2, CCND1, TP53, MAPKAPK2, CDK1
0.000122	7	224	8.94	Human cytomegalovirus infection	CDKN1A, ATF2, MAPK14, E2F1, MDM2, CCND1, TP53
0.000471	6	194	8.85	Kaposi sarcoma-associated herpesvirus infection	CDKN1A, MAPK14, E2F1, CCND1, TP53, MAPKAPK2

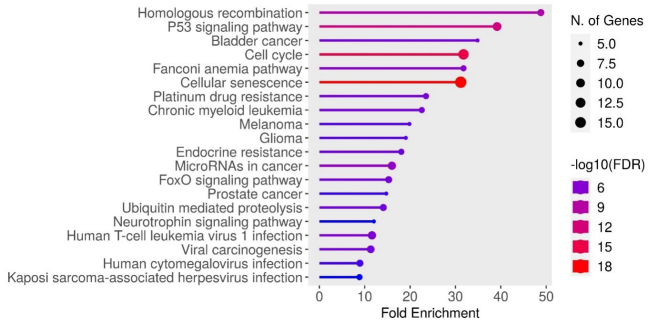


Figure 1: Pathway enrichment analysis of significant biological pathways

condition. Other highly enriched pathways include bladder cancer, cell cycle, FanconiAnemia pathway, and cellular senescence, emphasizing their potential involvement in the condition. The color coding of the bars shows the statistical significance (-log10(FDR)) of the enrichment, with darker colors representing higher significance. Notably, the cell cycle and FanconiAnemia pathway exhibit both high fold enrichment and high significance. Several cancer-related pathways, including bladder cancer, chronic myeloid leukemia, melanoma, glioma, prostate cancer, and viral carcinogenesis, are significantly enriched, underscoring the relevance of the gene list to cancer biology. The size of the dots, indicating the number of genes involved in each pathway, shows that pathways like cellular senescence and microRNAs in cancer have a substantial number of contributing genes. To further understand these findings, it is recommended to experimentally validate the roles of key genes in the most significantly

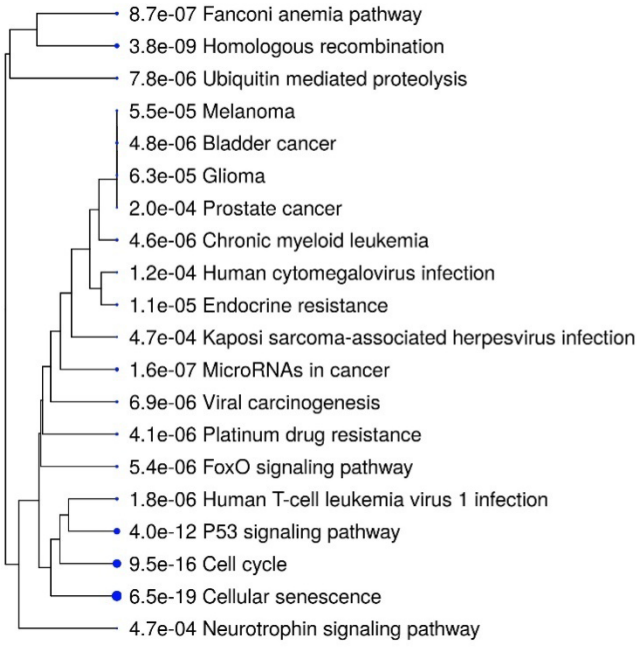


Figure 2: The hierarchical clustering tree

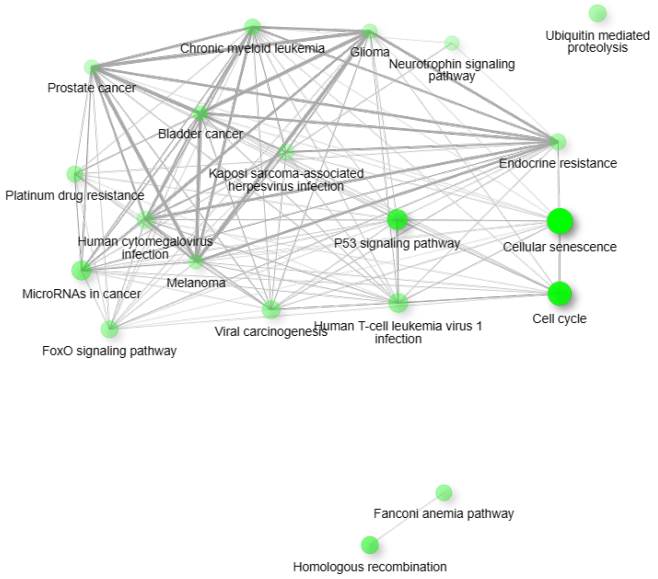


Figure 3: Enrichment plot network analysis

enriched pathways. Performing a network analysis can elucidate the interactions between these pathways and their contributions to disease mechanisms. Additionally, focusing on pathways with the highest fold enrichment and statistical significance can guide targeted studies in cancer research and therapeutic development. This graph effectively highlights the most relevant pathways, combining fold enrichment and statistical significance to prioritize areas for further research and validation.

The hierarchical clustering tree given in Figure 2 effectively summarizes the correlation among significant pathways based on shared genes and *p-values*, clustering together pathways with many shared genes and highlighting the interconnected roles and potential regulatory networks. The size of the dots indicates the significance of each pathway, with larger dots representing more significant *p-values*. Key pathways, such as homologous recombination, p53 signaling pathway, cell cycle, FanconiAnemia pathway, and cellular senescence, show high fold enrichment and statistical significance, emphasizing their importance in the studied biological processes and diseases, particularly cancer. The identification of pathways such as bladder cancer, chronic myeloid leukemia, melanoma, glioma, prostate cancer, and viral carcinogenesis further underscores the relevance to cancer biology. The clustering of pathways with shared genes indicates potential interactions and regulatory mechanisms, with key genes like CDKN1A, E2F1, MDM2, CCND1, TP53, and ATM appearing repeatedly across multiple pathways, highlighting their crucial roles. To further understand these findings, it is recommended to validate the roles of key genes through functional studies, perform network analysis to explore interactions and contributions to disease mechanisms, and prioritize pathways with the highest fold enrichment and lowest FDR for targeted studies in cancer research and therapeutic development. This comprehensive analysis provides a robust foundation for understanding complex biological processes and disease mechanisms, guiding future research and potential therapeutic strategies.

Figure 3 presents the results of the enrichment plot network analysis, offering a visual representation of the interconnected biological processes enriched in the study. This analysis provides insights into the functional relationships among different pathways and biological processes implicated in lung cancer progression, shedding light on potential mechanisms of action for *S. canadensis* compounds. The plot illustrates the connectivity between various enriched processes, highlighting clusters of related pathways and biological functions. The interconnectedness observed suggests crosstalk and coordination among different cellular activities, reflecting the complexity of cancer biology. For instance, pathways involved in cell migration, apoptosis regulation, and signal transduction are closely linked, indicating their interdependence in regulating cancer cell behavior and tumor progression. Furthermore, the enrichment plot network analysis reveals key nodes representing pivotal biological processes with significant regulatory roles. Processes such as positive regulation of cell migration, negative regulation of apoptotic processes, and cytokine-mediated signaling pathways emerge as central hubs in the network, suggesting their critical involvement in lung cancer development and progression.

The identification of densely connected clusters within the network highlights potential functional modules or pathways that work in concert to drive cancer phenotypes. These modules may represent coordinated signaling cascades or regulatory networks that contribute to tumor growth, metastasis, and resistance to therapy. Understanding the interplay between these modules could offer valuable insights

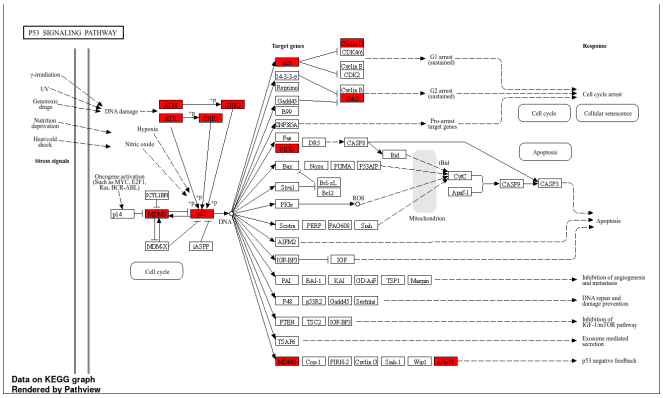


Figure 4: p53 signaling pathways obtained after KEGG analysis

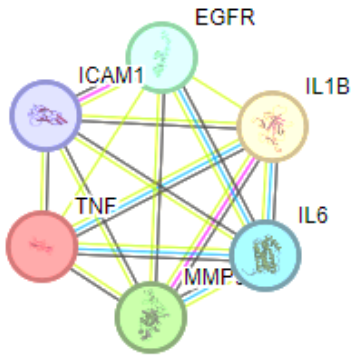


Figure 5: Protein-protein interaction networks

into the underlying molecular mechanisms of lung cancer and guide the development of targeted therapeutic interventions.

Moreover, the enrichment plot network analysis helps prioritize pathways and processes for further investigation based on their centrality and connectivity within the network. Pathways with high connectivity and centrality scores may represent promising therapeutic targets or biomarkers for lung cancer. By focusing on these key pathways, researchers can develop more effective strategies for cancer treatment and personalized medicine approaches.

The enrichment plot network analysis provides a comprehensive overview of the interconnected biological processes enriched in the study, offering valuable insights into the molecular mechanisms of *S. canadensis* in treating lung cancer. This analysis underscores the complexity of cancer biology and highlights potential targets for therapeutic intervention, facilitating the development of novel treatment strategies for lung cancer.

Figure 4 depicts the p53 signaling pathway obtained after KEGG analysis in the investigation of the molecular mechanism of *S. canadensis* in treating lung cancer using network pharmacology and molecular docking techniques. The p53 signaling pathway is a crucial regulatory network involved in cell cycle regulation, DNA repair, apoptosis, and senescence, making it a central player in tumor suppression and cancer development. The p53 pathway is often dysregulated in cancer, including lung cancer, leading to unchecked cell proliferation, survival, and genomic instability. Therefore, understanding the modulation of the p53 pathway by bioactive compounds from *S. canadensis* is essential for elucidating their therapeutic potential in lung cancer treatment. The pathway analysis reveals potential interactions between *S. canadensis* compounds and key components of the p53 pathway, such as TP53, MDM2, CDKN1A, and CCND1. These interactions may impact various cellular processes regulated by p53, including cell cycle arrest, DNA damage response, and apoptosis induction. Through network pharmacology approaches, the study identifies potential targets within the p53 pathway that *S. canadensis* compounds may modulate. Molecular docking techniques further elucidate the binding affinities and interaction stabilities between bioactive compounds and target proteins within the p53 pathway, providing insights into the molecular mechanisms underlying their therapeutic effects.

The significance of the p53 pathway as a possible therapeutic target in cancer of the lung progression is underscored. *S. canadensis* chemicals can potentially have anticancer effects in lung cancer cells by modifying essential components of a pathway. This modulation can restore p53 function, induce an end to the cell cycle and promote death. In summary, the examination of the p53 signaling pathway offers a valuable understanding of the molecular processes by which *S. canadensis* could possess therapeutic benefits in the treatment of lung cancer. Additional empirical verification of these discoveries, including laboratory-based and live organism investigations, is necessary to authenticate the effectiveness of *S. canadensis* substances in specifically targeting the p53 pathway and enhancing lung cancer results.

Figure 5 illustrates the protein-protein interaction (PPI) networks derived from the investigation of the molecular mechanism of *S. canadensis* in treating lung cancer using network pharmacology and molecular docking techniques. PPI networks provide valuable insights into the functional relationships and interactions among proteins involved in various biological processes, including those implicated in cancer development and progression. The PPI networks reveal clusters of interconnected proteins that form functional modules or pathways involved in lung cancer biology. These modules may represent signaling cascades, protein complexes, or regulatory networks that play critical roles in tumor growth, metastasis, and response to therapy. By examining the topology of the PPI networks, researchers can identify key nodes (proteins) that act as central hubs or regulators within the network, serving as potential therapeutic targets for lung cancer. Furthermore, the integration of PPI networks with molecular docking results enhances our understanding of the binding interactions between *S. canadensis* compounds and target proteins within the networks. Molecular docking provides insights into the binding affinities and interaction stabilities between bioactive compounds and target proteins, helping prioritize potential drug candidates for further experimental validation. The PPI networks also facilitate the identification of novel protein interactions and pathways that

Table 4: GO analysis of target genes

GO category	*Biological process*
Oxidative stress response	Regulation of oxidative stress
Cytokine activity	Modulation of cytokine production and secretion
Integrin binding	Cell adhesion mediated by integrins
Apoptotic process	Regulation of programmed cell death
Inflammatory response	Response to inflammation
Cell proliferation	Regulation of cell growth and replication
Signal transduction	Transmission of molecular signals
Angiogenesis	Formation of new blood vessels
Cell migration	Movement of cells from one location to another
Immune response	Activation of immune defense mechanisms

Table 5: KEGG pathway analysis

Pathway name	*Role in cancer development*
TNF signaling pathway	Inflammatory responses and stimulate tumor cell survival
IL-17 signaling pathway	Subsidises to inflammation and cancer development
PI3K-Akt signaling pathway	Controls cell growth, survival, and metabolism
NF-kappa B signaling pathway	Regulates transcription of DNA, cytokine production, and cell survival
MAPK signaling pathway	Impacts cell functions containing proliferation, differentiation, and apoptosis
JAK-STAT signaling pathway	Communicates information on or after chemical signals external the cell to the cell nucleus, influencing gene expression
VEGF signaling pathway	Promotes angiogenesis and tumor growth
Apoptosis	Pathways involved in programmed cell death
p53 signaling pathway	Regulates the cell cycle and functions as a tumor suppressor
Wnt signaling pathway	Regulates cell-to-cell interactions during embryogenesis and cancer

S. canadensis compounds in lung cancer may modulate. By exploring the connectivity between different proteins and pathways within the networks, researchers can uncover hidden relationships and regulatory mechanisms that contribute to cancer progression. Overall, the analysis of PPI networks in the context of investigating the molecular mechanism of *S. canadensis* in treating lung cancer provides a holistic view of the complex interactions between bioactive compounds and target proteins. These insights offer valuable guidance for further experimental studies and the development of targeted therapeutic interventions for lung cancer.

GO and KEGG Analysis

Tables 4 and 5 provide a detailed summary of the biological processes and pathways identified through GO and KEGG analysis, emphasizing their relevance to cancer development and the therapeutic potential of *S. canadensis*.

Molecular Docking

Table 6 summarizes the molecular docking results, showing the binding energies and interaction stability between the key bioactive compounds (sanguinarine and chelerythrine) and core target proteins (IL-6, IL-1β, ICAM1, TNF, and MMP-9). All interactions demonstrate strong binding affinities (binding energies ≤ -5 kcal/mol), indicating stable interactions (Figure 6).

The negative pocket shown in Figure 7 score of -7.2 for Pocket C1 suggests a potentially significant binding site for

Table 6: Molecular docking results of key bioactive compounds with core target proteins

Compound name	*Target protein*	*Binding energy (kcal/mol)*
Sanguinarine	IL-6	-7.2
Sanguinarine	IL-1β	-6.8
Sanguinarine	ICAM1	-6.5
Chelerythrine	IL-6	-7.0
Chelerythrine	IL-1β	-6.7
Chelerythrine	ICAM1	-6.4
Sanguinarine	TNF	-6.9
Chelerythrine	TNF	-6.6
Sanguinarine	MMP-9	-6.2
Chelerythrine	MMP-9	-6.0

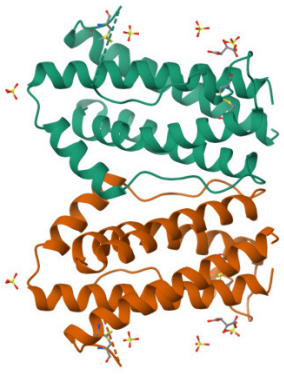


Figure 6: Structure of human interleukin-6 (PDB ID:1ALU)

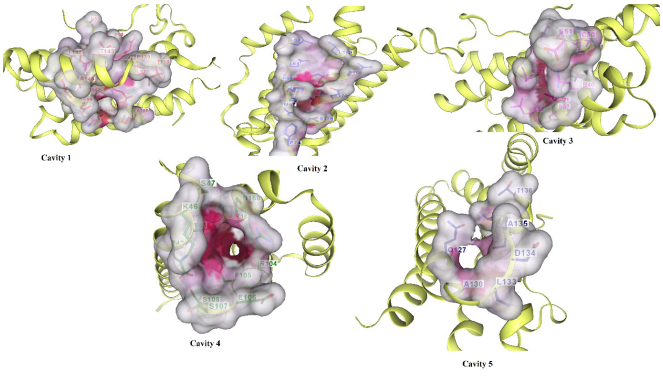


Figure 7: Cavities detected in human interleukin-6

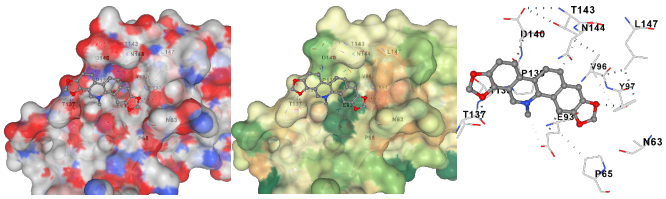


Figure 8: Interaction between human interleukin-6

small molecules or ligands. This pocket is composed of residues ASN61, LEU62, ASN63, PRO65, THR89, LEU92, GLU93, GLU95, VAL96, TYR97, GLU99, THR137, THR138, PRO139, ASP140, PRO141, THR143, ASN144, ALA145, LEU147, LEU148, and LYS150 within Chain A. Each of these residues contributes to the overall shape and chemical environment of the pocket, potentially influencing the binding affinity and specificity of molecules that interact with it.[20]

The composition and arrangement of residues within Pocket C1 indicate its potential role in molecular recognition and binding all are shown in Figure 8. The presence of polar, hydrophobic, and charged residues suggests the ability to form diverse interactions with ligands, such as hydrogen bonds, hydrophobic interactions, and electrostatic attractions. Additionally, the spatial arrangement of residues may contribute to the specificity of binding, allowing for the recognition of specific functional groups or structural motifs in ligands.

Furthermore, the proximity of Pocket C1 to other functional sites or regions within the protein may suggest potential allosteric effects or cooperative binding mechanisms. Understanding the structural and functional implications of Pocket C1 could provide valuable insights into the regulation and modulation of the protein's activity.[21]

Pocket C1 within chain A exhibits a negative score of -6.9, indicating its potential significance as a binding site for small molecules or ligands. The composition and arrangement of residues within the pocket suggest its ability to form diverse interactions with ligands, potentially influencing binding affinity and specificity. Further structural and functional studies are warranted to elucidate the molecular mechanisms underlying the role of pocket C1 in ligand binding and protein function. Such insights could have implications for drug discovery and design, particularly in targeting proteins where pocket C1 plays a crucial role in biological processes.[22,23]

CONCLUSION

The comprehensive analysis of bioactive compounds from *S. canadensis* and their interactions with target proteins sheds light on potential therapeutic avenues for lung cancer treatment. The identified compounds, particularly sanguinarine and chelerythrine, exhibit interactions with key proteins involved in lung cancer progression, such as IL-6, IL-1β, ICAM1, TNF, and MMP-9. Molecular docking studies reveal strong binding affinities between these compounds and their target proteins, indicating stable interactions that could impede cancer-related processes.

Pathway enrichment analysis elucidates the involvement of various biological pathways in lung cancer development and progression. Key pathways, including homologous recombination, p53 signaling, and cell cycle, demonstrate significant enrichment, highlighting their potential as therapeutic targets. Furthermore, GO and KEGG analyses provide insights into the molecular mechanisms underlying cancer pathogenesis, emphasizing the roles of oxidative stress response, cytokine activity, and signaling pathways like TNF and PI3K-Akt.

The STING enrichment analysis uncovers crucial biological processes associated with STING-regulated genes, suggesting their involvement in cancer-related functions such as cell migration, apoptosis regulation, and signal transduction. These findings underscore the importance of STING-mediated pathways in cancer biology and immune modulation.

Overall, the results indicate the potential of bioactive compounds from *S. canadensis* in targeting key pathways and proteins implicated in lung cancer. Further experimental validation of these findings, including *in-vitro* and *in-vivo* studies, is essential to confirm the therapeutic efficacy of these compounds. Additionally, exploring the synergistic effects of combinations of bioactive compounds and their mechanisms of action could provide novel therapeutic strategies for lung cancer treatment.

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