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EXPLORING QUINOVIC ACID AS A POTENTIAL LUNG CANCER THERAPY: INSIGHTS FROM NETWORK PHARMACOLOGY AND MOLECULAR DOCKING

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ABSTRACT :

Background: Lung cancer is the predominant cause of cancer-related death globally, attributed to delayed diagnosis and limited therapeutic effectiveness. Natural chemicals provide potential avenues for the development of innovative cancer therapeutics. **Objective:** This study seeks to investigate the anticancer efficacy of quinovic acid in lung cancer via a network pharmacology approach combined with molecular docking techniques. **Methods:** A network pharmacology analysis was conducted to discover the proteins targeted by quinovic acid. The targets were also analyzed for potential overlap with genes linked to lung cancer. A Protein-Protein Interaction (PPI) network was constructed to identify pivotal hub genes. Molecular docking simulations were conducted to evaluate the binding affinity of quinovic acid with the indicated targets. **Results:** Network pharmacology indicates that quinovic acid interacts with a diverse array of proteins, predominantly phosphatases (33.3%) and phosphodiesterases (26.7%). A substantial overlap of 49 genes was identified between quinovic acid targets and lung cancer-associated genes, suggesting potential therapeutic relevance. PPI analysis identified essential hub genes including TP53, EGFR, KRAS, BRAF, and PIK3CA, which are involved in significant signaling pathways such as PI3K-AKT, MAPK, and apoptosis. Computer-simulated ligand binding analyses demonstrated substantial binding affinities of quinovic acid, particularly with BRAF and PIK3CA (-9.2 kcal/mol). **Conclusion:** The results indicate that quinovic acid may inhibit cancer proliferation by altering many critical oncogenic pathways, rendering it a promising option for lung cancer treatment. Additional experimental validation is necessary to demonstrate its therapeutic effectiveness.

KEYWORDS: Lung cancer, quinovic acid, network pharmacology, molecular docking, A549, PI3K-AKT, BRAF.

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1. INTRODUCTION

Lung cancer continues to be a leading cause of cancer-related fatalities globally, with increased mortality rates linked to late-stage detection and the restricted effectiveness of traditional treatments such as chemotherapy and radiation.[1, 2] Therefore, there is an urgent need for innovative therapeutic procedures that are less harmful yet equally effective.[3] Natural products have traditionally been a source of potential anticancer agents due to their diverse bioactive constituents with unique mechanisms of action.[4, 5] Quinovic acid, a naturally occurring triterpenoid saponin, has attracted attention for its potential therapeutic advantages among these compounds.

Quinovic acid is predominantly present in plant species such as *Rhamnus* and *Strychnos*, and it has demonstrated potential in several pharmacological activities, including antibacterial, anticancer, and anti-inflammatory effects.[6, 7, 8] Not withstanding its recognized biological effects, the molecular mechanisms that support its anticancer efficacy, especially for lung cancer, remain little elucidated. Lung cancer, characterized by uncontrolled cellular proliferation in the lungs, has two histological subtypes: NSCLC (non-small cell lung cancer) and SCLC (small cell lung cancer).[9] Both types provide significant treatment challenges because of their aggressive nature and resistance to current drugs, rendering effective management challenging.

This study represents the first investigation of the anticancer efficacy of quinovic acid against lung cancer, utilizing a synthesis of integrated network pharmacology and molecular docking techniques. Integrative network pharmacology is an advanced methodology that combines systems biology and pharmacology to predict interactions between bioactive compounds and biological targets.[10, 11] This technique facilitates the identification of critical signaling pathways and biomarkers associated with the drug's mechanism of action. Molecular docking models the interactions of quinovic acid with target proteins at the molecular level, yielding crucial insights on its binding affinity and therapeutic potential.[12]

2. MATERIALS AND METHODS

Target identification and overlap analysis

The SwissTargetPrediction program (http://www.swisstargetprediction.ch) was utilized to identify potential molecular targets of quinovic acid following the input of its canonical SMILES structure. To ascertain relevance to lung cancer, disease-associated genes were extracted from the GeneCards database (https://www.genecards.org) utilizing the keyword "lung cancer."

Utilizing Venny 2.1 (https://bioinfogp.cnb.csic.es/tools/venny/), we identified overlapping genes between quinovic acid targets and genes associated with lung cancer. A Venn diagram was constructed to illustrate the intersection and emphasize shared aims, considered essential for subsequent study. These prevalent genes may indicate the pharmacological connection between quinovic acid and the etiology of lung cancer.

Construction of the PPI network

A protein-protein interaction (PPI) network was constructed utilizing the STRING database (https://string-db.org/) for the whole list of

quinovic acid targets and the subset of overlapped targets associated with lung cancer. The minimum needed interaction score was established as "Medium confidence" (0.400). Annotations of the Disease Ontology (DO) and pathway enrichment analyses from the Kyoto Encyclopedia of Genes and Genomes (KEGG) were conducted. Networks were analyzed via the Cytoscape tool (v3.10.1). Assessing essential network measures such as degree, betweenness, and closeness centrality facilitated the identification of hub gene nodes with significant connectivity and biological importance.

Molecular docking

Molecular docking employing AutoDock Vina was utilized to examine the interaction between quinovic acid and significant protein targets. The three-dimensional (3D) structures of quinovic acid were obtained from the PubChem database (CID: 119025). Crystal structures of lung cancer-associated proteins BRAF (PDB ID: 3C4C), PIK3CA (7LIC), EGFR (3POV), P53 (8DC7), and KRAS (8WB1) were obtained from the RCSB Protein Data Bank. AutoDockTools was utilized to add polar hydrogens, eliminate water molecules, and assign Kollman charges for the pre-processing of proteins. Grid boxes were delineated around the active sites based on co-crystallized ligands. Default parameters directed each docking simulation; the resulting sites were subsequently evaluated based on binding affinity (kcal/mol). Discovery Studio Visualizer was utilized to examine interactions such as hydrogen bonds, hydrophobic interactions, and van der Waals forces.

3. RESULTS

Network pharmacology

The first classification of the target proteins for quinovic acid, as illustrated in Figure 1a, indicates a diverse array of molecular targets. Most of these targets are phosphatases (33.3%), followed by phosphodiesterases (26.7%) and nuclear receptors (20%). Of the projected targets, the other kinds of enzymes, membrane receptors, and surface antigens each make 6.7%.

Figure 1b of the Venn diagram shows a notable overlap of 49 target genes between those linked with lung cancer and those forecast to interact with quinovic acid. This overlap, indicating a non-random intersection that may reveal significant biochemical pathways through which quinovic acid operates, arises from a broader dataset of 5,219 lung cancer-related genes and 100 quinovic acid-associated genes. The identification of these 49 shared genes is particularly noteworthy, since they connect many cancer-related metabolic pathways to the bioactivity of quinovic acid.

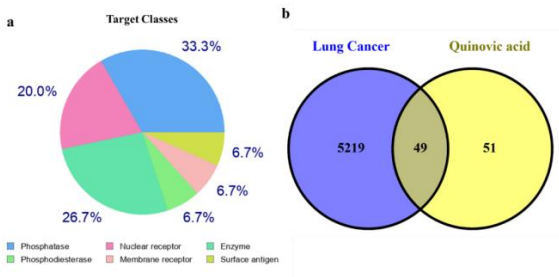

Figure 1. (a) Pie chart illustrating the categorisation of putative target proteins of quinovic acid. The targets are classified as follows: phosphatase (33.3%), phosphodiesterase (26.7%), nuclear receptor (20.0%), enzyme (6.7%), surface antigen (6.7%), and membrane receptor (6.7%). (b) A Venn diagram depicting the overlap between genes related with lung cancer (blue

circle) and targets connected with quinovic acid (yellow circle). A total of 49 shared targets were discovered between lung cancer and quinovic acid.

STRING analysis facilitated the construction of a PPI network. All anticipated targets of quinovic acid depicted in Figure 2a constitute a highly interconnected network, underscoring the extensive activity of quinovic acid. Figure 2b illustrates a complex and intricate network, specifically delineating the interactions among the 49 shared targets. This gene clustering suggests that the shared targets are functionally interconnected rather than operating independently, potentially converging on critical signalling pathways associated with the initiation and progression of lung cancer.

Functional enrichment analyses were performed to enhance comprehension of the biological roles of these prevalent targets. The bubble plots (Figure 2c and Figure 2d) visually depict the significantly improved connections between KEEG pathways and illness-related genes. The most enriched terms are cancer hallmarks, cell cycle regulation, PI3K-AKT signalling, apoptosis, MAPK signalling, and immune response modulation. These pathways are not only associated with the oncogenic transformation of cells but are also recognised as primary therapeutic targets in contemporary cancer treatment strategies. The PI3K-AKT pathway is essential for regulating cell growth, survival, and metabolism; its dysfunction has been associated with resistance to chemotherapy and radiation in lung cancer. In lung adenocarcinomas, the MAPK pathway frequently participates in the conveyance of mitogenic signals. Quinovic acid may mitigate carcinogenic actions by modifying these pathways, thereby warranting more investigation. An in-depth examination of the 49 frequent targets unveiled several hub genes, which are critical nodes in the interaction network due to their significant connectivity and biological importance. The hub genes include TP53, EGFR, KRAS, BRAF, and PIK3CA, all of which are prominent contributors to lung cancer (Figure 2e).

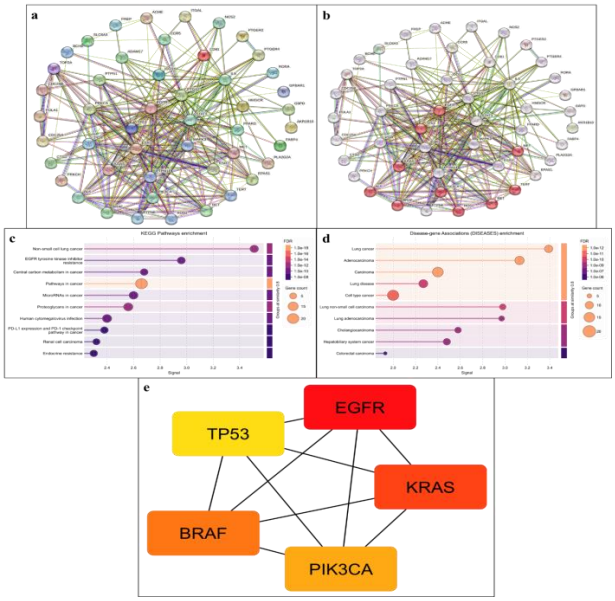

Figure 2. (a) Protein-protein interaction network comprising the 49 shared targets between quinovic acid and lung cancer, developed utilising the STRING database. (b) Hub gene network emphasising the most critical lung cancer proteins within the protein-protein interaction (PPI) network according to connectedness. (c) KEGG pathway enrichment study. (d) Enrichment analysis of disease gene associations. (e) Core regulatory network depicting essential cytohub genes (TP53, EGFR, KRAS, BRAF, and PIK3CA).

Molecular docking

Quinovic acid was shown by molecular docking studies to have significant binding affinities for

proteins linked to lung cancer, suggesting possible therapeutic relevance (Table 1 and Figure 3). Among the proteins examined, BRAF (PDB ID: 3C4C) and PIK3CA (PDB ID: 7LIC) had the highest binding affinities, each achieving a docking score of -9.2 kcal/mol. Van der Waals interactions were seen with ALA 481, HIS 539, and ASN 580, whereas hydrophobic π-alkyl interactions involved VAL 482, ILE 463, and LEU 514. BRAF's quinovic acid created hydrogen bonds with GLN 530 and SER 535. In PIK3CA, quinovic acid created hydrogen bonds with GLY 837 and ASP 836, van der Waals interactions with SER 806, TYR 836, and PRO 835, and hydrophobic contacts with ILE 634, VAL 827, and PHE 845.

-8.3 kcal/mol was a respectable docking score for the EGFR (PDB ID: 3POV). Apart from more van der Waals interactions with THR 166, HIS 168, and LEU 178, significant hydrogen bonds were formed with ASP 166, SER 167, and GLY 168. Observed with PRO 140 and PHE 161 were hydrophobic π-alkyl interactions. P53 (PDB ID: 8DC7) demonstrated a modest binding affinity of -6.7 kcal/mol, characterised by hydrogen bonds at MET 147 and SER 149, van der Waals interactions at ASP 148, THR 150, and ASP 228, and hydrophobic interactions involving VAL 143, PRO 223, and GLY 229.

With a docking score of -6.6 kcal/mol, KRAS (PDB ID: 8WB1) had the lowest binding affinity of all targets. Hydrogen bonding with GLU 64 and TYR 39 produced Van der Waals interactions involving ASN 85, ALA 60, GLN 70, and ARG 109. ALA 61, ALA 11, and ALA 9 took part in hydrophobic interactions. The interactions overall suggest that quinovic acid forms stable complexes with these proteins by combining hydrogen bonds, van der Waals forces, and hydrophobic interactions; the affinities for BRAF and PIK3CA are extremely strong.

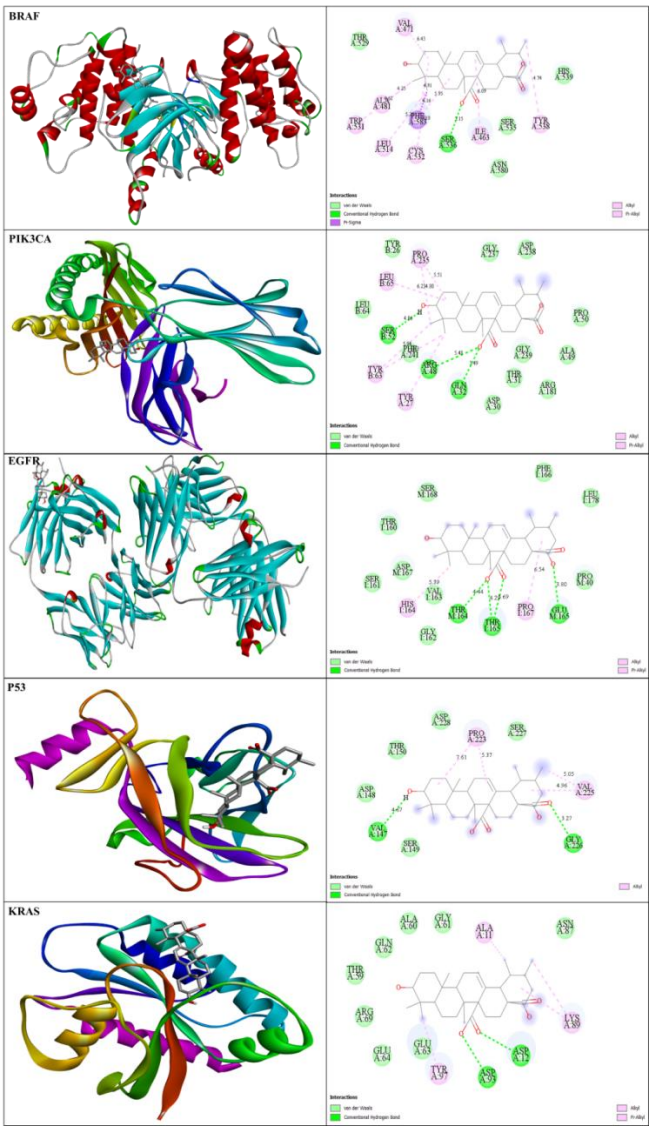

Figure 3. Molecular docking investigation of quinovic acid with principal lung cancer-related target proteins. For each target protein (BRAF, PIK3CA, EGFR, TP53, and KRAS), the left panel illustrates the three-dimensional binding conformation of quinovic acid within the protein's active site, while the right panel displays the two-dimensional interaction diagram emphasising critical molecular interactions.

Table 1. Docking score and amino acid interactions of the quinovic acid with target proteins

Protein	PDB ID	Docking score (kcal/mol)	Hydrogen Bond Interactions	Van der Waals Interactions	Hydrophobic Interactions (π-Alkyl/Alkyl)
BRAF	3C4C	-9.2	GLN 530, SER 535	ALA 481, HIS 539, CYS 532, SER 536, ASN 580	VAL 482, ILE 463, LEU 514
PIK3CA	7LIC	-9.2	GLY 837, ASP 836	SER 806, TYR 836, ARG 818, PRO 835	ILE 634, VAL 827, PHE 845
EGFR	3POV	-8.3	ASP 166, SER 167, GLY 168	THR 166, ASP 167, HIS 168, LEU 178, SER 164	PRO 140, PHE 161
P53	8DC7	-6.7	MET 147, SER 149	ASP 148, THR 150, ASP 228, THR 230	VAL 143, PRO 223, GLY 229
KRAS	8WB1	-6.6	GLU 64, TYR 39	ASN 85, ALA 60, ALA 61, GLN 70, ARG 109, ASP 38	ALA 61, ALA 11, ALA 9

4. DISCUSSION

Marked by uncontrolled cellular growth in pulmonary tissue, lung cancer ranks among the most common and deadly diseases worldwide. [1] Though non-smokers are affected as well, smoking is the main risk factor. [13] By 2020, the World Health Organization forecasted 1.8 million deaths from lung cancer. [14] Reducing the consequences of this condition depends on early detection and prevention.

Plants include natural substances called phytochemicals that offer many health benefits, including anti-inflammatory, anti-cancer, and antioxidant properties. [15] Quinovic acid, a bioactive component found in several plants, including *Quinoa*, has been demonstrated to improve immune function, reduce inflammation, and fight cancer. [16]. Present in several plants like Quinoa, quinovic acid, a bioactive chemical, has been found to fight cancer, reduce inflammation, and improve immunological function. Their possible medicinal uses have attracted great scientific attention.

To investigate the anticancer efficacy of quinovic acid in lung cancer, this paper used a comprehensive molecular docking and network pharmacology technique. The findings show many ways by which quinovic acid might be beneficial, thereby stressing its possible use as a candidate for the next pharmacological development.

Preliminary target prediction and classification suggested that quinovic acid interacts with a wide range of protein classes, with a notable percentage comprising phosphatases, phosphodiesterases, and nuclear receptors. These classes are functionally diverse and significantly involved in cellular control, suggesting that quinovic acid might affect several signaling axes simultaneously. Many natural chemicals with polypharmacological qualities have a broad targeting profile. Many natural chemicals with polypharmacological characteristics have a wide targeting spectrum. [17]

The junction of 49 genes between lung cancer-related genes and quinovic acid-associated targets indicates a remarkable convergence in biological importance. Quinovic acid's ability to change fundamental pathways connected to lung cancer is shown by the Venn diagram study. The PPI network revealed that these common targets are interconnected, suggesting potential co-regulation or convergence on similar signaling pathways. Particularly noteworthy is the discovery of hub genes, including TP53, EGFR, KRAS, BRAF and PIK3CA, as these genes are known major causes of lung cancer and its resistance mechanisms.

Molecular docking simulations produced further data showing notable binding affinities between quinovic acid and other main lung cancer targets. Indicating consistent and good interactions, the highest binding affinities were for BRAF and PIK3CA, both at -9.2 kcal/mol. Comprehensive interaction studies revealed a complicated interaction involving van der Waals forces, hydrogen bonding, and hydrophobic interactions, all of which improve binding stability. The molecular weight of quinovic acid (486.69 Da) is within the moderate range generally advantageous for oral medications, indicating adequate membrane permeability and systemic absorption. The molecular structure has 35 atoms, 5 heteroatoms and 5 rings, together with just 2 rotatable bonds, suggesting a rather stiff framework that often improves specificity and binding affinity by restricting conformational flexibility [18]. Structural studies reveal that quinovic acid has several pharmacophoric features suitable for molecular recognition and attachment. Amongst others, they include hydrogen bond donors and acceptors, including hydroxyl groups that likely interact with amino acid residues in the ATP-binding sites of BRAF and PIK3CA. The stiff pentacyclic triterpenoid core of the molecule also helps good hydrophobic interactions, thus imitating the interaction patterns usual of small-molecule kinase inhibitors. Perhaps this structural similarity explains the alleged inhibitory action of the chemical, which might interfere with kinase-mediated signaling pathways crucial for oncogenesis. Though EGFR and TP53 showed good binding energies, they were far lower than BRAF and PIK3CA; yet, their interaction patterns imply possible regulatory functions. KRAS, a notoriously difficult target because of its flat surface and absence of deep binding pockets, had the lowest binding affinity. Given KRAS's vital importance in lung cancer, even tiny binding interactions with it are significant.

5. CONCLUSION

Ultimately, quinovic acid has considerable therapeutic promise for lung cancer. A network pharmacology study identified multiple target proteins, including 49 genes linked to both lung cancer and quinovic acid. These targets are involved in fundamental cancer-related pathways, including MAPK and PI3K-AKT signaling. Molecular docking research revealed notable binding affinities between quinovic acid and important lung cancer-related proteins, namely BRAF, PIK3CA, and EGFR

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REFERENCES:

1. Thandra, K. C., Barsouk, A., Saginala, K., Aluru, J. S., & Barsouk, A. (2021). Epidemiology of lung cancer. *Contemporary oncology (Poznan, Poland)*, *25*(1), 45–52. https://doi.org/10.5114/wo.2021.103829
2. El-Hussein, A., Manoto, S. L., Ombinda-Lemboumba, S., Alrowaili, Z. A., & Mthunzi-Kufa, P. (2021). A Review of Chemotherapy and Photodynamic Therapy for Lung Cancer Treatment. *Anti-cancer agents in medicinal chemistry*, *21*(2), 149–161. https://doi.org/10.2174/1871520620666200403144945
3. Lau, S. C. M., Pan, Y., Velcheti, V., & Wong, K. K. (2022). Squamous cell lung cancer: Current landscape and future therapeutic options. *Cancer cell*, *40*(11), 1279–1293. https://doi.org/10.1016/j.ccell.2022.09.018
4. Asma, S. T., Acaroz, U., Imre, K., Morar, A., Shah, S. R. A., Hussain, S. Z., Arslan-Acaroz, D., Demirbas, H., Hajrulai-Musliu, Z., Istanbullugil, F. R., Soleimanzadeh, A., Morozov, D., Zhu, K., Herman, V., Ayad, A., Athanassiou, C., & Ince, S. (2022). Natural Products/Bioactive Compounds as a Source of Anticancer Drugs. *Cancers*, *14*(24), 6203. https://doi.org/10.3390/cancers14246203
5. Naeem, A., Hu, P., Yang, M., Zhang, J., Liu, Y., Zhu, W., & Zheng, Q. (2022). Natural Products as Anticancer Agents: Current Status and Future Perspectives. *Molecules (Basel, Switzerland)*, *27*(23), 8367. https://doi.org/10.3390/molecules27238367
6. Mostafa, M., Nahar, N., Mosihuzzaman, M., Sokeng, S. D., Fatima, N., Atta-Ur-Rahman, & Choudhary, M. I. (2006). Phosphodiesterase-I inhibitor quinovic acid glycosides from Bridelia ndellensis. *Natural product research*, *20*(7), 686–692. https://doi.org/10.1080/14786410600661658
7. Akesson, C., Lindgren, H., Pero, R. W., Leanderson, T., & Ivars, F. (2003). An extract of Uncaria tomentosa inhibiting cell division and NF-kappa B activity without inducing cell death. *International immunopharmacology*, *3*(13-14), 1889–1900. https://doi.org/10.1016/j.intimp.2003.07.001
8. Saleem, S., Jafri, L., ul Haq, I., Chang, L. C., Calderwood, D., Green, B. D., & Mirza, B. (2014). Plants Fagonia cretica L. and Hedera nepalensis K. Koch contain natural compounds with potent dipeptidyl peptidase-4 (DPP-4) inhibitory activity. *Journal of ethnopharmacology*, *156*, 26–32. https://doi.org/10.1016/j.jep.2014.08.017
9. Rodak, O., Peris-Díaz, M. D., Olbromski, M., Podhorska-Okołów, M., & Dzięgiel, P. (2021). Current Landscape of Non-Small Cell Lung Cancer: Epidemiology, Histological Classification, Targeted Therapies, and Immunotherapy. *Cancers*, *13*(18), 4705. https://doi.org/10.3390/cancers13184705
10. Noor, F., Asif, M., Ashfaq, U. A., Qasim, M., & Tahir Ul Qamar, M. (2023). Machine learning for synergistic network pharmacology: a comprehensive overview. *Briefings in bioinformatics*, *24*(3), bbad120. https://doi.org/10.1093/bib/bbad120
11. Sasikumar, D. S. N., Thiruselvam, P., Sundararajan, V., Ravindran, R., Gunasekaran, S., Madathil, D., Kaliamurthi, S., Peslherbe, G. H., Selvaraj, G., & Sudhakaran, S. L. (2024). Insights into dietary phytochemicals targeting Parkinson's disease key genes and pathways: A network pharmacology approach. *Computers in biology and medicine*, *172*, 108195. https://doi.org/10.1016/j.compbiomed.2024.108195
12. Ryntathiang I, Pooja Y, Khalid JP, Behera A, Murugesan M, Prasad M, Jothinathan MKD. (2025). Therapeutic potential of bioactive compounds from Millettia pinnata: Computational and in vitro approaches. *Int Res J Multidiscip Scope*. 6(1):263-273. https://doi.org/10.47857/irjms.2025.v06i01.02494
13. Cheng, E. S., Weber, M., Steinberg, J., & Yu, X. Q. (2021). Lung cancer risk in never-smokers: An overview of environmental and genetic factors. *Chinese journal of*

cancer research = Chung-kuo yen cheng yen chiu, *33*(5), 548–562. https://doi.org/10.21147/j.issn.1000-9604.2021.05.02

14. International Agency for Research on Cancer. World Health Organization Lung Factsheet Globocan 2020 Available from: https://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf accessed on February 3, 2021
15. Arumugam P. (2024). Emerging role of natural product-derived phytochemicals in the green synthesis of metal nanoparticles: a paradigm shift in sustainable nanotechnology. *Natural product research*, 1–2. Advance online publication. https://doi.org/10.1080/14786419.2024.2432012
16. Singla, R. K., Kumar, R., Khan, S., Mohit, Kumari, K., & Garg, A. (2019). Natural Products: Potential Source of DPP-IV Inhibitors. *Current protein & peptide science*, *20*(12), 1218–1225. https://doi.org/10.2174/1389203720666190502154129
17. Kabir, A., & Muth, A. (2022). Polypharmacology: The science of multi-targeting molecules. *Pharmacological research*, *176*, 106055. https://doi.org/10.1016/j.phrs.2021.106055
18. Aquino R, De Tommasi N, De Simone F, Pizza C. (1997) Triterpenes and quinovic acid glycosides from Uncaria tomentosa. Phytochemistry, 45(5):1035-40. https://doi.org/10.1016/S0031-9422(96)00716-9