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RESEARCH ARTICLE

Identification and *in-silico* analysis of phytochemicals from *Phyla nodiflora* (L.): Potential bioactive compounds for therapeutic applications

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Abstract

The increasing demand for safer and more sustainable alternatives to chemical-based medicines has driven significant interest in plant-derived bioactive compounds, which possess a wide range of therapeutic properties. Among these, *Phyla nodiflora* (L.), a medicinal plant traditionally used in various remedies, has garnered attention for its potential in treating numerous ailments. However, a comprehensive understanding of the bioactive compounds in *P. nodiflora* and their mechanisms of action remain limited. In this context, the present study aims to explore the therapeutic potential of phytochemicals derived from the hexane and methanolic leaf extract of *P. nodiflora*. Using GC-MS (gas chromatography and mass spectrometry) analysis, 50 distinct chemical compounds were identified, from which the 10 most predominant bioactive compounds were selected for further investigation based on their known pharmacological properties. These compounds were subjected to molecular docking studies against key protein targets, including protein tyrosine phosphatase 1B, androgen receptor, cyclin A, and Na-K-Cl Cotransporter 1 (NKCC1). The findings revealed that n-hexadecanoic acid, stigmasterol, and beta-sitosterol exhibit significant potential as drug candidates, demonstrating promising therapeutic applications for conditions such as diabetes, alopecia, cancer, and anti-diuresis. These findings provide valuable insights into the medicinal value of *P. nodiflora*, paving the way for further research, including *in vitro* and *in vivo* studies, to validate the efficacy of these compounds. Additionally, the study underscores the importance of plant-based drug discovery in the development of novel treatments for non-communicable diseases, thereby contributing to the growing body of research in ethnopharmacology and natural product chemistry.

Keywords

anti-diuresis; cancer; dandruff; diabetes; *in-silico* docking; non-communicable disease; *Phyla nodiflora*; phytochemicals

Introduction

The growing demand for safer and more sustainable alternatives to synthetic medicines has fuelled interest in the therapeutic potential of plant-derived compounds. *Phyla nodiflora* (L.), formerly known as *Lippia nodiflora*, is a perennial herb traditionally used in medicine that has gained attention for its

wide array of pharmacological activities, including anti-inflammatory, antimicrobial, and antipyretic properties (1, 2). While several phytochemicals have been identified in *P. nodiflora*, their specific therapeutic potential in addressing non-communicable diseases, such as diabetes, alopecia, cancer, and anti-diuresis conditions, remains insufficiently explored, particularly at the molecular level (3, 4).

Diabetes, characterized by chronic hyperglycaemia, is often treated by targeting enzymes such as protein tyrosine phosphatase 1B (PTP1B), which negatively regulates insulin signalling. Insulin signalling plays a critical role in regulating glucose homeostasis in the body. When insulin binds to its receptor on the surface of cells, it triggers a cascade of intracellular signals that facilitates glucose uptake in tissues like muscles and fat while suppressing glucose production in the liver. This process is essential for maintaining normal blood glucose levels. In diabetes, particularly type 2 diabetes, insulin signalling becomes impaired due to insulin resistance, wherein cells fails to respond effectively to insulin. This leads to reduced glucose uptake and elevated blood sugar levels, which can cause long-term damage to organs and tissues (5).

Similarly, alopecia can be potentially managed by inhibiting the androgen receptor (AR), which plays a key role in hair follicle development and regulation (6). In cancer therapy, targeting cell cycle proteins such as cyclin A, which plays a key role in tumour growth (7). Furthermore, the Na-K-Cl Cotransporter 1 (NKCC1), a crucial regulator of fluid balance in the body, is a target for addressing anti-diuretic conditions (8).

Several studies have highlighted the efficacy of molecular docking in identifying lead compounds from natural sources. For examples, phytochemicals isolated from *Curcuma longa* have been shown, through docking studies, to inhibit key proteins involved in cancer and inflammatory pathways, thereby encouraging further research into their therapeutic potential (9). Similarly, molecular docking has been successfully employed to identify natural inhibitors of enzymes such as acetylcholinesterase, which is implicated in alzheimer's disease, and the angiotensin-converting enzyme (ACE), a critical target for antihypertensive therapies (10). These successes underscore the value of computational tools in accelerating the discovery of plant-based drugs.

Given the therapeutic potential of *P. nodiflora* and the demonstrated efficacy of computational methods in drug discovery, this study aims to investigate the phytochemicals extracted using two distinct solvents, hexane, a non-polar solvent that extract lipophilic compounds such as fatty acids and terpenoids, and methanol, a polar solvent that extracts polar compounds like flavonoids, phenolics, and glycosides. By employing both solvents, a comprehensive profiling of non-polar and polar metabolites is achieved, providing a holistic understanding of the bioactive compounds present in *P. nodiflora*.

The study focuses on evaluating the potential of these compounds for treating diabetes, alopecia, cancer, and anti-diuresis. Using GC-MS analysis, the chemical constituents of the plant extract were identified, followed by *in silico* molecular docking studies to assess their interactions with key protein targets: protein tyrosine phosphatase 1B (PTP1B), androgen receptor (AR), cyclin A and NKCC1. These proteins are critically implicated in the pathogenesis of the aforementioned diseases, making them strategic targets for therapeutic intervention. By identifying compounds with strong binding affinities to these proteins, this research aims to provide valuable insights into the medicinal potential of *P. nodiflora*. Additionally, the findings contribute to the growing body of knowledge in plant-based drug discovery, highlighting the role of *P. nodiflora* as a promising source of bioactive compounds for future therapeutic development.

Materials and Methods

Plant material collection and preparation

Leaves of *P. nodiflora* were collected from the herbal garden, Department of Spices and Medicinal Crops, Tamil Nadu Agricultural University, Coimbatore, India, and authenticated by a horticulturist. Ten grams of leaves were shade-dried for 48 hrs. The dried leaf samples were then macerated with 50 mL hexane until no visible large particles remained. The macerated samples were soaked in hexane for 24 hrs at room temperature. Subsequently, the extracts were filtered using Whatmann filter paper and labelled as the hexane extract.

The sediment from the hexane extraction was then steeped in methanol and extracted at room temperature for 24 hrs to obtain the methanol extract. The filtrates from both extractions were condensed separately using a rotary evaporator at 40°C to yield the respective crude extracts. One microlitre of each crude extract was injected into a GC-MS system for fractionation and further analysis.

GC-MS analysis

The crude methanolic extract was analysed using gas chromatography-mass spectrometry (GC-MS) to identify its chemical constituents. The analysis was performed on a Perkin-Elmer GC Clarus 500 system equipped with an Elite-5MS fused silica column (5% biphenyl, 95% dimethylpolysiloxane, 30 m 0.25 mm ID 250m df). The separation of components was achieved at a steady flow rate of 1 mL/min using helium as the carrier gas. A 1µL sample was injected into the system, with the injector temperature set to 260°C. The oven temperature was programmed to start at 60° C and was held for 2 minutes, followed by a gradual increase to 300°C at a rate of 10°C/min. The final temperature of 300°C was maintained for 6 minutes. The transfer line and ion source temperatures of the mass detector were both set to 240°C. The National Institute of Standards and Technology (NIST) database was used to identify compounds based on mass spectral data (11, 12).

In-silico molecular docking

Docking studies were conducted using the "AutoDock Vina" software to evaluate the interactions between selected bioactive compounds and the target proteins. The 3D structures of the target proteins were retrieved from the Protein Data Bank (PDB), including tyrosine phosphatase 1B (PDB ID: 4Y14) for diabetes, AR (PDB ID: 4K7A) for dandruff, cyclin A (PDB ID: 6GUE) for cancer, and human NKCC1 (PDB ID: 6PZT) for anti-diuresis treatments. Ligands were prepared

and optimized using the PubChem database and MM2 force fields. The selection of bioactive compounds was based on their physicochemical properties, which were evaluated using ADMETLAB 2.0 and Lipinski's rule of five. This criteria consider factors such as molecular weight, log P (partial coefficient), the number of hydrogen bond donors, and the number of hydrogen bond acceptors, ensuring the drug-likeness of the selected compounds.

Target proteins and their role in disease

Tyrosine phosphatase 1B (PTP1B): A critical enzyme involved in the negative regulation of insulin signaling, making it a significant therapeutic target for type 2 diabetes (5).

Androgen receptor (AR): Plays a pivotal role in hair follicle development, and its dysregulation has been associated with alopecia (6).

Cyclin A: A key regulator of the cell cycle, whose overexpression is frequently observed in cancerous tissues, particularly in breast cancer (7).

NKCC1 (Na-K-Cl Cotransporter 1): Facilitates fluid balance in the body and serves as a therapeutic target for diuretics (8).

Molecular docking and visualization

Molecular docking studies were conducted using the "Vina Wizard" module in PyRx-Python Prescription 0.8 to evaluate the interactions between the receptor proteins and the selected ligands. The receptor and ligand molecules were imported into the software and appropriately categorized as macromolecules or ligands. Following the docking procedure, detailed data and docked structures were retrieved for analysis.

The docking analysis examined binding affinities, bond energies, van der Waals interactions, hydrogen bonds (H-bonds), and electrostatic energies. The results were visualized using Discovery Studio (DS4.5, Accelrys, Inc., San Diego, CA, USA) to provide detailed insights into the molecular interactions. This software allowed for the visualization of 3D molecular structures, identification of hydrogen bonds, and the nearest interacting amino acid residues. Additionally, it facilitated the generation of 2D interaction diagrams and the study of binding site conformations, providing a comprehensive understanding of the receptor-ligand interactions.

Results

GC-MS analysis of extracts

The GC–MS chromatogram of the hexane and methanol extract of *P. nodiflora* are presented in Fig. 1. The GC-MS analysis revealed the presence of approximately 50 compounds in both extracts (Table 1 and 2). Among these, ten bioactive compounds with an area percentage greater

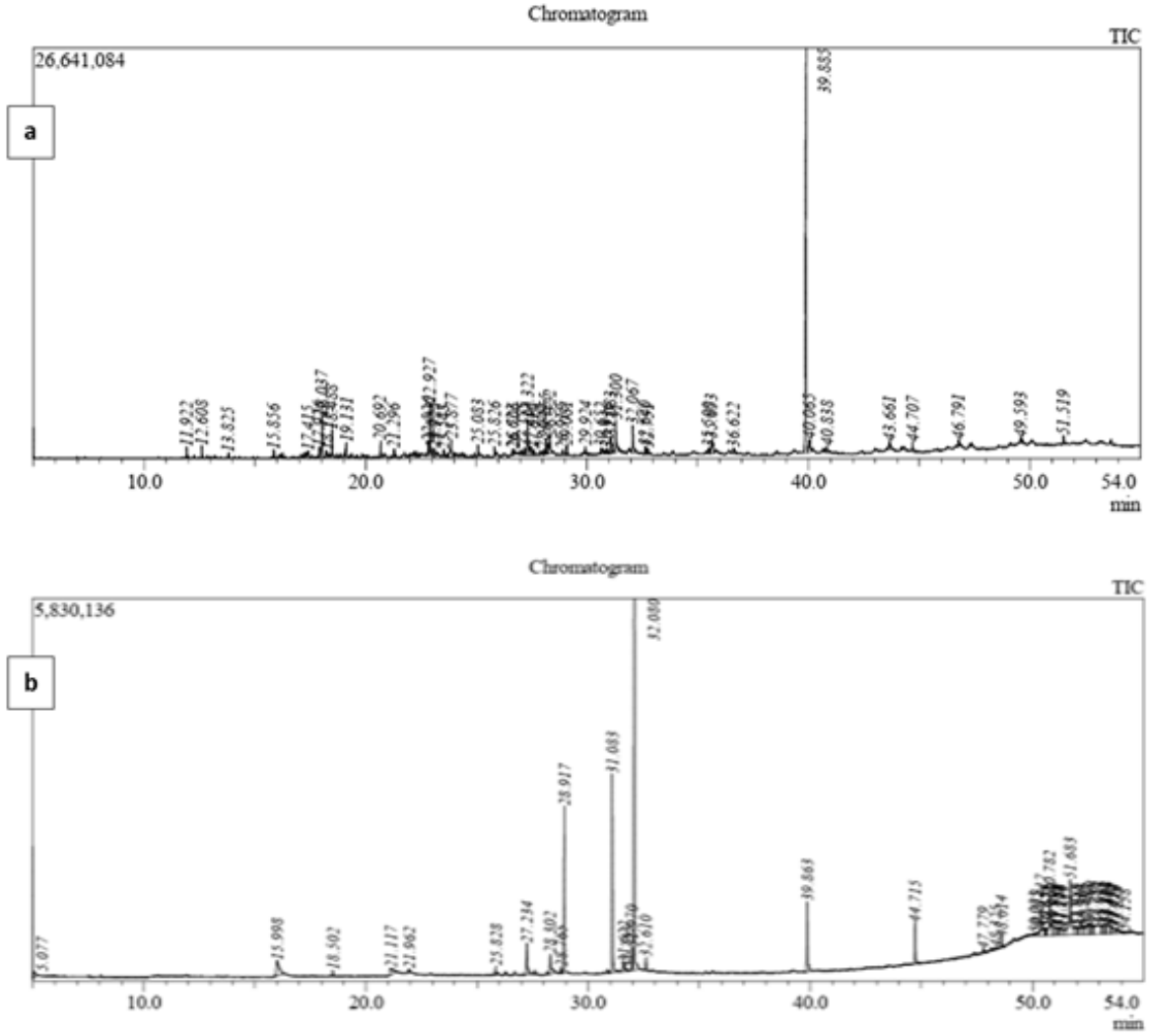


Fig. 1. GC–MS chromatogram of (a) hexane and (b) methanol extract of *P. nodiflora***.**

Table 1. GC-MS analysis of *P. nodiflora* for hexane extract

Peak	Retention time	Initial time	Final time	Area	Area %	Height	Height %	Area / Height	Name
43	39.885	39.775	39.967	88775476	40.23	25878148	40.28	3.43	Bis(2-ethylhexyl) phthalate
14	22.927	22.883	22.992	8607993	3.9	3260385	5.07	2.64	Eicosane
36	31.3	31.158	31.147	7898098	3.58	2014553	3.14	3.92	Eicosane
7	18.037	17.967	18.117	7416674	3.36	2623279	4.08	2.83	Hexadecane
24	27.322	27.233	27.367	7336767	3.32	2328001	3.62	3.15	Eicosane
37	32.067	32.008	32.183	6411296	2.91	1704324	2.65	3.76	9-Octadecen-12-ynoic acid, methyl ester
18	23.877	23.717	23.958	5384257	2.44	1118480	1.74	4.81	Eicosane
9	18.488	18.358	18.567	4798227	2.17	1692631	2.63	2.83	2,4-Di-tert-butylphenol
29	28.322	28.208	28.442	4656454	2.11	1158848	1.8	4.02	n-Hexadecanoic acid
41	35.653	35.567	35.75	4440271	2.01	902183	1.4	4.92	Tetrapentacontane

Table 2. GC-MS analysis of *P. nodiflora* for methanol extract

Peak	Retention time	Initial time	Final time	Area	Area %	Height	Height %	Area / Height	Name
15	32.08	32.017	32.35	15740023	20.01	5600027	27.95	2.81	9,12,15-Octadecatrienoic acid, ethyl ester
11	31.083	30.958	31.242	8926547	11.35	2975746	14.85	3	Phytol
10	28.917	28.825	29.075	6623609	8.42	2457434	12.27	2.7	Hexadecanoic acid, ethyl ester
34	51.683	51.55	51.858	4995879	6.35	831657	4.15	6.01	beta-Sitosterol
17	39.863	39.783	40.025	3752944	4.77	1066438	5.32	3.52	Bis(2-ethylhexyl) phthalate
27	50.782	50.692	50.9	3249394	4.13	638653	3.19	5.09	Stigmasterol
42	53.027	52.775	53.075	2373000	3.02	145513	0.73	16.31	Linoleic acid-TMS
2	15.998	15.925	16.333	2127777	2.71	233470	1.17	9.11	1'-Hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one
7	27.234	27.142	27.417	1925647	2.45	468123	2.34	4.11	Dimethyl palmitamine
18	44.715	44.642	44.792	1833720	2.33	618165	3.09	2.97	Squalene
24	50.417	50.3	50.517	1789319	2.27	282799	1.41	6.33	beta-Sitosterol

than 1% (Table 3) were selected for molecular docking with the four selected protein targets. The molecular structures of the ten bioactive compounds chosen for docking are detailed in Table 3.

Fig. 2 shows the 3D crystal structures of the four target proteins used in the docking studies, as retrieved from the PDB. These include tyrosine phosphatase 1B complexed with inhibitor (PDB ID: 4Y14), AR (PDB ID: 4K7A), cyclin A (PDB ID: 6GUE), and human NKCC1 (PDB ID: 6PZT).

In-silico docking analysis

The boiled egg model of the selected ligands, as represented in Fig. 3, predicts their potential for gastrointestinal absorption and blood-brain barrier permeability. This highlights its significance in evaluating the bioavailability of the compounds. Fig. 4 depicts the docking results of the

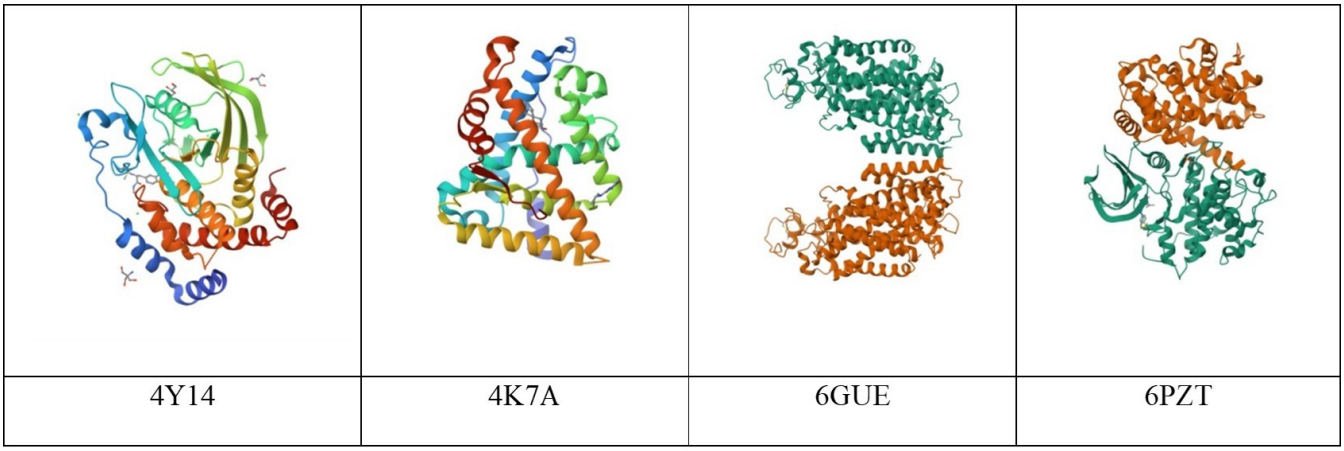
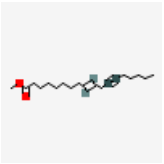
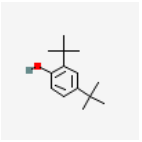
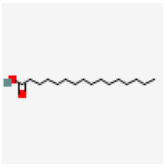
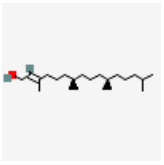
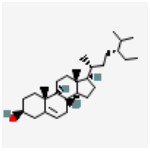
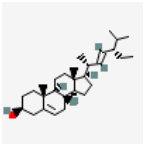
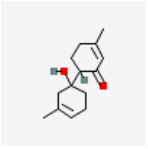
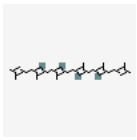


Fig. 2. 3D Crystal structure of four proteins taken from the PDB: Tyrosine phosphatase 1B complexed with inhibitor (PDB ID: 4Y14), AR (PDB ID: 4K7A), Cyclin A (PDB ID: 6GUE), and Human NKCC1 (PDB ID: 6PZT).

Table 3. Ligand structures of the ten compounds derived from GC-MS analysis of *P. nodiflora*

S. No.	Compound	2D Structure	Pubchem ID	Molecular formula
1.	Hexadecane		8343	$C_{16}H_{34}$
2.	9-Octadecen-12-ynoic acid, methyl ester		5363161	$C_{19}H_{32}O_2$
3.	2,4-Di-tert-butylphenol		7311	$C_{14}H_{22}O$
4.	n-Hexadecanoic acid		985	$C_{16}H_{32}O_2$
5.	Phytol		5280435	$C_{20}H_{40}O$
6.	beta-Sitosterol		222284	$C_{29}H_{50}O$
7.	Stigmasterol		5280794	$C_{29}H_{48}O$
8.	1'-Hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one		557446	$C_{14}H_{20}O_2$
9.	Dimethyl palmitamine		16221	$C_{18}H_{39}N$
10.	Squalene		638072	$C_{30}H_{50}$

bioactive compounds. Protein-ligand binding studies indicated that the binding patterns varied based on the nature of the ligands. The docking results, including binding energy values, the number of H-bonds, and the interacting residues of the selected compounds, as shown in Table 4.

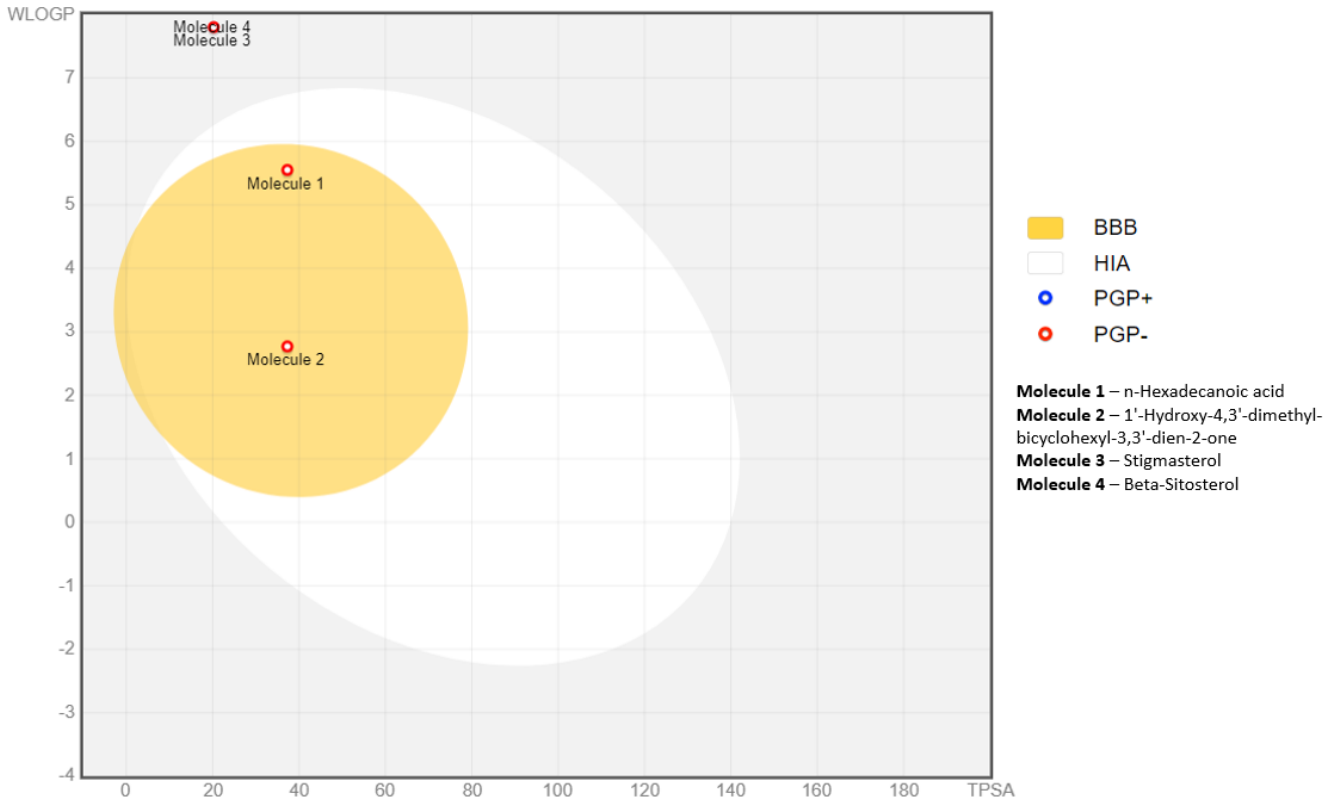


Fig. 3. Boiled egg model of the selected phytochemical compounds showing its ability for gastrointestinal absorption and blood brain barrier.

Docking with tyrosine posphatase 1B: The docking of n-Hexadecanoic acid with tyrosine phosphatase 1B (PDB ID: 4Y14), a protein implicated in pathogenesis of diabetes, yielded promising results. The compound exhibited a binding energy of -4.5 kcal/mol, forming two hydrogen bonds with the key residues LYS A 197 (lysine at position 197) and ASN A 193 (asparagine at position 193). This indicates that n-hexadecanoic acid interacts effectively with the active site of the protein, suggesting its potential as an anti-diabetic agent by modulating tyrosine phosphatase 1B activity.

Docking with androgen receptor: The docking analysis with the AR (PDB ID: 4K7A), a target involved in the pathogenesis of dandruff, demonstrated significant binding interactions with 1'-hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one and n-hexadecanoic acid. 1'-Hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one achieved a binding energy of -8 kcal/mol, forming one hydrogen bond, while n-hexadecanoic acid exhibited a binding energy of -5.2 kcal/mol with one hydrogen bond. These results underscore the potential of these compounds to modulate androgen receptor activity, which could be leveraged for anti-dandruff treatments.

Docking with cyclin A: The analysis of cyclin A (PDB ID: 6GUE), a critical protein in cancer progression, revealed the strongest interactions with stigmasterol and phytol. Stigmasterol exhibited a superior binding energy of -8.4 kcal/mol, forming one hydrogen bond at HIS A 84 (histidine residue at 84 position), while phytol exhibited a binding energy of -4.9 kcal/mol with multiple hydrogen bonds. This suggests that stigmasterol may be more effective in targeting cyclin A, a key player in cancer progression, thereby supporting its potential use in cancer therapy.

Docking with human NKCC1: For human NKCC1 (PDB ID: 6PZT), a target implicated in anti-diuresis, both beta-sitosterol and 1'-hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one demonstrated strong interactions. Beta-sitosterol exhibited a binding energy of -9.3 kcal/mol, forming a hydrogen bond with GLU B 363 (glutamic acid residue at 363 position of B chain), while 1'-hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one showed a binding energy of -7.8 kcal/mol, forming two hydrogen bonds. These results suggest that beta-sitosterol, due to its stronger binding affinity and interaction with the active site, may serve as a more effective diuretic agent.

Discussion

The findings of this study provide valuable insights into the therapeutic potential of phytochemicals derived from *P. nodiflora*. The *in silico* docking analysis identified n-hexadecanoic acid as a potent inhibitor of PTP1B, a critical enzyme in the regulation of insulin signaling and a promising target for the management of type 2 diabetes (5). Previous research has highlighted the antidiabetic properties of plant-derived fatty acids, and our results further support the investigation of n-hexadecanoic acid as a potential therapeutic agent (13).

Additionally, the inhibition of the AR by 1'-hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one highlights its potential role in treating androgen-related alopecia (4, 14). The AR, when activated by dihydrotestosterone (DHT) and other androgens, promotes the miniaturization of hair follicles, resulting in hair loss. The binding of 1'-hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one to the AR's active site

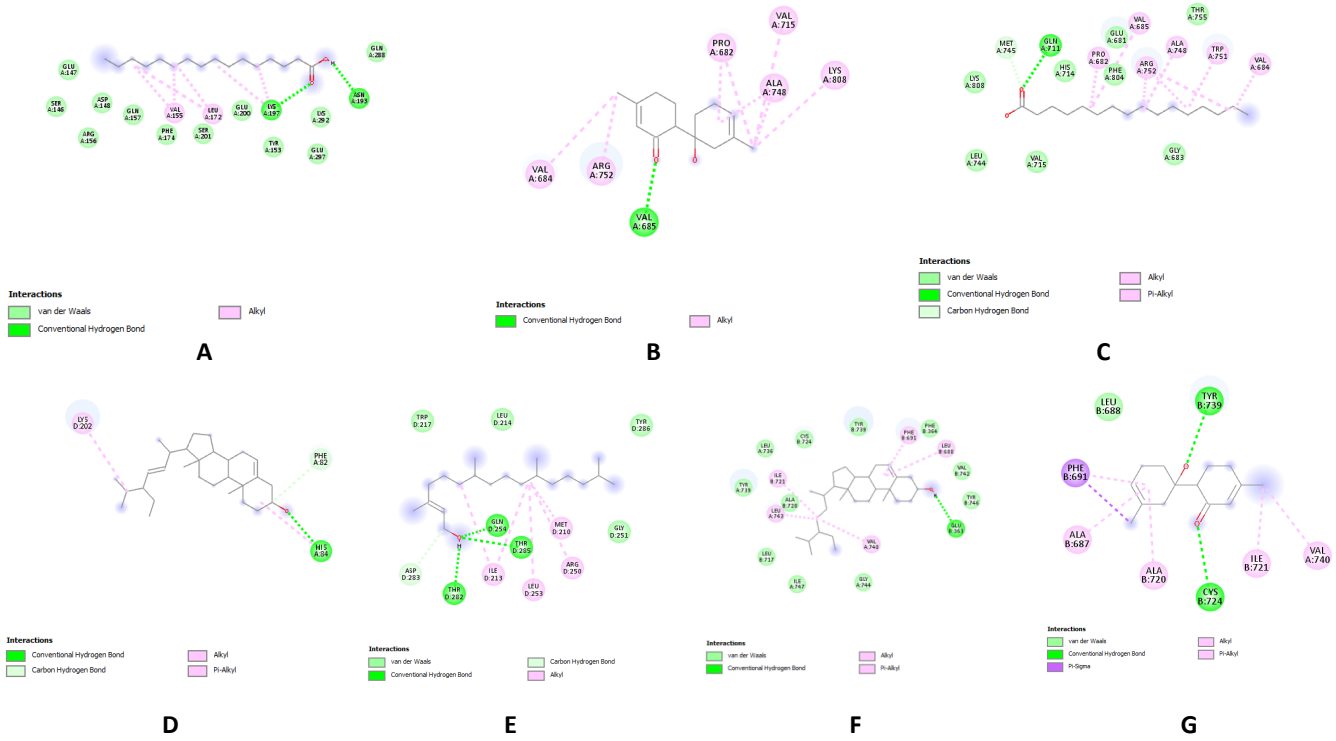


Fig. 4. Visualisation of molecular docking between tyrosine phosphatase 1B with (A) - n-Hexadecanoic acid; AR with (B) - 1'-Hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one and (C) - n-Hexadecanoic acid; cyclin A with (D) - Stigmasterol, (E) – Phytol; cryo-EM structure of human NKCC1 with (F) - beta-Sitosterol, (G) - 1'-Hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one.

could block DHT or similar androgens from interacting with the receptor, thereby reducing the downstream signalling that triggers hair follicle miniaturization. This inhibition could slow or stop the progression of androgen-related alopecia, making this compound a promising candidate for therapeutic development in hair loss treatments. Stigmasterol, a well-known phytosterol, exhibited strong binding affinity to cyclin A, a key regulator of the cell cycle and a protein frequently overexpressed in cancer cells. This finding aligns with earlier studies suggesting that phytosterols can inhibit cancer cell growth by modulating cell cycle pathways (7, 15). The ability of n-hexadecanoic acid and 1'-hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one to cross the blood-brain-barrier, as demonstrated by the boiled egg model, underscores their potential in drug development for neural disorders.

Additionally, beta-sitosterol, a widely studied phytosterol, showed significant binding affinity to NKCC1, a protein involved in fluid balance and diuresis. This finding aligns with earlier research suggesting the role of plant sterols in kidney function and fluid regulation. The interaction of beta-sitosterol with NKCC1 underscores its potential as a therapeutic agent for managing conditions associated with fluid retention and anti-diuresis (8).

Table 4. The binding energy, number of H-bonds, interacting residues of selected compounds

Protein ID	Property	PUBChem ID	Interacting residues at active sites	No. of H-bonds	Binding energy
4Y14	Anti-diabetic	985	LYS A: 197	2	-4.5
4K7A	Anti-alopecia	557446	VAL A: 685	1	-8
		985	VAL A: 711	1	-5.2
		5280794	HIS A: 84	1	-8.4
6GUE	Anti-cancer	5280435	GLN D: 254 THR D: 285 THR D: 285	3	-4.9
6PZT	Anti-diuretics	22284	GLU B: 363	1	-9.3
		557446	TYR B: 739	2	-7.8

Conclusion

Our *in-silico* docking study demonstrates the therapeutic potential of phytochemicals like n-hexadecanoic acid, 1'-hydroxy-4,3'-dimethyl-bicyclohexyl-3,3'-dien-2-one, stigmasterol and beta-sitosterol, derived from *P. nodiflora*, for the treatment of diabetes, alopecia, cancer, and anti-diuresis respectively. The findings from this research provide a strong foundation for further experimental validation and drug development efforts.

Future studies should focus on validating the therapeutic potential of these compounds through *in-vitro* and *in-vivo* experimental approaches to elucidate their mechanisms of action in greater detail. *In-vitro* assays using disease-relevant models, such as diabetes, cancer, and alopecia, followed by *in-vivo* animal studies, can help validate the efficacy of these compounds. Additionally, structure-activity relationship (SAR) studies can be employed to optimize the identified compounds by modifying their structure to improve activity and binding affinity to target proteins.

High-throughput screening (HTS) of additional phytochemicals from *P. nodiflora* and related species may reveal more bioactive compounds with therapeutic potential. Mechanistic studies, including gene expression profiling and protein interaction analysis, can provide insights into the effects of these compounds on disease-related pathways. Finally, clinical trials can be designed to evaluate the safety and efficacy of these compounds in humans after preclinical validation, ultimately paving the way for potential therapeutic applications.

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Authors' contributions

PS and UP performed the experiment and wrote the draft manuscript. RB conceived the idea, provided research facilities and wrote the final version of the manuscript. TAU verified the data and helped writing and correction of manuscript.

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During the preparation of this work, the authors used ChatGPT in order to improve language and readability, with caution. After using the tool, PS and UP reviewed and edited the content as needed and take full responsibility for the content of the publication.

References

1. Arumanayagam S, Arunmani M. Hepatoprotective and antibacterial activity of *Lippia nodiflora* Linn. against lipopolysaccharides on HepG2 cells. Pharmacogn Mag. 2015;11 (41):24-31. https://doi.org/10.4103/0973-1296.149689
2. Khdera HA, Saad SY. Chemical composition of organic extracts of *Phyla nodiflora* L. in Syria by GC-MS. Heliyon. 2024;10 (14):e34686. https://doi.org/10.1016/j.heliyon.2024.e34686
3. Alafnan A, Nadeem MF, Ahmad SF, Sarfraz M, Aalamri A, Khalifa NE, et al. A comprehensive assessment of phytochemicals from *Phyla nodiflora* (L.) Greene as a potential enzyme inhibitor and their biological potential: An *in-silico*, *in-vivo* and *in-vitro* approach. Arab J Chem. 2023;16(11):105233. https://doi.org/10.1016/j.arabjc.2023.105233
4. Sadgrove NJ. The new paradigm for androgenetic alopecia and plant-based folk remedies: 5α-reductase inhibition, reversal of secondary microinflammation and improving insulin resistance. J Ethnopharmacol. 2018;227:206-36. https://doi.org/10.1016/j.jep.2018.09.009
5. Teimouri M, Hosseini H, ArabSadeghabadi Z, Babaei-Khorzoughi R, Gorgani-Firuzjaee S, Meshkani R. The role of protein tyrosine phosphatase 1B (PTP1B) in the pathogenesis of type 2 diabetes mellitus and its complications. J Physiol Biochem. 2022;1-16. https://doi.org/10.1007/s13105-021-00860-7
6. Zhuo F, Xu W, Wang L, Wu Y, Xu Z, Zhao J. Androgen receptor gene polymorphisms and risk for androgenetic alopecia: A meta-analysis. Clin Exp Dermatol. 2012;37(2):104-11. https://doi.org/10.1111/j.1365-2230.2011.04186.x
7. Ding L, Cao J, Lin W, Chen H, Xiong X, Ao H, et al. The roles of cyclin-dependent kinases in cell-cycle progression and therapeutic strategies in human breast cancer. Int J Mol Sci. 2020;21(6):1960. https://doi.org/10.3390/ijms21061960
8. Koumangoye R, Bastarache L, Delpire E. NKCC1: Newly found as a human disease-causing ion transporter. Function. 2021;2 (1):zqaa028. https://doi.org/10.1093/function/zqaa028
9. Furlan V, Konc J, Bren U. Inverse molecular docking as a novel approach to study anticarcinogenic and anti-neuroinflammatory effects of curcumin. Molecules. 2018;23 (12):3351. https://doi.org/10.3390/molecules23123351
10. Iman K, Mirza MU, Mazhar N, Vanmeert M, Irshad I, Kamal MA. *In silico* structure-based identification of novel acetylcholinesterase inhibitors against Alzheimer's disease. CNS Neurol Disord Drug Targets. 2018;17(1):54-68. https://doi.org/10.2174/1871527317666180115162422
11. Balamurugan R, Duraipandiyan V, Ignacimuthu S. Antidiabetic activity of γ-sitosterol isolated from *Lippia nodiflora* L. in streptozotocin induced diabetic rats. Eur J Pharmacol. 2011;667 (1-3):410-18. https://doi.org/10.1016/j.ejphar.2011.05.025
12. Sudha A, Srinivasan P. Physicochemical and phytochemical profiles of aerial parts of *Lippia nodiflora* L. Int J Pharm Sci Res. 2013;4(11):4263. http://dx.doi.org/10.13040/IJPSR.0975-8232.4 (11).4263-71
13. Purushothaman R, Vishnuram MG, Ramanathan DT. Isolation and identification of N-hexadecanoic acid from *Excoecaria agallocha* L. and its antibacterial and antioxidant activity. JETIR.2024;11(1):332-42.
14. Balakrishna K, Gopal RH, Ramkumar V, Rao RB, Vasanth S, Narayanappa D. Antibacterial acivity of the essential oil of *Lippie nodiflora*. Anc Sci Life. 1996;16(1):79-81.
15. Teoh PL, Liau M, Cheong BE. *Phyla nodiflora* L. extracts induce apoptosis and cell cycle arrest in human breast cancer cell line, MCF-7. Nutr Cancer. 2019;71(4):668-75. https://doi.org/10.1080/01635581.2018.1559942