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Computational investigation of *Crateva religiosa* bark phytoconstituents as potential modulators of Hyperthyroidism

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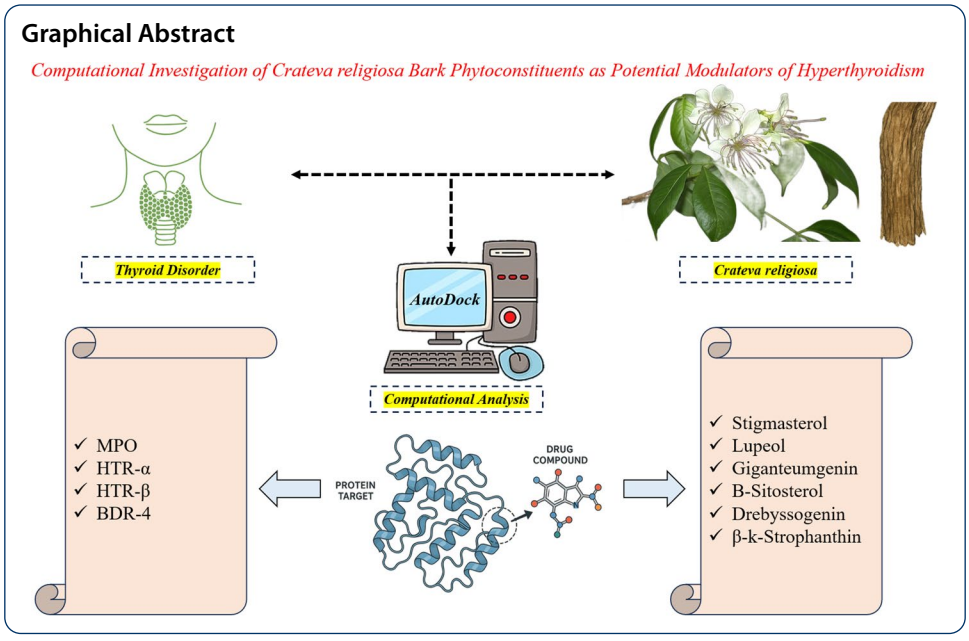
Abstract

Crateva religiosa possesses a diverse array of biologically and pharmacologically active phytoconstituents in its bark, including stigmasterol, β-k-strophanthin, drebyssogenin, β-sitosterol, lupeol, and giganteumgenin. These natural compounds are traditionally known for their therapeutic potential, including in managing hyperthyroid conditions. In this study, an in silico molecular docking approach was employed to investigate the binding affinities of major bark phytoconstituents of *Crateva religiosa* with key hyperthyroidism-related targets: myeloperoxidase (MPO, PDB: 1CXP), thyroid hormone receptors α and β (HTR-α, PDB: INAV; HTR-β, PDB: 1N46), and BDR-4 (PDB: 3MXF). Docking was conducted using AutoDock Tools 4.2.1, evaluating dock scores for each ligand-protein interaction. The results revealed that β-sitosterol and stigmasterol exhibited the most favorable binding affinities, with docking energies as low as −9.29 and −7.00 kcal/mol, respectively, against HTR-α, HTR-β, and BDR-4. Lepuol exhibit with −7.12 kcal/mol binding affinity towards MPO target. Drebyssogenin also showed notable affinity towards HTR-α (–9.06 kcal/mol). The standard reference inhibitor, methimazole, showed significantly interaction profiles (–3.37 to −3.55 kcal/mol) across all targets. These findings highlight β-sitosterol and stigmasterol as promising phytoconstituent leads for further antithyroid drug development. The noticeable binding efficiency of these compounds suggests their potential as selective thyroid hormone receptor modulators and warrants subsequent experimental validation for therapeutic application in hyperthyroidism management.

Keywords Molecular docking, *Crateva religiosa*, Myeloperoxidase, Hyperthyroidism, AutoDock



1 Introduction

Thyroid dysfunction is a prevalent endocrine issue that affects 200 million people globally, accounting for 40% of the global population [1]. Thyroid dysfunction affects individuals equally across developed, developing, and underdeveloped countries. These disorder appears to pose a significant risk to the Indian population, with reported prevalence rates that are both high and escalating [2–4]. Despite this trend, considerable variation exists among the different states within India regarding the incidence of thyroid dysfunction [2]. The underlying causes of hyperthyroidism exhibit geographical variations, largely influenced by regional iodine consumption levels [5]. In regions with adequate iodine intake, Graves disease is the predominant cause of hyperthyroidism, affecting 70–80% of patients. Conversely, in areas with iodine deficiency, Graves disease accounts for approximately 50% of cases, with toxic nodular goiter making up the remainder [5, 6]. A cross-sectional investigation in India by Singh et al.. concerning patients with thyrotoxicosis revealed that following the exclusion of drug-induced and pregnancy-induced thyrotoxicosis, Graves disease accounted for 84.21% of cases, subacute thyroiditis for 11.84%, and toxic nodular disease for 3.95% [7]. The clinical presentation of hyperthyroidism also differs based on its underlying cause. Specifically, patients with Toxic Nodular Goiter tend to be older, exhibit lower thyroid hormone levels, are more frequently subclinical than over hyperthyroidism, and present with a higher incidence of cardiovascular disorders when contrasted with patients diagnosed with graves disease [6, 8].

Current treatment modalities for the condition are all efficacious and encompass medical management with antithyroid drugs (ATD), surgical intervention, and radioactive iodine (RAI) therapy, each of which carries the potential for significant adverse effects. In guiding patients through shared decision-making to determine the most appropriate treatment option, physicians should evaluate both the immediate risks and benefits of the therapy, as well as its long-term implications [9]. In light of the substantial increase in the global adoption of traditional and complementary medicine, the World Health

Organization (WHO) has, over the past thirty years, highlighted the necessity of rejuvenating traditional medical practices in diverse regions worldwide [10]. Given the considerable adverse effects associated with synthetic antithyroid drugs, there is a growing need for natural, plant-based therapeutic alternatives. Phytoconstituents with multimodal mechanisms of action hold significant promise for the effective management of hyperthyroid disorders [11].

One important medicinal plant in the Capparidaceae family is *Crateva religiosa*, also referred to as the Temple plant or Sacred Garlic Pear. It can be found in areas of the South Pacific Islands, Japan, Australia, and Southeast Asia. Due to its traditional use and therapeutic potential, it is important in Indian Ayurvedic medicine for treating a variety of diseases [12, 13]. *Crateva religiosa* exhibits a broad spectrum of pharmacological activities that substantiate its traditional medicinal applications. The bark demonstrates strong diuretic and litholytic properties, making it effective in urinary disorders such as urolithiasis, renal stones, neurogenic bladder, and benign prostatic hyperplasia. It also possesses notable anti-inflammatory potential, alleviating edema and related conditions, while the whole plant powder shows cholinergic effects on smooth muscles, particularly in the urinary bladder, thereby aiding urinary dysfunction. Preparations from the bark and stem exhibit antimicrobial activity against urinary tract and other microbial infections, and the plant is also traditionally employed for hepatoprotective purposes, especially in liver enlargement. Gastrointestinal benefits include its use in diarrhea, dysentery, appetite stimulation, bile secretion, and bowel regulation. Additionally, the root juice is used in fever and cough management, reflecting antipyretic and expectorant potential, whereas wood smoke has been applied in syphilitic ulcerations and even cancer, indicating anticancer relevance.

Ethnomedicinal reports further highlight its antidiabetic effects, though detailed mechanistic studies remain limited, while its application in leprosy and scrofulous glandular enlargements suggests immunomodulatory and dermatological significance [14]. Phytochemical investigations of *C. religiosa* have revealed a diverse array of bioactive constituents, including steroidal sapogenins, triterpenoids, phytosterols, and cardiac glycosides. Key compounds such as giganteumgenin and drebyssogenin, classified as steroidal sapogenins, exhibit notable anti-inflammatory and cytotoxic activities, highlighting their potential in therapeutic applications. Phytosterols like stigmasterol and β-sitosterol contribute to cholesterol regulation, immunomodulation, and antioxidative effects, whereas triterpenoids such as lupeol demonstrate anti-inflammatory, anticancer, and hepatoprotective properties. Additionally, cardiac glycosides like β-k-strophanthin play a role in modulating cardiac function, underscoring the plant's relevance in cardiovascular health. The rich chemical diversity of *C. religiosa* underscores its pharmacological potential and provides a scientific basis for its traditional use. Understanding the classification and biological significance of its phytoconstituents is crucial for exploring novel therapeutic applications and guiding future drug discovery efforts. In order to address this gap, the current study investigated to assess the therapeutic potential of *Crataeva religiosa* bark on hyperthyroidism-targeted proteins through simulation studies.

2 Materials and methods

Molecular modelling technique is very most important method for the investigation and reorganization of receptor protein and compound structure potentially without giving more action and investment in research work. Structure prediction of target and the ligand is important for their interaction studies.

Various software tools and online databases were employed in this study.

Chemical structures of phytoconstituents were retrieved from PubChem (https://pubchem.ncbi.nlm.nih.gov) [15], while the target protein structures were obtained from the Protein Data Bank (http://www.rcsb.org/pdb/home/home.do) [16]. Online platforms including SwissADME (http://www.swissadme.ch) [17], and the Cheminformatics Property Explorer (https://www.cheminfo.org/flavor/cheminformatics/Utility/Property_explorer/index.html) [18] were utilized for evaluating pharmacokinetic and physicochemical properties. Additional analyses were performed using OSIRIS and molecular docking studies were carried out with AutoDockTools 4.2.1. Protein visualization and interaction analysis were conducted using Bio-Discovery Studio.

2.1 Retrieval of target enzyme structures

The three-dimensional structures of target enzymes associated with the pathogenesis of hyperthyroidism in *Homo sapiens* were retrieved from the Protein Data Bank (PDB). The selected targets included Myeloperoxidase (MPO; PDB ID: 1CXP), Thyroid Hormone Receptor Alpha (HTR-α; PDB ID: 1NAV), Thyroid Hormone Receptor Beta (HTR-β; PDB ID: 1N46), and Beta-adrenergic Receptor 4 (BDR-4; PDB ID: 3MXF) shown in Table 1. Prior to molecular docking, all water molecules and heteroatoms were removed from the protein structures to ensure optimized binding site preparation.

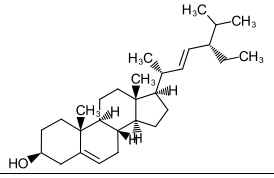
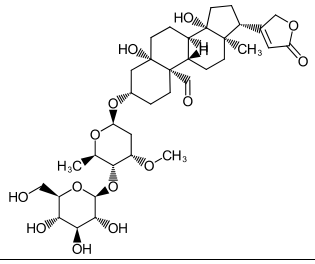
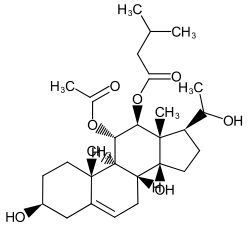
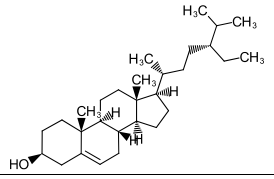
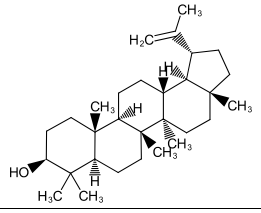
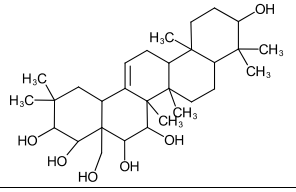
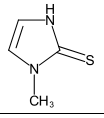
2.2 Retrieval of ligand

The structures of 6 phytoconstituents were retrieved from the PubChem database. These structures were used for docking studies. The selected 3D structure of the ligands was retrieved from PubChem compound database in SDF format followed by conversion in the PDB format and optimization using Bio-Discovery Studio. Structure, Compound, Molecular formula, and PubChem ID of phytoconstituents present in the study shown in Table 2.

Table 1 Selected target description

Target	Function / relevance	PDB ID	Notes
Myeloperoxidase (MPO)	Enzyme involved in oxidative stress and inflammation; elevated activity can contribute to thyroid tissue damage in autoimmune hyperthyroidism (e.g., Graves' disease).	1CXP	Potential target for antioxidant or anti-inflammatory modulation.
Thyroid Hormone Receptor Alpha (TR-α / HTR-α)	Nuclear receptor mediating thyroid hormone (T3/T4) effects on metabolism, cardiac, and bone functions.	1NAV	Modulation can affect tissue-specific thyroid hormone action.
Thyroid Hormone Receptor Beta (TR-β / HTR-β)	Nuclear receptor mainly expressed in liver, pituitary, and kidney; regulates feedback on TSH secretion.	1N46	Selective targeting may normalize TSH levels and hyperthyroid symptoms.
Beta-adrenergic Receptor 4 (BDR-4 / β4-AR)	G-protein coupled receptor mediating sympathetic responses; hyperthyroidism often causes elevated adrenergic activity.	3MXF	Targeting adrenergic receptors helps manage cardiac and metabolic symptoms.

Table 2 Selected phytoconstituents molecular formula, PubChem ID, structure

Sl. No	Structure	Compound	Molecular formula	PubChem ID
1		Stigmasterol	$C_{29}H_{48}O$	5280794
2		β -k-strophanthin	$C_{36}H_{54}O_{14}$	20055294
3		Drebyssogenin	$C_{28}H_{44}O_7$	12309358
4		β -sitosterol	$C_{29}H_{50}O$	222284
5		Lupeol	$C_{30}H_{50}O$	259846
6		Giganteumgenin	$C_{30}H_{50}O_6$	619407
7		Methimazole	$C_4H_6N_2S$	1349907

2.3 Prominent active site prediction

Before performing the docking analysis, the prominent active sites of the four selected target proteins were identified using the PDB sum database https://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/GetPage.pl?pdbcode=index.html, which provides detailed structural and ligand-binding information for protein–ligand complexes [19].

Table 3 Physiochemical properties of selected phytoconstituents

Sl. no	Ligand	Molecular weight	No of rotatable bonds	H bond acceptor	H bond donor	Clog *P*
1.	Stigmasterol	412.70	5	1	1	7.60
2.	β -k-strophanthin	710.81	8	14	6	−0.51
3.	Drebyssogenin	492.65	7	7	3	3.48
4.	β -sitosterol	414.72	6	1	1	7.86
5.	Lupeol	426.73	1	1	1	7.65
6.	Giganteumgenin	506.72	1	6	6	−4.55

Table 4 Toxicity risks predicted by OSIRIS property explorer

Sl. no	Ligand	Mutagenicity	Tumorigenicity	Skin irritation	Reproductive toxicity
1	Stigmasterol	Safe	Safe	Safe	Safe
2	β -k-strophanthin	Safe	Safe	Safe	Safe
3	Drebyssogenin	Safe	Safe	High toxicity	Mild toxicity
4	β -sitosterol	Safe	Safe	Safe	Safe
5	Lupeol	Safe	Safe	Safe	Safe
6	Giganteumgenin	Safe	Safe	Safe	Safe

2.4 In-silico ADME properties

In order to predict the ADME properties of the selected phytoconstituents, SwissADME web tool was used. It is a free web tool to compute pharmacokinetics, ADME properties, drug-likeliness, and medicinal chemistry friendliness of small molecules. The import tool on the input zone of the Swiss ADME submission page was used to retrieve the compound structure from databases, converted into SMILES format and then calculations were run. In some cases, the SMILE format of the compound was copied from the PubChem database and directly pasted before running. When results were loaded, they were saved as a CSV file present in Table 3.

2.5 In-silico toxicity risks assessment and drug likeliness

To assess the toxicity risks of the selected phytoconstituents, their SMILES were retrieved from PubChem database and illustrated in the OSIRIS Property Explorer open source program which computes toxicity risks and drug-relevant properties of compounds and provides results as safe, mild and moderate coded features shown in Table 4.

2.6 In silico molecular docking

Compounds representing different subclasses of the sterodial sapogenin, phytosterol, cardiac gycoside, triterpenoid were selected to evaluate their potential inhibitory activity against the chosen protein targets. The two-dimensional (2D) structures of six phytoconstituents were retrieved from the NCBI PubChem database in .sdf format. The ligand structures were then prepared, optimized, and converted into PDB format using BioDiscovery Studio for subsequent molecular docking analysis.

2.7 Molecular docking

Molecular docking studies were carried out using AutoDock 4.2.1, which employs the Lamarckian Genetic Algorithm (LGA) to predict the optimal binding conformation of ligands within the active site of target proteins. The algorithm integrates energy evaluation through affinity grid maps to identify the most favorable binding poses. Polar hydrogen atoms were added to all protein structures, and Kollman united atomic charges were

assigned. A grid box of dimensions 60 Å × 60 Å × 60 Å with a spacing of 0.375 Å was generated, centered around the identified active site residues of each target protein. For all ligands, random starting positions, orientations, and torsions were applied. Docking parameters were set as follows: number of Genetic Algorithm (GA) runs = 25, population size = 150, maximum number of evaluations = 2,500,000, and maximum number of generations = 27,000. The docked conformation with the lowest binding free energy was selected as the most stable complex. The docking results were visualized and analyzed using BioDiscovery Studio Visualizer [20–24].

3 Results & discussion

The present investigation was designed to explore the therapeutic potential of selected phytoconstituents in the management of hyperthyroidism through a comprehensive in silico approach integrating molecular docking, pharmacokinetic profiling, and toxicity prediction.

3.1 Pharmacokinetic profiling

Pharmacokinetic properties were evaluated using Lipinski's Rule of Five, which remains a cornerstone for assessing drug-likeness in orally administered compounds. Most of the tested phytoconstituents complied with these criteria, suggesting favorable absorption and distribution profiles. However, certain steroidal compounds such as stigmasterol, β-sitosterol, and lupeol exhibited a single violation due to elevated lipophilicity (LogP > 5) shown in Table 3. While this characteristic may limit aqueous solubility and oral bioavailability, it is not uncommon among bioactive natural products. Such findings highlight the importance of advanced drug delivery strategies—such as nano formulations or lipid-based carriers to overcome solubility constraints and optimize systemic availability.

3.2 Toxicity assessment

Toxicity risks were predicted using OSIRIS Property Explorer. The majority of compounds demonstrated no mutagenic, tumorigenic, irritant, or reproductive toxicity, underscoring their potential safety shown in Table 4. Drebyssogenin was an exception, showing mild reproductive toxicity and a higher likelihood of skin irritation. Although this does not preclude therapeutic relevance, it emphasizes the need for careful preclinical validation to ensure safety before clinical translation.

Table 5 Docking scores of selected ligands against various protein targets

Ligand	MPO (1CXP) (kcal/mol)	HTR-α (INAV) (kcal/mol)	HTR-β (1N46) (kcal/mol)	BDR-4 (3MXF) (kcal/mol)
Stigmasterol	−7.00	−9.21	−8.51	−8.51
β-k-strophanthin	−2.48	−5.23	69.85	16.82
Drebyssogenin	−5.61	−9.06	−5.35	−5.35
β-sitosterol	−5.61	−9.29	−9.02	−9.02
Lupeol	−7.12	−9.10	17.79	6.79
Giganteumgenin	−4.91	−4.28	69.85	16.82
Methimazole	−3.37	−3.55	−3.30	−3.30

Table 6 Top docked compound of MPO & HTR-α docking score and protein-ligand interactions

Sl. no	Compound	Docking Score Kcal/mol	No of H-bond interaction	Interacting residues
MPO (1CXP)				
1	Stigmasterol	−7.00	2	ARG 438 PHE 439
2	Methimazole	−3.37	1	ILE 498
HTR-α (INAV)				
1	β-sitosterol	−9.29	1	SER 319
2	Methimazole	−3.55	1	HIS 358

Table 7 Top docked compound of HTR-β & BDR-4 docking score and protein-ligand Interactions

Sl. No	Compound	Docking Score Kcal/mol	No of H-bond interaction	Interacting residues
HTR-β (1N46)				
1	β-sitosterol	−8.51	1	MET 442
2	Methimazole	−3.30	1	MET 313
BDR-4 (3MXF)				
1	β-sitosterol	−9.02	1	ASN 140
2	Methimazole	−3.30	1	GLN 85

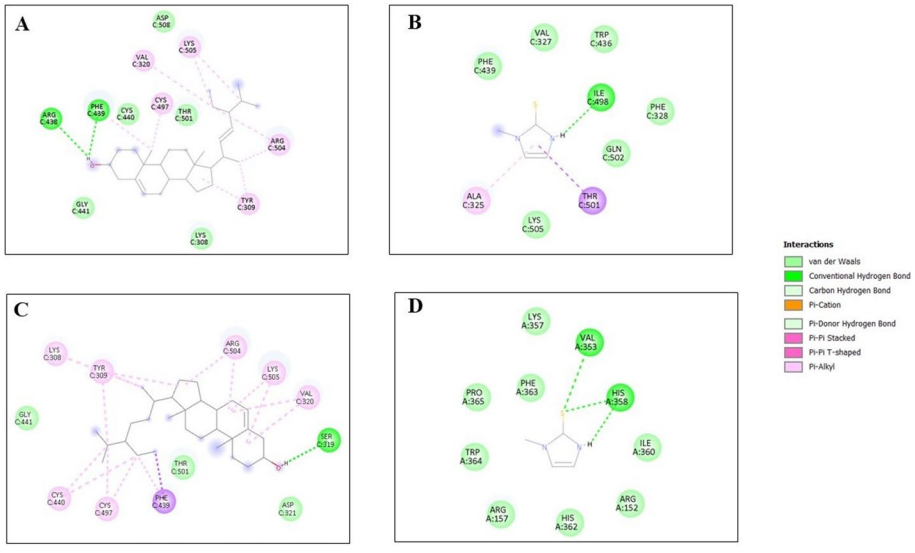


Fig. 1 2-D interaction diagram of top ranked screened phytoconstituents **A** Stigmasterol, **B** Methimazole interacted with MPO (1CXP); **C** β-sitosterol and **D** Methimazole interacted with HTR-α (INAV) respectively

3.3 Molecular docking

Molecular docking analysis was performed against four key protein targets implicated in thyroid regulation: Myeloperoxidase (MPO; 1CXP), Thyroid Hormone Receptor alpha (HTR-α; INAV), Thyroid Hormone Receptor beta (HTR-β; 1N46), and Bromodomain-containing protein 4 (BDR-4; 3MXF). Distinct binding interactions were observed across the phytoconstituents, with steroidal compounds such as β-sitosterol and stigmasterol consistently demonstrating strong affinities, achieving docking scores as low as − 9.29 kcal/mol. These interactions and selective binding to thyroid-related receptors, positioning them as promising modulators in hyperthyroid conditions shown in Table 5.

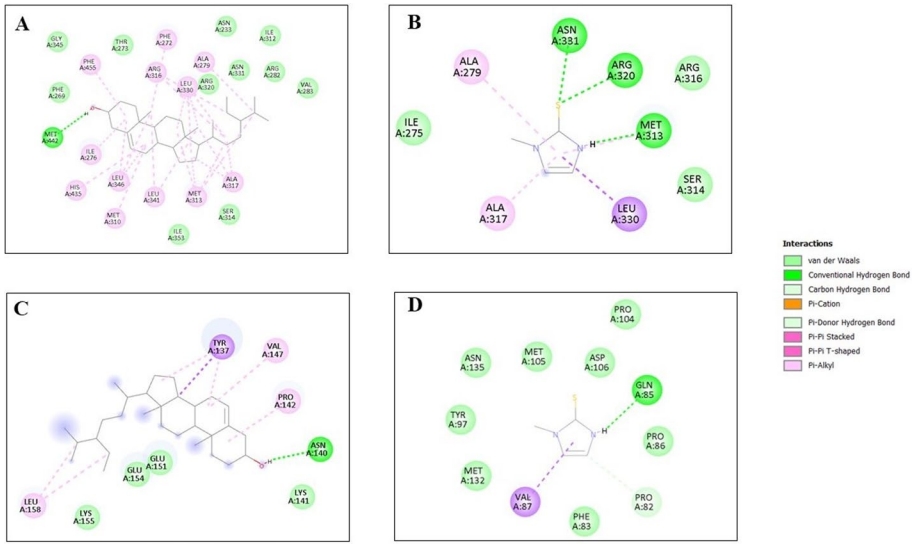


Fig. 2 2-D interaction diagram of top ranked screened phytoconstituents **A** β-sitosterol, **B** Methimazole interacted with HTR-β (1N46); **C** β-sitosterol and **D** Methimazole interacted with BDR-4 (3MXF) respectively

Drebyssogenin also exhibited notable affinity, particularly toward HTR-α, reinforcing the relevance of steroid-like scaffolds in thyroid hormone pathway modulation.

The function of specific amino acids in the ligand-binding domain of MPO, HTR-α & HTR-β, BDR-4 has been well documented in Tables 6 and 7. These amino acids are involved in non-covalent interactions with studied ligands, and they play a critical role in inhibiting the ligand-binding domain of MPO, HTR-α & HTR-β, BDR-4. These non-covalent interactions, van der waals, columbic interaction, u-u interaction, and hydrogen interaction are shown in Figs. 1 and 2.

Conversely, compounds such as β-k-strophanthin, giganteumgenin, and lupeol displayed weaker or non-favorable interactions, particularly with HTR-β and BDR-4. This variability may reflect structural incompatibility within binding pockets or limitations of docking algorithms, but it also points to potential molecular selectivity that could reduce off-target effects.

Interestingly, when compared with the standard drug methimazole, which showed relatively weak binding energies (–3.37 to – 3.55 kcal/mol), the selected phytoconstituents—especially β-sitosterol and stigmasterol—demonstrated superior binding potential. This comparative advantage underscores their promise as alternative or complementary therapeutic agents. Their strong binding affinities, acceptable pharmacokinetic profiles (with manageable limitations), and favorable safety predictions suggest significant potential in modulating thyroid hormone pathways. At the same time, the observed variability among other phytoconstituents emphasizes the importance of structural compatibility and selectivity in drug design. Although simulation work primarily focuses on the preliminary screening of compound to facilitate further in vitro and in vivo proof-of-concept studies. This approach aims to identify the most promising compound through in silico methods, which can then be translated into future applications based on the supporting data.

4 Conclusion

The in silico molecular docking study demonstrated that the natural phytosterols, β-sitosterol and stigmasterol, exhibit strong binding affinities across key thyroid hormone receptors and related target proteins, better than reference drug methimazole in binding potency. Collectively, the findings highlight β-sitosterol and stigmasterol as lead candidates for further in vitro and in vivo evaluation in the context of thyroid-related disorders or as multi-targeted modulators. These results provide a strong foundation for subsequent experimental studies to validate the biological activity and therapeutic potential of these phytoconstituents.

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Author contributions
Sittarthan Viswanathan, Gowrishankar Jayabalan: Conceptualization and Original Draft; Sittarthan Viswanathan, Gowrishankar Jayabalan: Data Collection and Analysis; Sittarthan Viswanathan, Jayaraman Rajangam: Methodology and Writing Original Draft; Sittarthan Viswanathan: Data Visualization and Resources; Sittarthan Viswanathan, Jayaraman Rajangam: Supervision and Project Administration.

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Data availability
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Consent for publication
Not applicable as no human study is involved.

Competing interests
The authors declare no competing interests.

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References

1. Kuyl JM. The evolution of thyroid function tests. J Endocrinol Metabolism Diabetes South Afr. 2015;20(2):11–6.
2. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metabol. 2011;15(Suppl2):S78–81.
3. Bagcchi S. Hypothyroidism in India: more to be done. lancet diabetes Endocrinol. 2014;2(10):778.
4. Singh SK, Singh R, Singh A. Prevalence of Thyroid Disorders (TD) in Newly Diagnosed Type 2 Diabetes Mellitus Patients-A Cross Sectional Study. J Assoc Phys India. 2021;69(10):11–2.
5. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, Okosieme OE. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Reviews Endocrinol. 2018;14(5):301–16.
6. Nyström HF, Jansson S, Berg G. Incidence rate and clinical features of hyperthyroidism in a long-term iodine sufficient area of Sweden (Gothenburg) 2003–2005. Clin Endocrinol. 2013;78(5):768–76.
7. Singh SK, Singh R, Singh SK, Iquebal MA, Jaiswal S, Rai PK. Aetiological sub-classification of thyrotoxicosis and relevance of TT3/TT4 ratio in sub-classification of patients with thyrotoxicosis; an Indian cross-sectional study. Int J Adv Med. 2023;10:830–5.
8. Biondi B, Kahaly GJ. Cardiovascular involvement in patients with different causes of hyperthyroidism. Nat reviews Endocrinol. 2010;6(8):431–43.
9. Shah R, Adamson SE, Jasim S. Management Aspects of Medical Therapy in Graves Disease. Endocr Pract. 2025;31(4):536–46.
10. Ghaffari-Saravi F, Jokar A. Herbal remedies for hypothyroidism: A systematic review and meta-analysis. Caspian J Intern Med. 2024;16(1):1.
11. Bharthi V, Kavya N, Shubhashree MN, Bhat S. Herbal approach to management of thyroid disease-a review. J Ayurvedic Herb Med. 2017;3(1):48–52.
12. Shinsy P, Thomas J. A Systematic Review of Crateva Species for It's Traditional and Modern Medicinal Uses. Eur Chem Bull. 2023;12(7):5822–41.
13. Srinivas V, Surendra G, Anjana M, Kiran AS. A scientific review on Crateva religiosa. Int J Adv Pharm Biol Chem. 2018;7(1):11–6.

14. Patil UH, Gaikwad DK. Medicinal profile of a scared drug in ayurveda: Crataeva religiosa A Review. J Pharm Sci Res. 2011;3(1):923.
15. Kim S, Chen J, Cheng T, Gindulyte A, He J, He S, Li Q, Shoemaker BA, Thiessen PA, Yu B, Zaslavsky L. PubChem 2019 update: improved access to chemical data. Nucleic Acids Res. 2019;47(D1):D1102–9.
16. Berman HM, Westbrook J, Feng Z, Gilliland G, Bhat TN, Weissig H, Shindyalov IN, Bourne PE. The protein data bank. Nucleic Acids Res. 2000;28(1):235–42. https://www.rcsb.org/
17. Daina A, Michielin O, Zoete V. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017;7:42717. http://www.swissadme.ch/
18. OSIRIS, an entirely in-house developed drug discovery informatics system. J Chem Inf Model. 2009;49(2):232–46. https://www.cheminfo.org/
19. Laskowski RA, Jabłońska J, Pravda L, Vařeková RS, Thornton JM. PDBsum: Structural summaries of PDB entries. Protein Sci. 2018;27(1):129–34 https://www.ebi.ac.uk/
20. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, Olson AJ. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. J Comput Chem. 2009;30(16):2785–91.
21. Syriopoulou A, Markopoulos I, Tzakos AG, Mavromoustakos T. Ligand–receptor interactions and drug design. InProtein-Ligand Interactions and Drug Design. Springer US. 2021; pp. 89–104
22. Bitencourt-Ferreira G, Pintro VO, de Azevedo WF Jr. Docking with autodock4. InDocking screens for drug discovery. Springer New York. 2019; (pp. 125–48)
23. Forli S, Huey R, Pique ME, Sanner MF, Goodsell DS, Olson AJ. Computational protein–ligand docking and virtual drug screening with the AutoDock suite. Nat Protoc. 2016;11(5):905–19.
24. Zaka M, Sehgal SA, Shafique S, Abbasi BH. Comparative in silico analyses of Cannabis sativa, Prunella vulgaris and Withania somnifera compounds elucidating the medicinal properties against rheumatoid arthritis. J Mol Graph Model. 2017;74:296–304.

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