INSILI 2 (2026) 100227

Contents lists available at ScienceDirect

In Silico Research in Biomedicine

journal homepage: www.sciencedirect.com/journal/in-silico-research-in-biomedicine

Molecular docking and dynamics reveal potential galactagogue mechanism of *Breynia patens* via D2R, OXTR, and TR_β modulation

Tushar R. Gaikwad, Nachiket M. Atale, Rajendra Choure, Ulhas K. Patil *

Microbiology Department, The Institute of Science, Dr. Homi Bhabha State University, Mumbai, 400032, India

ARTICLE INFO

Keywords:
Breynia patens
Lactation
Galactagogue
Dopamine receptor
Oxytocin receptor
Thyroid hormone receptor
Molecular dynamics

ABSTRACT

Objective: This study investigates the in-silico interactions of 17 active components from *Breynia patens* extract with lactation-related proteins.

Methods: The compounds were first screened via rigid docking using AutoDock Vina against three target receptors: dopamine receptor D2R, oxytocin receptor OXTR, and thyroid hormone receptor TR_β. Furthermore, flexible docking (AGFR) used to refine the results. The interaction between Stigmasterol and D2R further analysed by employing molecular dynamics (MD) simulations of 300 ns using Dopamine as a control. The lactation-related role of receptors was analysed by KEGG enrichment using the DAVID database.

Results: Rigid docking identified promising candidates, and flexible docking revealed that 11 of the 17 components strongly interacted with D2R. Stigmasterol (-9.6 kcal/mol), epifriedenalol (-9.0 kcal/mol), and β-sitosterol (-8.2 kcal/mol) exhibited the highest binding affinities. Three compounds; glochidonol, lupeol, and friedelanol interacted with the allosteric site of OXTR (-8.0, -7.2, and -7.8 kcal/mol), while quercetin (-6.8 kcal/mol) and kaempferol (-6.2 kcal/mol) interacted with TR_β. MD simulations showed Stigmasterol maintained interaction with the D2R active site for 300 ns, though with lower stability compared to dopamine, suggesting possible antagonism. KEGG enrichment confirmed all three receptors as part of hormone signaling pathways linked to lactation.

Conclusion: This in-silico analysis suggests *Breynia patens* may promote lactation via multi-receptor modulation, including D2R antagonism, OXTR allosteric modulation, and TR_β partial agonism. These findings align with its traditional galactagogue use, but experimental validation is required to confirm therapeutic relevance.

1. Introduction

Breynia patens, (Syn. *Breynia retusa*), is a plant of considerable traditional medical significance, widely used in Ayurveda and indigenous system of medicine. Various parts of the plant - leaves, stems, roots and fruits have been reported to exhibit therapeutic purposes like treating inflammation, diabetes, anti-oxidant activity, supporting lactation, etc. [1–3]. In Sanskrit, it is called *Bahupraja* and *Bahupushpa* (denoting its abundant seedlings and numerous flowers), while in local contexts, it is referred as *Kamboji*, indicating its integration into traditional practices [4].

Phytochemical investigations have identified the presence of flavonoids, tannins, alkaloids, and saponins in *Breynia patens* [5] classes of compounds known for antioxidant and endocrine-modulating properties. Clinical evidence further supports its role as a galactagogue. In a controlled trial, Leptaden an ayurvedic formulation containing equal parts of *Leptadenia reticulata* and *B. patens* was administered to lactating mothers, resulting in significant improvements in infant weight gain and milk secretion, without adverse effects [6]. Similarly, Vaishnav and Buch tested the Leptaden in low milk-yielding Gir cows, where some individual animals showed improved milk secretion, though the results were not statistically significant as overall increase was not observed in milk production. These findings indicate the need for controlled studies to confirm its lactogenic efficacy [7], suggesting that the bioactive constituents of *B. patens* might play a role as a galactagogue by modulating hormone pathways.

Prolactin is a principal hormone regulating milk synthesis. It is secreted by lactotroph cells in anterior pituitary gland. Numerous hormone signals that are mediated through particular receptors tightly control the activity of lactotrophs [8]. The release of prolactin is tightly controlled by hypothalamic dopamine, which binds to dopamine D2 receptor (D2R) on lactotrophs to inhibit prolactin secretion [9].

* Corresponding author at: Professor, Department of Microbiology, The Institute of Science, Dr. Homi Bhabha State University, Mumbai, 400032 (M.S.), India.
E-mail address: ulhas.patil@gov.in (U.K. Patil).

https://doi.org/10.1016/j.insi.2026.100227
Received 19 October 2025; Received in revised form 18 November 2025; Accepted 26 January 2026
Available online 27 January 2026

Oxytocin receptor (OXTR), although absent in lactotrophs, is expressed on mammary myoepithelial cells, wherein oxytocin binding triggers milk ejection during nursing [10]. Thyroid hormone receptor beta (TR_β), expressed in both pituitary and mammary tissue, indirectly influence lactotroph function by regulating gene transcription associated with prolactin synthesis, mammary development and cellular metabolism [11]. Therefore, the regulation of milk synthesis and secretion is a coordinated action of D2R, OXTR, and TR_β across central and peripheral sites.

Based on these facts, this study employs in-silico approaches like molecular docking and molecular dynamics simulations to investigate the interactions of the active components of *Breynia patens*. Ever evolving approaches in computational biology like molecular docking and molecular dynamics simulations, offer powerful, mechanistic insights into phytochemical–protein interactions. The study is useful to predict mechanism of lactation enhancement by exploring insights into the multi-receptor-based mechanisms of herbal products formulated using *Breynia patens*. This in-silico documentation could be useful to guide further in-vivo analysis using precise pharmacological methods.

2. Materials and methods

2.1. Selection of active components from Breyniapatens

The active components of *Breynia patens* were selected from Kirtikar and Basu, 1918 [4]. The 3D structures of all the components were retrieved from PubChem (PubChem) and saved in .sdf format. The 17 components selected for this study were: Stigmasterol, Beta-sitosterol, hydroxyfriedelin, p-coumaric acid, ellagic acid, kaempferol, pyrogallol, epifriedelanol, lupenol acetate, quercetin, friedelanol, lupeol, gallic acid, methylbrevifolin carboxylate, scopoletin, glochidonol, methy gallol.

2.2. Target selection

The target proteins were selected by studying their role in the physiological process of lactation. Dopamine receptor D2R (PDB ID: 6CM4) was selected as dopamine is a prolactin inhibitory factor (PIF) and inhibits the secretion of prolactin. The oxytocin receptor OXTR (PDB ID: 6TPK) was selected as oxytocin plays a direct role in milk ejection. Finally, thyroid hormone receptor TR_β (PDB ID: 3GWS) was selected as thyroid hormones regulate metabolism and energy balance and are prolactin releasing factors (PRLs) thus increasing the secretion of prolactin.

2.3. Ligand and receptor preparation for docking

The 3D structures of active components were prepared using UCSF Chimera version 1.19 All the active components along with native ligands of the targets were saved in .pdb format after preparation. Since oxytocin is a peptide hormone and the 3D structure was not available on PubChem, we used pyPept [12] to predict the 3D structure and saved it in .pdb format. The 3D structures of proteins were retrieved from Protein Data Bank (https://www.rcsb.org/). Target preparation in Chimera involved removing all non-standard atoms (water molecules and ions) followed by energy minimization [13]. The prepared targets were then saved in pdb format for subsequent docking studies.

2.4. Screening of activecomponentsby moleculardocking

All 17 active components from *Breynia patens* were docked against the proteins (D2R, OXTR, TR_β) using Dockit (https://github.com/aretasg/dockit) with the AutoDock Vina engine [14]. Blind docking was performed for all the target D2R, OXTR, and TR_β. For D2R, grid box dimensions (X, Y, Z centres) were set to 23.51, −0.89, −11.69 Å respectively and the size (X, Y, Z) was 76.30, 57.69, 81.86 Å respectively. Similarly, for OXTR, the grid box dimensions were 6.09, −3.48, 100.03 Å respectively and with dimensions 68.37, 62.02, 98.52 Å respectively. For TR_β, the dimensions were 4.32, 23.63, 17.42 Å respectively, and the size was 41.43, 53.95, 62.33 Å respectively. The exhaustiveness parameter was set to 16. To validate the docking protocol, each receptor was first docked with its native ligand (Dopamine for D2R, Oxytocin and Cholesterol for OXTR, T3 for TR_β).

2.5. Re-docking activecomponentswith targetreceptors

Following the initial screening, flexible docking was performed using AutoDockFR [15]. Based on the results of initial screening, the top three poses of each active components were analyzed and selected for flexible docking along with the target residues within a distance of 0.3 Å. Oxytocin, was redocked using Autodock CrankPep (ADCP) [16]. The maximum evaluation (maxEval) was set to 20,000. Docking was performed and the results were further analyzed using PyMOL [17] and Biovia Discovery Studio [18].

2.6. Molecular dynamicssimulations

Molecular dynamic simulation of D2R with dopamine and Stigmasterol were performed using GROMACS 2025.1 with AMBER force field [19,20]. The system was solvated using TIP3P water molecules [21], pH was adjusted to 7.0 and neutralized with Cl− ions. Energy minimization was carried using steepest descent algorithm followed by a 300 ns run. Post simulation, the system was centered and analyzed.

2.7. KEGG enrichmentanalysis

KEGG Pathway Enrichment analysis was performed using the DAVID database (https: //david.ncifcrf.gov/tools.jsp). All the target receptors as input were selected from Homo sapiens as reference species. Matplotlib, Pandas, and numpy was used to visualize the KEGG pathway enrichment.

3. Results

3.1. Screening of activecomponentsby interactionwith D2R, OXTR, TR_β

Rigid docking was performed using Dockit to screen 17 active components of *Breynia patens*. The binding affinities (kcal/mol) of all the components with the target receptors are in Fig. 1. The receptors D2R, OXTR, TR_β were validated by studying their interactions with native ligands Dopamine (for D2R), Oxytocin and Cholesterol (for OXTR) and T3 (for TR_β). For D2R, dopamine showed moderate binding affinity of −6.5 kcal/mol. Among 17 active components, 11 showed strong affinity with D2R near the active site of the receptor. Further, on analyzing the 3D structures using PyMOL (Figure S1), 5 components (Stigmasterol, epifriedelanol, β-sitosterol, quercetin, scopoletin) showed strongest interactions overlapping with dopamine binding site.

In oxytocin receptor, two sites were examined. First was the ligand-binding domain (active site) and the second was the allosteric site of the receptor. After analyzing the affinities (kcal/mol) of the active components, it was observed that among 17 components, only three components (lupeol acetate, hydroxyfriedelin and epifriedelanol) showed a strong interaction with the active site of OXTR (Figure S2). Whereas, seven components (Stigmasterol, β-sitosterol, methylbrevifolin, lupeol, glochidonol, friedelanol, and scopoletin) showed interactions with the allosteric site.

For TR_β, eight components (quercetin, scopoletin, pyrogallol, p-coumaric acid, methyl gallate, kaempferol, gallic acid, and ellagic acid) showed interactions near the active site of the receptor (Figure S3).

Next, 2-D interaction maps of all the native ligands (Dopamine, oxytocin, cholesterol, and T3) were studied to determine the residues of active site to be used for flexible docking. On analyzing the interaction of

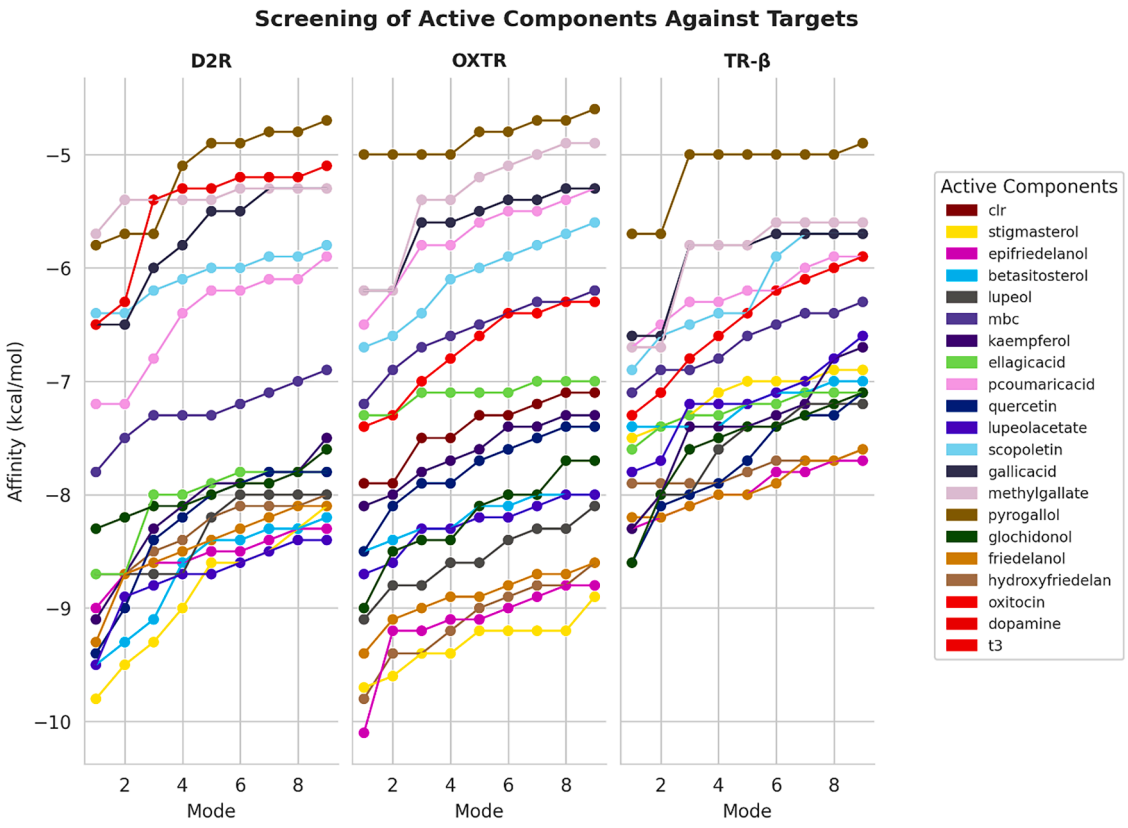

Fig. 1. Screening of all active components against target receptors (D2R, OXTR, and TR_{β}). All the native ligands of the targets are given in Red.

dopamine with D2R, it was observed that dopamine interacted with ASP:80, VAL:81, THR:85, SER:163 (Fig. 2A). The 2-D interaction map of oxytocin with OXTR revealed interactions with key residues of ligand binding domain such as LYS:116, MET:123 and hydrogen bonds with Cys:187, SER:298 (Fig. 2B); Whereas, cholesterol interacted strongly with PRO:170, TYR:200, ILE:192 and formed a hydrogen bond with VAL:190 (Fig. 2C). Similarly, the interaction map of TR_{β} revealed interactions with key residues of the active site such as HIS:435, ARG:282, and LEU:330 (Fig. 2D). These results validate rigid docking allowing meaningful comparisons of active components with native ligands.

3.2. *Re-docking of activecomponentswith D2R, OXTR, TR_{β}*

Re-docking of active components was performed using AGFR. During this, specific residues (< 0.3 Å) of the target receptors were kept flexible along with the ligand. Analysis data of all the flexible residues of the targets for each active component is given in supplementary data (Table S1, S2, and S3). The binding interactions of all the components against respective target receptors is illustrated in Fig. 3. For D2R, the binding affinities of top 3 poses ranged from −9.5 to −8.0 kcal/mol. Similarly, the top three poses of Stigmasterol, epifriedelanol, and β−sitosterol showed strong binding affinity near the active site as reflected by re-docking.

The binding affinity of oxytocin for OXTR was estimated to be very high, exceeding-14.0 kcal/mol. As oxytocin is a peptide hormone, the re-docking was performed using ADCP instead of AGFR. Among all the components interacting with the active site, lupeol acetate showed less binding affinity (−5.9 kcal/mol), while, epifriedelanol and hydroxyfriedelin showed moderate binding affinity; (−7.0 and −6.4 kcal/mol respectively), near the active site of the receptor. Cholesterol showed moderate binding affinity (−7.0 kcal/mol) at the allosteric site after re-docking. Glochidonol, lupeol and friedelanol showed similar interactions with the allosteric site of OXTR (−8.0, −7.2, and −7.8 kcal/mol) whereas other components showed less binding affinity compared to initial docking analysis.

Out of eight components screened out during initial docking, only two components; quercetin and kaempferol showed moderate binding affinity (−6.7, −6.1 kcal/mol, respectively) near the active site of the target.

For TR_{β}, the results were analyzed and compared using 2D interactions maps. The potential role of native ligands in inhibition/activation of the receptors. The 2D interaction map of dopamine with D2R revealed interaction of key residues within the active site ASP:80 and SER:169 with a salt bridge formation with ASP:80. Also, it was observed that Stigmasterol interacted with the active site pocket of the D2R (TRP:373, VAL:81, CYS:84) but did not interact with any of the key residues (Fig. 4). Similarly, epifriedelanol and β-sitosterol showed interactions with the D2R (Figure S4). The outcomes supports that these three compounds might act as antagonists of the D2R, probably blocking dopamine from binding with the active site.

For OXTR, the active site and the allosteric modulation was analyzed. Epifriedelanol interacted moderately with the active site of OXTR (−7.0 Kcal/mol) (Fig. 5B). Glochidonol showed strong interaction with the allosteric site with several interacting residues common with CLR-OXTR interaction; TRP:203, ILE:192, TYR:200 (Fig. 5C, 5D). Friedelanol and lupeol also showed similar interactions with the allosteric site (Figure S6). Thus, glochidonol, friedelanol, and lupeol might act as Positive Allosteric Modulators (PAMs) of OXTR and are predicted to enhance the binding of oxytocin to the receptor.

Re-docking the components with TR_{β} revealed that only two (quercetin and kaempferol) of the eight screened compounds interacted moderately with the active site of the receptor. The 2D interaction analysis of T3 (Fig. 6A) reflected several key interactions with the active site of the receptor like ARG:282, MET:313, HIS:435, ASN:331. Quercetin (Fig. 6B) also interacted with the same active site pocket of TR_{β} and interaction with many common residues like the conventional hydrogen

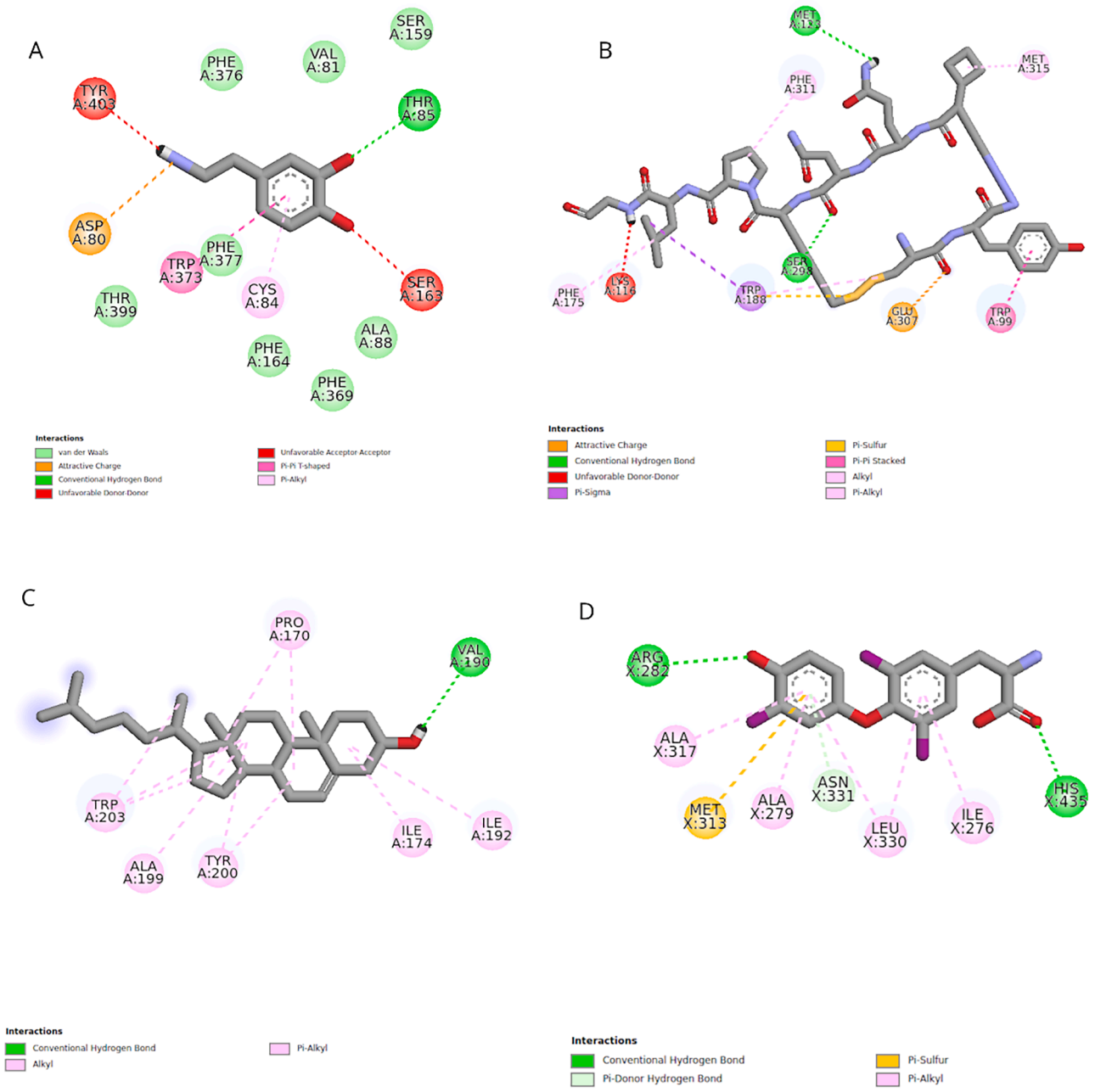

Fig. 2. Interaction of dopamine with D2R **(A)**, Oxytocin and cholesterol with OXTR **(B, C)**, and T3 with TR_{β} **(D)**.

bond with HIS:435 and ASN:331, interactions with MET:313, LEU:346, LEU:341 were observed. This suggests that quercetin might act as a partial agonist of the receptor.

3.3. Molecular dynamicssimulations

Molecular dynamics (MD) simulations were carried out for 300 ns to evaluate binding of Stigmasterol with D2R. Dopamine served as the native ligand. The RMSD analysis of ligands fitted to protein (Fig. 7A) revealed that Stigmasterol (yellow) underwent conformational adjustment within the first 50 ns and then remained relatively stable over the range of 0.8–1.2 nm for the rest of the duration. Dopamine, being the native ligand of the receptor showed stable RMSD in the range of 0.1–0.3 nm for the entire duration. This indicates that Stigmasterol rapidly changed its poses within first 50 ns and then achieved stability, whereas the initial pose of dopamine did not change and remained bound to the active site.

The RMSF analysis (Fig. 7B) revealed that the receptor conformation remained stable with both the ligand bound complexes, while it showed fluctuations in the flexible residues. The protein-ligand minimum distance (Fig. 7C) revealed that the minimum distance between protein-ligand for both the complexes was 0.14–0.22 nm which indicates that both ligands interacted with the receptor for 300 ns. The radius of gyration of both the complexes (Fig. 7D) was similar and stable for the entire duration. These results emphasize that Stigmasterol is interacting with the active site of D2R, however, the interaction is weaker as compared to dopamine.

3.4. KEGG enrichmentanalysis

KEGG enrichment analysis was performed using the target proteins as input in DAVID database. Out of 15 chart records obtained, 3 records

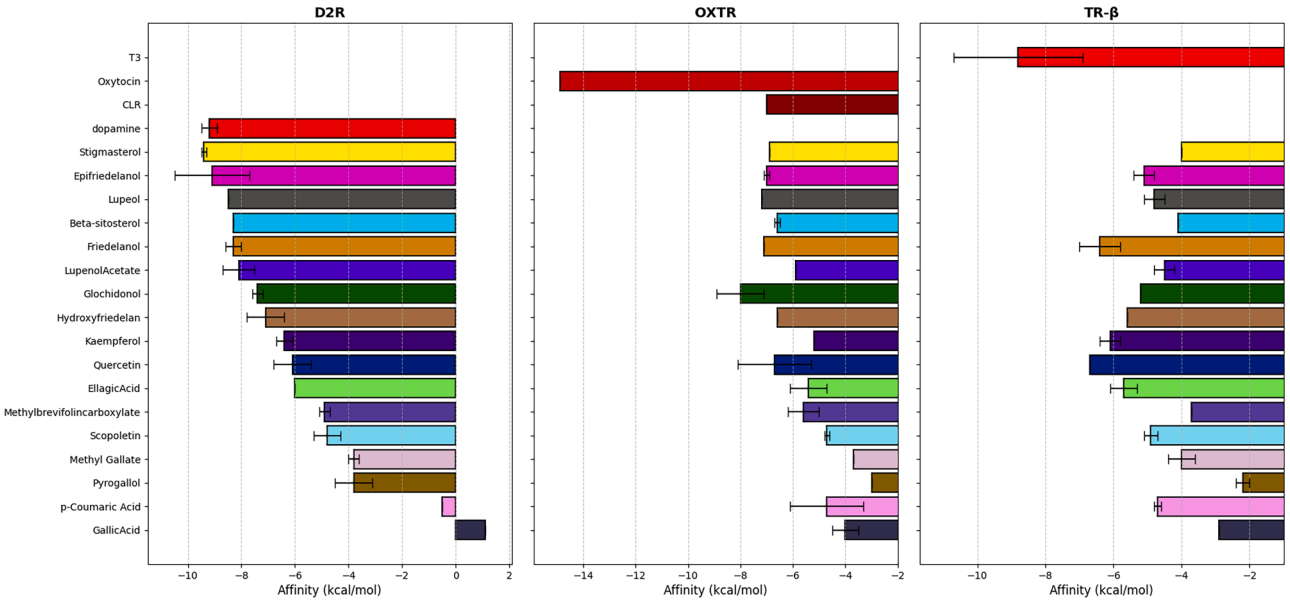

Fig. 3. Interactions of active components against target receptors (D2R, OXTR, and TR_{β}) by flexible docking using AGFR.

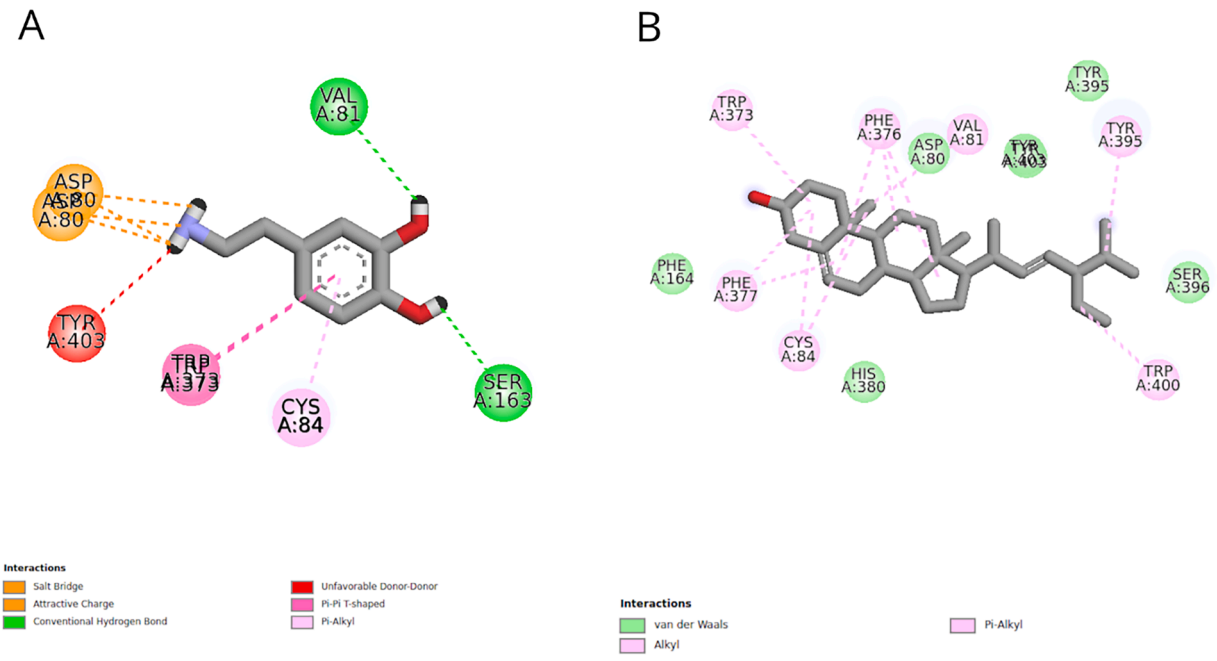

Fig. 4. 2D Interaction map of flexible docking of Dopamine **(A)** and Stigmasterol **(B)** with D2R.

were linked to KEGG Pathways. All the three targets were involved in hormone signaling pathway as well as neuroactive ligand-receptor interaction with the p-value < 0.05 (Fig. 8). The Fig. 8 is an analysis of the chart records and depicts the p-value, and number or targets (according to the bubble size) which are a part of a particular pathway. These results confirm the role of target receptors in the hormone signaling pathway which can ultimately be linked to lactation.

4. Discussion

The present silico analyses suggest the potential of *Breynia patens* phytoconstituents to enhance lactation through a multi-receptor mechanism that integrates dopaminergic, oxytocinergic, and thyroid signaling. This cross-receptor pharmacology is consistent with the neuroendocrine complexity of lactation and highlights how plant metabolites can modulate multiple hormonal pathways simultaneously.

Similar results have been reported in earlier studies showing that prolactin secretion is inhibited by hypothalamic dopamine acting through pituitary D2R. Dopamine binding involves a salt-bridge interaction with ASP:80, initiating a cascade that suppresses prolactin release [22,9]. Consistent with this, blocking D2R has been shown to disinhibit lactotrophs, increase prolactin secretion, and enhance milk synthesis, an effect underlying the clinical use of galactagogues such as domperidone and metoclopramide [23,24]. In contrast, our docking studies revealed that Stigmasterol, β-sitosterol, and epifriedelanol bind strongly near the D2R active site but do not engage key activating residues, suggesting potential antagonistic rather than agonistic activity. Importantly, similar receptor interactions have been observed in the central

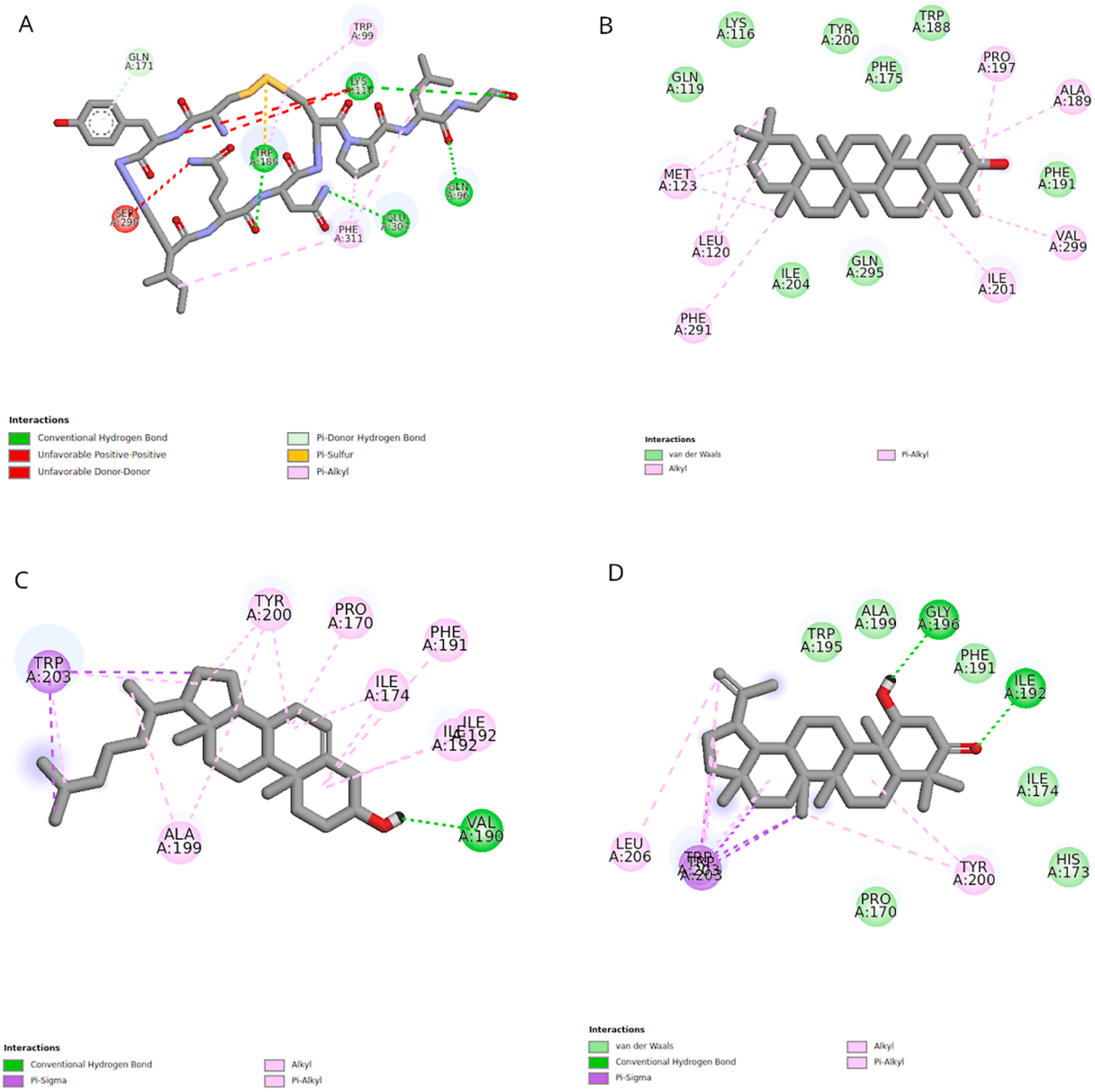

Fig. 5. 2D Interaction map of flexible docking of Oxytocin **(A)** and Epifriedelanol. **(B)** with OXTR at the active site and Cholesterol **(C)** and Glochidonol **(D)** with OXTR at the allosteric site.

amygdala, where D2R and OXTR form functional heteroreceptor complexes with allosteric facilitation enhancing anxiolytic responses [25].

Comparable mechanisms have also been described for the oxytocin receptor (OXTR). Oxytocin binding to OXTR on mammary myoepithelial cells is essential for milk letdown, and cholesterol has been identified as a positive allosteric modulator (PAM) that enhances OXTR signaling [26]. In accordance to this, present docking studies demonstrated that B. patens sterols such as friedelanol, lupeol, and glochidonol interact with the OXTR allosteric site, like cholesterol, suggesting their potential role as PAMs. Furthermore, recent genomic analyses have identified cis-regulatory enhancer elements controlling OXTR transcription, including OCE7, which was validated by luciferase assays [27]. These findings collectively emphasize that OXTR function can be regulated both allosterically and transcriptionally. In contrast to the cholesterol-centric model, our results highlight the potential of plant sterols to serve as natural modulators of oxytocin signaling, offering an alternative mechanism through which herbal compounds may influence lactation.

Similar evidence exists for the role of thyroid hormones in lactation. Thyroid hormones are known to support mammary gland development and metabolic adaptation, and synthetic as well as environmental ligands have been reported to act as weak agonists or antagonists of thyroid hormone receptor-β (TR_β) through conformational modulation of helix 12, influencing coactivator recruitment [28]. In agreement with these findings, our docking studies suggest that quercetin and kaempferol from *B. patens* exhibit partial TR_β agonist-like activity. In contrast to strong agonists such as triiodothyronine (T3), these flavonoids appear to exert more subtle conformational effects, suggesting their role in fine-tuning transcriptional programs relevant to prolactin synthesis and mammary gland function. The pharmacological strategies used in conventional galactagogue therapy, include individualistic approach based on (i) D2R antagonism may enhance prolactin release, (ii) OXTR allosteric modulation may facilitate oxytocin-mediated milk ejection, and (iii) TR_β partial agonism may optimize mammary gland readiness [29]. Based on computational investigation carried in this study, phyto-constituents of *B. patens* could be efficient galactagogue by

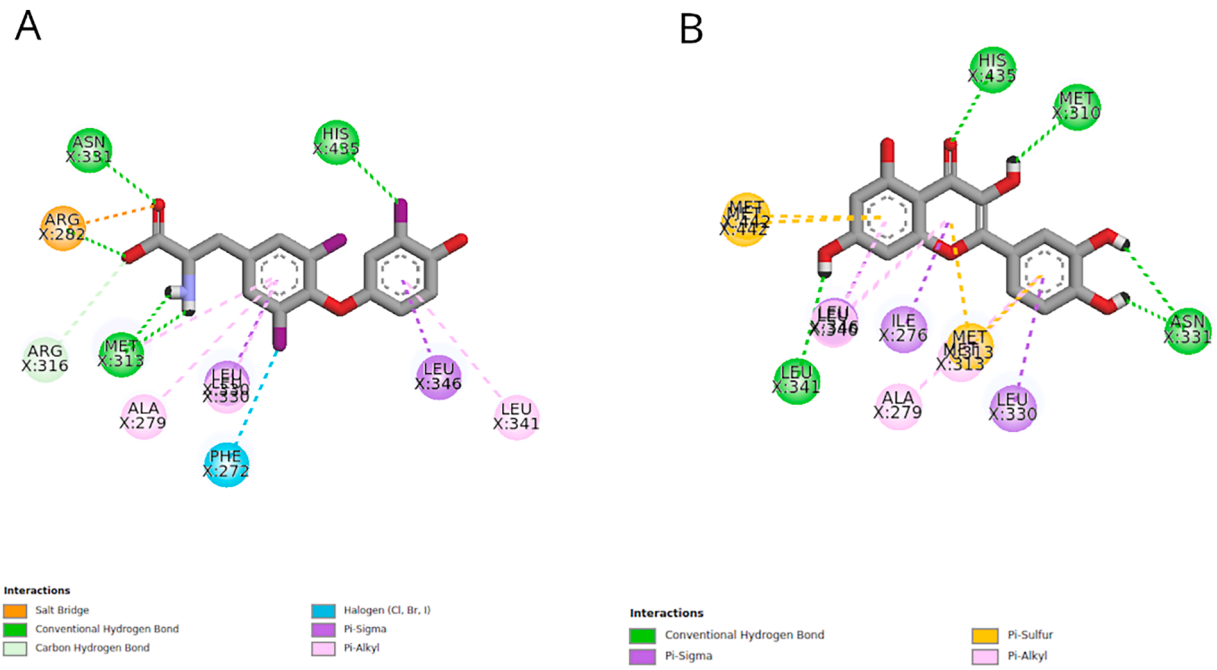

Fig. 6. 2D Interaction map of flexible docking of T3 **(A)** and Quercetin **(B)** with TR_{β}.

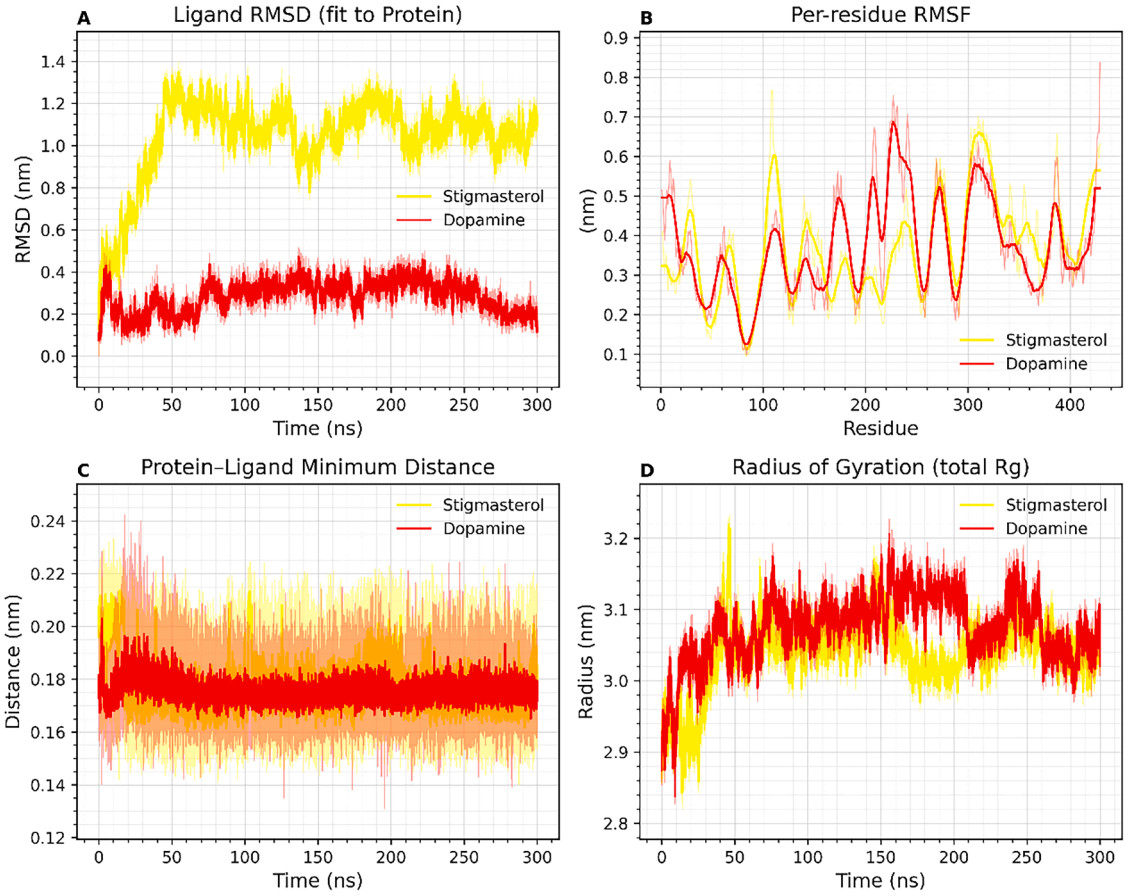

Fig. 7. RMSD analysis of ligands; Stigmasterol (yellow) and Dopamine (red) fit to Protein **(A)**, RMSF-per residue of the receptor backbone **(B)**. Contact residue distance between the ligands and protein over the course of 300 ns **(C)** and Radius of gyration of the complexes **(D)**.

modulating multiple receptors.

The integrative mechanism of lactogenic potential of *B. patens* is consistent with ethnopharmacological and ayurvedic observations where *Breynia patens* in combination with *Leptadenia reticulata* (Leptaden formulations) has been traditionally employed to improve lactation in both women and cattle [6,7]. Recent reviews similarly indicate

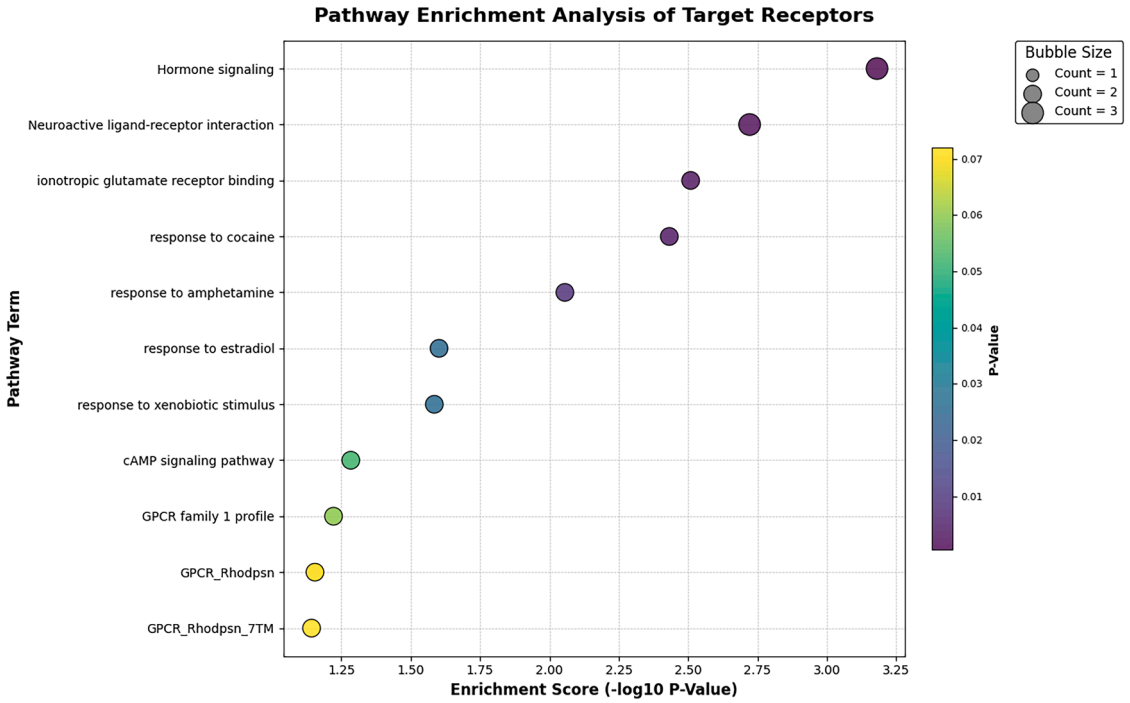

Fig. 8. KEGG Enrichment Analysis of targets.

that herbal galactagogues often act through combined modulation of dopaminergic, oxytocinergic, and thyroid pathways [30], supporting the broader relevance of our findings. Further experimental in-vitro and in-vivo validation of this scientifically predicted pharmacological potential of *Breynia patens* is underway and subsequent part of this study.

5. Conclusions

The present in-silico investigation highlights the potential of *Breynia patens* phytoconstituents to modulate lactation through a multi-receptor mechanism involving dopaminergic, oxytocinergic, and thyroid pathways. Sterols such as Stigmasterol, β-sitosterol, and epifriedelanol displayed binding profiles consistent with D2R antagonism, suggesting a role in relieving prolactin inhibition. Other sterols, including friedelanol, lupeol, and glochidonol, showed cholesterol-like interactions with OXTR, indicating possible positive allosteric modulation of oxytocin signaling. In addition, flavonoids such as quercetin and kaempferol exhibited partial agonist-like activity at TR_{β}, implying a fine-tuning effect on transcriptional programs relevant to mammary gland function.

Overall, these findings propose that *B. patens* may enhance lactation through synergistic actions across multiple receptor systems rather than a single-target mechanism. This integrative pharmacological profile not only supports its traditional ethnomedicinal and ayurvedic use but also provides a mechanistic basis for exploring *B. patens* as a source of novel lactogenic agents. Future experimental validation, including in-vitro and in-vivo studies, will be essential to confirm these interactions and assess their therapeutic potential in clinical and veterinary context.

Author contributions

Tushar R. Gaikwad & Nachiket M. Atale: Writing – original draft, Visualization, Methodology, Investigation, Data curation. **Ulhas K. Patil & Rajendra G. Choure:** Writing – Review & Editing, Validation, Formal analysis.

Funding

Not applicable.

Data Availability

The data presented in this study are available on request from the corresponding author. The csv files of affinities and the codes of graphs, simulation data, movie, etc. can be requested from the corresponding author

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors would like to thank Mr. Mahesh Atale (*Alarsin Pvt. Ltd.)*

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.insi.2026.100227.

Data availability

Data will be made available on request.

References

[1] Lal K, Singh B, Gupta YV, Tiku CN, Jamwal DS. A controlled trial of Leptaden in lactational failure and an experimental study in lactating rats. Indian Pract 1980 Oct 1;33(10):557–64.
[2] Chowdury MIA, Rahman MH, Alam MN, Chowdhury S, Biozid MS, Bhuiyan MNI, Alam SAB. Ex-vivo anti-arthritic and membrane stabilizing activity of aqueous extract of Breynia retusa. World J Pharm Pharm Sci 2015;4:89–95.
[3] Murugan R, Prabu J, Chandran R, Sajeesh T, Iniyavan M, Parimelazhagan T. Nutritional composition, in vitro antioxidant and anti-diabetic potentials of Breynia retusa (Dennst.) Alston. Food Sci Hum Wellness 2015;4:1–35.
[4] Kirtikar KR, Basu BD. Indian medicinal plants. Bhuwaneśwari Áśrama, 2; 1918.
[5] Sharma S, Kumar S. Phyllanthus reticulatus Poir. An important medicinal plant: a review of its phytochemistry, traditional uses and pharmacological properties. Int J Pharm Sci Res 2013;4(7):2528–36.

[6] Bhandari N, Soni S. A controlled trial on Leptaden in weight gain of infants and as a galactagogue in lactation cases. Indian Pract 1979;32:229–40.
[7] Vaishnav V, Buch H. A preliminary note on the study of lactogenic properties of Leptaden. Indian Vet J 1965;42:796–8.
[8] Al-Chalabi M., Bass A.N., Alsalman I. Physiology, Prolactin. StatPearls.
[9] Ben-Jonathan N, Hnasko R. Dopamine as a prolactin (PRL) inhibitor. Endocr Rev 2001;22(6):724–63. https://doi.org/10.1210/edrv.22.6.0451.
[10] Gimpl G, Fahrenholz F. The oxytocin receptor system: structure, function, and regulation. Physiol Rev 2001;81(2):629–83. https://doi.org/10.1152/physrev.2001.81.2.629.
[11] Vasudevan N, Pfaff DW. Non-genomic actions of estrogens and their interaction with genomic actions in the brain. Front Neuroendocrinol 2008;29(2):238–57. https://doi.org/10.1016/j.yfrne.2007.08.003.
[12] Ochoa R, Brown JB, Fox T. pyPept: a python library to generate atomistic 2D and 3D representations of peptides. J Cheminform 2023 Sep 12;15(1):79.
[13] Pettersen EF, Goddard TD, Huang CC, Couch GS, Greenblatt DM, Meng EC, Ferrin TE. UCSF Chimera a visualization system for exploratory research and analysis. J Comput Chem 2004;25(13):1605–12. https://doi.org/10.1002/jcc.20084.
[14] Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. J Comput Chem 2010;31(2):455–61. https://doi.org/10.1002/jcc.21334.
[15] Ravindranath PA, Forli S, Goodsell DS, Olson AJ, Sanner MF. AutoDockFR: advances in protein–ligand docking with explicitly specified binding site flexibility. PLoS Comput Biol 2015;11(12):e1004586. https://doi.org/10.1371/journal.pcbi.1004586.
[16] Zhang Y, Sanner MF. AutoDock CrankPep: combining folding and docking to predict protein–peptide complexes. Bioinformatics 2019;35(24):5121–7. https://doi.org/10.1093/bioinformatics/btz459.
[17] DeLano WL, et al. PyMOL: an open-source molecular graphics tool. CCP4 Newsl Protein Crystallogr 2002;40:82–92.
[18] BIOVIA DS. Discovery studio modeling environment. San Diego: Dassault Systèmes; 2017.
[19] Wang J, Wolf RM, Caldwell JW, Kollman PA, Case DA. Development and testing of a general Amber force field. J Comput Chem 2004;25(9):1157–74. https://doi.org/10.1002/jcc.20035.
[20] Van Der Spoel D, Lindahl E, Hess B, Groenhof G, Mark AE, Berendsen HJ. GROMACS: fast, flexible, and free. J Comput Chem 2005;26(16):1701–18. https://doi.org/10.1002/jcc.20291.
[21] Jorgensen WL, Chandrasekhar J, Madura JD, Impey RW, Klein ML. Comparison of simple potential functions for simulating liquid water. J Chem Phys 1983;79(2):926–35. https://doi.org/10.1063/1.445869.
[22] Shi L, Javitch JA. The binding site of aminergic G protein-coupled receptors: the transmembrane segments and second extracellular loop. Annu Rev Pharmacol Toxicol 2002;42:437–67. https://doi.org/10.1146/annurev.pharmtox.42.091801.154806.
[23] Gabay MP. Galactogogues: medications that induce lactation. J Hum Lact 2002;18(3):274–9. https://doi.org/10.1177/089033440201800309.
[24] Fitzgerald P, Dinan TG. Prolactin and dopamine: what is the connection? A review article. J Psychopharmacol 2008;22(2):12–9. https://doi.org/10.1177/0269881107086946. Suppl.
[25] Hernández-Mondragón JC, DA Hernández-Hernández, Crespo-Ramírez M, Prospero-García O, Rocha-Arrieta L, Fuxe K, Borroto-Escuela DO, Perez de la Mora M. Evidence for the existence of facilitatory interactions between the dopamine D2 receptor and the oxytocin receptor in the amygdala of the rat: relevance for anxiolytic actions. Front Pharmacol 2023;14:1251922.
[26] Marlow B, Vogel A, Kuenze G, Pankonin M, Reinhardt F, Stadler PF, Hildebrand PW, Meiler J. Cholesterol allosteric modulation of the oxytocin receptor. Biophys J 2025;124(12):1930–43.
[27] Laboy Cintrón D, Sheng RR. Ahituv N. Functional characterization of OXTR-associated enhancers. Hum Mol Genet 2025;34(10):837–42.
[28] Zhang M, Shi J, Li B, Ge H, Tao H, Zhang J, Li X, Cai Z. Thyroid hormone receptor agonistic and antagonistic activity of newly synthesized dihydroxylated polybrominated diphenyl ethers: an In Vitro and In Silico coactivator recruitment study. Toxics 2024 Apr 11;12(4):281.
[29] Grzeskowiak LE, Wlodek ME, Geddes DT. What evidence do we have for pharmaceutical galactagogues in the treatment of lactation insufficiency? A narrative review. Nutrients 2019;11(5):974.
[30] Bazzano AN, Cenac L, Brandt AJ, Barnett J, Thibeau S, Theall KP. A review of herbal and pharmaceutical galactagogues for breastfeeding. Ochsner J 2016;16(4):511–24. PMID:27999594.