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Original Article

Dentistry Section

Exploring the Antibacterial Potential of *Murraya koenigii* Phytochemicals: An In-silico Docking Approach against *Porphyromonas gingivalis*

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ABSTRACT

Introduction: *Porphyromonas gingivalis*, a primary bacterium in dental plaque, is a key pathogen in periodontal disease. *Murraya koenigii* has got a range of therapeutic properties, including antioxidant, antibacterial, antifungal, antidiarrhoeal, antidiabetic, and anti-inflammatory effects. The specific phytocompound in *M. koenigii* responsible for inhibiting *P. gingivalis* has not yet been identified.

Aim: The present study was aimed to identify the *Murraya koenigii* phytocompounds against *Porphyromonas gingivalis* proteins using molecular docking and with Molecular dynamics (MD) simulations for the phytocompound Koenigine. The secondary objective was to Evaluate the drug-likeness of *Murraya koenigii* phytocompounds by assessing its gastrointestinal absorption and compliance with Lipinski's Rule of Five.

Materials and Methods: The present in-silico computational study was conducted in the Department of Periodontics, Thaimoogambigai Dental College, Chennai, Tamil Nadu, India from October 2024 to November 2024. Predominant phytochemicals, including o-methyl murrayamine, koenigine, koenigicine, and murrayone, were identified from *Murraya koenigii*. The three-dimensional structures of *Porphyromonas gingivalis* virulence proteins, gingipain and FimA type 4 protein were retrieved from the Research Collaboratory for Structural Bioinformatics (RCSB) Protein Data Bank (PDB), and molecular docking was performed to predict the binding efficacy of these compounds.

Results: Koenigine demonstrated the highest binding affinity of -4.123 kcal/mol, forming a stable hydrogen bond with Ser156 of gingipain. Additionally, koenigine showed strong binding to the FimA type 4 protein, with a docking score of -5.675 kcal/mol, interacting with Asp53 through two hydrogen bonds. Koenigine also exhibited high gastrointestinal absorption, and adhered to Lipinski's Rule of Five.

Conclusion: The present study emphasises the promising therapeutic potential of the phytocompound koenigine from *Murraya koenigii* in inhibiting *P. gingivalis* activity associated with periodontitis. Incorporating the active compounds of *Murraya koenigii* into oral healthcare products, such as mouthwashes and gels, may help reduce the progression of periodontal disease.

Keywords: Antimicrobial agents, Molecular docking simulation, Periodontitis, Virulence factors

INTRODUCTION

Periodontitis is a common condition that affects the oral cavity. The inflammatory response associated with periodontal disease is triggered by pathogenic bacteria and the accumulation of microbial plaque. This disease is characterised by inflammation of the tissues supporting the teeth and is primarily caused by the build-up of dental biofilm [1]. These pathogens initiate an immune response, resulting in tissue inflammation and contributing to disease development [2]. *Porphyromonas gingivalis*, a key periodontopathic bacterium frequently found in dental plaque, plays a major role in the development of periodontal disease [3]. *Porphyromonas gingivalis* is a Gram-negative bacterium and is a key pathogen in periodontal disease, possessing a variety of virulence factors that disrupt the host-microbial balance, ultimately resulting in inflammatory bone loss [4]. These virulence factors enable *P. gingivalis* to directly and indirectly damage periodontal tissues by promoting inflammation. *Porphyromonas gingivalis* evades immune system clearance, takes advantage of inflammation, invades host cells, forms protective biofilms, and adapts to survive in the challenging environment of the oral cavity, ensuring its long-term persistence in host tissues [5]. In recent years, there has been increasing interest in bioactive natural products as potential treatments for preventing or curing periodontitis [6]. Additionally, a variety of natural product-based therapies may emerge as viable alternative treatments for periodontitis [7].

Murraya koenigii, popularly known as curry leaves, is a tropical to subtropical tree belonging to the Rutaceae family. It demonstrates a wide array of therapeutic properties, such as antioxidant, antibacterial, antifungal, antidiarrhoeal, antidiabetic, and anti-inflammatory activities [8]. Extracts derived from traditional medicinal plants, along with their phytochemicals, have been reported to inhibit dental plaque build-up, prevent bacterial adhesion, and ease symptoms associated with oral diseases [9]. Given that *P. gingivalis* is a prominent pathogen in the oral microbiome and a leading contributor to periodontitis, targeting this bacterium through medicinal plant extracts holds significant potential in periodontal therapy.

Molecular docking is a computational method commonly used in bioinformatics and pharmaceutical research to predict the interaction between a protein receptor and a small molecule ligand [10]. This technique enables researchers to analyse the biochemical interactions between small molecules, such as nutraceuticals, and their target proteins. By simulating these interactions, molecular docking provides valuable insights that are essential for understanding the molecular mechanisms at play [11]. It is crucial in drug discovery and development as it helps identify potential lead compounds, which can later undergo further experimental validation.

Nakao R et al., showed that the curry leaf extract has the strongest growth inhibitory activity, and it was maintained even after extensive heat treatment [12]. Bacterial membrane potential assay revealed that curry leaf extract induced depolarisation of the bacterial membrane.

Uma Maheswari K et al., reported the inhibitory potential of *M koenigii* phytocompounds against the cariogenic bacteria *Streptococcus mutans* [13]. At present, there is a lack of effective drugs targeting biofilm formation or resistant pathogens, driving the search for natural phytocompounds that can effectively inhibit biofilm formation. Previous studies have demonstrated the in-vitro antimicrobial activity against *P. gingivalis* [14,15]. However, to the best of our knowledge, the exact phytocompound in *M. koenigii* responsible for this inhibitory effect has not yet been identified.

A prior study converted all 14 phytocompounds of *M. koenigii* into PDB format and performed molecular docking with the glycosyltransferase protein of S. mutans [13]. Among these, O-methyl murrayamine, koenigine, koenigicine, and murrayone demonstrated inhibitory potential against the glycosyltransferase protein, while also complying with Lipinski's Rule of Five. Consequently, the present study concentrated on these four phytocompounds of *M. koenigii* for molecular docking analysis targeting *P. gingivalis*.

The present study aimed to evaluate the major bioactive compounds of *Murraya koenigii* against the key surface proteins of the bacterium with MD simulations to investigate the conformational changes for the phytocompound Koenigine. The secondary objective was to assess the drug-likeness of phytocompounds from *Murraya koenigii* by examining their gastrointestinal absorption and adherence to Lipinski's Rule of Five.

MATERIALS AND METHODS

The present in-silico computational study was conducted in the Department of Periodontics, Thaimoogambigai Dental College, Chennai, Tamil Nadu, India from October 2024 to November 2024. The study was approved by the Institutional Review Board. (Dr. MGRDU/TMDCH/RES/2024/2582A).

The protein structures were prepared using the protein preparation wizard in Schrödinger 2022-1, where protonation states of ionizable residues were assigned at physiological pH (7.4) using Epik to accurately reflect biological conditions. Missing hydrogen atoms were added, and crystallographic water molecules beyond 5 Å from the binding site were removed to avoid interference. Energy minimisation was performed using the Optimised Potentials for Liquid Simulations (OPLS)2005 force field with restrained minimisation, allowing side chains and hydrogens to relax while keeping the backbone fixed until convergence {Root Mean Square Deviation (RMSD) < 0.3 Å}, ensuring a stable and realistic protein conformation. Phytochemicals from *Murraya koenigii* were selected based on their documented bioactivity and availability of Three-dimensional (3D) structures in the PubChem database. The compounds were converted from SDF to PDB format using OpenBabel, then prepared using LigPrep in Schrödinger 2022-1.LigPrep corrected bond orders, protonation states, and optimized geometries using the OPLS2005 force field, ensuring that ligands were in their energetically favourable conformations prior to docking. Selection prioritised compounds with structural diversity and functional groups capable of key interactions with the target protein.

Study Procedure

Ligand preparation: The 3D structures of four phytochemicals from *Murraya koenigii* namely Methylmurrayamine A (PDB id: 14892681) Koenigicine (278055) Koenigine (5318825) and Murrayone (5319964) with the correct resolution were obtained from PubChem database (https://pubchem.ncbi.nlm.nih. gov/) in the Structure-Data File (SDF) format. The SDF format of ligand was converted to PDB using OpenBabel Software (https://sourceforge. net/projects/openbabel/). The ligand molecules were prepared using Ligprep module of Schrodinger. The bond orders and angles along with the charges of the ligands were corrected while preparation and OPLS2005 forcefeild was used to optimise the ligands. All the Schrodinger modules were carried out in Schrodinger 2022-1 version. The converted PDB files were further processed using the LigPrep module of the Schrödinger Suite (version 2022-1). LigPrep is designed to prepare high-quality, all-atom 3D structures of small molecules for computational studies. Correct bond orders, angles, charges; optimize geometry with OPLS2005 [13].

Protein preparation: The Gingipain R2 and Major fimbrium subunit (FimA type 4) of *P. gingivalis* were selected as the target proteins. The three-dimensional structure of Gingipain R2 was retrieved from RCSB PDB (PDB ID: 1CVR) and due to the unavailability of FimA type 4 in RCSB-PDB, 3D model was obtained from AlphaFold. The Research Collaboratory for Structural Bioinformatics (RCSB) PDB is a database for the 3D structural data of large biological molecules such as proteins and nucleic acids [16]. After retrieval, the structures were pre processed and prepared using Protein Preparation Wizard of Schrodinger, in which the unbound water molecules were removed, with addition of hydrogen atoms, and further the structures were optimised and minimised using OPLS2005 forcefeild. Since the crystal structure of Gingipain R2 has the co-crystalised inhibitor, which was directly considered as the active site or molecular docking analysis. SiteMap module of Schrodinger was used to predict the active site of the major fimbrial subunit. The active site residues were defined as receptor grid to facilitate molecular docking.

Selection of phytocompounds: Phytochemicals like O-methyl murrayamine, koenigine, koenigicine, and murrayone from *M. koenigii* were chosen for the study due to their potential antioxidant, anti-inflammatory, and antimicrobial properties [9]. Using this previous study as a standard reference, 4 phytochemicals of *M. koenigii* were selected for in present study [13].

Molecular Docking and Molecular Dynamic (MD) Simulations: The prepared ligands and the proteins were used for molecular docking analysis. The Schrodinger Glide XP module was used to dock the ligands against the respective protein targets to determine the binding affinity of the compounds. For each ligand, the molecule was docked one at a time against the target protein. The binding scores of the ligands with better binding affinity were further analysed using MDs simulations, and the most promising compound koenigine was chosen from amongst them based on their scores, the binding efficacy and the number of stable hydrogen bonds formed. Desmond 2021 version was used to simulate the ligand bound protein complexes. OPLS2005 forcefeild was used during the simulation. In order mimic the physiological environment, 300K temperature and one bar pressure was maintained during the simulation process. The protein with ligand was solvated in a single point charge water model in an orthorombhic periodic boundary condition. Upon the equilibration, the production run was carried out for 100 nanoseconds (ns).

Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) properties: The important aspect of a drug are efficacy and safety, and this underscores the importance of the ADMET properties of a molecule during the drug discovery and development process. Therefore, it is necessary to find effective molecules with better ADMET properties. The compounds O-methyl murrayamine, koenigine, koenigicine and murrayone from *M. koenigii* were selected for the prediction of drug likeliness and their ADMET properties. In the pharmacodynamic analysis of the compounds, the interactions with the proteins, metabolic enzymes and transporters, effects on gene expression of different proteins and the possible side effects were predicted using the Way2Drug PASS Online server [17]. The Way2Drug informational-computational platform (www.way2drug.

com/dr) provides access to the data on drugs approved for medicinal use.

The phytochemical properties, such as lipophilicity, water solubility, pharmacokinetics, and drug-likeness including Topological Polar Surface Area (TPSA), cytochrome inhibition, and gastrointestinal absorption potential were evaluated using the Swiss ADME online server and the scores for each drug were then recorded. The Swiss ADME web tool presented here is freely accessible at http://www.swissadme.ch and meant for user-friendly submission and easy analysis of the results [18]. For each drug that was processed in the program, Simplified Molecular Input Line Entry System (SMILES) was supplied as a modular input. The SMILES list is a fully editable text field and is the actual input for a SwissADME run. Probability of being active, (Pa), is the probability that the drug is active and belongs to the subclass of active compounds. P1 is the probability of being inactive, which is computed in the server as well.

MD Simulation: All-atom MD simulations offer a powerful means of examining the structural dynamics of proteins and their interactions with ligands. This technique has revolutionised computer-aided drug design and discovery by allowing in-depth, atomic-level insights into molecular behaviour. In the present study, MD simulations were conducted to investigate the conformational changes associated with receptor-ligand complex formation. Key metrics-including RMSD, Root Mean Square Fluctuation (RMSF), and protein-ligand contact profiles-were assessed for both the apo (unbound) protein and the ligand-bound complex.

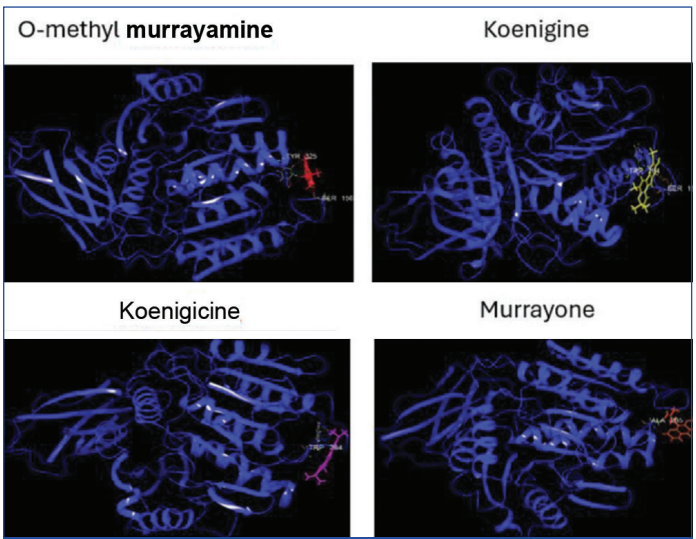
STATISTICAL ANALYSIS

Descriptive Statistics were used to analyse data.

RESULTS

The present study investigated the phytochemicals of *Murraya koenigii* {O-methyl murrayamine, koenigine, koenigicine, and murrayone} have inhibitory potential against the virulence factors Gingipain R2 and major fimbrium subunit (Fim type 4) of *P. gingivalis*.

Molecular docking analysis of four selective compounds- O-methylmurrayamine, koenigine, koenigicine, and murrayone- against the active site of the Gingipain R2 protein from *Porphyromonas gingivalis* revealed varying binding affinities [Table/Fig-1]. The docking score and the amount of hydrogen bond formation between the compound and the ligand were utilised to estimate the binding affinity in the molecular docking experiment. For non-covalent binders, participation in electrostatic hydrogen bonding as a donor and acceptor is an important interaction that involves not just ionic interactions but covalent and van der Waals interactions. The docking score has been another important parameter to evaluate the binding affinity of any two molecules. The more negative the docking score, the greater the binding. The most negative energy value out of the four compounds with hydrogen bonding represents the compound that binds to the residues with the strongest binding affinity. Hydrogen bonds contribute to the binding affinity and specificity of the protein-ligand interactions. Pi-Pi stacking contributes to the stability of the drugs.



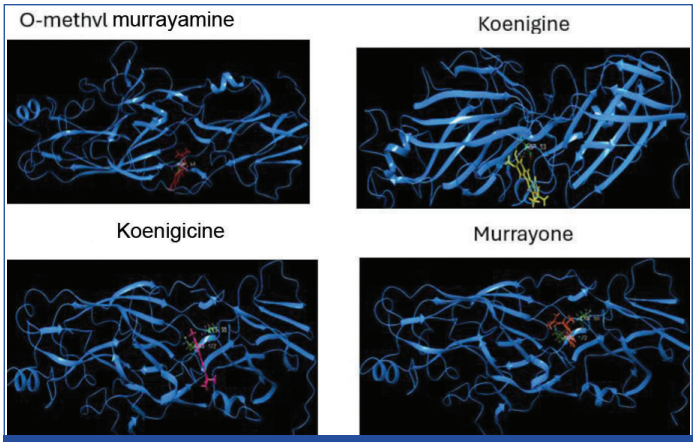
[Table/Fig-1]: Molecular docking of phytocompounds of M.koenigii with Gingipain R2 protein of *P. gingivalis*.

O-methylmurrayamine displayed a docking score of -3.404 kcal/mol, forming stable hydrogen bonds with Ser156 and pi-pi stacking interactions with Tyr325. Koenigicine showed a slightly stronger docking score of -3.495 kcal/mol, with pi-pi stacking interactions with Trp284. Koenigine exhibited the highest binding affinity at -4.123 kcal/mol, with a stable hydrogen bond to Ser156. Murrayone had the lowest binding affinity (-3.061 kcal/mol), interacting with Ala285 through a hydrogen bond. All compounds demonstrated effective binding via hydrogen bonds and pi-pi interactions with key amino acids such as Ser156, Trp284, and Tyr325. The results suggest that these compounds, particularly koenigine, could act as potential inhibitors of Gingipain R2 due to their strong interactions with the protein's active site [Table/Fig-2]. In O-methylmurrayamine, the combination of hydrogen bonding and pi-pi stacking likely contributes to the moderate binding affinity. The methoxy substituent increases electron density, possibly strengthening the pi-pi interaction with Tyr325. In koenigicine, the lack of hydrogen bonding suggests that hydrophobic and pi-pi interactions are the primary contributors to binding. The slightly better docking score than O-methylmurrayamine may be due to the optimal stacking geometry and surface complementarity with Trp284. The superior binding affinity is attributed to the strong hydrogen bond with Ser156 and possible additional van der Waals contacts. In Koenigine, the absence of reported pi-pi stacking may indicate a more buried or polar binding mode, maximising hydrogen bond strength. In murrayone, the lower affinity is consistent with limited interaction options- primarily a single hydrogen bond and fewer hydrophobic or pi-pi contacts.

Similarly, docking of four compounds into the active site of the FimA type-4 protein showed stable binding. Crucial interactions were identified, including hydrogen bonds and pi-pi interactions involving amino acid residues such as Asp53, Lys55, and Arg172, which stabilise ligand binding [Table/Fig-3]. The molecular docking results revealed that O-methylmurrayamine showed the strongest binding affinity against the FimA Type-4 protein of *P. gingivalis* with a docking score of -5.795 kcal/mol, forming a stable hydrogen bond with Asp53. Koenigicine followed with a score of -4.149 kcal/mol, forming hydrogen bonds with Lys55 and Arg172. Koenigine also exhibited strong binding with a score of -5.675 kcal/mol, interacting with Asp53 through two hydrogen bonds. Murrayone, though exhibiting a weaker binding affinity of -3.909 kcal/mol, formed multiple hydrogen bonds with Lys55 and Arg172. These findings

S. No	Compound Name	Pubchem ID	Docking score (kcal/mol)	Interacting Amino acid	Hydrogen Bond	Bond Length (Å)
1	O-Methy-lmurrayamine A	14892681	-3.404	Ser156	1	1.95
				Tyr325	1	11
						42
2	Koenigicine	278055	-3.495	Trp284	Pi-Pi Stacking	3.81
3	Koenigine	5318825	-4.123	Ser156	1	1.83
4	Murrayone	5319964	-3.061	Ala285	1	2.11

[Table/Fig-2]: Molecular Interaction of phytocompounds of M.koenigii with Gingipain R2 protein of *P. gingivalis*.



[Table/Fig-3]: Molecular docking of phytocompounds of M.koenigii with Major fimbrium subunit FimA type-4 protein of *P. gingivalis*.

highlight O-methylmurrayamine and Koenigine as promising inhibitors of the FimA Type-4 protein, suggesting their potential as therapeutic agents [Table/Fig-4].

S. No	Compound name	Docking score (kcal/mol)	Interacting Amino acid	Hydrogen bond	Bond length (Å)
1	O-Methyl-murrayamine A	-5.795	Asp53	1	1.98
2	Koenigicine	-4.149	Lys55	2	2.01
			Arg172		05
3	Koenigine	-5.675	Asp53 (2)	2	1.75
					19
4	Murrayone	-3.909	Lys55	1	2.79
			Arg172 (2)	2	08
					07

[Table/Fig-4]: Molecular interaction of phytocompounds of *M. koenigii* with major fimbrium subunit FimA type-4 protein of *P. gingivalis*.

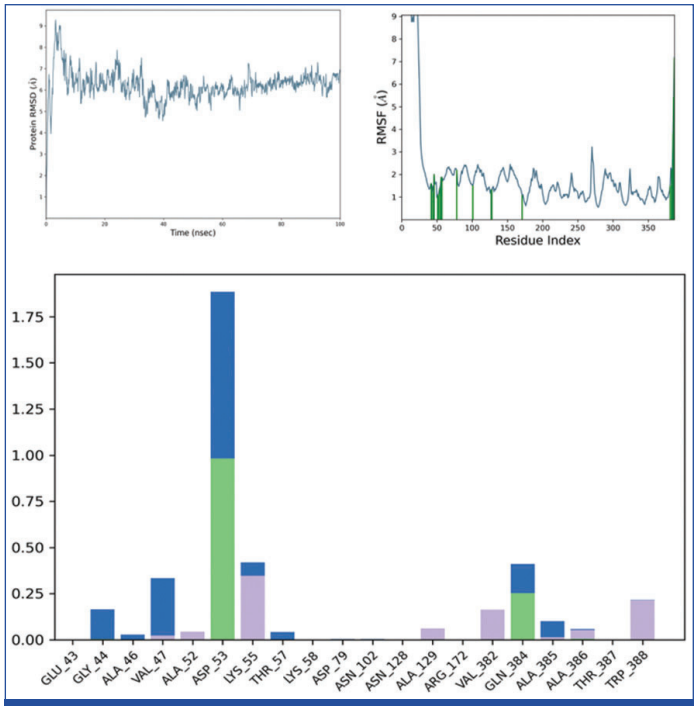
The pharmacokinetic evaluation of four compounds-O-methylmurrayamine, Koenigine, Koenigicine, and Murrayone-revealed high GI absorption, compliance with Lipinski's Rule of Five, and moderate bioavailability (0.55). While O-methylmurrayamine and Koenigicine were poorly soluble, Koenigine and Murrayone showed moderate solubility. All compounds, except O-methylmurrayamine, were predicted to cross the blood-brain barrier. Koenigine and Koenigicine inhibited key CYP enzymes, indicating drug-drug interaction risks, whereas Murrayone did not, making it safer for combination therapies [Table/Fig-5].

Parameters	O-methyl murrayamine	Koenigine	Koenigicine	Murrayone
TPSA	42.09 Å²	54.48 Å²	43.43 Å²	56.51 Å²
Inhibitors of CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4	Yes	Yes	Yes	No
GI absorption	High	High	High	High
Consensus Log Po/w	5	3.78	4.12	2.56
Water solubility class	Poorly soluble	Moderately soluble	Poorly soluble	Moderately soluble
BBB permeant	No	Yes	Yes	Yes
Lipinski	Yes; zero violations	Yes; zero violations	Yes; zero violations	Yes; zero violations
Bioavailability score	0.55	0.55	0.55	0.55

[Table/Fig-5]: Pharmacokinetic (ADMET) properties of the selected four compounds.

MDs simulation analysis of the ligand bound protein complexes: The ligand Koenigine individually bound with the target proteins Gingipain R2 and Major fimbrium subunit were MD simulated for 100 nano seconds (ns). The Koenigine bound Gingipain R2 have shown an average RMSD of 1.89Å, which less than 2 Å depicts that the ligand bound protein is more stable [Table/Fig-6]. To understand the residue wise fluctuations, RMSFs were analysed, which shows that the residues were fluctuated within 1.5 Å on average and the terminal residues along with loop regions have shown slightly higher fluctuations. Majority of the Gingipain R2 residues have established a hydrogen bond with koenigine molecule, and few residues has involved in hydrophobic interactions to support the koenigine within the active site of Gingipain R2. Similarly, RMSD pattern of koenigine bound with target protein FimA type 4 have displayed an average deviation of 7 Å from the initial to the end of the simulation [Table/Fig-7]. This stable plateau of RMSD profile showed that the ligand bound protein complex is more stable throughout the simulation time frame. To understand amino acid movements, RMSF was computed, and the average was observed to be 2 Å, which also reflects that the protein has maintained rigid conformations during the simulations with minimal fluctuation of residues. The protein-ligand contact shows that two residues namely Asp53 and Gln384 has involved in hydrogen bond formation during the simulation, however the ligand molecule binding is stabilised by water bridge and hydrophobic interactions. The MD simulation results well correlate with docking results in support of establishing the ligand molecule koenigine as strongly bound with target proteins.

[Table/Fig-6]: RMSD, RMSF and Protein- ligand contact of Koenigine bound Gingipain R2.



[Table/Fig-7]: RMSD, RMSF and Protein- ligand contact of Koenigine bound FimA type 4.

DISCUSSION

The present study comprehensively analysed the inhibitory potential of phytocompounds derived from *Murraya koenigii* against the periodontal pathogen *Porphyromonas gingivalis* using molecular docking computation analysis. *Porphyromonas gingivalis* is a late coloniser of biofilms in subgingival pockets and a pathobiont that disrupts the oral microbiome, leading to dysbiosis [19,20]. Targeting the key pathogen *P. gingivalis* with medicinal plant extracts offers a promising approach for managing and treating periodontal diseases [21].

Murraya koenigii, is loaded with bioactive compounds known for their therapeutic effects, including antitumour, antioxidant, anti-inflammatory, antihyperglycaemic, and hypoglycaemic properties [22,23]. Nutraceuticals and plant-based medicines like *M. koenigii* have gained attention for their natural origins, affordability, and minimal side-effects, with clinical studies supporting their role in preventing various health conditions [24]. Previous studies have shown that *M. koenigii* exhibits in-vitro antimicrobial activity against *P. gingivalis*. However, to the best of our knowledge, the specific phytocompound responsible for this inhibitory effect has not yet been identified. Given the importance of *P.gingivalis* virulence factors gingipain and fimbriae protein in periodontal disease, the investigators have targeted these virulence factors in this study.

Molecular docking studies of four selective compounds, O-methylmurrayamine, koenigine, koenigicine, and murrayone, against the active site of the Gingipain R2 protein from *Porphyromonas gingivalis* showed different binding affinities. Among them, koenigine showed the strongest binding affinity at -4.123 kcal/mol, forming a stable hydrogen bond with the amino acid residue Ser156. These results depict that these compounds, especially koenigine, have the potential to inhibit Gingipain R2 due to their significant interactions within the protein's active site.

Similarly, docking analyses of the same four compounds with the active site of the FimA type-4 protein revealed stable binding interactions. Koenigine again exhibited the highest binding affinity with a score of -5.675 kcal/mol, establishing two hydrogen bonds with Asp53. This suggests that koenigine is also a promising inhibitor of the FimA type-4 protein, highlighting its potential as a therapeutic agent targeting *P. gingivalis* virulence factors.

With respect to ADMET properties, all four compounds inhibit CYP enzymes, except for murrayone, and all have high gastrointestinal absorption. None of the four compounds violate any of the Lipinski rules.

The binding scores of ligands exhibiting superior affinity were further evaluated through MD simulations. Among these, the compound koenigine was identified as the most promising based on its binding scores, binding efficacy, and the number of stable hydrogen bonds formed. The koenigine-bound Gingipain R2 complex demonstrated an average RMSD of 1.89 Å, which is below 2 Å, indicating a stable ligand-protein interaction. In contrast, the koenigine complex with the target protein FimA type 4 showed an average RMSD of 7 Å from the start to the end of the simulation. The consistent plateau observed in the RMSD profile indicates that the ligand-bound protein complex remains stable throughout the entire simulation period. Most residues of Gingipain R2 formed hydrogen bonds with koenigine, while some residues contributed hydrophobic interactions that helped stabilise koenigine within the active site. Overall, the MD simulation findings align well with the docking results reinforcing the conclusion that koenigine binds strongly to the target proteins. Overall, these findings underscore koenigine's strong binding capabilities to critical proteins involved in *P. gingivalis* pathogenicity, supporting its candidacy as a potential inhibitor for therapeutic development against periodontal disease. In future to validate the computational findings antimicrobial assays against P gingivalis will be conducted.

Limitation(s)

The present study thoroughly examined the phytocompounds of *M. koenigii* for their potential applications in human healthcare. However, it faced certain limitations, including the lack of validation through in-vitro antimicrobial assays, animal models and human clinical trials. This study did not include antibiotics or any inhibitors to evaluate their effectiveness against *P. gingivalis*. Since this study involved only molecular docking, further in-vitro studies could explore the antioxidant, antimicrobial and anti-inflammatory properties.

CONCLUSION(S)

The present study highlights the potential of koenigine a phytocompound derived from *Murraya koenigii*, as a promising therapeutic agent against *Porphyromonas gingivalis*, a key pathogen in periodontitis. Koenigine demonstrated strong binding affinities with critical virulence factors- gingipain R2 and FimA 4 proteins- and formed stable protein-ligand complexes, as validated by MDs simulations. These findings suggest that koenigine could serve as a novel, plant-based antimicrobial candidate capable of mitigating *P. gingivalis*-mediated periodontal destruction. To translate these results into clinical relevance, further in-vivo investigations are essential to confirm its safety and therapeutic efficacy.

REFERENCES

[1] Abdulkareem AA, Al-Taweel FB, Al-Sharqi AJB, Gul SS, Sha A, Chapple ILC. Current concepts in the pathogenesis of periodontitis: from symbiosis to dysbiosis. J Oral Microbiol. 20232;15:2197779.
[2] Darveau RP. Periodontitis: A polymicrobial disruption of host homeostasis. Nature Reviews Microbiology. Nat Rev Microbiol. 2010;8:481-90.
[3] How KY, Song KP, Chan KG. Porphyromonas gingivalis: An overview of periodontopathic pathogen below the gum line. Front Microbiol. 2016;7:53.
[4] Xu W, Zhou W, Wang H, Liang S. Roles of Porphyromonas gingivalis and its virulence factors in periodontitis Adv Protein Chem Struct Biol. 2020;120:45-84.
[5] Hajishengallis G. Periodontitis: From microbial immune subversion to systemic inflammation. Nat Rev Immunol. 2015;15:30-44.
[6] Hashim NT, Babiker R, Rahman MM, Mohamed R, Priya SP, Chaitanya NC, et al. Natural bioactive compounds in the management of periodontal diseases: a comprehensive review. Molecules. 2024;29(13):3044.
[7] Fydrych D, Jeziurska J, Wełna J, Kwiecińska-Piróg J. Potential use of selected natural compounds with anti-biofilm activity. Int J Mol Sci. 2025;13:607.
[8] Nishan M, Subramanian P. Murraya koenigii (curry leave)- A review on its potential. International Journal of PharmTech Research. 2014;7:566-72.
[9] Palombo EA. Traditional medicinal plant extracts and natural products with activity against oral bacteria: potential application in the prevention and treatment of oral diseases. Evid Based Complement Alternat Med. 2011;12:680354.
[10] Pinzi L, Rastelli G. Molecular docking: shifting paradigms in drug discovery. Int J Mol Sci. 2019;20:4331.
[11] Morris GM, Lim-Wilby M. Molecular docking. Methods Mol Biol. 2008;443:365-82.
[12] Nakao R, Ikeda T, Furukawa S, Morinaga Y. Curry leaf triggers cell death of P. gingivalis with Membrane Blebbing. Pathogens. 2021;10:1286.
[13] Uma Maheswari K, Sathish S. In silico molecular docking of phytochemicals of murraya koenigii against streptococcus mutans. Cureus. 2024;16:e53679.
[14] Kalburgi NB, Koregol AC, Patil RS, Puttarevanna T. Anti-microbial efficacy of an ethanolic extract of murraya koenigii against periodontal pathogens like porphyromonas gingivalis and aggregatibacter actinomycetemcomitans: in vitro analysis. International Journal of Research in Ayurveda and Pharmacy. 2021;12(3):41-45.
[15] Chandra Shekar BR , Nagarajappa R, Jain R, Singh R, Suma S, et al. Antimicrobial efficacy of Acacia nilotica, Murraya koenigii L. Sprengel, Eucalyptus hybrid, Psidium guajava extracts and their combinations on Fusobacterium nucleatum and Porphyromonas gingivalis. Indian J Dent Res. 2018;29(5):641-45.
[16] WW PDB, Consortium. "Protein data bank: the single global archive for 3D macromolecular structure data". Nucleic Acids Res. 2019;47(D1):520-28.
[17] Computational platform Way2Drug: from the prediction of biological activity to drug repurposing Bulletin of the Academy of Sciences of the USSR Division of Chemical Science. 2017;66(10):1832-41.
[18] 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.
[19] Preshaw PM, Taylor, JT. How has the pathogenesis of periodontitis changed with the discovery of the role of the immune response? J Clinical Periodontol. 2011;38:03-13.
[20] Aleksijević LH, Aleksijević M, Škrlec I, Šram M, Šram M, Talapko J. Porphyromonas gingivalis virulence factors and clinical significance in periodontal disease and coronary artery diseases. Pathogens. 2022;11;11:1173.
[21] Balakrishnan R, Vijayraja D, Jo S-H, Ganesan P, Su-Kim I, Choi D-K. Medicinal profile, phytochemistry, and pharmacological activities of Murraya koenigii and its primary bioactive compounds. Antioxidants (Basel). 2020;24:101.

[22] Kumar R, Gupta S, Kaur P, Sahu SK. Exploring the potential of curry leaves for their therapeutic action. BIO Web of Conferences. 2024;86:01037.
[23] Ma Q, Tian J, Yang J, Wang A, Ji T, Wang Y, Su Y. Bioactive carbazole alkaloids from Murraya koenigii (L.) Spreng. Fitoterapia. 2013;87:01-06.
[24] Ghasemzadeh A, Jaafar HZ, Rahmat A, Devarajan T. Evaluation of bioactive compounds, pharmaceutical quality, and anticancer activity of curry leaf (Murraya koenigii L.). Evid Based Complement Alternat Med. 2014;2014:873803.

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