INDONESIAN JOURNAL OF INNOVATION AND APPLIED SCIENCES (IJIAS)
Journal Homepage: https://ojs.literacyinstitute.org/index.php/ijias
ISSN: 2775-4162 (Online)
Research Article

Volume 5	Issue 3	October (2025)	DOI: 10.47540/ijias.v5i3.1679	Page: 339 – 347

Molecular Docking of Allicin with PBP2a in MRSA: Insights into Antibacterial Mechanisms

Onche, E. P.[1], Abdulrazak, N. [1], Michael, E. I.[2], Attah, A. A.[3]

[1]Department of Medical Microbiology, School of Medical Laboratory Science, Usman Danfodiyo University Sokoto, Nigeria

[2]Department of Microbiology, University of Benin, Nigeria

[3]Department of Public Health, University of Port Harcourt, Nigeria

Corresponding Author: Onche, E. P; Email: ochochephilip0007@gmail.com

ARTICLE INFO

Keywords: Allicin, Methicillin, Resistant, *Staphylococcus aureus*.

Received : 09 October 2024
Revised : 08 November 2024
Accepted : 04 October 2025

ABSTRACT

Methicillin-resistant Staphylococcus aureus (MRSA) is a significant universal public health challenge owing to its resistance to β-lactam antibiotics, mostly methicillin. Primarily, resistance is mediated through the acquisition of the mecA gene encoding penicillin-binding protein 2a (PBP2a), which diminishes the effectiveness of β-lactams. A sulfur-containing compound known as allicin, often derived from Allium sativum (garlic), has proven broad-spectrum properties of antibacteria; nevertheless, its information regarding interactions with resistance protein PBP2a and its likes remains understudied. This study made use of molecular docking analysis to examine the binding interactions between allicin and PBP2a. The binding score of allicin was -3.9 kcal/mol, which shows that allicin has a moderate affinity for the PBP2a active site when compared to vancomycin (positive control) binding energy of -15.6 kcal/mol. The interaction of allicin with key amino acids in the PBP2a catalytic site showed no hydrogen bond formation. The outcome of this research shows that allicin can serve as a potential adjunct or alternative intervention against MRSA by targeting PBP2a. The study reveals insights into allicin's mode of action and presents a basis for further research on the application of compounds derived from plants in combating antibiotic resistance.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is currently one of the most challenging clinical pathogens in the medical practice owing to its resistance to β-lactam antibiotics, thus complicating treatment selections (Tong *et al.,* 2015; Lee et al., 2018; Turner et al., 2019). Primarily, this resistance is conferred by the *mecA* gene acquisition, penicillin-binding protein 2a (PBP2a) encoding, which decreases the β-lactams effectiveness through lowering their binding affinity (Peacock and Paterson, 2015; Miragaia, 2018; Shalaby et al., 2020). The MRSA infections prevalence is particularly common in hospitals and healthcare settings, which has driven a crucial search for new therapeutic agents that can circumvent the mechanism of resistance (Hassoun et al., 2017; Avershina et al., 2021).

Allicin is a bioactive sulfur compound derived from garlic (*Allium sativum*) and has expressed potential as an effective antibacterial agent against a broad spectrum of pathogens, together with gram-positive bacteria like *S. aureus* (Bhatwalka et al., 2021; Sasi et al., 2021; Jikah and Edo, 2023; Jikah et al., 2024). Allicin is enzymatically formed when a sulfur-containing amino acid called alliin is converted by alliinase following the mechanical disruption of garlic cells. Its powerful antimicrobial activity is held to stem from its capacity to react with thiol groups in proteins, with effect on cellular functions and bacterial metabolism (Shang et al., 2019). In spite of its recognized antibacterial properties, the precise interactions between MRSA

resistance proteins and allicin, such as PBP2a, have not been explored thoroughly.

With the computational methods emergence and drug discovery, molecular docking has turned out to be a critical tool for exploring drug-protein interactions (Katsila et al., 2016; Sarvagalla et al., 2019; Oyedele et al., 2023). Molecular docking is applied to predict the binding affinity and orientation of small molecules, such as allicin, to target proteins, like PBP2a, presenting insights into possible inhibition mechanisms. Recent research has adopted molecular docking to assess natural compounds' binding potentials against antibiotic-resistant bacteria, presenting new directions for therapeutic development (Álvarez-Martínez et al., 2020; Terreni et al., 2021; Pancu et al., 2021).

In this study, we adopted molecular docking analysis to investigate the allicin and PBP2a interaction, aiming to illuminate the antibacterial potential mechanism of allicin against MRSA. This provided an understanding of how allicin binds to PBP2a, revealing novel inhibitory pathways and suggesting avenues to potentiate its antibacterial activity, also as a combination and standalone treatment with β-lactam antibiotics. Through applying cutting-edge computational methods, we aimed to contribute to the unending search for natural compounds with the potential to mitigate the public health threat caused by MRSA.

The insights gained from this molecular docking research will enhance our understanding of allicin's mechanism of action to inform future research on applying plant-derived compounds as potential replacements or adjuncts to conventional antibiotics, particularly in the face of growing antibiotic resistance.

METHODS

Preparation of Protein (Staphylococcus aureus Penicillin Binding Protein 2a (SauPBP2a))

The three-dimensional coordinate of SauPBP2a was obtained from the Protein Data Bank (PDB) database, which is available at https://www.rcsb.org with PDB codes of 4CJN (X-ray resolution = 1.95A). The 4CJN files has two polypeptide chains as A and B. Since PBP2a is a dimeric structure, the chain B was selected for further analysis, which contained 642 residues in the 4CJN file. The chain B also included a ligand ((E)-3-(2-(4-cyanostyryl)-4-oxoquinazolin-3(4H)-yl) benzoic acid) and a water molecule (Ibrahim et al., 2021; Masumi et al., 2022). Autodock Mgltools was used to remove the ligand and water molecule (Arcon et al., 2021; Sheikholeslami et al., 2024). Polar hydrogen and charge were then added. The protein was then renamed and converted to PDBQT format (Ravi & Kannabiran, 2016).

Preparation of Ligand (Allicin, Gentamicin, and Vancomycin)

The three-dimensional (3D) coordinates of allicin and vancomycin in a structure data file (SDF) were collected from the PubChem database (https://pubchem.ncbi.nlm.nih.gov). The software PyMol was then used to convert the SDF files to PDB files since SDF files cannot be used for docking simulation. The PBP files were then subjected to Autodock Mgltool for renaming and conversion to PDBQT format.

Energy Minimizing (EM) of Prepared Protein and Ligands

Energy minimization of the prepared protein was done before the docking simulation. Swiss-PDB Viewer version 4.1.0 was used. Energy minimization was administered to all prepared Ligands using UCSF Chimera 1.15 (Akher et al., 2019; Lima et al., 2022; Xiao, 2023). Energy minimization helps to refine the initial 3D structure of the molecules, it stabilizes the structures by finding the energetically favorable conformations, it reduces steric hindrance, it also allows for conformational sampling, it improves docking accuracy, it enhances predictive power, and minimizes artifacts (Mirzaei et al., 2015; Pagadala et al., 2017; Tripathi & Misra, 2017).

Molecular Docking with the SauPBP2a Active Site

The following features from a Windows-based system: installed RAM (8GB), system type (64 bit), processor (Intel Pentium), and processor speed (1.60GHz), was used. AutoDock vina (https://autodock.scripps.edu) was used to perform docking simulation (Chauhan et al., 2021; Blanes-Mira et al., 2022). AutoDock vina predicts the ligand docking pose using an algorithm (Lamarckian genetic) and applies partial flexibility in the receptor (Forli et al., 2016; Chen et al., 2023). Docking simulation of allicin and vancomycin (positive control) compounds was done considering the catalytic site of SauPBP2a. In the binding site of SauPBP2a, 14 amino acid residues were noted

Met681, Thr600, Gly599, Ser598, Gly549, Ser548, Thr500, Asn464, Ser462, Tyr446, Lys406, Ser403, Lys340 and Ser337 (Masumi et al., 2022; Tabassum et al., 2023). But 8 amino acid residues (Ser403, Lys 406, Try446, Ser462, Asn464, Ser598, Gly599, Thr600) out of the 14 amino acid residues were used. The following are grid box settings: X-dimension, 40; Y-dimension, 40; Z-dimension, 40; X-center, 24.464; Y-center, -20.988; Z-center, -8.583; spacing, 0.603A. Individual component docking poses were set at 8. The binding affinity of ligand to receptor was considered when the Root Mean Square Deviation (RMSD) and tolerance of 2.0A, along with the lowest binding involved in the largest cluster. The amino acid residues within the binding site of SauPBP2a interacted with ligands after docking simulation.

Docking Validation

Following the validation protocol carried out by Saliu et al. (2021), the docking procedure was validated using the oxoquinazolin inhibitor from the Sau PBP2a. Oxoquinazolin was removed and re-docked into the active site using AutoDock vina. Autodock Mgltool was used to open the co-crystallized structure, then the oxoquinazolin was removed and saved as an inhibitor, while the Sau PBP2a was saved as a receptor all in PDBQT files. An unchanged grid parameter and docking protocols was followed to ensure precision and minimize deviation when compared to the actual co-crystallized complex. PyMol was then used to superimpose the re-docked multifacet with the reference co-crystallized complex and calculate the Root Mean Square Deviation (RMSD).

RESULTS AND DISCUSSION

It was observed that allicin bound to the PBP2a catalytic site with a binding energy of -3.9 kcal/mol. The docking scores of allicin and vancomycin (positive control) were shown in Table 1, with allicin having a score of -3.9 and vancomycin having a docking score of -15.6. Table 2 shows the polar and non-polar interactions of allicin and vancomycin (positive control) with the amino acid residue of chain B. Allicin formed non-polar interactions with 9 amino acid residues and no hydrogen bond interaction, while vancomycin formed 1 hydrogen bond, 1 polar interaction, and 45 non-polar interactions with the amino acid residue. The validation interaction of quinazolione, amino acid interaction, and RMSD value were all represented in Table 3. Quinazolione had a binding score of -7.8, RMSD value of 0.6791, non-polar interaction with 55 amino acid residues, and a polar (hydrogen) bond interaction with 3 amino acid residues in Table 3.

Figure 1 shows allicin interacting in the pocket region of PBP2a chain B and the crystallographic binding mode of allicin in the PBP2a chain B active site. Figure 2 shows vancomycin interacting in the pocket region of PBP2a chain B and the crystallographic binding mode of vancomycin in the PBP2a chain B active site. Figure 3 shows quinazolione interacting in the pocket region of PBP2a chain B and the crystallographic binding mode of quinazolione in the PBP2a chain B active site.

Table 1. Docking scores of Allicin, Gentamicin, and Vancomycin (positive control)

Ligand	Mode	Affinity (kcal/mol)
Allicin	1	-3.9
Vancomycin (Positive control)	1	-15.6

Table 2. Interactions and Binding Energy of Allicin and Vancomycin (positive control) with PBP2a

Ligand	Binding energy (kcal/mol)	Interacting amino acid residues	Number of hydrogen bond	Hydrogen bond interactions
Allicin	-3.9	ILE 614, VAL 633, ASN 632, LEU 603, SER 400, LYS 604, GLY 345, SER 346, PRO 528, THR 344, THR 399, THR 398, LYS 394, ILE 397, GLU 389, LEU 392, LYS 634	0	0

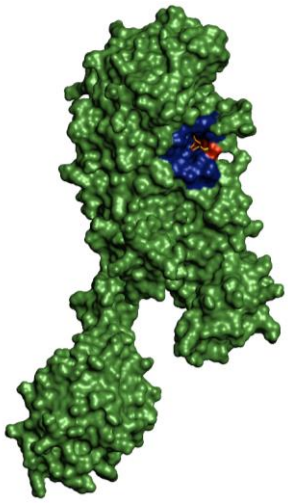
Vancomycin (Positive control)	-15.6	TRP 438, GLY 440, TYR 441, ASN 442, LYS 430, LEU 513, VAL 449, THR 444, ASP 516, GLN 457, VAL 448, ARG 445, ASN 464, TYR 519, GLY 522, GLU 447, TYR 446, SER 598, MET 641, ALA 642, HIS 583, SER 643, LYS 639, TYR 644, LYS 584, GLU 584, ASP 586, GLU 609, GLU 523, GLN 521, GLY 520, LEU 603, SER 400, GLN 613, THR 600, ALA 601, GLU 602, GLY 611	1	GLY 640

Table 3. Validation interaction, binding energy, and RMSD value of Quinazolione

Ligand	Binding energy (kcal/mol)	Interacting amino acid residues	RMSD (Å)	Hydrogen bond interactions
Quinazolinone	-7.8	LYS 581, LYS 584, THR 582, GLU 585, GLU 460, HIS 583, ASP 586, SER 462, GLU 447, LYS 430, TYR 440, ASN 464, VAL 443, SER 643, SER 598, GLY 599, ALA 642, GLY 540, MET 641, THR 600, ASN 442, GLY 520, ASP 516, GLY 402, ILE 512, TRP 438, TRP 441, GLY 440, GLN 521, GLY 522, GLU 602, ILE 614, ASN 632, PRO 528, VAL 633, SER 346, LYS 634, LEU 525, GLU 523, GLY 345, THR 399, THR 398, TYR 344, LYS 394, ILE 397, LEU 392, GLU 389, LYS 387, LEU 603, LYS 604, ARG 612, THR 610, MET 605, GLU 609, LYS 606.	0.6791	SER 480, TYR 519, THR 444.

RMSD: Root Mean Square Deviation

(A)



(B)

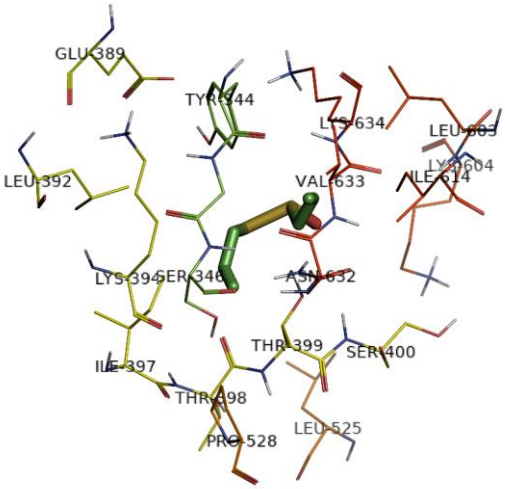
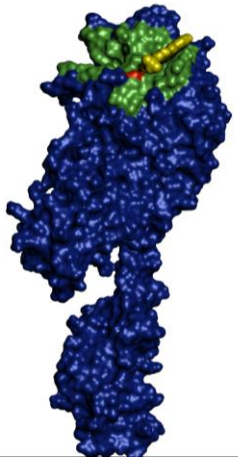


Figure 1. (A) Allicin interacting in the pocket region of protein chain B (B) Crystallographic binding mode of allicin in chain B active site

(C)



(D)

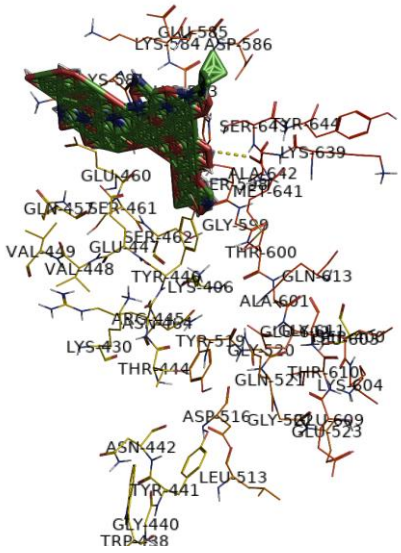
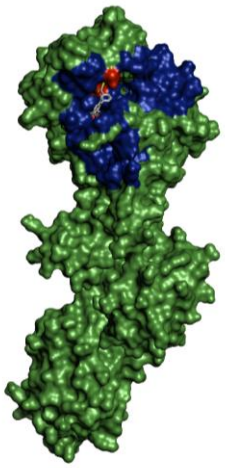


Figure 2. (C) Vancomycin interacting in the pocket region of protein chain B (D) Crystallographic binding mode of Vancomycin in chain B active site

(E)



(F)

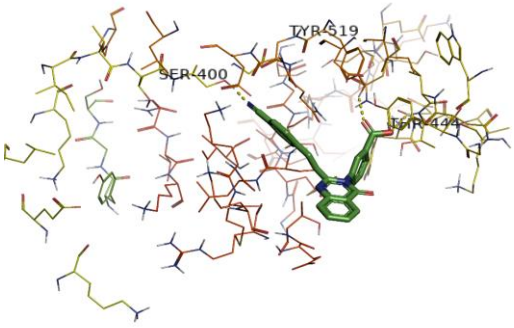


Figure 3. (E) Quinazolione interacting in the pocket region of protein chain B (F) Crystallographic binding mode of quinazolione in chain B active site

Docking analysis results show that allicin exhibits a moderate binding affinity to PBP2a, which is the main enzyme responsible for methicillin resistance in MRSA. The binding energy of allicin (-3.9 kcal/mol) was considerably lower than that of the positive control vancomycin (-15.6 kcal/mol), indicating a weaker interaction (Bouley et al., 2015; Khameneh et al., 2021). Regardless of the weak interaction, allicin still interacted with critical amino acid residues in the active site of PBP2a, including ILE 614, VAL 633, and SER 400. Allicin- PBP2a lacks hydrogen bond formation, suggesting that the lack of non-polar interaction may play a more significant role in stabilizing the allicin binding conformation.

Allicin's binding score, although it may not be as potent as vancomycin, has potential as a supplementary agent (Wüllner et al., 2019; Bhatwalkar et al., 2021). With the rising interest in the use of plant-derived compounds to fight antibiotic resistance, the capacity of allicin to bind to PBP2a provides a novel avenue for exploration and research (Shang et al., 2019; Ashraf et al., 2023; Jo et al., 2024). Furthermore, complementary therapy using allicin alongside β-lactam antibiotics may improve their effectiveness against MRSA by potentially disrupting the bacterial resistance mechanisms.

The validation process using quinazolione showed consistent results, further supporting the accuracy of the docking procedure (Huang et al., 2019; Patel et al., 2019; El-Sayed et al., 2021; Sarkar et al., 2021; Eissa et al., 2021). This supports the evidence that allicin could disrupt MRSA resistance, although its binding affinity is lower than traditional antibiotics like vancomycin.

CONCLUSION

In conclusion, this study on molecular docking has provided insights into the interface between allicin and PBP2a, a critical enzyme in MRSA's resistance to β-lactam antibiotics. Allicin revealed moderate binding affinity, stressing its potential as a natural compound with antibacterial properties. Although allicin may not substitute current antibiotics such as vancomycin, it could aid as an adjunctive therapy, enhancing the usefulness of conventional antibiotics. Additional experimental validation and optimization of allicin derivatives may advance its binding affinity and antibacterial effectiveness against MRSA.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

REFERENCES

1. Akher, F. B., Farrokhzadeh, A., Olotu, F. A., Agoni, C., & Soliman, M. E. (2019). The irony of chirality–unveiling the distinct mechanistic binding and activities of 1-(3-(4-amino-5-(7-methoxy-5-methylbenzo [b] thiophen-2-yl)-7 H-pyrrolo [2, 3-d] pyrimidin-7-yl) pyrrolidin-1-yl) prop-2-en-1-one enantiomers as irreversible covalent FGFR4 inhibitors. *Organic & Biomolecular Chemistry*, *17*(5), 1176-1190.
2. Álvarez-Martínez, F. J., Barrajón-Catalán, E., & Micol, V. (2020). Tackling antibiotic resistance with compounds of natural origin: A comprehensive review. *Biomedicines*, *8*(10), 405.
3. Arcon, J. P., Turjanski, A. G., Martí, M. A., & Forli, S. (2021). Biased docking for protein–ligand pose prediction. *Protein-ligand interactions and drug design*, 39-72.
4. Ashraf, M. V., Pant, S., Khan, M. H., Shah, A. A., Siddiqui, S., Jeridi, M., ... & Ahmad, S. (2023). Phytochemicals as antimicrobials: prospecting Himalayan medicinal plants as source of alternate medicine to combat antimicrobial resistance. *Pharmaceuticals*, *16* (6), 881.
5. Avershina, E., Shapovalova, V., & Shipulin, G. (2021). Fighting antibiotic resistance in hospital-acquired infections: current state and emerging technologies in disease prevention, diagnostics and therapy. *Frontiers in Microbiology*, *12*, 707330.
6. Bhatwalkar, S. B., Mondal, R., Krishna, S. B. N., Adam, J. K., Govender, P., & Anupam, R. (2021). Antibacterial properties of organosulfur compounds of garlic (Allium sativum). *Frontiers in Microbiology*, *12*, 613077.
7. Blanes-Mira, C., Fernández-Aguado, P., de Andrés-López, J., Fernández-Carvajal, A., Ferrer-Montiel, A., & Fernández-Ballester, G. (2022). Comprehensive survey of consensus docking for high-throughput virtual screening. *Molecules*, *28*(1), 175.

8. Bouley, R., Kumarasiri, M., Peng, Z., Otero, L. H., Song, W., Suckow, M. A., Schroeder, V. A., Wolter, W. R., Lastochkin, E., Antunes, N. T., Pi, H., Vakulenko, S., Hermoso, J. A., Chang, M., & Mobashery, S. (2015). Discovery of antibiotic (E)-3-(3-carboxyphenyl)-2-(4-cyanostyryl) quinazolin-4(3H)-one. *Journal of the American Chemical Society, 137*(5), 1738–1741.
9. Chauhan, S., Srivastava, M., & Singh, J. (2021). DocVSP (Docking-based Virtual Screening Perl-script) for Automating and Integrating AutoDock and SBDD. In *SCRS Conference Proceedings on Intelligent Systems* (pp. 287-291).
10. Chen, T., Shu, X., Zhou, H., Beckford, F. A., & Misir, M. (2023). Algorithm selection for protein–ligand docking: strategies and analysis on ACE. *Scientific Reports*, *13*(1), 8219.
11. Eissa, I. H., Ibrahim, M. K., Metwaly, A. M., Belal, A., Mehany, A. B., Abdelhady, A. A., ... & Mahdy, H. A. (2021). Design, molecular docking, in vitro, and in vivo studies of new quinazolin-4 (3H)-ones as VEGFR-2 inhibitors with potential activity against hepatocellular carcinoma. *Bioorganic Chemistry*, *107*, 104532.
12. El-Sayed, N. N., Al-Otaibi, T. M., Alonazi, M., Masand, V. H., Barakat, A., Almarhoon, Z. M., & Ben Bacha, A. (2021). Synthesis and Characterization of Some New Quinoxalin-2 (1H) one and 2-Methyl-3 H-quinazolin-4-one Derivatives Targeting the Onset and Progression of CRC with SAR, Molecular Docking, and ADMET Analyses. *Molecules*, *26*(11), 3121.
13. Forli, S., Huey, R., Pique, M. E., Sanner, M. F., Goodsell, D. S., & Olson, A. J. (2016). Computational protein–ligand docking and virtual drug screening with the AutoDock suite. *Nature protocols*, *11*(5), 905-919.
14. Hassoun, A., Linden, P. K., & Friedman, B. (2017). Incidence, prevalence, and management of MRSA bacteremia across patient populations—a review of recent developments in MRSA management and treatment. *Critical care*, *21*, 1-10.
15. Huang, S., Feng, K., & Ren, Y. (2019). Molecular modelling studies of quinazolinone derivatives as MMP-13 inhibitors by QSAR, molecular docking and molecular dynamics simulations techniques. *Medchemcomm*, *10*(1), 101-115.
16. Ibrahim, M. A., Abdeljawaad, K. A., Abdelrahman, A. H., Alzahrani, O. R., Alshabrmi, F. M., Khalaf, E., ... & Atia, M. A. (2021). Non-β-lactam allosteric inhibitors target methicillin-resistant Staphylococcus aureus: an insilico drug discovery study. *Antibiotics*, *10*(8), 934.
17. Jikah, A. N., & Edo, G. I. (2023). Mechanisms of action by sulphur compounds in Allium sativum. A review. *Pharmacological Research-Modern Chinese Medicine*, 100323.
18. Jikah, A. N., Edo, G. I., Makia, R. S., Yousif, E., Gaaz, T. S., Isoje, E. F., ... & Umar, H. (2024). A review of the therapeutic potential of sulfur compounds in Allium sativum. *Measurement: Food*, 100195.
19. Jo, D. M., Tabassum, N., Oh, D. K., Ko, S. C., Kim, K. W., Yang, D., ... & Khan, F. (2024). Green Medicine: Advancing Antimicrobial Solutions with Diverse Terrestrial and Marine Plant-Derived Compounds. *Processes*, *12*(11), 2316.
20. Katsila, T., Spyroulias, G. A., Patrinos, G. P., & Matsoukas, M. T. (2016). Computational approaches in target identification and drug discovery. *Computational and Structural Biotechnology Journal*, *14*, 177-184.
21. Khameneh, B., Eskin, N. M., Iranshahy, M., & Fazly Bazzaz, B. S. (2021). Phytochemicals: a promising weapon in the arsenal against antibiotic-resistant bacteria. *Antibiotics*, *10*(9), 1044.
22. Lee, A. S., De Lencastre, H., Garau, J., Kluytmans, J., Malhotra-Kumar, S., Peschel, A., & Harbarth, S. (2018). Methicillin-resistant Staphylococcus aureus. *Nature reviews Disease primers*, *4*(1), 1-23.
23. Lima, C. C., Silva, D. S. N., & de Sá, É. R. A. (2022). Computational Analysis of Sulfonamide-Based Compounds by Molecular Docking and ADME/T in the Inhibition of Acetylcholinesterase (AChE) in Alzhaimer's Disease. *Open Access Library Journal*, *9*(3), 1-13.
24. Masumi, M., Noormohammadi, F., Kianisaba, F., Nouri, F., Taheri, M., & Taherkhani, A. (2022). Methicillin-Resistant Staphylococcus

aureus: Docking‐Based Virtual Screening and Molecular Dynamics Simulations to Identify Potential Penicillin‐Binding Protein 2a Inhibitors from Natural Flavonoids. *International Journal of Microbiology*, 2022(1), 9130700.

25. Miragaia, M. (2018). Factors contributing to the evolution of mecA-mediated β-lactam resistance in staphylococci: update and new insights from whole genome sequencing (WGS). *Frontiers in Microbiology*, *9*, 2723.
26. Mirzaei, H., Zarbafian, S., Villar, E., Mottarella, S., Beglov, D., Vajda, S., ... & Kozakov, D. (2015). Energy minimization on manifolds for docking flexible molecules. *Journal of Chemical Theory and Computation*, *11*(3), 1063-1076.
27. Oyedele, A. Q. K., Ogunlana, A. T., Boyenle, I. D., Adeyemi, A. O., Rita, T. O., Adelusi, T. I., ... & Odunitan, T. T. (2023). Docking covalent targets for drug discovery: stimulating the computer-aided drug design community of possible pitfalls and erroneous practices. *Molecular Diversity*, *27*(4), 1879-1903.
28. Pagadala, N. S., Syed, K., & Tuszynski, J. (2017). Software for molecular docking: a review. *Biophysical Reviews*, *9*, 91-102.
29. Pancu, D. F., Scurtu, A., Macasoi, I. G., Marti, D., Mioc, M., Soica, C., ... & Dehelean, C. (2021). Antibiotics: conventional therapy and natural compounds with antibacterial activity-a pharmaco-toxicological screening. *Antibiotics*, *10*(4), 401.
30. Patel, T. S., Bhatt, J. D., Dixit, R. B., Chudasama, C. J., Patel, B. D., & Dixit, B. C. (2019). Green synthesis, biological evaluation, molecular docking studies and 3D-QSAR analysis of novel phenylalanine linked quinazoline-4 (3H)-one-sulphonamide hybrid entities distorting the malarial reductase activity in folate pathway. *Bioorganic & Medicinal Chemistry*, *27*(16), 3574-3586.
31. Peacock, S. J., & Paterson, G. K. (2015). Mechanisms of methicillin resistance in Staphylococcus aureus. *Annual Review of Biochemistry*, *84*(1), 577-601.
32. Ravi, L., & Kannabiran, K. (2016). A handbook on protein-ligand docking tool: AutoDock 4. *Innovare Journal of Medical Sciences*, 28-33.
33. Saliu, T. P., Umar, H. I., Ogunsile, O. J., & others. (2021). Molecular docking and pharmacokinetic studies of phytocompounds from Nigerian medicinal plants as promising inhibitory agents against SARS-CoV-2 methyltransferase (nsp16). *Journal of Genetic Engineering and Biotechnology, 19*(1), 172.
34. Sarkar, M. A. A. S. U., Nath, A., Kumer, A., Mallik, C., Akter, F., Moniruzzaman, M., & Ali, M. A. (2021). Synthesis, molecular docking screening, ADMET and dynamics studies of synthesized 4-(4-methoxyphenyl)-8-methyl-3, 4, 5, 6, 7, 8-hexahydroquinazolin-2 (1H)-one and quinazolinone derivatives. *Journal of Molecular Structure*, *1244*, 130953.
35. Sarvagalla, S., Syed, S. B., & Coumar, M. S. (2019). An overview of computational methods, tools, servers, and databases for drug repurposing. *In silico drug design*, 743-780.
36. Sasi, M., Kumar, S., Kumar, M., Thapa, S., Prajapati, U., Tak, Y., ... & Mekhemar, M. (2021). Garlic (Allium sativum L.) bioactives and its role in alleviating oral pathologies. *Antioxidants*, *10*(11), 1847.
37. Shalaby, M. A. W., Dokla, E. M., Serya, R. A., & Abouzid, K. A. (2020). Penicillin binding protein 2a: An overview and a medicinal chemistry perspective. *European Journal of Medicinal Chemistry*, *199*, 112312.
38. Shang, A., Cao, S.-Y., Xu, X.-Y., Gan, R.-Y., Tang, G.-Y., Corke, H., & Li, H.-B. (2019). Bioactive compounds and biological functions of garlic (*Allium sativum* L.). *Foods, 8*(7), 246.
39. Sheikholeslami, M., Nazari, M. H., & Fassihi, A. (2024). M01 tool: An automated, comprehensive computational tool for generating small molecule-peptide hybrids and docking them into curated protein structures.
40. Tabassum, R., Kousar, S., Mustafa, G., Jamil, A., & Attique, S. A. (2023). In Silico Method for the Screening of Phytochemicals against Methicillin‐Resistant Staphylococcus Aureus. *BioMed Research International*, *2023*(1), 5100400.
41. Terreni, M., Taccani, M., & Pregnolato, M. (2021). New antibiotics for multidrug-resistant bacterial strains: latest research developments and future perspectives. *Molecules*, *26*(9), 2671.

42. Tong, S. Y., Davis, J. S., Eichenberger, E., Holland, T. L., & Fowler, V. G. (2015). *Staphylococcus aureus* infections: Epidemiology, pathophysiology, clinical manifestations, and management. *Clinical Microbiology Reviews, 28*(3), 603–661.
43. Tripathi, A., & Misra, K. (2017). Molecular docking: A structure-based drug designing approach. *JSM Chem*, *5*(2), 1042-1047.
44. Turner, N. A., Sharma-Kuinkel, B. K., Maskarinec, S. A., Eichenberger, E. M., Shah, P. P., Carugati, M., ... & Fowler Jr, V. G. (2019). Methicillin-resistant Staphylococcus aureus: an overview of basic and clinical research. *Nature Reviews Microbiology*, *17*(4), 203-218.
45. Wüllner, D., Haupt, A., Prochnow, P., Leontiev, R., Slusarenko, A. J., & Bandow, J. E. (2019). Interspecies comparison of the bacterial response to allicin reveals species‐specific defense strategies. *Proteomics*, *19*(24), 1900064.
46. Xiao, Y. (2023). *Computational Simulations of Protein-Ligand Binding with a Focus on Carbohydrates* (Doctoral dissertation, University of Georgia).