Clinical and Experimental Health Sciences

Comparative Molecular Docking Analysis of Carbapenem Antibiotics With NDM-1 and OXA-23 B-Lactamases: Insights Into Binding Mechanisms

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ABSTRACT

Objective: This study aimed to investigate the molecular interactions between carbapenem antibiotics (imipenem and meropenem) and two β-lactamase enzymes, NDM-1 (class B) and OXA-23 (class D), to understand the structural basis of carbapenem resistance.

Methods: The study employed molecular docking methods using the crystal structures and homology models of the NDM-1 and OXA-23 enzymes to analyze binding affinities and interaction patterns.

Results: The results revealed distinct binding characteristics for each enzyme. NDM-1 exhibited a polar, hydrophobic active site, with imipenem forming hydrogen bonds with ASP124, ASN220, and LYS211, while meropenem relied on weaker interactions like Van der Waals forces. In contrast, OXA-23 featured a hydrophobic cavity with charged residues, where imipenem bonded with ARG259 and meropenem interacted with SER79, TRP219, and ARG259. A key finding was the significantly lower binding energy for the OXA-23-imipenem complex in the crystal structure (-8.06 kcal/mol) compared to its homology model (-5.34 kcal/mol), highlighting the importance of accurate structural representation. The study demonstrated strong agreement between the computational and experimental data.

Conclusion: These findings provide critical insights into the structural basis of carbapenem resistance, offering potential avenues for designing inhibitors to combat β-lactamase-mediated antibiotic resistance. The integrated approach validates the utility of computational methods in elucidating molecular interactions and guiding therapeutic strategies.

Keywords: NDM-1, OXA-23, imipenem, meropenem, molecular docking

1. INTRODUCION

Antibiotics are among the most essential therapeutic agents used in the treatment of infectious diseases, playing a pivotal role in modern medicine (1). Among these, carbapenems stand out as powerful β-lactam antibiotics, effectively combating a broad spectrum of bacterial pathogens. They function by inhibiting bacterial cell wall synthesis through the irreversible binding to penicillin-binding proteins (PBPs). This binding disrupts the critical process of peptidoglycan cross-linking, which is vital for maintaining the structural integrity of bacterial cell walls (2).

However, the widespread and often inappropriate use of antibiotics has precipitated an alarming rise in antibiotic resistance, significantly undermining the efficacy of these vital medications. Antibiotic resistance has escalated into a global health crisis, characterized by the emergence of bacteria that have developed sophisticated mechanisms to circumvent the effects of antibiotics. One prominent defense mechanism involves the production of β-lactamases—enzymes that specifically inactivate β-lactam antibiotics, thereby diminishing their therapeutic effectiveness (1).

β-lactamases are categorized into two major groups based on their enzymatic mechanisms: serine β-lactamases (which encompass Classes A, C, and D) and metallo-β-lactamases (Class B). Serine β-lactamases utilize a pivotal catalytic serine residue located in their active site to facilitate the hydrolysis of β-lactam antibiotics. In contrast, metallo-β-lactamases rely on zinc ions for their hydrolytic activity, which creates a different enzymatic environment for the inactivation of these antibiotics (3).

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The role of zinc ions extends beyond merely assisting in the enzymatic process; they are also crucial for the recognition and binding of various β-lactam antibiotics. Additionally, specific amino acid residues within the active site of β-lactamases contribute significantly to substrate binding and catalysis, influencing the overall activity and specificity of these enzymes (4). Understanding the intricate mechanisms by which β-lactamases operate is essential for developing strategies to combat antibiotic resistance and enhance the effectiveness of existing antibiotics (5).

Among clinical isolates, New Delhi metallo-β-lactamase (NDM) has emerged as the most prevalent and concerning variant of metallo-β-lactamase enzymes. NDM was first identified in 2009 in a male patient who had recently traveled to New Delhi, India, highlighting the global connectivity that can facilitate the spread of antibiotic resistance (6). The identification of the NDM-1 variant, along with its numerous genetic variants, has sparked significant alarm within the medical community due to its remarkable ability to inactivate nearly all β-lactam antibiotics, with the notable exception of aztreonam. This extensive resistance renders infections caused by NDM-producing bacteria particularly challenging to treat and often leads to severe, life-threatening complications, necessitating the urgent need for alternative therapeutic strategies (7).

In the realm of β-lactamases, Class D enzymes are particularly noteworthy, with over 250 distinct variants documented to date. These enzymes exhibit considerable structural diversity, which is closely linked to their ability to confer broad-spectrum antibiotic resistance across various bacterial species. Among these, some Class D β-lactamases are capable of hydrolyzing carbapenems—powerful antibiotics often used as a last resort—earning them the designation of carbapenem-hydrolyzing class D β-lactamases (CHDLs). One of the prominent members of this group is OXA-23, characterized by a distinct structural framework that comprises two α-helices and six β-sheets. Initially observed in Scotland, OXA-23 has since shown a widespread geographical distribution, raising concerns about its presence in various healthcare settings worldwide (8-9).

In particular, during an outbreak investigation at Kocaeli University Hospital in Turkey, a significant number of blaOXA-23-positive Acinetobacter baumannii isolates were identified. This finding underscores the clinical relevance of OXA-23 in the context of nosocomial infections and the urgent need for ongoing surveillance and research to understand the mechanisms of resistance and to develop effective countermeasures against such formidable pathogens (10).

Molecular docking studies have emerged as a crucial methodology in modern scientific research, particularly in the fields of biochemistry and pharmacology. This computational technique allows researchers to simulate and analyze the interactions between chemical compounds and biologically relevant macromolecules, such as proteins or nucleic acids, within three-dimensional structures that have been resolved using techniques like X-ray crystallography or NMR spectroscopy (11). By accurately positioning potential drug candidates in these target sites, molecular docking facilitates the prediction of various binding modes, interaction energies, and the resulting molecular conformations of both the ligand and its target (11,12).

The significance of docking methods is particularly pronounced in drug discovery, where they serve as powerful tools for identifying novel ligands that can modulate specific biological targets effectively. This predictive capability not only accelerates the early-stage screening of compounds but also enhances the likelihood of discovering therapeutic agents that might not be readily apparent through traditional experimental methods (11). Furthermore, docking studies provide substantial advantages in terms of time efficiency and resource conservation; they allow for preliminary assessments of compound efficacy and specificity without the need for extensive laboratory work, thus streamlining the drug development process and reducing costs associated with experimental screening (12).

In this study, molecular interactions between β-lactam antibiotics, specifically imipenem and meropenem, and both the crystallographic structure and the homology model of two important β-lactamases, New Delhi Metallo-β-lactamase-1 (NDM-1) and Oxacillinase-23 (OXA-23), were explored in this study. Advanced molecular docking techniques were utilized to analyze the binding affinities of these antibiotics to the enzyme targets, with a focus on the various interaction patterns that emerge during the binding process. By systematically comparing the docking results, insights were provided into the structural mechanisms underlying antibiotic resistance facilitated by these enzymes. This investigation not only enhances our understanding of the biochemical basis for resistance but also aids in the development of more effective therapeutic strategies against β-lactam-resistant bacterial infections.

2. METHODS

The crystal structures of NDM-1 (PDB ID: 5YPL) and OXA-23 (PDB ID: 4JF5) were retrieved from the Protein Data Bank database. Using these template structures, homology models of OXA-23 and NDM-1 were generated using Swiss-Model (13-17). Model validation was performed using ERRAT (18), VERIFY3D (19,20), PROCHECK (21,22), and Swiss-Model's built-in quality assessment tools (13-17).

The ligand preparation of meropenem and imipenem in pdbqt format was conducted using MGLTools (23). Molecular docking were performed with AutoDock4.2 (24), targeting the known binding sites of both the homology models and crystal structures. The hydrolyzed forms of meropenem and imipenem were used in this study. The binding site coordinates were defined as (-7.925, 39.154, 11.045) for OXA-23 and (2.250, 7.779, 24.903) for NDM-1.

The docking protocol utilized an advanced Genetic Search Algorithm, which was specifically designed to assess the conformational relationships between potential binding partners. This was complemented by the Lamarckian Genetic Algorithm, which played a crucial role in determining the optimal binding pose for each complex. As a result of this

Table 1. *Validation Metrics of NDM-1 and OXA-23 Homology Models*

	QMEANDisCo Global		MolProbity Score		Clash Score		Ramachandrana Favoured (%)		ERRAT		VERIFY (%)	
	Crys. Strc.	Hom. Strc.	Crys. Strc.	Hom. Strc.	Crys. Strc.	Hom. Strc.	Crys. Strc.	Hom. Strc.	Crys. Strc.	Hom. Strc.	Crys. Strc.	Hom. Strc.
NDM-1	0.94	0.93	1.06	0.63	2.68	0.28	99.12	97.91	97.1963	91.5929	91.70	97.10
OXA-23	0.87	0.89	1.11	0.96	0.96	0.00	98.33	96.27	90.411	94.3723	86.36	93.00

NDM-1; New Delhi metallo-β-lactamase-1, OXA-23; Oxacillinase-23

Table 2. *Comparative binding analysis of carbapenems with NDM-1 and OXA-23 β-lactamases*

System	Binding Energy (kcal/mol)		Key Interacting Residues	
	Homology	Experimental	Homology Model	Experimental Structure
NDM-1/Imipenem	-4.26	-3.82	ASN220, ASP124, LYS211	ASN220, GLN123, LYS211
NDM-1/Meropenem	-6.19	-5.74	LYS211, ASN220, ASP124	LYS211, ASN220, ASP124
OXA-23/Imipenem	-5.34	-8.06	ARG259	THR217, ARG259, VAL128
OXA-23/Meropenem	-6.57	-7.59	ARG259, TRP219, SER79	LYS82, LYS216, ARG259,

NDM-1; New Delhi metallo-β-lactamase-1, OXA-23; Oxacillinase-23

comprehensive approach, a total of 10 distinct binding models were generated for each complex analyzed.

To visualize and analyze these generated models, PyMol and Schrödinger Maestro were employed, both of which are powerful tools in molecular visualization (25-26). The analysis process involved creating two-dimensional interaction diagrams in Schrödinger Maestro. These diagrams were constructed based on carefully defined parameters, which included a maximum hydrogen bond distance of 2.8 Å to ensure relevant interactions were captured, a minimum donor angle of 120.0° to optimize the spatial orientation of hydrogen bond donors, and a minimum acceptor angle of 90.0° to maintain effective interaction geometry. This structured approach facilitated a thorough evaluation of the binding interactions within the complexes, providing insight into their potential biological implications.

3. RESULTS

The quality of the generated homology models for NDM-1 and OXA-23 was rigorously assessed using a combination of validation tools, and the results are summarized in Table 1.

In this study, an in-depth examination of the molecular interactions between imipenem and meropenem with two distinct classes of β-lactamases: the class D OXA-23 and the class B NDM-1 were conducted. Utilizing both crystallographic structures and homology models of these enzymes, molecular docking to elucidate the binding characteristics of these antibiotics was performed . A comparative analysis was performed between the docking poses generated in this work and the native ligand conformations observed in the relevant crystal structures retrieved from the Protein Data Bank (PDB) (Table 2).

4.DISCUSSION

The models demonstrated a high degree of reliability, as evidenced by their scores across all metrics. The ERRAT scores for NDM-1 and OXA-23, respectively, indicate a high-quality model with a significant percentage of the protein structure falling within the 91% rejection limit. Similarly, the VERIFY3D analysis showed that over 80% of the residues for both models had an averaged 3D-1D score of >0.2, confirming that the models' 3D structures are consistent with their amino acid sequences (Table 1).

Further validation by PROCHECK confirmed the stereochemical quality of the models. The Ramachandran plots revealed that residues for the NDM-1 model and for the OXA-23 model were located in the most favored regions, with no residues in the disallowed regions. This favorable residue distribution highlights the stereochemical accuracy of the generated models. The built-in quality assessment tools from Swiss-Model also supported these findings, with high Global Model Quality Estimation (GMQE) scores of and for NDM-1 and OXA-23, respectively. Collectively, these validation results confirm that the generated homology models are of high quality and reliable for subsequent analyses.

The extensive binding energy calculations to quantify the strength of the interactions were carried out. Our comparative analysis revealed that while the binding energies of imipenem and meropenem showed only minimal differences across the various systems studied, a significant anomaly in the binding profile of the OXA-23-imipenem complex was identified. Notably, the binding energy derived from the crystal structure of OXA-23 was markedly lower at – 8.06 kcal/mol compared to the binding energy of the homology model, which registered at – 5.34 kcal/mol (Table 2). This discrepancy implies that the binding affinity of imipenem to the OXA-23 enzyme is notably enhanced in the experimentally determined crystal structure, highlighting the importance of accurate structural representation in predicting molecular interactions.

To enable comparison, the interactions of imipenem and meropenem with both a homology model and the crystal structure of NDM-1 were analyzed using 2D diagrams,

alongside the interaction diagram of the native complex from the Protein Data Bank (PDB).

Two-dimensional structure of the NDM-1 (homology model) – Imipenem complex, highlighting the intricate molecular interactions that imipenem forms within the active site of the NDM-1 enzyme. In this analysis, it was found that imipenem establishes critical hydrogen bonds with the residues located at positions ASP124, ASN220, and LYS211 in the NDM-1 sequence, which play a pivotal role in stabilizing the drug-enzyme interaction (Figure 1a). Similar interaction poses were also observed in the molecular docking study performed using the experimental structure of NDM-1. Furthermore, analysis of the crystal structure from the Protein Data Bank (PDB) revealed that this binding mode is largely conserved (Figure 1c). Beyond these primary interactions, additional amino acids surrounding the active site are predicted to engage in weaker interactions, further contributing to the overall binding stability. Notably, the interacting residues collectively create a negatively charged polar hydrophobic binding pocket, which is essential for accommodating the imipenem molecule. In the context of NDM-1 (New Delhi metallo-beta-lactamase-1), Lysine 211 (Lys211) is a crucial amino acid residue that plays a significant role in the enzyme's catalytic activity and broad substrate specificity. The NDM-1 enzyme relies on zinc ions in its active site to hydrolyze and inactivate beta-lactam antibiotics (27).

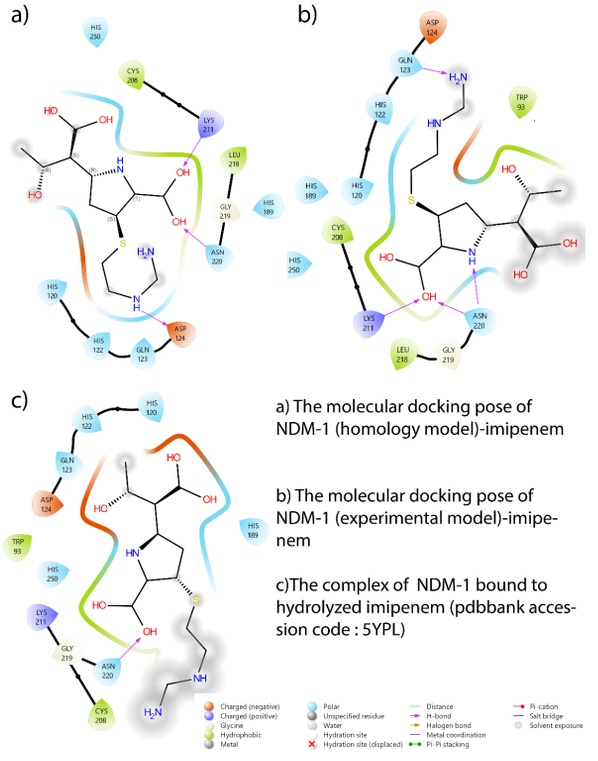

Figure 1. *Two-dimensional schematic representation of protein-ligand binding modes a) NDM1 (homology model)-Imipenem, b) NDM1 (experimental model)-Imipenem, c) The complex of NDM1-Imipenem (pdb code: 5YPL)*

The structural representation of the NDM-1 (homology model) – Meropenem complex, along with an analysis of the interaction profile of meropenem. Unlike imipenem, meropenem does not form direct hydrogen bonds with any of the NDM-1 residues; however, the presence of weak molecular interactions—including Van der Waals forces and hydrophobic contacts—significantly contributes to the stabilization of the complex. Furthermore, analysis of the post-docking pose in the experimental model revealed a hydrogen bond with Lys211 (Figure 2b). Upon examining the structure of the NDM-1-meropenem complex from the Protein Data Bank (PDB), it was observed that while the overall binding cavity was consistent with previous findings, meropenem formed hydrogen bonds with residues Asp124, Asn220, and Lys211, based on established hydrogen bonding criteria (Figure 2c). The binding site for meropenem mirrors that of the imipenem complex, characterized by a negatively charged polar hydrophobic pocket that is critical for binding efficacy.

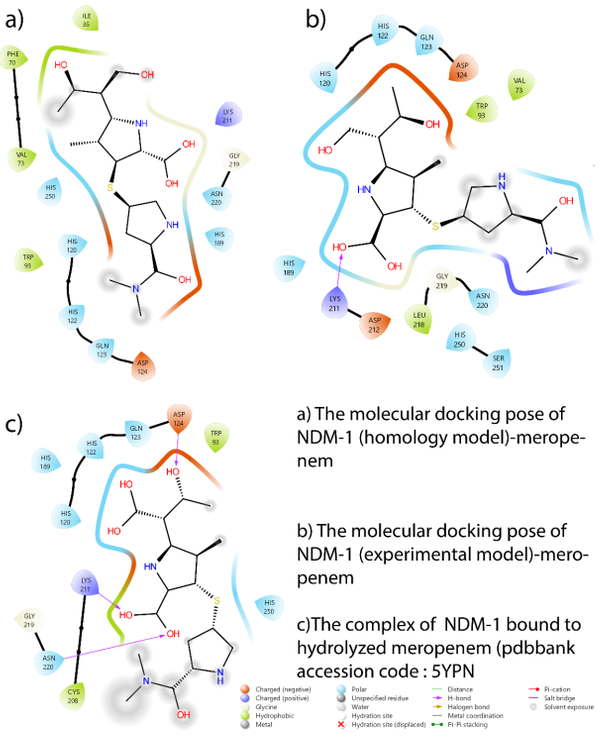

Figure 2. *Two-dimensional schematic representation of protein-ligand binding modes a) NDM1 (homology model)-Meropenem, b) NDM1 (experimental model)-Meropenem, c) The complex of NDM1-Meropenem (pdb code: 5YPN)*

The two-dimensional interaction map of the OXA-23 (homology model) – Imipenem complex was shown. Here, imipenem establishes a direct hydrogen bond with the residue located at ARG259 in the OXA-23 enzyme, which is crucial for effective binding (Figure 3a). In addition to this strong interaction, other amino acids within the proximity of the binding site support the interaction through weaker forces. Based on the 2D analysis of the post-docking results from the experimental model, imipenem formed hydrogen bonds with Val128, Thr217, and Arg259. For the control

group structure, meropenem was observed to form hydrogen bonds with Ser79 and Arg259 (Figure 3b-c). The interaction site of OXA-23 is formed as a polar hydrophobic binding cavity, optimizing the fit of the imipenem molecule.

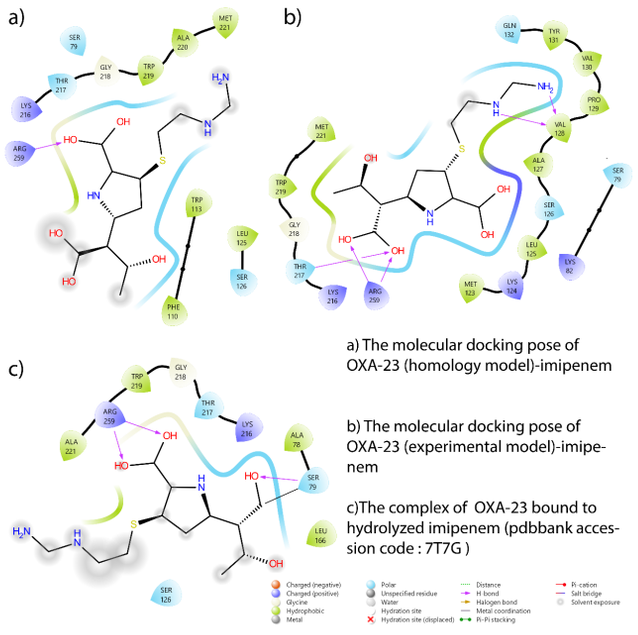

Figure 3. *Two-dimensional schematic representation of protein-ligand binding modes a) OXA-23 (homology model) – Imipenem, b) OXA-23 (experimental model) – Imipenem, c) The complex of OXA-23 – Imipenem (pdb code: 7T7G)*

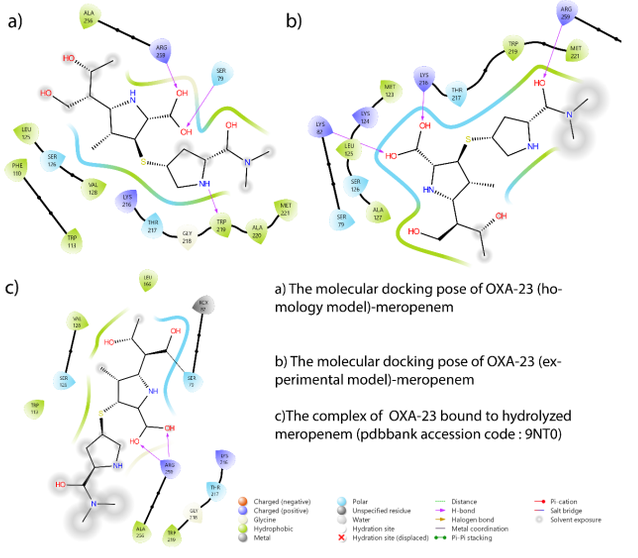

Figure 4. *Two-dimensional schematic representation of protein-ligand binding modes a) OXA-23 (homology model) – Meropenem, b) OXA-23 (experimental model) – Meropenem, c) The complex of OXA-23 – Meropenem (pdb code: 7T7G)*

Finally, Figure 4 provides a detailed structural analysis of the OXA-23/Meropenem complex. In this complex (homology model), meropenem forms significant hydrogen bonds with the residues SER79, TRP219, and ARG259 in the OXA-23 enzyme, which not only stabilizes the binding but also enhances the overall affinity of the complex (Figure 4a). Weak interactions from surrounding amino acids further augment this binding process. Docking analysis of meropenem to the experimental model revealed hydrogen bond interactions with Lys82, Lys216, and Arg259. Conversely, the control group complex exhibited a single hydrogen bond interaction, exclusively with Arg259 (Figure 4b-c). The binding site of OXA-23 is also organized as a polar hydrophobic pocket, showcasing structural similarities to the NDM-1 complex and illustrating the strategic nature of these interactions in antibiotic binding and efficacy. Arg259 is a fundamental part of the OXA-23 active site, playing a direct role in substrate binding and orientation. Its interactions are essential for the enzyme's carbapenemase activity, making it a critical residue to consider in the design of new inhibitors aimed at overcoming antibiotic resistance (28).

5. CONCLUSION

This study conducted a comprehensive comparative analysis of computational and experimental models to examine the binding interactions between carbapenem antibiotics (imipenem and meropenem) and β-lactamase enzymes (NDM-1 and OXA-23). Molecular docking studies revealed distinct binding characteristics for each enzyme. In the case of NDM-1, the binding pocket was found to consist of polar, hydrophobic, and partially charged residues, forming a well-defined active site. Imipenem demonstrated specific hydrogen bonding interactions with ASP124, ASN220 and LYS211 residues, while additional weaker interactions contributed to complex stabilization. Notably, the computational models showed strong agreement with experimental data, confirming a consistent binding mode. For OXA-23, structural analysis identified a predominantly hydrophobic binding cavity containing charged residues. While imipenem formed a hydrogen bond with ARG259, meropenem exhibited more extensive interactions with SER79, TRP219 and ARG259. Both computational and experimental approaches confirmed similar binding geometries for the antibiotics in OXA-23, suggesting a conserved recognition mechanism. The comparative analysis highlighted key differences between the enzymes, with NDM-1 displaying a more polar character in its binding site compared to the more hydrophobic nature of OXA-23's active site. Importantly, both enzymes maintained consistent binding architectures across different analytical methods, with minor variations reflecting their distinct catalytic requirements. These findings provide valuable structural insights that could inform the development of new β-lactamase inhibitors and strategies to overcome carbapenem resistance. The strong correlation between computational predictions and experimental observations validates the integrated approach used in this study for investigating antibiotic-enzyme interactions at the molecular level. Despite these valuable insights, this study is limited by its reliance on a purely computational model, which may not fully capture the dynamic complexity of biological systems.

Therefore, future work will focus on validating these findings through *in vitro* and *in vivo* experiments to further our understanding of the binding mechanisms and to inform the rational design of new inhibitors.

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Research idea: ES, GA
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Acquisition of data for the study: ES, GA
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Interpretation of data for the study: ES, GA
Drafting the manuscript: ES, GA
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REFERENCES

[1] Rahman M, and Khan MKA. In silico based unraveling of New Delhi metallo-β-lactamase (NDM-1) inhibitors from natural compounds: a molecular docking and molecular dynamics simulation study. Journal of Biomolecular Structure and Dynamics. 2020; 38(7):2093-2103. https://doi.org/10.1080/07391.102.2019.1627248

[2] Ali A, Gupta D, Srivastava G, Sharma A, Khan AU. Molecular and computational approaches to understand resistance of New Delhi metallo β-lactamase variants (NDM-1, NDM-4, NDM-5, NDM-6, NDM-7)-producing strains against carbapenems. Journal of Biomolecular Structure and Dynamics. 2019;37(8)2061-2071. https://doi.org/10.1080/07391.102.2018.1475261

[3] Zmarlicka MT, Nailor MD, Nicolau DP. Impact of the New Delhi metallo-beta-lactamase on beta-lactam antibiotics. Infection and Drug Resistance. 2015;8:297-309. https://doi.org/10.2147/IDR.S39186

[4] Chiou J, Leung TYC, Chen S. Molecular mechanisms of substrate recognition and specificity of New Delhi metallo-β-lactamase. Antimicrobial Agents and Chemotherapy. 2014;58(9):5372-5378. https://doi.org/10.1128/aac.01977-13

[5] Kar B, Kundu CN, Pati S, Bhattacharya, D. Discovery of phyto-compounds as novel inhibitors against NDM-1 and VIM-1 protein through virtual screening and molecular modelling. Journal of Biomolecular Structure and Dynamics. 2023;41(4):1267-1280. https://doi.org/10.1080/07391.102.2021.2019125

[6] Rolain J, Parola P, and Cornaglia G. New Delhi metallo-beta-lactamase (NDM-1): towards a new pandemia? Clinical Microbiology and Infection. 2010;16(12):1699-1701. https://doi.org/10.1111/j.1469-0691.2010.03385.x

[7] Nagulapalli Venkata, KC, Ellebrecht M, Tripathi SK. Efforts towards the inhibitor design for New Delhi metallo-beta-lactamase (NDM-1). European Journal of Medicinal Chemistry. 2021;225:113747. https://doi.org/10.1016/j.ejmech.2021.113747

[8] Smith CA, Antunes NT, Stewart NK, Toth M, Kumarasiri M, Chang M, Mobashery S, Vakulenko SB. Structural basis for carbapenemase activity of the OXA-23 β-lactamase from Acinetobacter baumannii. Chemistry & Biology. 2013;20(9):1107-1115. https://doi.org/10.1016/j.chembiol.2013.07.015

[9] Arrigoni R, Ballini A, Santacroce L, Palese LL. The Dynamics of OXA-23 β-Lactamase from Acinetobacter baumannii. International Journal of Molecular Sciences. 2023;24(24):17527. https://doi.org/10.3390/ijms242417527

[10] Torol S, Kasap M. Purification and characterization of OXA-23 from Acinetobacter baumannii. Journal of Enzyme Inhibition and Medicinal Chemistry. 2013;28(4):836-842. https://doi.org/10.3109/14756.366.2012.689296

[11] Paggi JM, Pandit A, Dror RO. The art and science of molecular docking. Annual Review of Biochemistry. 2024;93(1):389-410. https://doi.org/10.1146/annurev-biochem-030.222.120000

[12] Stanzione F, Giangreco I, Cole and JC. Use of molecular docking computational tools in drug discovery. Progress in Medicinal Chemistry. 2021;60: p. 273-343. https://doi.org/10.1016/bs.pmch.2021.01.004

[13] Waterhouse A, Bertoni M, Bienert S, Studer G, Tauriello G, Gumienny R, Heer TF, Beer TAP, Rempfer C, Bordoli L, Lepore R, Schwede T. Swiss-Model: homology modelling of protein structures and complexes. Nucleic Acids Res. 2018;46(W1):W296-w303. https://doi.org/10.1093/nar/gky427

[14] Bienert S, Waterhouse A, De Beer TA, Tauriello G, Studer G, Bordoli L, Schwede T. The Swiss-Model repository-new features and functionality. Nucleic Acids Research. 2017;45(D1): D313-319. https://doi.org/10.1093/nar/gkw1132

[15] Guex N, Peitsch MC, Schwede T. Automated comparative protein structure modeling with Swiss-Model and Swiss-PdbViewer: a historical perspective. Electrophoresis. 2009;30 Suppl 1: 162-173. https://doi.org/10.1002/elps.200900140

[16] Studer G, Rempfer C, Waterhouse AM, Gumienny R, Haas J, Schwede T. QMEANDisCo-distance constraints applied on model quality estimation. Bioinformatics, 2020;36(6):1765-1771. https://doi.org/10.1093/bioinformatics/btz828

[17] Bertoni M, Kiefer F, Biasini M, Bordoli L, Schwede T. Modeling protein quaternary structure of homo – and hetero-oligomers beyond binary interactions by homology. Scientific reports. 2017;7(1):10480. https://doi.org/10.1038/s41598.017.09654-8

[18] Colovos C, Yeates TO. Verification of protein structures: patterns of nonbonded atomic interactions. Protein Sci. 1993;2(9):1511-1519. https://doi.org/10.1002/pro.556.002.0916

[19] Bowie JU, Lüthy R, Eisenberg D. A method to identify protein sequences that fold into a known three-dimensional structure. Science 1991;253(5016):164-170. https://doi.org/10.1126/science.1853201

[20] Lüthy R, Bowie JU, Eisenberg D. Eisenberg, Assessment of protein models with three-dimensional profiles. Nature. 1992;356(6364):83-85. https://doi.org/10.1038/356083a0

[21] Laskowski RA, Rullmann JAC, MacArthur MW, Kaptein R, Thornton JM. AQUA and PROCHECK-NMR: programs for checking the quality of protein structures solved by NMR. J Biomol NMR. 1996;8(4):477-486. https://doi.org/10.1007/BF00228148

[22] Laskowski RA, MacArthur MW, Moss DS, Thornton JM. Procheck: a program to check the stereochemical quality of protein structures. Journal of Applied Crystallography. 1993;26(2):283-291. https://doi.org/10.1107/S002.188.9892009944

[23] Sanner MF. Python: A programming language for software integration and development. J Mol Graph Model. 1999;17(1):57-61.

[24] Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, Olson AJ. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. J Comput Chem. 2009;30(16):2785-2791. https://doi.org/10.1002/jcc.21256

[25] PyMOL, in Version 2.0. Schrödinger. LLC.

[26] Schrödinger Release 2024-4: Maestro, S., LLC, New York, NY, 2024.

[27] King D, Strynadka N. Crystal structure of New Delhi metallo-β-lactamase reveals molecular basis for antibiotic resistance. Protein Science. 2011;20(9):1484-1491. https://doi.org/10.1002/pro.697

[28] Smith CA, Antunes NT, Stewart NK, Toth M, Kumarasiri M, Chang M, Vakulenko SB. Structural basis for carbapenemase activity of the OXA-23 β-lactamase from Acinetobacter baumannii. Chemistry & Biology. 2013;20(9):1107-1115. https://doi.org/10.1016/j.chembiol.2013.07.015.