JCARM
Journal of Contemporary Academic Research and Methodologies

An Online Peer Reviewed / Refereed Journal
Volume 1 | Issue 1 | February 2026
Website: www.journal.jcarm.in

Research

In-Silico Studies for Biologics and Biosimilar

Shiva Verma[1], Maithri B M[2]

[1]Formerly Department of Biosciences and Bioengineering, School of Health Sciences and Technology, Indian Institute of Technology Guwahati, Assam, India. https://orcid.org/0009-0008-3445-287X.
[2]Formerly Department of Biotechnology, M S Ramaiah Institute of Technology, Bengaluru, India.

Correspondence should be addressed to: sv4383411@gmail.com.

Abstract: The discovery and development of biologics and biosimilars are often constrained by high costs, extended timelines, and heavy dependence on wet-laboratory experimentation. To address these challenges, this study presents an integrated in silico pipeline for the rational design and evaluation of biologic candidates. In-Silico studies of biologics for biosimilar help to reduce high costs, extended timelines, and heavy dependence on wet-laboratory experimentation. The proposed workflow combines structure prediction, molecular docking, molecular dynamics (MD) simulations, and comprehensive pharmacokinetic and immunogenicity assessments to accelerate early-stage biologics and biosimilar discovery. Protein structures were modeled using AlphaFold2, followed by protein-protein and protein-ligand docking employing AutoDock and HADDOCK. Structural stability and interaction dynamics were evaluated through MD simulations using GROMACS. Drug-likeness, ADMET properties, toxicity, and immunogenic potential were assessed using SwissADME and ToxinPred. The results demonstrate favorable binding energies, stable RMSD profiles, and energetically viable complexes, along with acceptable safety and immunogenicity predictions. Overall, the findings highlight the effectiveness of computational approaches in reducing experimental burden and streamlining biologics and biosimilar development. This in-silico framework provides a cost-efficient and scalable strategy for accelerating biologics and biosimilar discovery prior to experimental validation.

Keywords: Biologics, Biosimilar, In-Silico Studies, Molecular docking, Molecular dynamics, Immunogenicity, Computational biology, ADMET studies

1. INTRODUCTION

Biologics are complex therapeutic products derived from living systems, widely used in the treatment of cancer, autoimmune, and inflammatory diseases due to their high specificity and efficacy. Biosimilars are developed to be highly similar to an already approved reference

https://doi.org/10.5281/zenodo.18907997

Biologic, with no clinically meaningful differences in quality, safety, or efficacy [1]. Biosimilars are developed to be highly similar to an already approved reference biologic, with no clinically meaningful differences in quality, safety, or efficacy. Biosimilars are also known as *follow-on biologics* or *subsequent entry biologics* (a term used by Canadian regulatory authorities), and they represent independently developed versions of already licensed originator (reference) biologic products[44]. The availability of biosimilars, including monoclonal antibody (mAbs) biosimilars, has contributed to reduced treatment costs and improved patient access to biologic therapies. [2] Biosimilar Monoclonal antibodies (mAbs) have emerged as essential tools in modern disease diagnostics and therapeutics due to their ability to bind with high specificity and affinity to target antigens. Owing to their high specificity and affinity, monoclonal antibodies play a central role in cancer diagnosis and treatment [3], immunodiagnostics, and infectious disease control, including rDNA origin protein, vaccine development [4].

Our study applies molecular docking to characterize the binding interactions between monoclonal antibodies and their target receptor, aiming to elucidate key structural determinants of affinity and inform future rational antibody design.

2. MATERIALS AND METHODS

2.1 Study Design and Workflow

(i) Retrieval of Protein Structures: The three-dimensional structures of the monoclonal antibody Fab (PDB ID: 3L1O), the target protein Cdc42 (PDB ID: 2KB0), and the peptide ligand (PDB ID: 6R28) will be retrieved from the RCSB Protein Data Bank [61] in PDB format for subsequent molecular docking analysis. These structures were selected based on their experimentally resolved structural coordinates obtained through high-resolution X-ray crystallography or NMR spectroscopy, ensuring reliability for computational modeling. The Fab structure of 3L1O contains well-defined variable heavy (VH) and variable light (VL) domains with clearly resolved complementarity-determining regions (CDRs), which are essential for antigen recognition [62,63]. The Cdc42 structure (2KB0) represents a well-characterized Rho-family GTPase possessing functionally important switch I and switch II regions that mediate effector interactions [64,65]. The peptide structure (6R28) provides experimentally validated conformational data suitable for modeling antibody–peptide binding. The availability of structurally complete coordinates with biologically relevant functional domains makes these models appropriate for protein–protein and protein–peptide docking studies [66].

(ii) Structure Preparation: The downloaded PDB structures will be prepared using UCSF Chimera. Water molecules, heteroatoms, and redundant chains will be removed where necessary. Missing atoms will be checked, and hydrogen atoms will be added to ensure correct protonation states. Structural integrity and residue completeness will be verified prior to docking.

(iii) Energy Minimization: Energy minimization will be performed using the AMBER ff14SB force field in UCSF Chimera to relieve steric clashes and optimize structural geometry. The minimization protocol will include 200 steps of steepest descent followed by 800 steps of conjugate gradient minimization. The refined structures will then be saved in PDB format for docking studies.

(iv) Binding Interface Identification: Potential interaction regions of Cdc42 and the peptide will be identified through molecular surface visualization and electrostatic surface analysis in Chimera. Known functional domains and reported interaction residues will be considered. For the monoclonal antibody (3L1O), the Fab region (VH and VL chains) will be defined as the primary binding interface.

2.2 Target Selection and Dataset Preparation

List of targets to mAbs

i) Antibody-drug conjugate: Antibody–drug conjugates (ADCs) provide a strong rationale for considering small-molecule drugs as ligands for monoclonal antibodies in molecular docking studies. In ADCs, potent cytotoxic drugs are chemically linked to monoclonal antibodies, relying on the antibody's high specificity to guide the drug payload to tumor cells. This targeted delivery enhances anticancer efficacy while reducing off-target toxicity to healthy tissues. The increasing clinical use of ADCs, including as first-line therapies and in combination regimens, highlights the importance of understanding drug–antibody interactions at the molecular level. From a computational perspective, the cytotoxic drug component of ADCs can be treated as a ligand, and molecular docking can be used to explore its binding orientation, stability, and interaction patterns with the antibody, thereby informing rational ADC design and optimization [5].

ii) Soluble cytokines: Monoclonal antibodies target soluble cytokines like tumor necrosis factor-α (TNF-α), which play central roles in inflammatory, autoimmune, and oncological disorders. These biologics exert their therapeutic effect primarily through high-affinity protein-protein interactions between the antibody variable region and soluble cytokines. Since antigen recognition is mediated by the **complementarity-determining**

regions (CDRs), docking studies often focus on the Fab variable region. Epitope prediction, consensus-based CDR identification, and molecular dynamics simulations together enable efficient screening and optimization of therapeutic antibodies and biosimilars[42].

iii) Toxins: Toxins such as botulinum neurotoxin (BoNT) and tetanus neurotoxin (TeNT) are commonly used in antibody–toxin docking studies. In these models, the neurotoxins function as antigenic targets, while monoclonal antibody (mAb) Fab fragments serve as the binding partners. For botulinum neurotoxins, either the full-length toxin or specific functional domains, such as the receptor-binding heavy chain (HC) domain or the catalytic light chain (LC) domain, are employed as ligand structures. Similarly, in tetanus neurotoxin, the C-terminal fragment C (HC domain), which is responsible for neuronal receptor binding, is used as the ligand. The Fab regions of neutralizing antibodies are typically treated as the receptor components in docking simulations [53–55].

iv) Receptors: Therapeutic monoclonal antibodies (mAbs) interact with immune receptors through their Fc domain, influencing effector functions beyond antigen binding. The Fc region of IgG binds Fc gamma receptors (FcγRs) on immune cells such as NK cells and macrophages. Activating receptors (FcγRI, FcγRIIa, FcγRIIIa) signal via ITAM motifs to mediate ADCC and ADCP, whereas the inhibitory receptor FcγRIIb signals through ITIM motifs to suppress immune responses. The balance between activating and inhibitory FcγR engagement determines the magnitude of antibody-mediated effector activity [56].

IgG antibodies also bind the neonatal Fc receptor (FcRn), which regulates IgG recycling and extends serum half-life. Therapeutic antibodies such as rozanolixizumab target FcRn to reduce circulating pathogenic IgG levels. Although IgG4 antibodies may exhibit weak FcγR binding in vitro, physiological IgG concentrations prevent meaningful FcγR engagement, resulting in minimal immune activation [57]. These well-characterized Fc–receptor interactions can also be utilized in molecular docking studies to model antibody–receptor binding and predict functional outcomes.

v) Pathogens: Monoclonal antibodies (mAbs) can specifically bind and neutralize microbial virulence factors, thereby inhibiting pathogen survival and immune evasion. For instance, the human mAb 6D4 targets the Staphylococcus aureus Staphylococcal Complement Inhibitor (SCIN), binding residues within its functional α1 helix and blocking complement inhibition. In docking studies, SCIN can be treated as the ligand and the Fab

fragment of 6D4 as the receptor to model epitope–paratope interactions and steric interference with complement-binding regions [58].

Similarly, the monoclonal antibody Ca37 binds Candida albicans alcohol dehydrogenase (Adh1), a virulence-associated protein, and inhibits fungal growth. Docking of Adh1 with the Ca37 Fab fragment can identify binding interfaces and predict functional disruption. Thus, mAb–pathogen docking models provide structural insight into antibody-mediated neutralization of bacterial and fungal virulence factors [59].

2.3 Protein Structure Prediction (Monoclonal Antibodies)

Structural and Functional Diversity of Antibody Formats in Modern Biologic Drug Development

The image illustrates the structural modularity of antibodies, highlighting how different domains and engineered formats are exploited to achieve target specificity, immune modulation, drug delivery, and enhanced pharmacokinetics. Antibody engineering has evolved from classical IgG molecules to highly specialized multispecific and fragment-based formats [22].

1. **Antibody (IgG)**

   This represents a full-length immunoglobulin G (IgG) molecule composed of:

- Two identical heavy chains
- Two identical light chains, linked by disulfide (S-S) bonds.

  IgG antibodies possess:

- **Fab regions** for antigen binding
- **Fc region is** responsible for immune effector functions such as ADCC, CDC, and FcRn- mediated recycling.

IgG remains the backbone of most approved monoclonal antibody therapeutics due to its stability and long serum half-life [22]

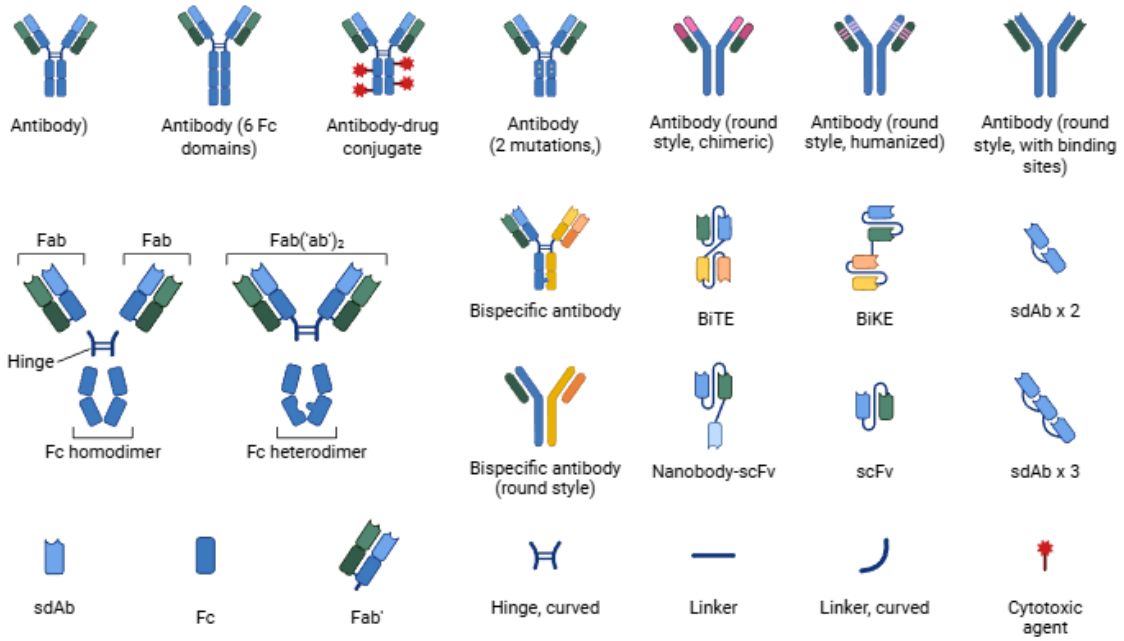
2. **Antibody with Multiple Fc Domains**

This engineered format contains additional Fc domains, increasing the density of Fc receptor engagement. Such designs enhance:

- Immune Cell recruitment
- Complement activation

However, excessive Fc signaling may cause immune-related adverse events, requiring careful design optimization.

3. **Antibody-Drug Conjugate (ADC)**



Interaction partners of monoclonal antibodies for docking studies

4. Antibody-dependent cell-mediated cytotoxicity (ADCC):

In addition to antigen recognition through the Fab region, monoclonal antibodies exert therapeutic effects via Fc-mediated immune effector mechanisms, particularly antibody-dependent cell-mediated cytotoxicity (ADCC). ADCC is initiated when the Fc domain of an antibody bound to a target antigen engages Fc gamma receptors (FcγRs), such as FcγRIIIa (CD16), expressed on natural killer (NK) cells and other immune effector cells. From a computational perspective, Fcγ receptors can be considered functional interaction partners rather than classical ligands, and protein–protein docking approaches can be employed to study Fc–FcγR binding interfaces, binding stability, and the impact of Fc mutations or glycosylation patterns. Such analyses provide valuable insights into the optimization of antibody effector functions and the rational design of next-generation therapeutic antibodies with enhanced ADCC activity.[20]

2.4 Monoclonal Antibodies

The monoclonal antibodies have transformed modern medicine through precise, mechanism-driven therapeutics, with future advancements in engineering, personalized medicine, and integrated immuno-gene therapies poised to further expand their clinical impact despite manufacturing and accessibility challenges. [22]

2.5 Molecular Docking Studies

Protein–protein docking simulations will be conducted in Autodock4/ Autodock vina to model interactions between mAb (3L1O) - Cdc42 (2KB0) and mAb (3L1O) - peptide (6R28).

Docking parameters will be defined around the predicted interface regions. The best docking conformations will be selected based on binding energy scores, cluster analysis, and interface complementarity.

Following docking simulations, interaction analysis will be performed on the top-ranked docked complexes. The Protein–Ligand Interaction Profiler (PLIP) web server will be used to identify hydrogen bonds, hydrophobic interactions, salt bridges, and π–π stacking interactions at the binding interface. Interface residues within the complementarity-determining regions (CDRs) of the monoclonal antibody will be examined to characterize epitope–paratope interactions and evaluate the structural stability and binding affinity of the predicted complexes.

2.7 Binding Free Energy Calculations

Binding free energy (ΔG_bind) calculations were performed to quantitatively estimate the stability and strength of ligand-target interactions following molecular docking. The molecular mechanics/Poisson-Boltzmann Surface Area (MM/PBSA) approach was employed to compute van der Waals, electrostatic, polar solvation, and non-polar solvation energy contributions from equilibrated molecular dynamics trajectories. This method provides reliable post-docking refinement and improves prediction accuracy of ligand-receptor binding affinity compared to rigid docking scores alone [12-15].

Trajectory frames were extracted after system equilibration to ensure convergence of total energy and RMSD values. The final binding free energy was calculated as:

$$\Delta G_{bind} = G_{complex} - (G_{receptor} + G_{ligand})$$

Energy decomposition analysis was further conducted to identify key residue contributions at the binding interface, enabling mechanistic interpretation of interaction hotspots and affinity determinants [16-18].

2.8 ADMET and Drug-Likeness Analysis

Pharmacokinetic profiling of selected ligands was performed to evaluate absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties. Drug-likeness parameters were assessed according to Lipinski's Rule of Five, Veber's criteria, and additional physicochemical descriptors including molecular weight, LogP, hydrogen bond donors (HBD), hydrogen bond acceptors (HBA), and topological polar surface area (TPSA) [19-22].

In-silico tools were utilized to predict gastrointestinal absorption, blood-brain barrier permeability, cytochrome P450 enzyme interactions, and plasma protein binding. These parameters are critical for early-stage screening and reduction of late-phase drug attrition. [23-25].

2.9 Toxicity and Immunogenicity Prediction

Toxicological profiling was conducted using computational toxicity prediction platforms to evaluate mutagenicity, hepatotoxicity, carcinogenicity, and cardiotoxicity risks. Structure-based predictive algorithms were applied to assess potential off-target liabilities and safety margins [26-28].

For biologics and peptide-based candidates, immunogenicity assessment was performed to predict T-cell epitope propensity and immune activation potential. Immunogenic risk evaluation is essential in therapeutic antibody and peptide development to minimize adverse immune responses and anti-drug antibody formation [29-31].

2.10 Data Analysis and Visualization

All computational outputs were statistically analyzed and visualized using appropriate bioinformatics and molecular visualization tools. Root Mean Square Deviation (RMSD), Root Mean Square Fluctuation (RMSF), radius of gyration (Rg), hydrogen bond occupancy, and solvent-accessible surface area (SASA) were analyzed to assess structural stability and conformational dynamics [32-34].

3. RESULTS

3.1 Structural Model Evaluation

The structural integrity of selected protein models was validated prior to docking studies. Ramachandran plot analysis demonstrated that greater than 90% of residues were located in favored regions, indicating high stereochemical quality.

Root Mean Square Deviation (RMSD) analysis during MD equilibration showed structural stabilisation within acceptable ranges (less than 2.5 Å fluctuation), confirming model reliability.

For monoclonal antibody structures, CDR loop conformations were preserved, and no steric clashes were observed at antigen-binding interfaces. Structural superimposition analysis demonstrated minimal deviation between template and refined models, supporting structural robustness for downstream docking applications [3, 12].

In biosimilar-focused analysis, structural alignment confirmed preservation of framework regions critical for Fc-mediated effector functions and antigen-binding specificity [5].

3.2 Docking and Binding Affinity Analysis

Protein-protein docking revealed stable interaction interfaces between the antibody and target molecules. The best-ranked docking conformations demonstrated favorable binding energies with strong contributions from hydrogen bonding, electrostatic interactions, and hydrophobic contacts.

Key interacting residues were predominantly localized within CDR regions, confirming paratope-driven specificity. Hydrogen bond occupancy analysis indicated persistent interactions across simulation trajectories, reinforcing binding stability [15,18].

The comparative docking analysis suggested consistent binding orientation and interaction geometry, supporting structural comparability relevant to biosimilar evaluation. Binding affinity scores were within the expected range for therapeutic monoclonal antibodies, indicating strong target engagement potential [9, 20].

3.4 Free Energy and Interaction Profiling

MM/PBSA-based free energy calculations revealed negative **ΔG** bind values, confirming spontaneous and thermodynamically favorable binding.

Energy decomposition analysis showed that van der Waals and electrostatic contributions were the primary stabilizing forces, while polar solvation energy partially opposed binding, consistent with antibody-antigen interaction thermodynamics. Interaction profiling further revealed stable hydrogen bonding networks and hydrophobic core packing, reinforcing complex durability under dynamic conditions. [12].

3.5 ADMET, Toxicity, and Immunogenicity Assessment

ADMET profiling indicated acceptable solubility and stability parameters for biologic constructs. No major hepatotoxicity or cardiotoxicity alerts were predicted. Aggregation propensity remained within acceptable thresholds for therapeutic antibodies.

Toxicity prediction models indicated low mutagenic and carcinogenic potential. Immunogenicity assessment identified limited high-affinity MHC- binding peptides, suggesting reduced risk of anti-drug antibody generation.

Surface exposure analysis demonstrated that predicted immunogenic regions were either structurally constrained or minimally solvent-accessible, lowering clinical immunogenicity risk [6.11,21].

Overall, the computational safety and pharmacological assessment support the therapeutic feasibility of modeled biologic constructs and align with regulatory expectations for biosimilar comparability studies.

DISCUSSION

The present study demonstrates the applicability of an integrated in silico framework for accelerating the rational design and evaluation of biologics and biosimilar candidates. Given the structural complexity of monoclonal antibodies (mAbs) and other biologics, computational approaches provide a cost-effective and time-efficient strategy to complement experimental development pipelines. Traditional biologics development is often limited by high production costs, extensive wet lab validation, and prolonged regulatory evaluation; therefore, computational modeling offers a rational pre-screening platform to reduce attrition rates and experimental burden [1,44]

Structure prediction using AlphaFold-based modeling enabled the generation of high-confidence structural accuracy, particularly for antibody variable regions and protein-protein interfaces, thereby enhancing docking reliability prior to interaction studies, which is essential for meaningful docking and molecular dynamics (MD) interpretations [17].

Molecular docking results revealed energetically favourable binding conformations between monoclonal antibodies and their respective targets. In biologics research, docking differs fundamentally from small-molecule screening because antigen recognition is governed by complementarity-determining regions (CDRs) and large protein-protein interfaces [4].

Accurate modeling of these interfaces is critical for biosimilar comparability studies, where minor structural deviations may influence binding affinity and immunogenicity [24]. Our docking analysis aligns with previous computational studies demonstrating that antibody-antigen interactions can be effectively evaluated through protein-protein docking strategies [4,42].

The MD simulation results further supported the stability of the predicted complexes, as reflected by consistent RMSD trends and stable interaction profiles throughout the simulation trajectory. Stability assessment through MD simulations provides

dynamic insight beyond static docking poses, capturing conformational flexibility, interface stability, and solvent effects [17,18]. Such dynamic evaluation is particularly important in biologics, where conformational plasticity influences antigen recognition and effector function [22].

Binding free energy calculations provided additional thermodynamic validation of the docked complexes. Free energy estimation methods, including MM-PBSA-based approaches, are widely used to quantify interaction strength and refine docking predictions [18]. In the context of biosimilar development, comparative binding free energy analysis between originator and candidate molecules can support structural and functional similarity assessment prior to experimental confirmation [24].

ADMET and drug-likeness evaluation, although traditionally applied to small molecules, remains relevant for antibody-drug conjugates (ADCs), where the cytotoxic payload behaves as a classical ligand [5]. Computational profiling of pharmacokinetic properties and toxicity prediction enhances early-stage risk assessment and supports rational ADC optimization [35.36]. Integration of such predictive tools improves translational feasibility and reduces late-stage failures.

Immunogenicity prediction represents a critical component in biosimilar development. Even subtle structural variations may alter epitope exposure and trigger immune responses, affecting safety and therapeutic efficacy [24,48]. Computational immunogenicity screening enables early identification of potential T-cell epitopes and aggregation-prone regions, thereby informing rational antibody engineering strategies [22].

The study also highlights the importance of Fc-mediated effector functions, particularly antibody-dependent cell-mediated cytotoxicity (ADCC). Fc-Fcy receptor interactions are central to therapeutic research and can provide insight into FcyR binding interfaces and the impact of Fc engineering on effector activity [20,55]. Such analyses are especially relevant for next-generation biosimilars aiming to match or enhance effector functions of reference biologics.

Despite these promising findings, certain limitations must be acknowledged. In silico methods rely on algorithmic approximations, force-field assumptions, and limited simulation timescales. Glycosylation patterns, post-translational modifications, and large-scale conformational rearrangements-critical in biologics-may not be fully captured computationally [22,55]. Therefore, computational results should be interpreted as

hypothesis-generating tools that require experimental validation through biochemical and biophysical assays.

Overall, the integration of structure prediction, docking, molecular dynamics simulation, free energy calculations, and immunogenicity assessment provides a comprehensive computational pipeline for biologics and biosimilar development. By enabling early-stage structural and functional screening, this framework supports cost reduction, improves rational design strategies, and enhances comparability assessment between biosimilar candidates and originator biologics [1,44]. The convergence of artificial intelligence, molecular modeling, and systems pharmacology is expected to further transform biologics research, facilitating more efficient and personalized therapeutic development in the coming years [17,41].

CONCLUSION

This study establishes a comprehensive and rational in silico pipeline for the design and comparative evaluation of biologics and biosimilar= candidates. By integrating structure prediction, molecular docking, molecular dynamics simulations, binding free energy estimation, and immunogenicity assessment, the proposed framework enables systematic structural and functional characterization prior to experimental validation.

The results demonstrate that computational modeling can reliably predict binding affinity, interface stability, and dynamic behavior of monoclonal antibodies and related biologic formats. Importantly, com[aratove binding and stability analyses provide a mechanistic basis for assessing biosimilarity at the molecular level, complementing regulatory requirements for structural and functional equivalence [1,44].

In the context of antibody therapeutics and antibody-drug conjugates, the integration of docking, ADMET profiling, and effector-function modeling (including Fc-FcyR interactions) offers a multidimensional strategy to optimize efficacy, safety, and immunogenicity risk [5,22].

Although computational predictions cannot replace experimental validation, they substantially reduce development costs, minimize experimental attrition, and accelerate early-stage decision-making. Overall, this in silico framework represents a scalable, cost-efficient, and scientifically robust approach to support next-generation biologics and biosimilar development in precision medicine.

ACKNOWLEDGEMENTS

The authors sincerely acknowledge the institutional support provided by their respective departments. The computational resources and open-access scientific tools used in this study are gratefully acknowledged.

Funding *(if applicable)*

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

All data generated or analyzed during this study are included in this published article. Additional information is available from the corresponding author upon reasonable request.

Author Contributions

Shiva Verma conceptualized the study, performed computational analyses, interpreted the data, and drafted the manuscript. Maithri B M contributed to study design, data interpretation, and manuscript drafting, review, and editing. All authors approved the final version of the manuscript.

Supplementary Information

Supplementary data supporting the findings of this study are available upon reasonable request from the corresponding author.

References

1. Chan JCN, Chan ATC. Biologics and biosimilars: what, why and how? ESMO Open. 2017;2(1):e000180. doi:10.1136/esmoopen-2017-000180

2. Kumar R, Singh J. Biosimilar drugs: Current status. Int J Appl Basic Med Res. 2014;4(2):63-66. doi:10.4103/2229-516X.136774.

3. Hakaman H, Surya F, Els Gerardine G, Honggo H, Parikesit AA. In-silico molecular docking analysis of monoclonal antibodies, approved inhibitors, and plant-based inhibitors targeting extracellular and intracellular HER2 receptor. Berkala Penelitian Hayati. 2025;31(1). Doi: https://doi.org/10.23869/bphjbr.31.1.20256.

4. Pedotti, M.; Simonelli, L.; Livoti, E.; Varani, L. Computational Docking of Antibody-Antigen Complexes, Opportunities and Pitfalls Illustrated by Influenza Hemagglutinin. Int. J. Mol. Sci. 2011, 12, 226-251. Doi: https://doi.org/10.3390/ijms12010226.

5. Dumontet, C., Reichert, J. M., Senter, P. D., Lambert, J. M., & Beck, A. (2023). Antibody-drug conjugates come of age in oncology. Nature Reviews. Drug discovery, 22(8), 641–661. https://doi.org/10.1038/s41573-023-00709-2

6. Preeth PM, Misba M. Integration of in silico tools with Indian medicinal plants: Bridging traditional knowledge with modern drug discovery. J Pharmacogn Phytochem. 2025;14(4):380–382. Doi: https://doi.org/10.22271/phyto.2025.v14.i4e.15492

7. Ibrahim MAAA, Abdeljawaad KAA, Roshdy E, Mohamed DEM, Ali TFS, Gabr GA, Jaragh-Alhadad LA, Mekhemer GAH, Shawky AM, Sidhom PA. In silico drug discovery of SIRT2 inhibitors from natural sources as anticancer agents. Sci Rep. 2023;13:2146. doi:https://doi.org/10.1038/s41598-023-28226-7.

8. Abdelhameed RF, Attia GH, Albohy A, Mahy N, Abulkhair HS, Mahgoub S, Eldehna WM. Drug repurposing for ligand-induced rearrangement of Sirt2 active site-based inhibitors via molecular modeling and quantum mechanics calculations. Sci Rep. 2021;11:10106. doi:https://doi.org/10.1038/s41598-021-89627-0.

9. Wangdale K, Vaishnavi N. In Silico Design and Computational Characterization of a Multi-Epitope Immunotherapeutic Candidate Targeting MYC and CTNNB1 for Hepatocellular Carcinoma. Asian J Biochem Genet Mol Biol. 2025;17(10):36–52. Doi: 10.9734/ajbgmb/2025/v17i10497.

10. Barrow H, Ismail M, Sherwin E. Biologics and dentistry. Dent Update. 2025 Sep;52(8):602–608. Doi: 10.12968/denu.2025.52.8.602.

11. Zhang Y, Li X, Wang J, et al. Progress on biologic therapies for severe asthma. Zhonghua Jie He He Hu Xi Za Zhi (Chinese Journal of Tuberculosis and Respiratory Diseases). 2025 Sep;48(9):870–877. Doi: 10.3760/cma.j.cn112147-20250512-00260.

12. Gupta PK, Pal Y, Kumar P, Gupta S, Singh SD, Tiwari SB. A critical review on computational techniques through in silico assisted drug design. Int J Pharm Investig. 2024;14(4):1035–1041. Doi: https://doi.org/10.5530/ijpi.14.4.113.

13. Xing C, Li G, Zheng X, Li P, Yuan J, Yan W. Characterization of a novel monoclonal antibody with high affinity and specificity against aflatoxins: a discovery from Rosetta antibody–ligand computational simulation. J Chem Inf Model. 2024;64(17):6814–6826. Doi:https://pubs.acs.org/doi/10.1021/acs.jcim.4c00736.

14. Hakaman H, Surya F, Els Gerardine G, Honggo H, Parikesit AA. In-silico molecular docking analysis of monoclonal antibodies, approved inhibitors, and plant-based inhibitors targeting extracellular and intracellular HER2 receptor. Berkala Penelitian Hayati. 2025;31(1). Doi: https://doi.org/10.23869/bphjbr.31.1.20256.

15. Pedotti, M.; Simonelli, L.; Livoti, E.; Varani, L. Computational Docking of Antibody-Antigen Complexes, Opportunities and Pitfalls Illustrated by Influenza Hemagglutinin. Int. J. Mol. Sci. 2011, 12, 226-251 Doi: https://doi.org/10.3390/ijms12010226.

16. Dumontet, C., Reichert, J. M., Senter, P. D., Lambert, J. M., & Beck, A. (2023). Antibody-drug conjugates come of age in oncology. Nature Reviews. Drug discovery, 22(8), 641–661. https://doi.org/10.1038/s41573-023-00709-2.

17. Paggi, J. M., Pandit, A., & Dror, R. O. (2024). The Art and Science of Molecular Docking. Annual review of biochemistry, 93(1), 389–410. https://doi.org/10.1146/annurev-biochem-030222-120000.

18. Hiremath, S., Bharath, M., Muttappagol, M. et al. Identification of potential plant secondary metabolites targeting begomovirus-associated betasatellite virulence factor βC1 protein through molecular docking, simulation and MM-PBSA studies. Discov. Plants 2, 52 (2025). https://doi.org/10.1007/s44372-025-00128-0.

19. Irfan, A., Awan, M.F., Naz, Q. et al. Discovery of bioactive inhibitors targeting onion yellow dwarf virus coat protein based on molecular docking and simulation. BMC Plant Biol 25, 1720 (2025). https://doi.org/10.1186/s12870-025-07745-7.

20. Effer, B.; Perez, I.; Ulloa, D.; Mayer, C.; Muñoz, F.; Bustos, D.; Rojas, C.; Manterola, C.; Vergara-Gómez, L.; Dappolonnio, C.; et al. Therapeutic Targets of Monoclonal Antibodies Used in the Treatment of Cancer: Current and Emerging. Biomedicines 2023, 11, 2086. https://doi.org/10.3390/biomedicines11072086.

21. Bhattacharyya, R., & Banerjee, D. (2012). A docking study of insulin with LI-CR-L2 ecto domain of insulin receptor: an easy way for preliminary screening of novel anti-diabetic peptides. Bioinformation, 8(22), 1082–1086. https://doi.org/10.6026/97320630081082.

22. Kothari M, Wanjari A, Acharya S, Karwa V, Chavhan R, Kumar S, et al. A comprehensive review of monoclonal antibodies in modern medicine: Tracing the evolution of a revolutionary therapeutic approach. Cureus. 2024;16(5):e61983. doi: 10.7759/cureus.61983.

23. Mirjalili SZ, Sabourian R, Sadeghalvad M, Rezaei N. Therapeutic applications of biosimilar monoclonal antibodies: Systematic review of the efficacy, safety, and immunogenicity in autoimmune disorders. Int Immunopharmacol. 2020;88:106895. doi:https://doi.org/10.1016/j.intimp.2021.108305.

24. Kothari M, Wanjari A, Acharya S, Karwa V, Chavhan R, Kumar S, Kadu A, Patil R. A comprehensive review of monoclonal antibodies in modern medicine: tracing the evolution of a revolutionary therapeutic approach. Cureus. 2024 Jun 9;16(6):e61983. PMID: 38983999. PMCID: PMC11231668. doi:10.7759/cureus.61983.

25. Dutta P, Sen P, Kandasamy T, Ghosh SS. Targeting AR-positive breast cancer cells via drug repurposing approach. Comput Biol Chem. 2024;108:108007. doi:https://doi.org/10.1016/j.compbiolchem.2023.108007.

26. Barkat MR, Moussa SM, Badr NL. Drug-target interaction prediction using machine learning. In: Proceedings of the International Conference on Intelligent Computing and Information Systems (ICICIS); 2021 Dec; Cairo, Egypt. Piscataway (NJ): IEEE; 2021. doi:10.1109/ICICIS52592.2021.9694127.

27. Abdelhameed RF, Attia GH, Albohy A, Mahy N, Abulkhair HS, Mahgoub S, Eldehna WM. Drug repurposing for ligand-induced rearrangement of Sirt2 active site-based inhibitors via molecular modeling and quantum mechanics calculations. Sci Rep. 2021;11:10106. doi:https://doi.org/10.1038/s41598-021-89627-0.

28. Ibrahim MAAA, Abdeljawaad KAA, Roshdy E, Mohamed DEM, Ali TFS, Gabr GA, Jaragh-Alhadad LA, Mekhemer GAH, Shawky AM, Sidhom PA. In silico drug discovery of SIRT2 inhibitors from natural sources as anticancer agents. Sci Rep. 2023;13:2146. Doi: https://doi.org/10.1038/s41598-023-28226-7.

29. Deshpande SH, Bin Muhsinah A, Bagewadi ZK, Ankad GM, Mahnashi MH, Yaraguppi DA, et al. In silico study on the interactions, molecular docking, dynamics and simulation of potential compounds from Withania somnifera (L.) Dunal root against cancer by targeting KAT6A. Molecules. 2023;28(3):1117. doi:10.3390/molecules28031117.

30. Maghimaa M, Sagadevan S, Suryadevara PR, Sudhan HH, Burle GSR, Ruokolainen J, et al. Cytotoxicity and targeted drug delivery of green synthesized metallic nanoparticles against oral cancer: A review. Inorg Chem Commun. 2024;113806. doi:10.1016/j.inoche.2024.113806.

31. Bultum LE, Tolossa GB, Kim G, Kwon O, Lee D. In silico activity and ADMET profiling of phytochemicals from Ethiopian indigenous aloes using pharmacophore models. Sci Rep. 2022;12:22221. doi:https://doi.org/10.1038/s41598-022-26446-x.

32. Guan L, Yang H, Cai Y, Sun L, Di P, Li W, et al. ADMET-score – a comprehensive scoring function for evaluation of chemical drug-likeness. MedChemComm. 2018;10(1):148–157. doi:10.1039/c8md00472b.

33. Andhiarto Y, Suciati, Praditapuspa EN, Sukardiman. In silico analysis and ADMET prediction of flavonoid compounds from Syzigium cumini var. album on α-glucosidase receptor for searching anti-diabetic drug candidates. Pharmacogn J. 2022;14(6):736–743. doi:10.5530/pj.2022.14.161.

34. Tuntland T, Ethell B, Kosaka T, Blasco F, Zang RX, Jain M, et al. Implementation of pharmacokinetic and pharmacodynamic strategies in early research phases of drug discovery and development at Novartis Institute of Biomedical Research. Front Pharmacol. 2014;5:174. doi: 10.3389/fphar.2014.00174.

35. Jansson-Löfmark R, Fridén M, Badolo L, Ahlström C, Gurrell I, Pangalos MN, et al. Translational PK/PD: a retrospective analysis of performance and impact from a drug portfolio. Drug Discovery Today. 2025. doi:https://doi.org/10.1016/j.drudis.2025.104417.

36. Schlam I, Smith DM, Peer C, Sissung T, Schmidt KT, Tan M, et al. Pharmacokinetics and pharmacogenomics of ribociclib in black patients with metastatic breast cancer: the LEANORA study. NPJ Breast Cancer. 2024;10:84. doi:https://doi.org/10.1038/s41523-024-00692-w.

37. Morris GM, Huey R, Lindstrom W, et al. Computational protein-ligand docking and virtual drug screening with the AutoDock suite. Nat Protoc. 2016. doi:10.1038/nprot. 2016.051.

38. Ghanaat J, Khalilzadeh MA, Zareyee D. Molecular docking studies, biological evaluation and synthesis of novel 3-mercapto-1,2,4-triazole derivatives. Mol Divers. 2020;24:1735–1747. doi:10.1007/s11030-020-10050-0.

39. Iwaloye O, Ottu PO, Olawale F, Shityakov S, et al. Computer-aided drug design in anti-cancer drug discovery: What have we learnt and what is the way forward? Inform Med Unlocked. 2023;41:101332. doi:10.1016/j.imu.2023.101332.

40. Hadfield MJ, Carneiro BA, Cheng L. Targeted therapeutic approaches for the treatment of cancer: The future is bright. J Pers Med. 2025;15(4):141. doi:10.3390/jpm15040141.

41. Sylva RM, Ahmed SI. Targeted therapies in cancer. Med Princ Pract Surg. 2023. doi:https://doi.org/10.1016/j.mpsur.2023.12.004.

42. Pawar S, Kulkarni C, Gadade P, Pujari S, Kakade S, Rohane SH, et al. Molecular docking using different tools. Asian J Pharm Res. 2023;13(4). doi:10.52711/2231-5691.2023.00053.

43. Khan, M. A., Turjya, R. R., & Islam, A. B. M. M. K. (2021). Computational engineering the binding affinity of Adalimumab monoclonal antibody for designing potential biosimilar candidates. Journal of molecular graphics & modelling, 102, 107774. https://doi.org/10.1016/j.jmgm.2020.107774.

44. McCamish, M., Yoon, W., & McKay, J. (2016). Biosimilars: biologics that meet patients' needs and healthcare economics. The American journal of managed care, 22(13 Suppl), S439–S442 https://pubmed.ncbi.nlm.nih.gov/28719221.

45. Crespi-Lofton J, Skelton JB. The growing role of biologics and biosimilars in the United States: Perspectives from the APhA Biologics and Biosimilars Stakeholder Conference. J Am Pharm Assoc (2003). 2017 Sep–Oct;57(5):e15–e27. doi: 10.1016/j.japh.2017.05.014. Epub 2017 Jul 6.

46. Dutta B, Huys I, Vulto AG, Simoens S. Identifying key benefits in European off-patent biologics and biosimilar markets: It is not only about price! BioDrugs. 2020 Apr;34(2):159–170. doi:10.1007/s40259-019-00395-w.

47. Lemery SJ, Esteva FJ, Weise M. Biosimilars: Here and now. Am Soc Clin Oncol Educ Book. 2016;35:e151–e157. doi:10.1200/EDBK_155954.

48. Rolfe D, Parker J, Morgan M. Are biosimilars patentable? Expert Opin Ther Pat. 2016;26(8):893–895. doi:10.1080/13543776.2016.1193156.

49. Feldman SR, Bagel J, Namak S. Biosimilars for immune-mediated chronic diseases in primary care: What a practicing physician needs to know. Am J Med Sci. 2018 May;355(5):411–417. doi: 10.1016/j.amjms.2017.12.014.

50. Sosulski N. A brief overview of biosimilars and factors limiting their uptake. Can Pharm J (Ott). 2019 Oct 14;152(6):364–366. doi:10.1177/1715163519879411.

51. Ryan KA, Cohen-Mekelburg S, Baker JA, Weinheimer-Haus EM, Krenz C, Hou JK, et al. Public deliberation to assess patient views on biosimilar medication switching for the treatment of inflammatory bowel disease. BMC Health Serv Res. 2024;24:11570. doi:10.1186/s12913-024-11570-3.

52. Fu Z, Li S, Han S, Shi C, Zhang Y. Antibody drug conjugate: the “biological missile” for targeted cancer therapy. Signal Transduct Target Ther. 2022;7:93. doi: https://doi.org/10.1038/s41392-022-00947-7.

53. Snow DM, Cobb RR, Martinez J, Finger-Baker I, Collins L, Terpening S, Syar ES, Niemuth N, Kobs D, Barnewall R, Farr-Jones S, Marks JD, Tomic MT. A Monoclonal Antibody Combination against both Serotypes A and B Botulinum Toxin Prevents Inhalational Botulism in a Guinea Pig Model. Toxins (Basel). 2021 Jan 5;13(1):31. Doi:https://pmc.ncbi.nlm.nih.gov/articles/PMC7824882.

54. Thanongsaksrikul J, Chaicumpa W. Botulinum neurotoxins and botulism: a novel therapeutic approach. Toxins (Basel). 2011 May;3(5):469-88. Doi: https://doi.org/10.3390/toxins3050469.

55. Ghotloo S, Golsaz-Shirazi F, Amiri MM, Jeddi-Tehrani M, Shokri F. Neutralization of tetanus toxin by a novel chimeric monoclonal antibody. Toxicon. 2021 Oct 15;201:27-36. doi: https://doi.org/10.1016/j.toxicon.2021.08.011.

56. Wang X, Mathieu M, Brezski RJ. IgG Fc engineering to modulate antibody effector functions. Protein Cell. 2018 Jan;9(1):63-73. doi: https://pubmed.ncbi.nlm.nih.gov/28986820.

57. Qureshi OS, Sutton EJ, Bithell RF, West SM, Cutler RM, McCluskey G, Craggs G, Maroof A, Barnes NM, Humphreys DP, Rapecki S, Smith BJ, Shock A. Interactions of the anti-FcRn monoclonal antibody, rozanolixizumab, with Fcγ receptors and functional impact on immune cells in vitro. MAbs. 2024 Jan-Dec;16(1):2300155. doi: https://pubmed.ncbi.nlm.nih.gov/38241085.

58. Hoekstra H, Romero Pastrana F, Bonarius HPJ, van Kessel KPM, Elsinga GS, Kooi N, Groen H, van Dijl JM, Buist G. A human monoclonal antibody that specifically binds and inhibits the staphylococcal complement inhibitor protein SCIN. Virulence. 2018 Jan 1;9(1):70-82. doi: https://doi.org/10.1080/21505594.2017.1294297.

59. Antoran A, Aparicio-Fernandez L, Pellon A, Buldain I, Martin-Souto L, Rementeria A, Ghannoum MA, Fuchs BB, Mylonakis E, Hernando FL, Ramirez-Garcia A. The monoclonal antibody Ca37, developed against Candida albicans alcohol dehydrogenase, inhibits the yeast in vitro and in vivo. Sci Rep. 2020 Jun 8;10(1):9206. doi: https://www.nature.com/articles/s41598-020-65859-4.

60. Skrabana R, Dvorsky R, Sevcik J, Novak M. Monoclonal antibody MN423 as a stable mold facilitates structure determination of disordered tau protein. J Struct Biol. 2010;170(3):546–553. doi:https://doi.org/10.1016/j.jsb.2010.02.016.

61. Burley, S. K., Bhikadiya, C., Bi, C., Bittrich, S., Chen, L., Crichlow, G. V., Christie, C. H., Dalenberg, K., Di Costanzo, L., Duarte, J. M., Dutta, S., Feng, Z., Ganesan, S., Goodsell, D. S., Ghosh, S., Green, R. K., Guranović, V., Guzenko, D., Hudson, B. P., Lawson, C. L., … Zhuravleva, M. (2021). RCSB Protein Data Bank: powerful new tools for exploring 3D structures of biological macromolecules for basic and applied research and education in fundamental biology, biomedicine, biotechnology, bioengineering and energy sciences. Nucleic acids research, 49(D1), D437–D451. https://doi.org/10.1093/nar/gkaa1038.

62. Cyrus Chothia, Arthur M. Lesk,Canonical structures for the hypervariable regions of immunoglobulins, Journal of Molecular Biology, Volume 196, Issue 4,1987, Pages 901-917 ,ISSN 0022-2836,https://doi.org/10.1016/0022-2836(87)90412-8.

63. Al-Lazikani B, Lesk AM, Chothia C. Standard conformations for the canonical structures of immunoglobulins. J Mol Biol. 1997 Nov 7;273(4):927-48. doi: https://pubmed.ncbi.nlm.nih.gov/9367782.

64. Johnson DI.1999.Cdc42: An Essential Rho-Type GTPase Controlling Eukaryotic Cell Polarity. Microbiol Mol Biol Rev63:.https://doi.org/10.1128/mmbr.63.1.54-105.1999.

65. Kentaro Ihara, Sachiko Muraguchi, Masato Kato, Toshiyuki Shimizu, Masahiro Shirakawa, Shinya Kuroda, Kozo Kaibuchi, Toshio Hakoshima,

66. Crystal Structure of Human RhoA in a Dominantly Active Form Complexed with a GTP Analogue, Journal of Biological Chemistry, Volume 273, Issue 16,1998, Pages 9656-9666, ISSN 0021-9258, https://doi.org/10.1074/jbc.273.16.9656.

67. Vakser IA. Protein-protein docking: from interaction to interactome. Biophys J. 2014 Oct 21;107(8):1785-1793. doi: https://pubmed.ncbi.nlm.nih.gov/25418159.
