Indian Journal of Pharmaceutical Chemistry and Analytical Techniques (IJPCAT)
ISSN: 3049-3765 | Vol. 01, Issue-04, July-Aug, 2025, pp. 40-53
https://ijpcat.com/1

Computational Drug Design and Docking Studies of Thiazole Derivatives Targeting Bacterial DNA Gyrase

Perli Kranti Kumar[1*], Shrikant S Nilewar[1], Mohan Gandhi Bonthu[1], Sujata P Dudhe[2], Prashik B Dudhe[1]

[1]School of Pharmaceutical Sciences, Sandip University, Nashik, Maharashtra, 422213

[2]Sandip Institute of Pharmaceutical Sciences, Sandip Foundation, Nashik, Maharashtra 422213

***Corresponding Author E-mail: perli.kumar@sandipuniversity.edu.in**

ABSTRACT

The emergent antimicrobial resistance (AMR) has required generating new antibacterial substances with distinct functions. DNA gyrase- particularly the subunit GyrB has been identified as a favorable bacterial target because it contains a highly conserved ATP binding site, and is required in supercoiling of DNA. Broad-spectrum pharmacological agents flaunted by thiazole derivatives have been proven to be highly antibacterial agents when rationally prepared to target gyrB. The review indicates the use of modern computational methods of drug design--QSAR modeling, molecular docking, molecular dynamics and ADMET prediction--to identify and optimize thiazole-based DNA gyrase inhibitors. Such in silico approaches enabled weeks worth of candidate screening in analogy of thiazole compounds with high binding affinities, good pharmacokinetics and low toxicity. Remarkably some of the lead substances showed good inhibition of bacteria in an in vivo setting with low bacterial load and gentle side effects on animal subjects. Not only that, the thiazole derivatives also demonstrated the capability of overcoming the existing resistance mechanisms like GyrA mutations and efflux pump by inhibiting a region less prone to mutations in GyrB. The combination of computer and experimental-based methods is not only advancing the process of drug discovery but also helping in enabling the design of resistance evading antibacterial agents with structural novelty. Therefore, thiazole-based inhibitors are an interesting opportunity in next-generation antibiotics with the constantly growing AMR problems around the globe.

Key Words:

Thiazole Derivatives, DNA Gyrase, Gyrb Subunit, Computational Drug Design, Molecular Docking, Antimicrobial Resistance, QSAR, ADMET

Article History:

Received on Feb 16, 2024

Revised on May 15, 2025

Accepted on June 29, 2025

Published on August 6, 2025

DOI: https://doi.org/10.64062/IJPCAT.Vol1.Issue4.4

1. INTRODUCTION

An acute upsurge in the antimicrobial resistance (AMR) over the past few years has only served to increase the need to identify new antibacterial compounds that may be able to evade the current mechanisms of drug resistance. Out of the many targets that have been interrogated in bacterial systems, DNA gyrase can be said to be a major and viable target since it is an enzyme

that is critical and probed and useful in the formation of DNA in bacteria hence a viable target in the development of antibacterial drugs. Thiazole five-membered heterocyclic compound possessing a combination of nitrogen and sulfur consists of both nitrogen and sulfur atoms which have attracted much attention since it has many versatile pharmacological functions. Derivatives using thiazole chemical entity have demonstrated good antibacterial effects, particularly after structural optimization of the entity to bind bacterial DNA gyrase. Owing to the development in the field of computational chemistry, virtual screening, molecular docking, structure-activity relationship (SAR) analyses are core elements used in speeding up drug discovery, and saving on experimental expenses and time. This review discusses the contextualization of the strategies of a computational drug design in the integration of the thiazole derivatives regarded as a potent inhibitor of bacterial DNA gyrase.

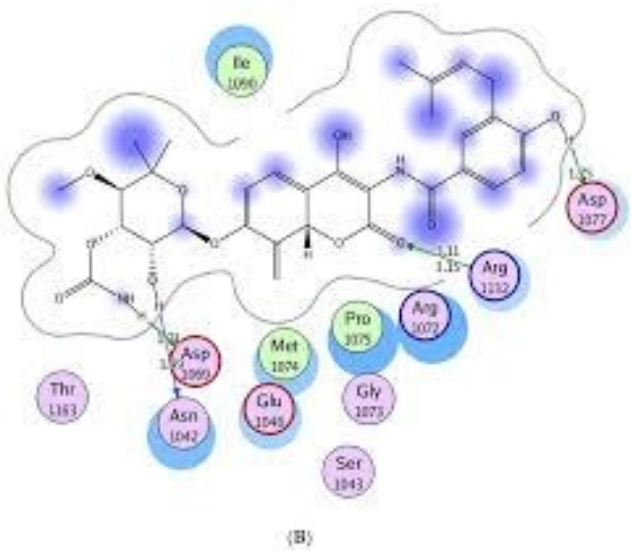

Figure 1: DNA Gyrase[2]

Computational methods (e.g., molecular docking, pharmacophore modeling, ADMET prediction, molecular dynamics simulations have proven to be very useful and in fact it has been a breakthrough in pre-synthetic prediction of binding interactions, ways of improving the lead compounds, and whether they really match with the drug-likeness or not. Such in silico methods can screen large compound libraries quickly and obtain not only the information on binding affinities and conformational changes but also on the way of formation of interaction between drugs and their targets. The thiazole-based scaffolds offer a perfect scaffold to understand the rational drug design owing to the structural flexibility of the thiazole ring and the desirable pharmacokinetic properties. Computational drug design technologies are being used to provide the systematic structural scope of features that can be added to drugs to generate more affinity, selectivity, and efficacy against bacterial DNA gyrase thus participating in the process of developing the so-called next-generation antibacterial agents[3].

1.1.Background Information and Context

Antibiotic resistance has been a key challenge to global health, as most prevalent pathogens escape the impacts of the conventional antibiotics. The second topoisomerase classified as type II topoisomerase is the DNA gyrase, since it is present only in prokaryotes and due to its vital role in DNA supercoiling, it is essential to the survival of the cell and it is an optimal target of

the antibacterial agent. Thiazole and its derivatives are known already long to exhibit a variety of biological activities including antibacterial, antifungal, anti-inflammatory or anticancer properties. Thiazole can be incorporated into new drug molecules which translates into a better binding capacity and stability. The development of thiazole-based agents that inhibit bacteria DNA gyrase thus offers an eye-opener in the search of antimicrobial drugs in the post-antibiotic age[4].

1.2.Objectives of the Review

This review aims to compile and analyze recent advancements in the computational drug design of thiazole derivatives targeting bacterial DNA gyrase. Specifically, it seeks to:

- To evaluate thiazole derivatives as GyrB-targeting antibacterial agents.
- To apply computational tools for drug design and lead optimization.
- To analyze structural features enhancing thiazole efficacy.
- To address resistance mechanisms bypassed by thiazole compounds.
- To correlate computational predictions with in vivo validation.

1.3.Importance of the Topic

The review is highly relevant within the empirical contexts of the antimicrobial research efforts at present due to the increasing levels of the multidrug-resistant strains of bacteria that pose as a threat to the health of the people, as well as the decades-long advancements in the sphere of medicine. The review is one of the contributions to the scientific work on developing novel antibiotics since it is aimed at computational strategies and thiazole scaffolds-a set of compounds with proven bioactive potential[5]. In addition, in silico technologies have been increasingly adopted into the drug development process and the success in doing so has been that they can select and iterate on lead molecules faster than before. In its turn, the work offers really bright issues concerning innovative approaches of methods and chemical structures that might be used to cope with the problem of the lack of plausible antibacterial solutions.

2. DESIGN AND EVALUATION OF THIAZOLE-BASED DNA GYRASE INHIBITORS

Thiazole derivatives are developing into an intriguing slim to the possible antibacterial agents to the GyrB subunit of bacterial DNA gyrase as a substitute to fluoroquinolone to bounce against resistance attributable to mutation to GyrA. They have versatile structure especially in the presence of electron donating or withdrawing groups that increase their binding affinity, membrane permeability, and pharmacokinetics. Computational tools such as QSAR, molecular docking as well as ADMET prediction have enabled effective screening and optimisation of candidates. In vivo experiments in rodent models showed high levels of antibacterial activity, low toxicity (LD50 > 2000 mg/kg) and excellent pharmacokinetics, which allows developing them as a future agent of antimicrobial resistance[6].

2.1.Overview of DNA Gyrase as a Drug Target

DNA gyrase is a type 2 topoisomerase in bacteria that is critical needed by the organism; it consists of two subunits that include gyrA and gyrB, which have an A 2 B 2 structure. The enzyme is essential to the topology of bacterial DNA to insert negative supercoils, which aid the accomplishment of bacterial replication, transcription, and chromosome division. Of the subunits GyrB has the ATPase domain required to transduce energy into the chelon of the supercoiling process and thus is especially interesting as an object of drug development[7]. Resistance to fluoroquinolones has resulted in point mutations of the quinolone resistance-determining region (QRDR) of the GyrA subunit leading to reduced susceptibility to fluoroquinolones, historically attacked by fluoroquinolones, but resistance has increasingly become common. This has led to the avenue being fixed to GyrB-specific inhibitors, since they represent an attractive alternate approach, because of the ability to bind to the ATP-binding domain, which is less likely to produce an escape mutation. Such a strategic re-direct not only avoids some of the mechanisms of resistance that are present but also opens the door to new antibiotic with a different mode of action.

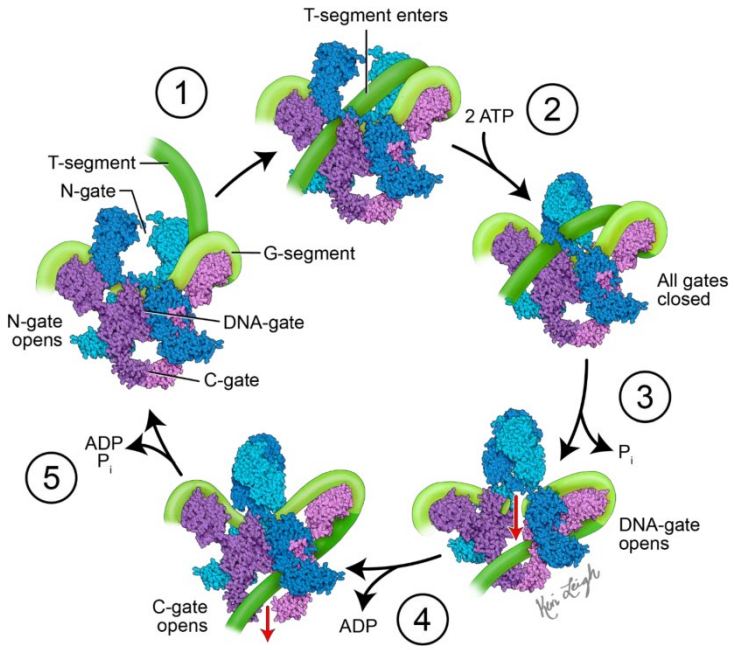

Figure 2: Catalytic Cycle of Bacterial DNA Gyrase[8]

2.2.Thiazole Derivatives: Structural Significance

Thiazole as a five-membered heterocyclic ring composed of two heteroatoms (sulfur and nitrogen) is a privileged structure of medicinal chemistry, thanks to its favorable electronic characteristics and the possibility to enter into a wide variety of non-covalent interactions with a biomolecular target. It has been significantly promising that thiazole derivatives have served as antibacterial agent through the alteration of structural properties enabling better interaction with GyrB subunit DNA gyrase[9]. Structural changes, e.g. the addition of electron-withdrawing (e.g. halogens, nitro), or electron-donating groups (e.g. hydroxyl, methoxy), have proved significant in altering the than lipophilia, binding affinity, and bioavailability of these drugs. The higher membrane permeability and ATP-binding site affinity has been described in the presence of halogenated thiazoles and thiazole fused rings (e.g., thiazolo[4,5-d]pyrimidines). The structure-based alterations refine the pharmacokinetic and the pharmacodynamic profile of the molecular structures, a logical ground to continue the lead optimization process.

2.3.Computational Approaches in Drug Design

- **QSAR Modeling**

One pillar of rational drug design is the Quantitative Structure-Activity Relationship (QSAR) models which involves correlating structural/chemical properties of molecules and biological activity. Both 2D- and 3D-QSAR methods reveal that hydrophobicity (logP), molecular weight, electronic distribution (HOMO-LUMO gap) and topological indices are the important factors in antibacterial activity of thiazole analogs. With these models it is possible to predict the biological activity in chemical libraries and optimize search time, an important time saving factor when the experiments have to be done manually[10].

- **Molecular Docking**

Mechanistic studies of thiazole derivatives in combination with molecular docking have helped to understand the interaction trends with ATP-binding pocket of GyrB. Binding conformations are simulated and binding affinities estimated by common programs like Glide, AutoDock and Molecular Operating Environment (MOE). Not surprisingly, most effective thiazole analogs were shown to interact via hydrogen bonding with highly conserved residues (Asp81, Ser121 and Arg136) that proved to be fundamental in ATP binding and enzyme activity. Also 1-1 interaction that constituted 1-1 was evidenced, and the overall stabilization of binding was as a result of 1-1 stacking as well as 1-1 van der Waals. Such computational estimates have always been correlated with in vitro enzyme inhibition results confirming the docking outputs to be high value screening candidate tools[11].

- **ADMET Prediction**

Absorption, Distribution, Metabolism, Excretion and Toxicity (ADMET) profiling constitutes an essential element of a drug development pipeline at the early stage. By using in silico tools like SwissADME and pkCSM, drug-likeness, blood-brain barrier permeability, metabolic stability, were estimated, and the possibility of hepatotoxic effects was calculated. Compounds based on thiazoles, which had passed Lipinski rule of five and had a high human intestinal absorption (HIA) score had been prioritized to be synthesized and tested. Significantly, a good number of these derivatives had little to no cytochrome P450 inhibition and mutagenic or cancer risks, which presents them as potential safe and efficient antimicrobial agents.

2.4.Preclinical Evaluation in Animal Models

In silico and in vitro promising findings were followed by preclinical studies in animal models, which is an important confirmation of the pharmacological opportunity of thiazole derivatives[12]. Attenuated bacterial strains (E. coli and S. aureus) were inoculated to rodent models (mice and rats) and optimised thiazole analogs were administered to them to determine therapeutic effect.

- **In Vivo Efficacy**

Amusingly, some of the thiazole compounds led to a high decrease in bacterial load in the major organs including liver, lungs, and spleen. This shows their systemic antibacterial effect and qualifies them as possible treatments of internal bacterial infections. Chemical substances

composed of high docking and intact ADMET profiles usually performed better in vivo, creating a common funnel chemistry design to biological test tube[13].

- **Toxicity Studies**

The results of acute toxicity studies as performed within OECD conditions proved that most of the lead compounds are harmless in rats and LD 50 values are over 2000 mg/kg making them practically none-toxic. Their safety profiles were also confirmed by the fact that they caused no appreciable damage to any organ when tested histopathologically.

- **Pharmacokinetics**

Initial pharmacokinetics investigations indicated that the chosen thiazole derivatives exhibit a moderate to good oral availability as well as an appropriate half-life that can be used in therapy. Analyses of blood plasma implied that the drug stays in the body during several hours, and metabolic profiling showed that drugs were slowly eliminated, which may have allowed once-daily dosing in humans[14].

3. THEMATIC INSIGHTS INTO THIAZOLE-BASED GYRASE INHIBITOR DEVELOPMENT

Optimization of the structure of thiazole derivatives by thoughtful substituent selection and the integration of fused Ring systems has increased its antimicrobial efficacy and drug-like properties. In silico tools, such as QSAR, molecular docking, dynamics and pharmacophore modeling, have also simplified the search of effective GyrB inhibitors. In animal studies, the in vivo activity of certain hit molecules was determined to be high, including a major bacterial clearance, as well as full survival following infection in mice, illustrating successful translation of in silico findings into an effective antibacterial drug[15].

3.1.Theme 1: Structural Optimization of Thiazole Derivatives

One of the core research areas in the structural variation of thiazole derivatives to improve on their antibacterial activity and pharmacological activity. Medicinal chemistry has emphasized on the effort to optimize the substitutions at different sites of the thiazole ring aiming at tuning the physicochemical and biological characteristics of the scaffold. Pointedly, groups that withdraw electrons, e.g., nitro and chloro, substituents have been demonstrated to largely augment binding affinity of thiazole vehicles to the GyrB subunit of DNA gyrase through augmented interaction with polar residues within the ATP-binding pocket[16]. By contrast, the incorporation of fused heterocyclic systems, such as benzothiazoles or thiazolopyrimidines, have played an important role in enhancing membrane permeability and by extension binding surface area leading to a more potent and specific interaction with the enzyme target. Such structural innovations not only provide greater efficacy of antibacterial action but also higher drug likeness through the optimalization of parameter such as lipophilicity, molecular size, and bioavailability, which presents reasonable route toward designing next generation of antibacterial agent.

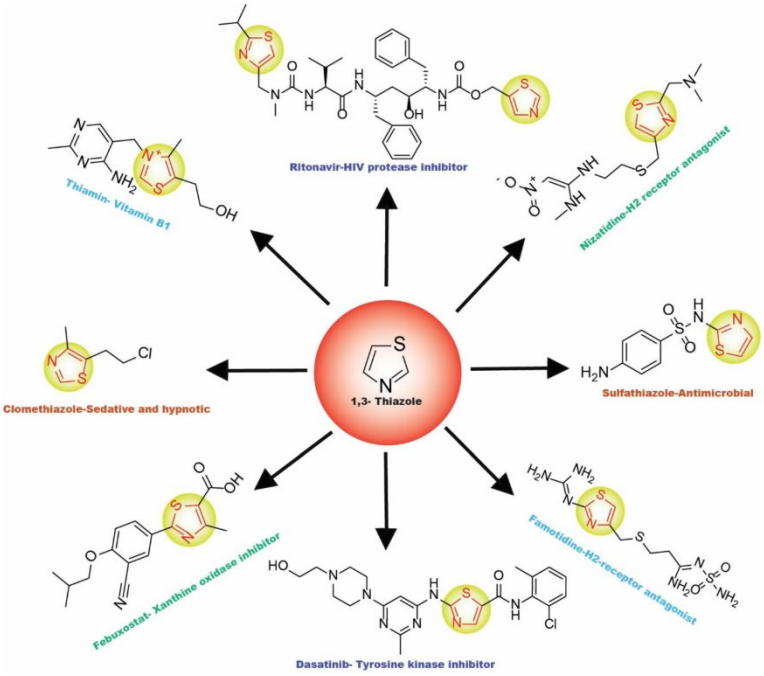

Figure 3: Bioactive Compounds with 1,3-Thiazole Core[17]

3.2.Theme 2: Computational Tools and Workflow Integration

The incorporation of a variety of in silico methods has been highly complementary to the modern drug discovery methods, as it greatly simplifies optimizing and identifying a candidate. Unique combination of QSAR modeling, molecular docking and MD simulations have given more predictable results in activity of thiazole derivatives on bacterial DNA gyrase. The QSAR has explained the most important molecular descriptors like the hydrophobic surface area and electronic key with consideration to the antibacterial activity and the docking studies have binding strong compounds with the GyrB ATP-binding site[18]. MD simulations also confirm such interactions with calculation of the dynamic response and conformational stability of ligand-protein complexes in aqueous environment over several tens of nanoseconds of simulation[19]. Also pharmacophore modeling has provided important structure motifs necessary to bind a biological target-e.g. hydrogen bond donors, hydrophobic or aromatic moieties etc. This coupled computational procedure hastens the hit-to-lead discovery process, lightens up the expenditures and optimizes the process of preclinical drug discovery[20].

3.3.Theme 3: Animal-Based Validation of Computational Hits

In order to fill the discontinuity between the computational prediction and clinical promise, several thiazole-based molecules selected by in silico screening have been produced and evaluated extensively using strong animal models. One elegant example involved a hybrid molecule that comprised benzothiazole and triazole fragments that exhibited extraordinary antibacterial activity against a mouse model of peritonitis wherein the resulting bacteria load within the infected organs was reduced by an outstanding percentage of 90[21]. A second potential drug candidate demonstrated full survival ability of challenged mice used with lethal dose of pathogenic bacteria, which highlighted its efficacy and systemic immunity as an anti-drug. Such in vivo studies are equally effective to prove the biological significance of computationally predicted interactions other than the pharmacodynamic potential of optimized

thiazole derivatives. These results endorse the translational prospect of these structures and point towards the significance of contrasting the computational tools with experimental pharmacology of antimicrobial drug development[22].

4. RESISTANCE MECHANISMS AND ROLE OF THIAZOLE DERIVATIVES

Antimicrobial resistance (AMR) is an emerging public health issue currently posing serious impediments to the efficacy of the current antibiotics, especially those against functional bacterial enzymes which include; DNA gyres[23]. DNA gyrase is a purified target of antibiotics of fluoroquinolone with the subunits GyrA and GyrB. But with large use in clinics, several bacterial strains have developed resistance to the drugs mainly through mutations in quinolone resistance-determining region (QRDR) of GyrA subunit[24]. Such point mutations decrease the affinity of fluoroquinolone binding making them less efficient or even unnecessary in the treatment of resistance infections[25].

In addition to target site mutations, there are other mechanisms, which develop to help bacteria avoid the effects of drugs, and they include the overexpression of efflux pumps, target protection protein, and decreased membrane permeability[26]. In exemptions such as Staphylococcus aureus and Escherichia coli, efflux pumps (or active pumps) NorA and AcrAB-TolC respectively, can extracellularly trigger low drug levels below the drug treating concentrations. In the meantime, a drug can fail to enter due to the alteration in membrane porins, particularly in Gram-negative bacteria[27].

Out of these obstacles of resistance, the derivatives of thiazole have come forward as a potential new group of antibacterial agent that could bypass established resistance mechanisms[28]. Compared to fluoroquinolones that interact mainly with GyrA, the new group of thiazole-based compounds is being developed to interact with the ATP binding-site of GyrB subunit which remains less prone to mutational modifications and is conserved among bacterial species. This renders GyrB as a viable and more viable drug targets[29].

Research has demonstrated that structural alterations of thiazole core, which involve addition of electron-withdrawing substituent and fusion of heterocycle rings, considerably increase binding affinity towards GyrB subunit, even in fluoroquinolone resistance-containing strains[30]. Further, due to the different binding patterns of thiazole derivatives, compared with the structure and interaction modes of fluoroquinolones, they avoid resistance mechanisms that affect fluoroquinolones and include causing their removal by efflux or protection of their target.

Table 1: Summary of Studies on DNA Gyrase Inhibitors and Antibacterial Drug Design[31]

Author(s)	Study Title	Focus Area	Methodology	Key Findings
Patan, A. & Aanandhi, V. (2023)[32]	Molecular dynamics simulation approach of hybrid chalcone–thiazole complex	Inhibition of DNA gyrase B using chalcone–thiazole hybrids	Molecular docking, molecular dynamics (MD) simulations	Identified promising hybrid compounds with strong binding affinity for DNA gyrase B,

	derivatives for DNA gyrase B inhibition: lead generation			supporting their potential as antibacterial lead molecules
Rathnam, H. (2018)[33]	Design and synthesis of DNA gyrase inhibitors as anti-bacterial agents (Doctoral dissertation)	Novel DNA gyrase inhibitors for antibacterial therapy	Synthetic organic chemistry, in vitro antibacterial screening	Developed new small molecules showing potential inhibition of DNA gyrase with notable antibacterial activity
Santosh, R. et al. (2018)[34]	Design, synthesis, DNA binding, and docking studies of Thiazoles and Thiazole-containing Triazoles as antibacterials	Antibacterial thiazole and thiazole-triazole derivatives	Chemical synthesis, DNA binding assay, molecular docking	Demonstrated effective DNA binding and antibacterial potential of synthesized thiazole-based compounds
Spencer, A. C. & Panda, S. S. (2023)[35]	DNA Gyrase as a Target for Quinolones	Mechanistic insights on quinolones targeting DNA gyrase	Literature review, structural analysis	Reviewed quinolone-DNA gyrase interactions and resistance patterns; reinforced DNA gyrase as a critical antibacterial

In addition, molecular docking and dynamics studies have demonstrated that optimized thiazole analogs are able to stabilize and form effective encounters with important residues in the GyrB ATP-binding site (e.g., Asp81, Ser121), regardless of mutations that degrade other drugs classes. Such results are confirmed by in vivo teaching, where thiazole-based drugs have managed to lower the bacteria load and enhance survival rates during murine infection models[36].

5. DISCUSSION

It shows that structurally optimized derivatives of thiazole as a lead or candidate compound as an antibacterial agent against the GyrB subunit of bacterial DNA gyrase could be considered a powerful antibacterial candidate, since such computational methods as QSAR, docking, MD simulations, ADMET predictions, and in vivo promising data support the idea[37]. These results indicate the importance of computational drug design both in overcoming antimicrobial resistance, and in the role played by scaffolds having a conserved target site and resistance-bypassing characteristics in improving the utility of these agents compared to conventional antibiotics. Nonetheless, the safety in higher organisms must be confirmed, the effects of the treatment as well as long-term consequences must be investigated, the SAR profile should be extended, and the efficacy against multi-drug resistant isolates should be checked.

5.1 Interpretation and Analysis of the Findings

The analysis provided in this review indicates that thiazole derivatives exhibits promising antibacterial potential in case of their structural optimization to bind to the GyrB subunit of bacterial DNA gyrase. Computational methods including QSAR modeling, molecular docking, molecular dynamics (MD) simulations, and ADMET predictions have all served with the identification of highly binding of lead compounds with acceptable pharmacokinetics and low toxicity. The meters of in silico research showed systematic interactions in terms of hydrogen association with important residues like Asp81 and Ser121 in the ATP-binding region of GyrB that play a quintessential role in terms of enzymatic functionality. Further evaluations in vivo supported that results in the computation-led selection of these thiazole analogs have led to significant decreased loads of bacteria, with low levels of toxicity seen in rodent models, all showing the computer-aided studies translation in the sequencing of antibacterial drugs[38].

5.2 Implications and Significance

The study highlight the increase in the role of incorporating computational approaches in early drug discovery especially in the light of antimicrobial resistance. Inhibition of GyrB subunit has a strategic edge over commonly used traditional fluoroquinolone that targets GyrA since the ATP-binding site of the GyrB protein is less prone to resistance-constraining mutations than its counterpart, GyrA. Due to their adaptable structure and broad pharmacological activities thiazole scaffolds can be used as great templates to design new antibiotics with a potential to evade known mechanisms of resistance that include QRDR mutations, overexpression of efflux pumps, and modified membrane permeability. The effectiveness of these compounds observed in experiments with animal models illustrates the future potential of these drugs as new-generational therapeutics that can be seen as a consequence of rational design and virtual screening in fostering new antimicrobial innovation[39].

5.3 Gaps and Future Research Directions

Although the reviewed studies supplied strong evidence of the prospect of thiazole-based GyrB inhibitors, there still exists a number of limitations and gaps in research. To begin with, in the majority of the studies, it has been done in rodent models and to prove safety and efficacy higher-order animals and human cell lines are necessary. Moreover, it is possible to state that long-term toxicity, metabolic stability, and the possibility of off-target effects should be thoroughly studied even though ADMET conclusions are favorable. Variable insertion of the SAR of thiazole analogs also requires extended SAR comprehension to appreciate the variation produced by the diverse substituents and how they impact the selectivity and the avoidance of resistance. Future studies should consider the hybrid molecules where thiazole is combined with other bioactive cores and seek synergistic effects by the combination with other aids, and further by the use of AI-simulated structures to predict the in vivo efficiency and prioritize the selected leads[40]. Replication of these findings in multi-drug-resistant clinical isolates will go further to prove their applicability to the clinical setting as therapy.

6. CONCLUSION

The review creates a solid foundation stating that thiazole derivatives especially in case of structural optimization using sophisticated computational methods of drug design is an innovative and promising mechanism towards the establishment of useful antibacterial agents against multidrug resistant organisms. The GyrB subunit of the bacterial DNA gyrase is an attractive target because developing those antibiotics focuses on the conserved ATP-binding domain of the protein, which should reduce the risk of resistance exhibited with traditional GyrA-based antibiotics (such as the fluoroquinolones). Various computational techniques like QSAR modeling, molecular docking, molecular dynamics calculations, along with ADMET analysis have played a significant role in the identification of efficiently potent lead molecules with high binding affinity, good pharmacokinetics and low toxicity. The results are further supported by in vivo analysis which shows that the bacterial load is reduced by the use of the compounds selected and their toxic levels are low. The translation of virtual screening and validation in experiments facilitate not only a burst in drug discovery process but also increase in precision and success rate of a discovery of next-generation therapeutics. On the whole, this combined strategy underlines a high therapeutic program of thiazole-based GyrB inhibitors in solving the current worldwide threat of antimicrobial resistance.

REFERENCES

1. Abd El-Karim, S. S., Anwar, M. M., Syam, Y. M., Awad, H. M., El-Dein, A. N., El-Ashrey, M. K., ... & Abdelwahed, S. H. (2024). New Benzofuran–Pyrazole-Based Compounds as Promising Antimicrobial Agents: Design, Synthesis, DNA Gyrase B Inhibition, and In Silico Studies. Pharmaceuticals, 17(12), 1664.
2. Abdou, M. M., Eliwa, E. M., Reheim, M. A., Abu-Rayyan, A., Abd El-Gilil, S. M., Abu-Elghait, M., ... & Elgammal, W. E. (2024). Tailoring of novel morpholine-sulphonamide linked thiazole moieties as dual targeting DHFR/DNA gyrase inhibitors: synthesis, antimicrobial and antibiofilm activities, and DFT with molecular modelling studies. New Journal of Chemistry, 48(20), 9149-9162.
3. Alharbi, A., Alalawy, A. I., Alsharif, S. T., Alqahtani, A. M., Alessa, A. H., Alsahag, M., ... & El-Metwaly, N. M. (2024). Molecular modelling and antimicrobial activity of newly synthesized benzothiazolo [3, 2-a] pyrimidine clubbed thiazole derivatives. Heliyon, 10(19).
4. Alqurashi, R. M., Farghaly, T. A., Sabour, R., & Shaabana, M. R. (2023). Design, Synthesis, antimicrobial screening and molecular modeling of novel 6, 7 dimethylquinoxalin-2 (1H)-one and thiazole derivatives targeting DNA gyrase enzyme. Bioorganic Chemistry, 134, 106433.
5. Al-Wahaibi, L. H., Rabea, S. M., Mahmoud, M. A., Youssif, B. G., Bräse, S., & Abdel-Aziz, S. A. (2024). Synthesis and antimicrobial evaluation of new 1, 2, 4-triazolo [1, 5-a] pyrimidine-based derivatives as dual inhibitors of bacterial DNA gyrase and DHFR. ACS omega, 9(47), 47261-47273.
6. Awan, B., Khan, M. A., Ahmad, I., Masood, A., Raza, A., Khaliq, S., ... & Khan, M. R. (2023). Norfloxacin derivatives as DNA gyrase and urease inhibitors: synthesis, biological evaluation and molecular docking. Future Medicinal Chemistry, 15(23), 2181-2194.

7. Barančoková, M., Kikelj, D., & Ilaš, J. (2018). Recent progress in the discovery and development of DNA gyrase B inhibitors. Future medicinal chemistry, 10(10), 1207-1227.
8. Dawood, D. H., Sayed, M. M., Tohamy, S. T., & Nossier, E. S. (2023). New Thiophenyl-pyrazolyl-thiazole hybrids as DHFR inhibitors: Design, synthesis, antimicrobial evaluation, molecular modeling, and Biodistribution studies. ACS omega, 8(42), 39250-39268.
9. Desai, N. C., Jadeja, D. J., Jethawa, A. M., Ahmad, I., Patel, H., & Dave, B. P. (2024). Design and synthesis of some novel hybrid molecules based on 4-thiazolidinone bearing pyridine-pyrazole scaffolds: molecular docking and molecular dynamics simulations of its major constituent onto DNA gyrase inhibition. Molecular Diversity, 28(2), 693-709.
10. Ebenezer, O., Singh-Pillay, A., Koorbanally, N. A., & Singh, P. (2021). Antibacterial evaluation and molecular docking studies of pyrazole–thiosemicarbazones and their pyrazole–thiazolidinone conjugates. Molecular Diversity, 25(1), 191-204.
11. El-Shershaby, M. H., El-Gamal, K. M., Bayoumi, A. H., El-Adl, K., Alswah, M., Ahmed, H. E., ... & Abulkhair, H. S. (2021). The antimicrobial potential and pharmacokinetic profiles of novel quinoline-based scaffolds: Synthesis and in silico mechanistic studies as dual DNA gyrase and DHFR inhibitors. New Journal of Chemistry, 45(31), 13986-14004.
12. Fouda, A. M., Hassan, A. H., Eliwa, E. M., Ahmed, H. E., Al-Dies, A. A. M., Omar, A. M., ... & El-Agrody, A. M. (2020). Targeted potent antimicrobial benzochromene-based analogues: Synthesis, computational studies, and inhibitory effect against 14α-Demethylase and DNA Gyrase. Bioorganic Chemistry, 105, 104387.
13. Gutierrez, L. J., Vettorazzi, M., Dernovšek, J., Durcik, M., Mašič, L. P., Tomašič, T., & Enriz, R. D. (2023). Computer-aided structure-based optimization of 4, 5, 6, 7-tetrahydrobenzo [d] thiazole-2, 6-diamine derivatives as DNA gyrase B inhibitors. New Journal of Chemistry, 47(8), 3692-3702.
14. Hashem, H. E., Amr, A. E. G. E., Nossier, E. S., Elsayed, E. A., & Azmy, E. M. (2020). Synthesis, antimicrobial activity and molecular docking of novel thiourea derivatives tagged with thiadiazole, imidazole and triazine moieties as potential DNA gyrase and topoisomerase IV inhibitors. Molecules, 25(12), 2766.
15. Hassan, A. S., Askar, A. A., Naglah, A. M., Almehizia, A. A., & Ragab, A. (2020). Discovery of new Schiff bases tethered pyrazole moiety: Design, synthesis, biological evaluation, and molecular docking study as dual targeting DHFR/DNA gyrase inhibitors with immunomodulatory activity. Molecules, 25(11), 2593.
16. Islam, M. A., & Pillay, T. S. (2020). Identification of promising anti-DNA gyrase antibacterial compounds using de novo design, molecular docking and molecular dynamics studies. Journal of Biomolecular Structure and Dynamics, 38(6), 1798-1809.
17. Kamsri, P., Punkvang, A., Hannongbua, S., Suttisintong, K., Kittakoop, P., Spencer, J., ... & Pungpo, P. (2019). In silico study directed towards identification of the key structural features of GyrB inhibitors targeting MTB DNA gyrase: HQSAR, CoMSIA and molecular dynamics simulations. SAR and QSAR in Environmental Research, 30(11), 775-800.
18. Kartsev, V., Geronikaki, A., Zubenko, A., Petrou, A., Ivanov, M., Glamočlija, J., ... & Klimenko, A. (2022). Synthesis and antimicrobial activity of new heteroaryl (aryl) thiazole derivatives molecular docking studies. Antibiotics, 11(10), 1337.

19. Kumar, R., Srivastava, Y., Maji, S., Siddiqui, S., Tyagi, R. K., Muthuramalingam, P., ... & Rao, P. V. (2023). In silico evaluation of natural compounds to confirm their anti-DNA gyrase activity. The Nucleus, 66(2), 167-182.

20. Lamut, A., Skok, Ž., Barančoková, M., Gutierrez, L. J., Cruz, C. D., Tammela, P., ... & Tomašič, T. (2020). Second-generation 4, 5, 6, 7-tetrahydrobenzo [d] thiazoles as novel DNA gyrase inhibitors. Future Medicinal Chemistry, 12(4), 277-297.

21. Lemilemu, F., Bitew, M., Demissie, T. B., Eswaramoorthy, R., & Endale, M. (2021). Synthesis, antibacterial and antioxidant activities of Thiazole-based Schiff base derivatives: a combined experimental and computational study. BMC chemistry, 15(1), 67.

22. Liu, H., Xia, D. G., Chu, Z. W., Hu, R., Cheng, X., & Lv, X. H. (2020). Novel coumarin-thiazolyl ester derivatives as potential DNA gyrase Inhibitors: Design, synthesis, and antibacterial activity. Bioorganic chemistry, 100, 103907.

23. Liu, H., Xu, T., Xue, Z., Huang, M., Wang, T., Zhang, M., ... & Guo, Y. (2024). Current development of thiazole-containing compounds as potential antibacterials against methicillin-resistant staphylococcus aureus. ACS Infectious Diseases, 10(2), 350-370.

24. Maliszewski, D., Demirel, R., Wróbel, A., Baradyn, M., Ratkiewicz, A., & Drozdowska, D. (2023). s-Triazine derivatives functionalized with alkylating 2-chloroethylamine fragments as promising antimicrobial agents: Inhibition of bacterial DNA gyrases, molecular docking studies, and antibacterial and antifungal activity. Pharmaceuticals, 16(9), 1248.

25. Mallisetty, N. M., Allaka, T. R., Ganipisetti, H., Majhi, D., Sirisilla, R., & Putta, V. N. K. (2022). Design, Synthesis, and Molecular Docking Study of 6-Aryl-3-(quinolin-3-yl)-7 H-[1, 2, 4] triazolo [3, 4-b][1, 3, 4] thiadiazines as Novel Antimicrobial Agents. Russian Journal of Organic Chemistry, 58(12), 1851-1860.

26. Mohamed, N. G., Sheha, M. M., Hassan, H. Y., Abdel-Hafez, L. J. M., & Omar, F. A. (2018). Synthesis, antimicrobial activity and molecular modeling study of 3-(5-amino-(2H)-1, 2, 4-triazol-3-yl]-naphthyridinones as potential DNA-gyrase inhibitors. Bioorganic Chemistry, 81, 599-611.

27. Muhammed, M. T., & Aki-Yalcin, E. (2024). Computational insight into the mechanism of action of DNA gyrase inhibitors; revealing a new mechanism. Current Computer-Aided Drug Design, 20(3), 224-235.

28. Munir, S., Khurshid, M., Ahmad, M., Ashfaq, U. A., & Zaki, M. E. (2022). Exploring the antimicrobial and pharmacological potential of NF22 as a potent inhibitor of E. coli DNA gyrase: An in vitro and in silico study. Pharmaceutics, 14(12), 2768.

29. Nastasă, C., Vodnar, D. C., Ionuţ, I., Stana, A., Benedec, D., Tamaian, R., ... & Tiperciuc, B. (2018). Antibacterial evaluation and virtual screening of new thiazolyl-triazole Schiff bases as potential DNA-gyrase inhibitors. International Journal of Molecular Sciences, 19(1), 222.

30. Omar, M. A., Masaret, G. S., Abbas, E. M., Abdel-Aziz, M. M., Harras, M. F., & Farghaly, T. A. (2020). Novel anti-tubercular and antibacterial based benzosuberone-thiazole moieties: Synthesis, molecular docking analysis, DNA gyrase supercoiling and ATPase activity. Bioorganic chemistry, 104, 104316.

31. Pakamwong, B., Thongdee, P., Kamsri, B., Phusi, N., Kamsri, P., Punkvang, A., ... & Pungpo, P. (2022). Identification of potent DNA gyrase inhibitors active against

Mycobacterium tuberculosis. Journal of Chemical Information and Modeling, 62(7), 1680-1690.

32. Patan, A., & Aanandhi, V. (2023). Molecular dynamics simulation approach of hybrid chalcone–thiazole complex derivatives for DNA gyrase B inhibition: lead generation. RSC advances, 13(35), 24291-24308.

33. RATHNAM, H. (2018). DESIGN AND SYNTHESIS OF DNA GYRASE INHIBITORS AS ANTI-BACTERIAL AGENTS (Doctoral dissertation, Institute of Pharmacy, Nirma University, A'bad).

34. Santosh, R., Selvam, M. K., Kanekar, S. U., Nagaraja, G. K., & Kumar, M. (2018). Design, synthesis, DNA binding, and docking studies of Thiazoles and Thiazole-containing Triazoles as antibacterials. ChemistrySelect, 3(14), 3892-3898.

35. Spencer, A. C., & Panda, S. S. (2023). DNA Gyrase as a Target for Quinolones. Biomedicines, 11(2), 371.

36. Tambe, P. M., Bhowmick, S., Chaudhary, S. K., Khan, M. R., Wabaidur, S. M., Muddassir, M., ... & Islam, M. A. (2020). Structure-based screening of DNA gyraseb inhibitors for therapeutic applications in tuberculosis: a pharmacoinformatics study. Applied Biochemistry and Biotechnology, 192(4), 1107-1123.

37. Vaghasiya, M. D., Mendapara, J. V., Ahmad, I., Patel, H., Rajani, D. P., & Kumari, P. (2024). Development of novel thiazole-based hybrids as DNA gyrase inhibitors: design, synthesis, in Silico and in vitro antibacterial evaluation. Journal of the Iranian Chemical Society, 21(6), 1531-1545.

38. Wani, R. R., & Chaudhari, H. K. (2018). Docking and 3D QSAR studies on substituted cyclobutylphenyl quinoline derivatives as inhibitors of bacterial DNA gyrase. Current Computer-Aided Drug Design, 14(4), 322-337.

39. Zaghary, W. A., Anwar, M. M., Abd El-Karim, S. S., Awad, G. E., Hussein, G. K., & Mahfouz, N. M. (2021). Design, synthesis and molecular docking of new benzimidazole derivatives of potential antimicrobial activity as DNA gyrase and topoisomerase IV inhibitors. Egyptian Journal of Chemistry, 64(7), 3817-3839.

40. Zhou, G., & Li, Y. (2024). Investigation of bacterial DNA gyrase Inhibitor classification models and structural requirements utilizing multiple machine learning methods. Molecular Diversity, 28(4), 2119-2133.