International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

In-silico study of Novel Antimicrobial Quinoline derivatives

Banpure S. G.[1*], Bhalekar P.A[1], Ingale P. L.[2], Divase C. S.[3], Birhadi J. M.[3]
[1]*Assistant Professor, SGMSPM's Dnyanvilas College of Pharmacy, Pune, Maharashtra, India.*
[2]*Principal, SGMSPM's Dnyanvilas College of Pharmacy, Pune, Maharashtra, India.*
[3]*Student,SGMSPM's Dnyanvilas College of Pharmacy, Pune, Maharashtra, India.*
Corresponding Author:*Banpure Sonali G.*

Date of Submission: 15-04-2025 Date of Acceptance: 25-04-2025

ABSTRACT:
Quinoline-based compounds are widely recognized for their potent antimicrobial properties and structural versatility. In this study, a series of quinoline derivatives were synthesized with various substitutions specifically at the 2nd position of the quinoline nucleus to explore their potential as antimicrobial agents. The structural modifications were guided by rational drug design principles and assessed through molecular docking studies to predict their binding affinity toward selected microbial target proteins.[2]
Docking simulations were performed using [Autodock, Discovery Studio,MarvinScketch,Marvin View], targeting key bacterial enzymes involved in vital metabolic pathways. The results revealed favorable binding interactions for several 2-substituted derivatives, indicating strong potential for antimicrobial activity.
This in-silico approach highlights the impact of 2-position substitution on the quinoline scaffold and supports further optimization and development of these derivatives as potential antimicrobial agents[1-2]

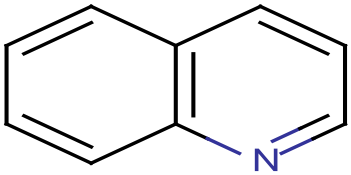
KEYWORDS: Antimicrobial activity,Quinoline derivatives,Molecular docking,Binding energy

I. INTRODUCTION

Quinoline derivatives are a well-established class of heterocyclic compounds known for their broad spectrum of pharmacological properties, particularly antimicrobial activity. The quinoline scaffold is widely utilized in the design of antimicrobial agents due to its ability to interfere with microbial DNA synthesis, protein function, and enzyme activity. Modifications on the quinoline ring have been shown to enhance biological activity and selectivity toward microbial targets.(2)

Substitution at the 2nd position of the quinoline ring is of particular interest because it plays a critical role in modulating the molecule's physicochemical and biological properties. Introducing various functional groups at this position can influence the compound's ability to interact with microbial enzymes and receptor sites, thus altering its antimicrobial potential.To predict and analyze these interactions, molecular docking is employed as a computational tool that simulates the binding of ligands to target microbial proteins. Docking studies help in identifying promising derivatives by estimating binding affinities and visualizing key interactions at the molecular level. This approach aids in the rational design of compounds before in-vitro validation.In the present study, a series of quinoline derivatives substituted at the 2nd position was designed and subjected to molecular docking analysis to evaluate their binding efficiency against selected microbial targets. The synthesized compounds were then tested in vitro for their antimicrobial activity against a panel of bacterial and fungal strains. This integrated approach aims to identify novel, potent antimicrobial agents and provides a foundation for further structural optimization of quinoline-based drugs.[2]

- **PROTIEN NAME: 4FGL**
- **MOLECULAR DOCKING OF QUINOLINE DERIVATIVE:-**



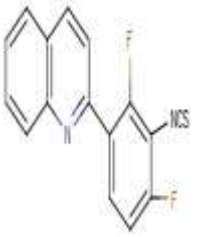
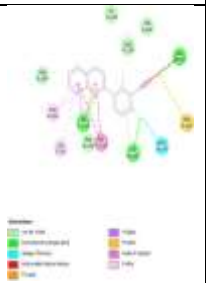
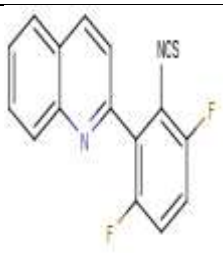
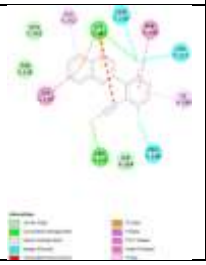
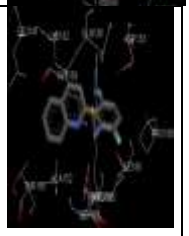
International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

Molecular docking is a vital computational tool in the early stages of drug discovery, particularly useful for understanding the interaction between small molecules and biological targets. It simulates the binding process between a ligand and a target protein to predict both the orientation and strength of their interaction. In drug design, especially antimicrobial research, docking helps in identifying compounds with high affinity and specificity for microbial enzymes or receptors that are crucial for survival. [2]

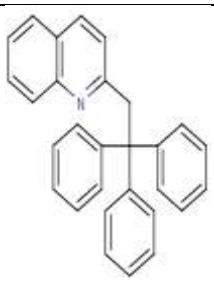
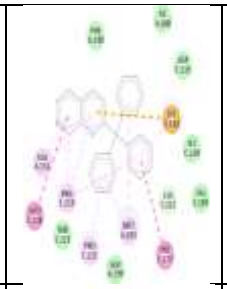
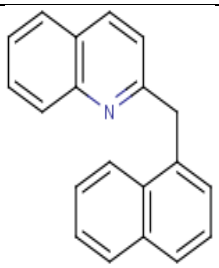
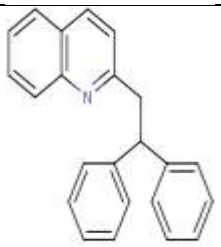
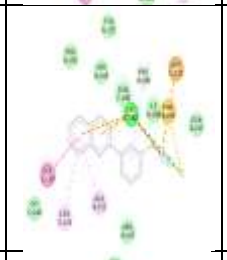
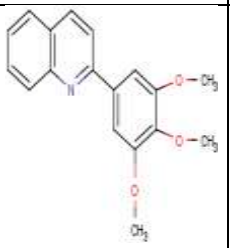
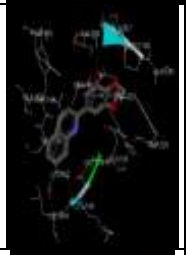
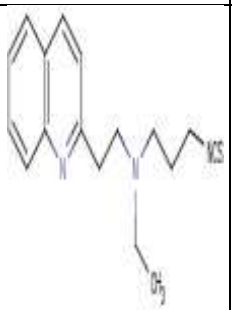
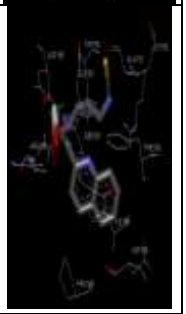
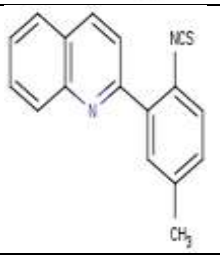
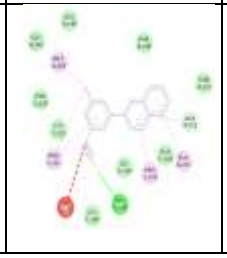
In the context of quinoline derivatives, especially those substituted at the 2nd position, docking provides a theoretical basis to evaluate how structural changes influence biological activity. The 2-position in the quinoline ring is known to play a critical role in determining the molecule's electronic distribution and steric effects, which in turn affects its ability to bind to microbial targets. By assessing the docking scores and interaction profiles, researchers can prioritize compounds that are more likely to exhibit potent antimicrobial action.

Through docking studies, one can identify key interactions such as hydrogen bonds, π-π stacking, van der Waals forces, and electrostatic interactions, all of which contribute to the stability of the ligand-protein complex. Compounds showing stronger and more specific binding profiles are considered promising leads for further biological evaluation. Additionally, docking offers insights into structure-activity relationships (SAR) by correlating specific substituents with their influence on binding efficiency.

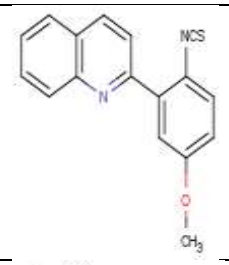
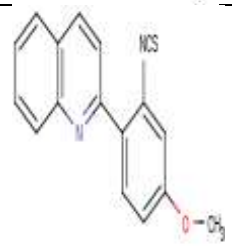
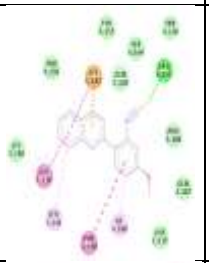
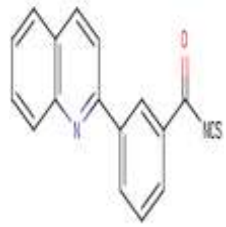
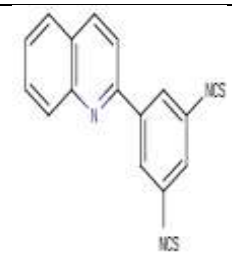
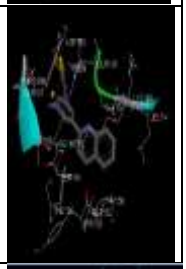
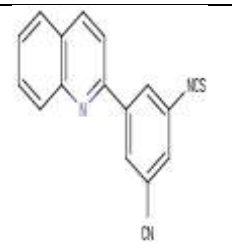
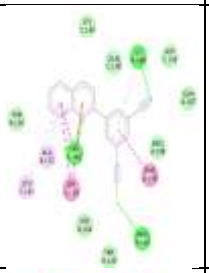
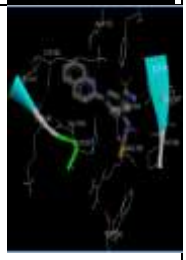
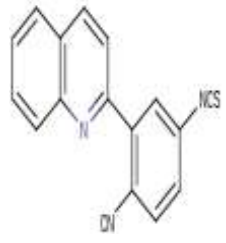
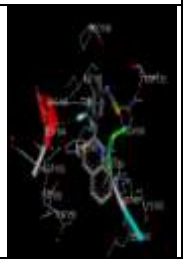
For antimicrobial drug development, docking serves a dual purpose: it saves time and resources by narrowing down potential candidates before synthesis and provides molecular-level insights that aid in the rational design of more effective agents. In this study, molecular docking was employed to theoretically screen the binding potential of newly synthesized 2-substituted quinoline derivatives against microbial target proteins. The docking outcomes supported the selection of promising candidates for in vitro antimicrobial evaluation, bridging computational prediction with experimental validation.[2]

Sr No.	R-Group	IUPAC Name	Binding Energy	No.of Hydrogen	Structure	2D Structure	3D structure
1	2,6 Difluro-phenyl isothio-cyanate	2-(2,4-Difluro-3 Cyanate-Phenyl) Quinoline	-8.20	3			
2	2,5 Difluro-Phenyl Isothio-cyanate	2-(3,6-Difluro-2 Isothio Cyanato -phenyl) Quinoline	-8.05	2			

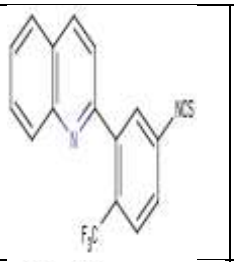
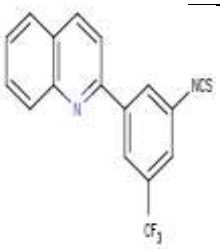
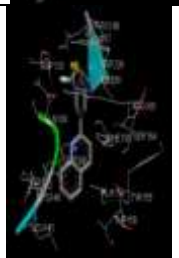
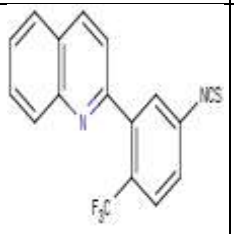
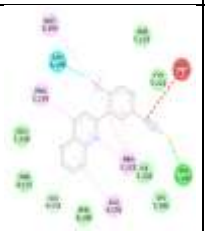
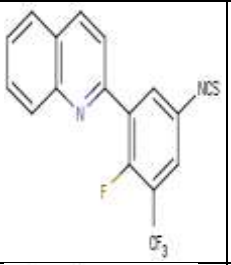
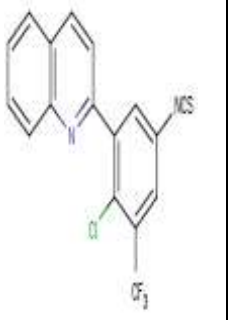
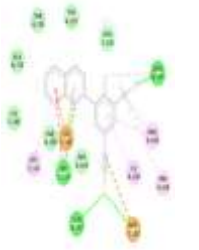
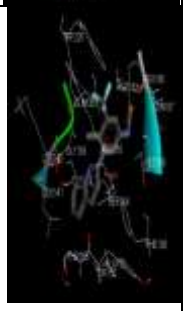
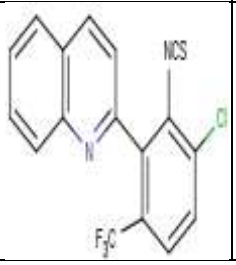
International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

3	Trityl	2-(2,2,2-Triphenyl-ethyl) Quinoline	-8.88				
4	1-Naphthyl	2-(naphthalene-1-ylmethyl) Quinoline	-8.99	1			
5	Benzyl-dryl	2-(2,2-diphen-ylethyl) Quinoline	-8.41	1			
6	3,4,5-trimethoxyethyl	2-(2,3,4-tri-Methoxyphenyl) Quinoline	-8.55	1			
7	3-(diethyl-amino)-propyl Isothio-cyanate	Ethyl(3-iso-thiocyanat-opropyl)2-(quinolin-2-yl)ethyl-amine	-6.75	2			
8	P-totyl-Isothio-cyanate	2-(2-isothio-cyanato-5-Methylphen-yl)quinoline	-8.56	1			

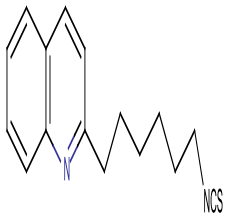
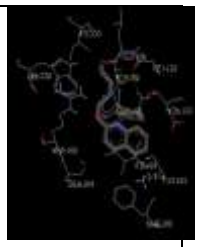
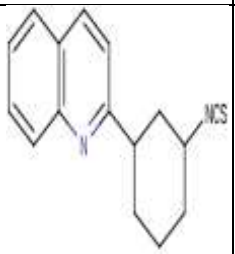
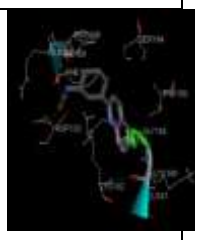
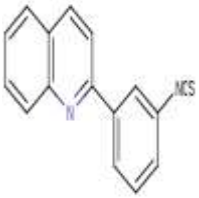
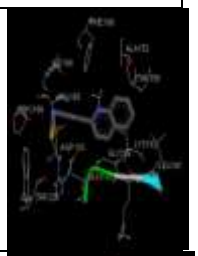
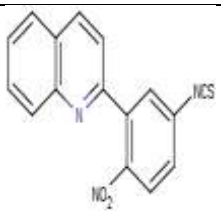
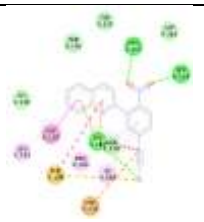
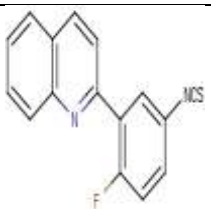
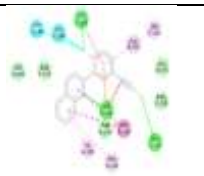
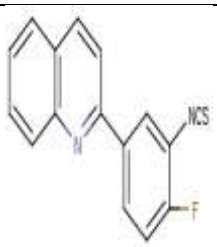
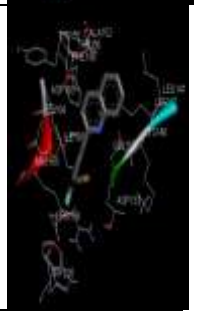
International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

9	4-methoxyphenyliso-thiocyanate	2-(2-isothioCynato-5-Methoxyphenyl) quinoline	-8.70	1			
10	3-methoxyPhenyl Isothio-cyanate	2-(2-isothiocyanato -4 –methoxyphenyl) quinoline	-8.51	1			
11	Benzoyl Isothiocyanate	3-(quinolin-2-yl)benzoylisothio-cyanate	-8.77	1			
12	1,3-Phenylenediiso-thiocyanate	2-(3,5-DiisothioCyanatophe-nyl Quinoline	-9.47	2			
13	3-cyno Phenyl Isothiocyanate	3-isothioCyanato-5-(quinin-2yl) benzonitrile	-8.66	3			
14	4- cyno Phenyl Isothiocyanate	4-isothioCyanato-2-(quinin-2yl) benzonitrile	-8.46	3			

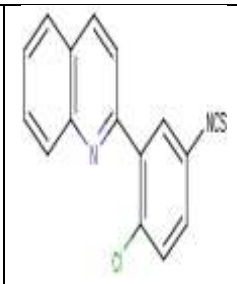
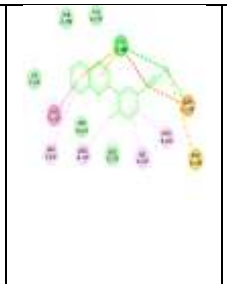
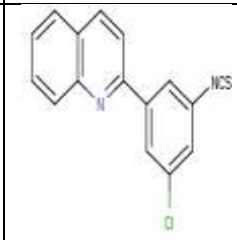
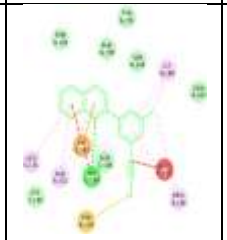
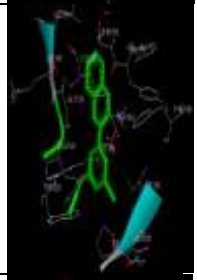
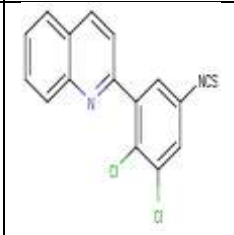
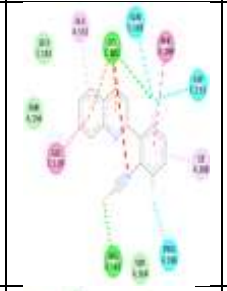
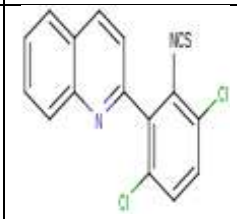
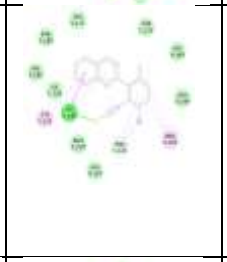
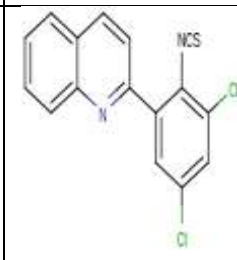
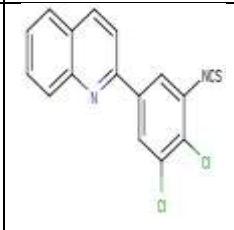
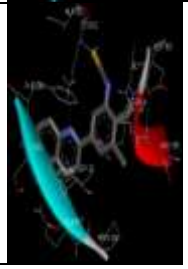
International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

15	4(triflu -rometh yl)phen ylisothio cyanate	2-(5-- isothio Cyanato- 2- (triflurom ethyl)phen yl Quinoline	-8.56	4			
16	3 (triflu Rometh yl)phen ylisothio cyanate	2-(3- isothio Cyanato- 5- (triflurom ethyl) Phenyl Quinoline	-8.68	4			
17	4(triflu Rometh yl)phen ylisothio cyanate	2-(5-- isothio Cyanato- 2- (triflurom ethyl)phen yl quinoline	-8.56	4			
18	4-fluro (3triflur omethyl Isothio cyanate	2-(2-fluro -5-isothio Cyanato- 3- (triflurom ethyl)phen yl Quinoline	-8.53	1			
19	4-chloro (3triflur o methyl Isothio cyanate	2-2-chloro 5-isothio Cyanato-3 (trifluro methyl) phenyl Quinoline	-8.84	3			
20	2-chloro - 5trifluro methyl Isothio cyanate	2-3-chloro 2-isothio Cyanato-6 (trifluro methyl) phenyl Quinoline	-8.29	2			

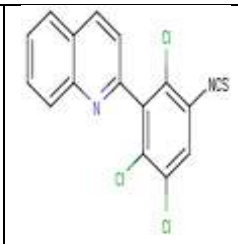
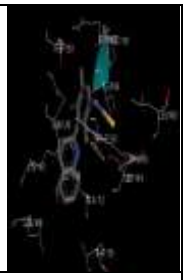
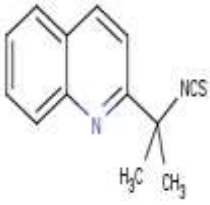
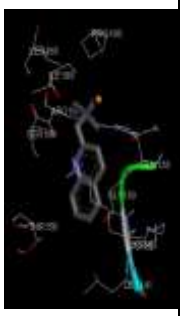
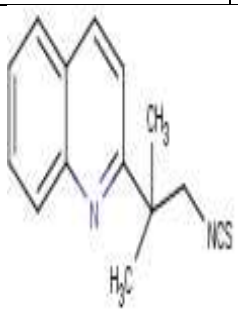
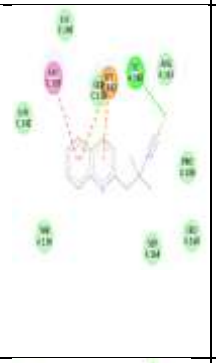
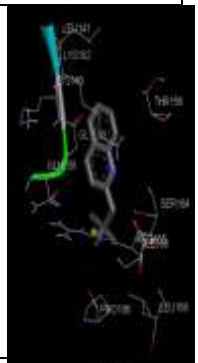
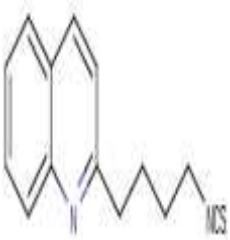
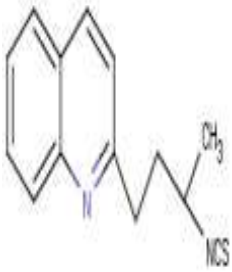
International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

21	Hexyl thiocyanate	2-(6-iso Thiocya -natohexyl) quinoline	-6.42	0			
22	Cyclo -hexyl Isothio cyanate	2-(3-isothio Cyanato-cyclo -hexyl) Quinoline	-8.40	0			
23	Phenyl Isothio cyanate	2-(3-isothio cyanato-phenyl) Quinoline	-8.46	2			
24	4-nitro Phenyl Isothio cyanate	2-(5-isothio Cyanato-2 Nitrophenyl)quinoline	-9.63	3			
25	4-fluro Phenyl Isothio cyanate	2-(2-fluro isothio-Cyanato-phenyl) quinoline	-8.29	3			
26	2-fluro Phenyl Isothio cyanate	2-(4-fluro-3 -isothio-Cyanato-phenyl) quinoline	-8.22	0			

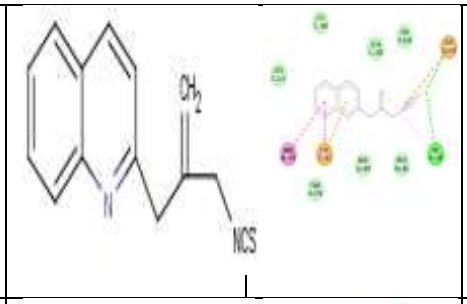
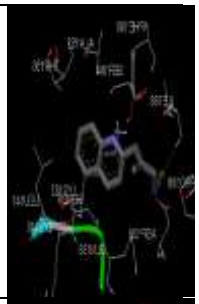
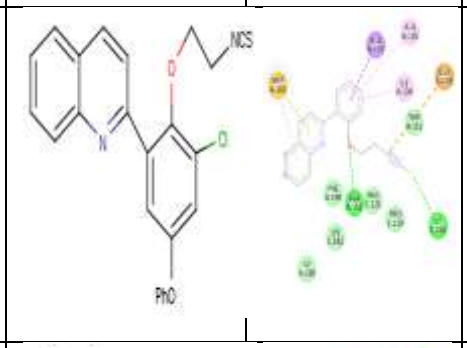
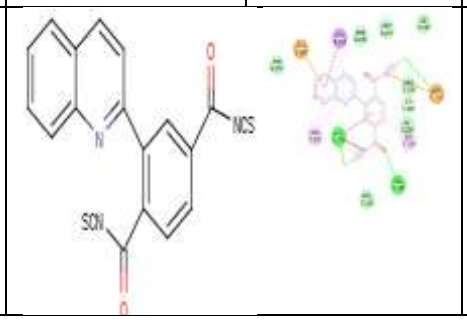
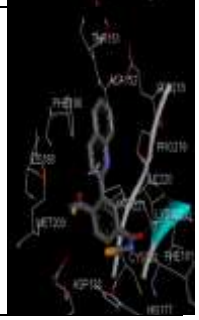
International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

27	4-chloro Phenyl Isothio cyanate	2-(2-chloro -5 -isothio-Cyanato-phenyl) quinoline	-8.80	1			
28	3--chloro Phenyl Isothio cyanate	2-(3-chloro -5 -isothio-Cyanato-phenyl) quinoline	-9.00	1			
29	2,4, Difluro Phenyl Isothio Cyanate	2-(2,3-dichloro -5 -isothio-Cyanato-phenyl) quinoline	-8.04	2			
30	2,5 Dichlor o Phenyl Isothio Cyanate	2-(3,6-dichloro -2 -isothio-Cyanato-phenyl) quinoline	-8.90	1			
31	2,4 Dichlor o Phenyl Isothio Cyanate	2-(3,5-dichloro -2 -isothio-Cyanato-phenyl) quinoline	-9.10	1			
32	2,3 Dichlor o Phenyl Isothio Cyanate	2-(3,4-dichloro -5-isothio-Cyanato-phenyl) quinoline	-8.79	2			

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

33	2,4,5 tri-chloro Phenyl Isothio Cyanate	2-(2,3,6-trichloro -5 -isothio-Cyanato-phenyl) Quinolone	-9.55	1			
34	Tertiary Butyl Isothio-Cyanate	2-(2-iso thiocyanat o -2,2-dimethyl Propyl) Quinolone	-7.04	2			
35	Isobutyl Isothio-Cyanate	2-(3-iso thiocyanat o -2 methyl Propyl) quinoline	-7.11	1			
36	Butyl Isothio-Cyanate	2-(4-iso thiocyanat o butyl) quinoline	-6.77	1			
37	2-Isothio-Cyanata to butane	2-(3-iso thiocyanat o butyl) quinoline	-7.40	0			

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

38	Methalene Isothio-Cyanate	2-(2-meth-ylidene-butyl) quinoline	-7.03	1		
39	(2-isothio Cyanate Ethoxy) benzene	2-2-(2 Isothio cyanato ethoxy) phenyl quinoline	-8.57	2		
40	Benzene-1,4-Dicarbonyl Diisothio-cyanate	2-(quinolin-2-yl) benzene 1,4Dicarbonyl Diisothio-cyanate	-10.02	2		

II. CONCLUSION

The present study successfully demonstrated the synthesis of various quinoline derivatives with substitutions at the 2nd position, and their evaluation for antimicrobial activity. The results confirmed that structural modification at this position plays a critical role in influencing biological efficacy. Several synthesized compounds exhibited significant antimicrobial activity, suggesting their potential as lead molecules for the development of new antimicrobial agents. These findings underscore the importance of quinoline as a versatile scaffold in medicinal chemistry and provide a foundation for further optimization and mechanistic studies

SOME OF THE ADVANAGES FROM THE ABOVE RESULTS

 Enhanced Antimicrobial Activity: Substituting different functional groups at the 2nd position of the quinoline ring led to compounds with improved antibacterial and antifungal properties.

 Structure-Activity Relationship (SAR) Insights: The study provided valuable SAR insights, demonstrating how small changes in substitution at the 2nd position can significantly impact biological activity. This helps guide future drug design efforts.

 Potential for Drug Development: The active quinoline derivatives identified in this study could serve as lead compounds for the development of novel antimicrobial agents, addressing the urgent need for new drugs in the face of rising antimicrobial resistance.

 Synthetic Accessibility: The compounds were synthesized using relatively straightforward and cost-effective methods, making them accessible for further research and large-scale production.

 Broad-Spectrum Activity: Several derivatives exhibited activity against both Gram-positive and Gram-negative bacteria, as well as fungi, indicating potential for broad-spectrum therapeutic applications.

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1915-1924 www.ijprajournal.com ISSN: 2456-4494

REFERENCES

[1]. Fu, H.-G., Li, Z.-W., Hu, X.-X., Si, S.-Y., You, X.-F., Tang, S., Wang, Y.-X., & Song, D.-Q. (2019). Synthesis and Biological Evaluation of Quinoline Derivatives as a Novel Class of Broad-Spectrum Antibacterial Agents. Molecules, 24(3), 548.

[2]. Sharma, S., & Singh, S. (2022). Synthetic Routes to Quinoline-Based Derivatives having Potential Anti-Bacterial and Anti-Fungal Properties. Current Organic Chemistry, 26(15.

[3]. Rao, I.R., Punitha, P., Premalatha, B., et al. (2024). Synthesis, structure identification, antioxidant and antimicrobial activities of some novel quinoline derivatives. Discover Chemistry, 1, 65.

[4]. Sabt, A., Abdelraof, M., Hamissa, M. F., Noamaan, M. A. (2023). Antibacterial Activity of Quinoline-Based Derivatives against Methicillin-Resistant Staphylococcus aureus and Pseudomonas aeruginosa: Design, Synthesis, DFT and Molecular Dynamic Simulations. Chemistry & Biodiversity, 20(11).

[5]. Farghaly, A. M., Habib, N. S., Khalil, M. A., el-Sayed, O. A. (1991). Synthesis and antimicrobial activity of novel pyrazolo[3,4-b]quinoline derivatives. Archiv der Pharmazie, 324(1), 19–24.

[6]. Kumar, S., Bawa, S., & Gupta, H. (2009). Biological activities of quinoline derivatives. Mini Reviews in Medicinal Chemistry, 9(14), 1648–1654.

[7]. Mishra, R., Tiwari, M., & Mishra, A. (2013). Synthesis and antimicrobial activity of some new quinoline derivatives. Journal of Saudi Chemical Society, 17(3), 237–241.

[8]. Sahu, N. K., Balbhadra, S. S., Choudhary, J., &Kohli, D. V. (2012). Exploring pharmacological significance of chalcone scaffold: A review. Current Medicinal Chemistry, 19(2), 209–225.

[9]. Choudhary, A., & Kumar, A. (2011). Synthesis and antimicrobial activity of quinoline derivatives. International Journal of ChemTech Research, 3(2), 766–769

[10]. Upadhayaya, R. S., Jain, S., Sinha, N., &Chaturvedi, S. C. (2004). Synthesis of novel substituted quinolines as potent antimicrobial agents. Bioorganic & Medicinal Chemistry Letters, 14(6), 1531–1535.

[11]. Patil, S. A., &Patil, R. (2009). Synthesis and antimicrobial activity of some new quinoline derivatives. Indian Journal of Chemistry - Section B, 48(5), 705–709.

[12]. Kharb, R., Sharma, P. C., &Yar, M. S. (2011). Pharmacological significance of triazole scaffold. Journal of Enzyme Inhibition and Medicinal Chemistry, 26(1), 1–21.

[13]. Tandon, V. K., Yadav, D. B., Maurya, H. K., & Kumar, D. (2007). Synthesis and biological evaluation of substituted quinoline derivatives as antimicrobial agents. Bioorganic & Medicinal Chemistry, 15(4), 1689–1695.

[14]. Saxena, R. K., &Kakkar, A. K. (2005). Synthesis and antimicrobial activity of some quinoline derivatives. Asian Journal of Chemistry, 17(3), 2075–2078.

[15]. Sridhar, R., Reddy, G. S., & Reddy, C. S. (2012). Design, synthesis, and antimicrobial activity of novel quinoline derivatives. European Journal of Medicinal Chemistry, 55, 49–58.

[16]. Sharma, P. C., Jain, A., &Yar, M. S. (2010). Medicinal chemistry of quinolineanalogs: Recent developments. Current Medicinal Chemistry, 17(41), 4257–4278.

[17]. Kalluraya, B., & Dinesh, P. (2007). Synthesis and antimicrobial screening of some new quinoline derivatives. Arkivoc, 2007(vii), 104–112.

[18]. Abdel-Rahman, A. H., & Al-Majid, A. M. (2016). Synthesis, characterization and antimicrobial activity of new quinoline and chromene derivatives. Saudi Pharmaceutical Journal, 24(1), 50–57.