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Research Article

Synthesis & Biological Evaluation of Oxime Based Derivatives as Antibacterial Agents

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The rapid emergence of bacterial resistance to existing antibiotics has created an urgent need for new antimicrobial agents. Oxime-based compounds are recognized for their wide range of biological activities and structural versatility. In the present investigation, a series of novel oxime-based derivatives were synthesized and evaluated for their antibacterial potential. The compounds were prepared by the reaction of selected carbonyl compounds with hydroxylamine derivatives under controlled conditions. The synthesized products were purified and characterized using melting point, infrared spectroscopy, nuclear magnetic resonance, and mass spectrometry. The antibacterial activity of the synthesized oxime derivatives was assessed against selected Gram-positive and Gram-negative bacterial strains using standard in-vitro methods. Several derivatives demonstrated moderate to good antibacterial activity in comparison with standard drugs. Preliminary structure–activity relationship analysis revealed that substitution patterns on the aromatic ring significantly influenced antibacterial efficacy. These results indicate that oxime-based derivatives may serve as promising lead molecules for the development of new antibacterial agents.

Keywords: Oxime derivatives, Antibacterial activity, Medicinal chemistry, Synthesis, Structure–activity relationship.

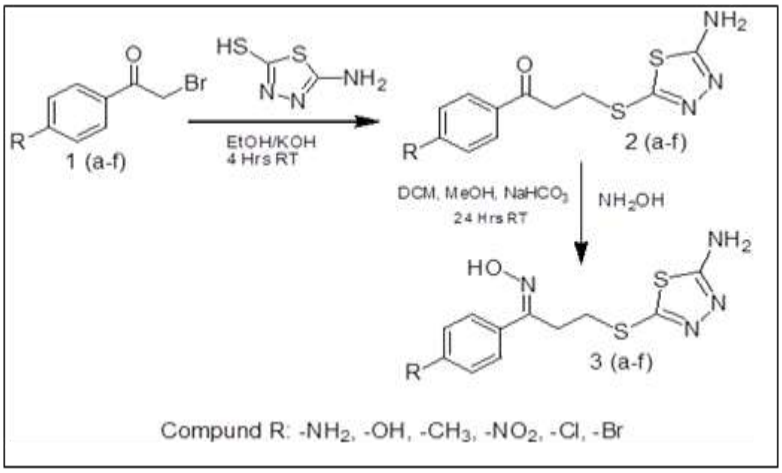
INTRODUCTION

Bacterial infections remain a major concern for global public health, even with notable progress in antimicrobial therapy and infection-control measures. Disease-causing bacteria are responsible for numerous clinical conditions, ranging from respiratory and gastrointestinal infections to skin, soft-tissue, and urinary tract diseases, as well as severe systemic illnesses such as sepsis and tuberculosis. The excessive and improper use of antibiotics has accelerated the development of antimicrobial resistance (AMR), reducing the effectiveness of many traditional antibacterial drugs. As a result, multidrug-resistant strains of Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Mycobacterium tuberculosis have become increasingly common, leading to poorer therapeutic outcomes, higher death rates, and rising healthcare expenditures across the world. Antimicrobial resistance develops through several biological processes, including the breakdown of drugs by bacterial enzymes, modification of drug-binding targets, decreased uptake through cell membranes, and the activation of efflux systems that expel antibiotics from the cell. These resistance traits can emerge through spontaneous genetic mutations or be transferred between bacteria via horizontal gene exchange, allowing resistance to spread rapidly. At the same time, the discovery of new classes of antibacterial agents has slowed, while existing therapies continue to lose effectiveness. This situation highlights the urgent need for new antibacterial compounds that offer greater activity, broader coverage, and novel modes of action. Consequently, modern medicinal chemistry increasingly emphasizes the redesign of established pharmacophores and the introduction of new functional groups to overcome resistance.

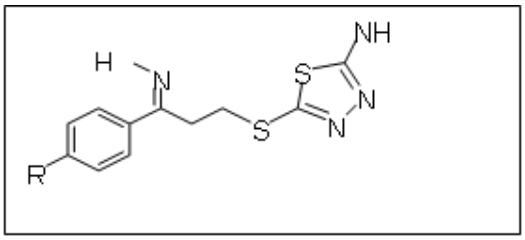
MATERIAL AND METHODS

All chemicals employed in the synthesis were procured from Merck (Mumbai), Sigma, Loba Chemie (Mumbai), Rankem (Haryana), and Avera Laboratories (Hyderabad). All solvents, reagents, and catalysts were of analytical grade and were used without further purification. The progress and purity of the synthesized compounds were monitored by thin-layer chromatography (TLC) using silica gel–coated glass plates as the stationary phase, with dichloromethane: methanol (10:1) as the mobile phase. The crude products were purified by recrystallization using suitable solvents. Further purification of the final compounds was achieved by column chromatography employing silica gel (230–400 mesh) packed in a sintered glass column. Melting points were determined by the open capillary method using an Analab scientific melting point apparatus and are reported as uncorrected values. Infrared (IR) spectra were recorded using the KBr pellet technique on an FT-IR 8400S spectrophotometer (Shimadzu, Japan). ^1H-NMR and ^13C-NMR spectra of the synthesized compounds were recorded on a BRUKER AVANCE II 400 spectrometer operating at 400 and 100 MHz, respectively. Mass spectra were obtained using a WATERS Q-TOF MICROMASS (LC-MS) instrument at the Sophisticated Analytical Instrument Facility (SAIF), Panjab University, Chandigarh. Chemical shift values are expressed in δ (ppm). In vitro antimicrobial studies were carried out in the Department of Biotechnology, Maharaja Ranjeet Singh College, Indore, India.

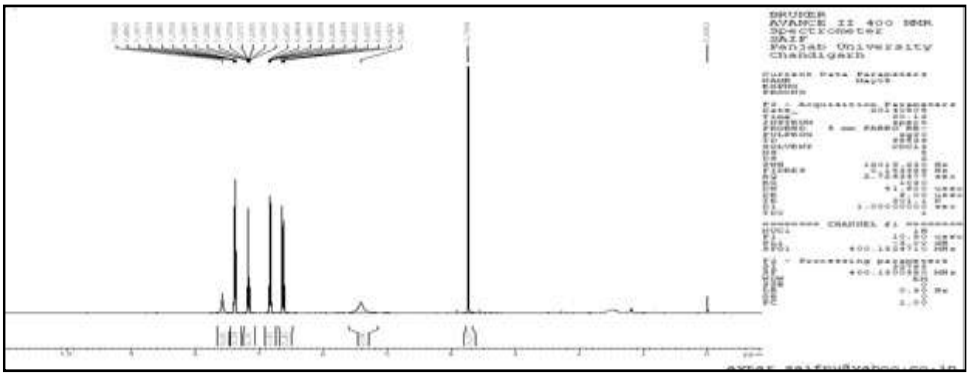
Scheme

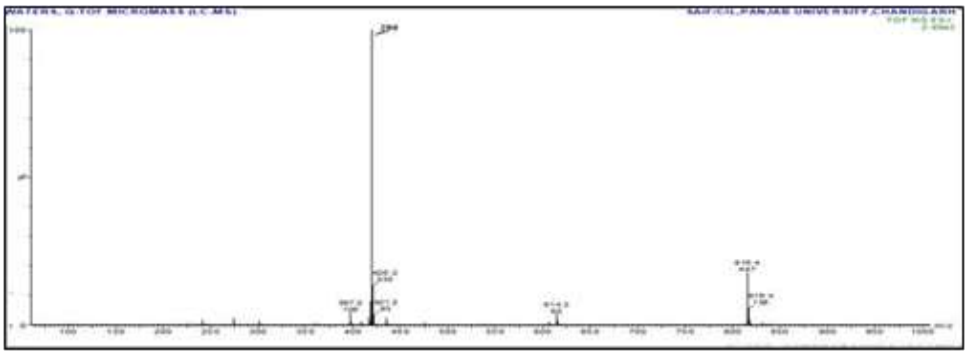


Physical data of title Compound IV(a-f)

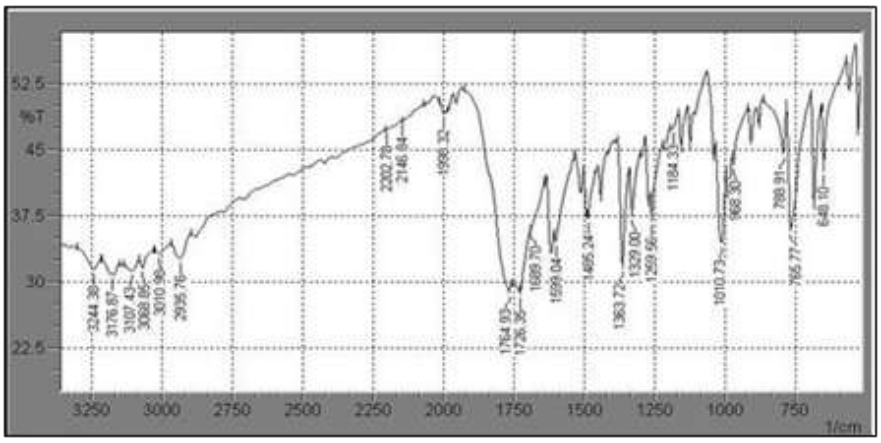


Compound	R	Molecular weight	Molecular formula	Rfvalue
IV(a)	-NH2	295	C11H13N5OS2	0.36
IV(b)	-OH	296	C11H12N4O2S2	0.38
IV(c)	-CH3	294	C12H14N4OS2	0.33
IV(d)	-NO2	325	C11H11N5O3S2	0.34
IV(e)	-Cl	315	C11H11ClN4OS2	0.37
IV(f)	-Br	359	C11H11BrN4OS2	0.41

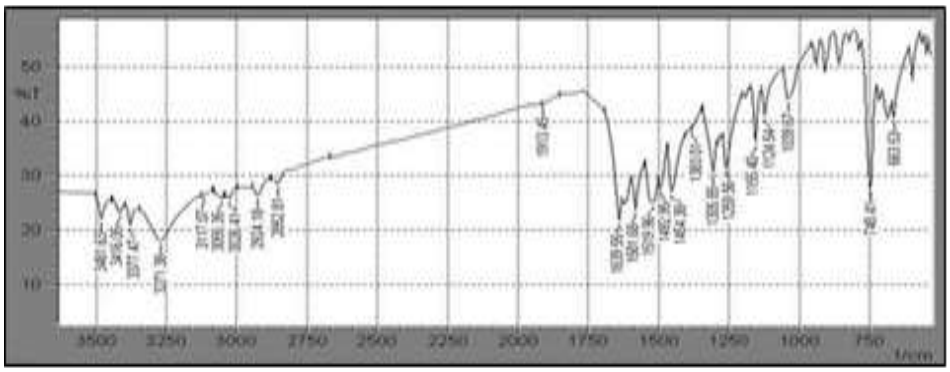




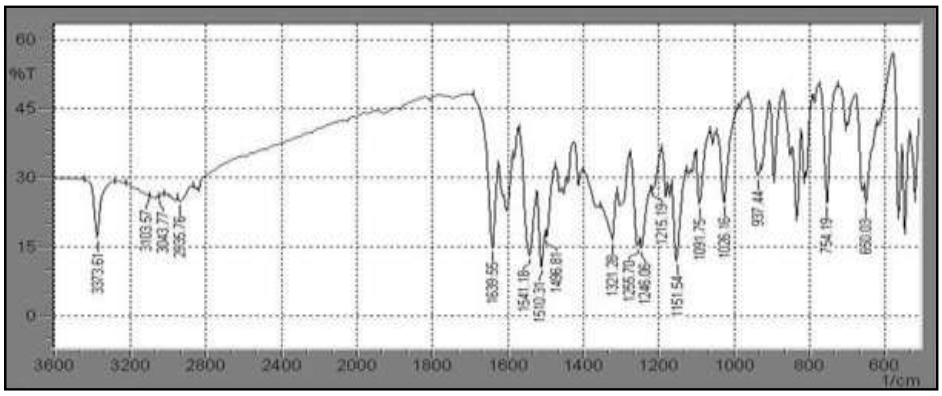
Compound	IVa	**Meltingpoint:**159-161^{0}C
Molecularweight	295	
FT-IR (cm^{-1})	1599.04(C=Nstr.),3244.38(N-Hstr.),2935.76(Aro.C-Hstr.),3244.38 (AmineN-Hstr.),3010.98(Aro.C=Cstr.),1332,1192(O-H), 1010.73(S-H).	
^{1}HNMRδ (ppm)	2.30(3H, s,methyl-H),3.76(3H,s,methoxy-H),6.90-6.93(4H,m, Arom-H),7.16-7.23(4H, m, Arom-H),7.44-7.62(4H, m, Arom-H), 10.15(1H, s, Amide-H), 10.85(1H, s, -H).	
LC-MS(m/z)	295(M+1)	



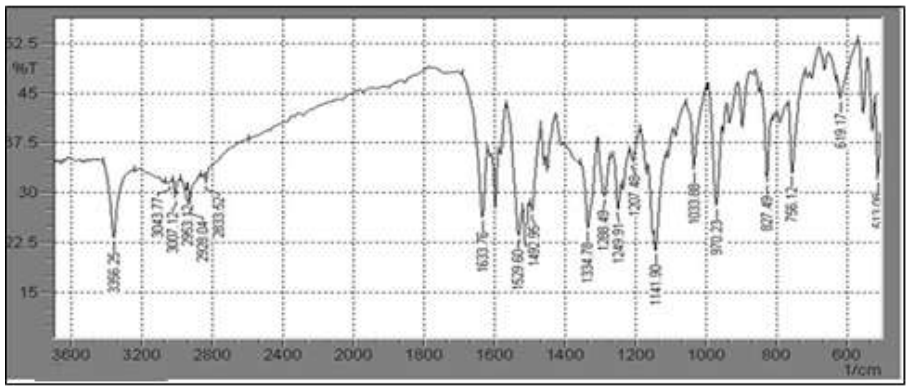
Compound	IVb	**Meltingpoint:**170-172^{0}C
Molecularweight	296	
FT-IR (cm^{-1})	1633.76(C=Nstr.),3277(AmideN-Hstr.),3466,3362(AmineN-H str.),3076(C=Cstr.),2922(Aro.C-Hstr.)	

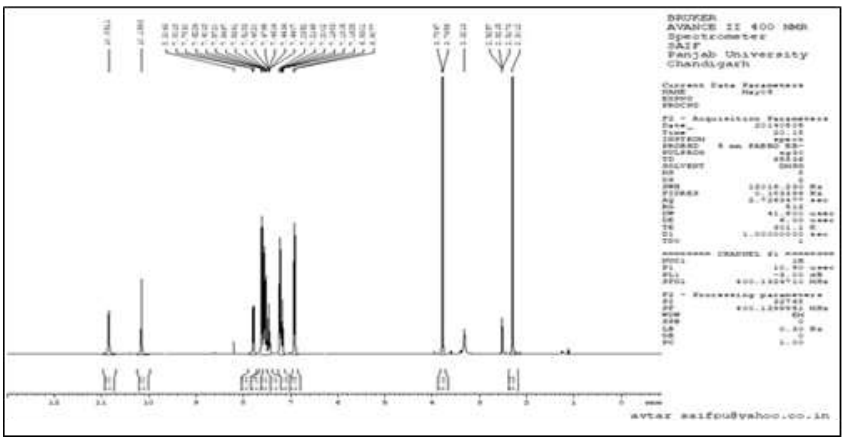


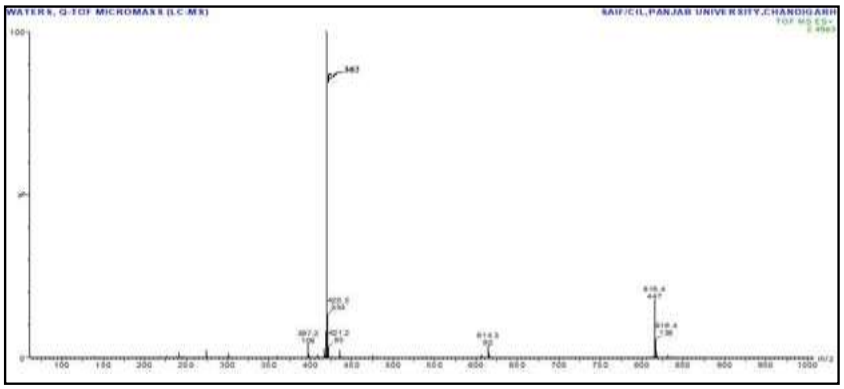
Compound	IVc	**Meltingpoint:**140-144^{0}C
Molecularweight	294	
FT-IR (cm^{-1})	1639(C=Ostr.),3271(AmideN-Hstr.),3481,3371(AmineN-Hstr.), 2924(Aro.C-Hstr.),3026(C=Cstr.).	



Compound	IVd	**Meltingpoint:**156-158^{0}C
Molecularweight	325	
FT-IR (cm^{-1})	1639(C=Ostr.),3373(AmideN-Hstr.),2935(Aro. C-Hstr.),1510(Aro. C=Cbend.),1321,1151(S=Ostr.)	







General procedure for the preparation of II (a-f)

General Procedure for Synthesis of 2 (a–f). Add (0.1 mol) of 80% KOH to a suspension of (0.1 mol) of 2-amino-5- mercapto-1,3,4-thiadiazole, in 15 mL of water. Solution was clarified with activated charcoal and diluted with 32 mL of ethanol, 0.1 mol of 1 (a–f) was added rapidly with stirring. Thick reaction mixture was formed, stirred vigorously at room temperature, and then diluted with 200 mL of cold water. The solid was obtained by filtration, washed with water and ether. 2 (a–f) were obtained. General procedure for the preparation of III (a-f) A mixture of compound II (a-f) (1 mmol), hydroxylamine hydrochloride (2 mmol) and sodium bi-carbonate (2 mmol) were taken in 10mL sealed; add equal volume of absolute methanol and dichloromethan into the sealed vial. The reaction was carried out at room temperature for 24 hrs to give the crude compound III (a-f). Recrystallized the crude III (a-f) by the mixture of ethanol and dichloromethane to gave the pure brownish amorphous compound IV (a-f). m.p. (°C) IV(a)159-161, IV(b)170-172, IV(c)140-144, IV(d)168-170, IV(e)164-166, IV(f)181 182; Yield (%) IV(a) 65, IV(b) 61, IV(c) 69, IV(d) 55, IV(e) 63, IV(f)68.

Antibacterial Evaluation

In-vitro Antibacterial Activity of Title Compounds III (a–f) All synthesized compounds were screened for their in-vitro antibacterial activity against selected Gram-positive and Gram-negative bacterial strains. Standard antibacterial agents, namely ciprofloxacin, gatifloxacin, and streptomycin, were employed as reference drugs. The Gram-positive organisms used in the study were Staphylococcus aureus (NCIM 2079) and Bacillus subtilis (NCIM 2250), while the Gram-negative organisms included Escherichia coli (NCIM 2109) and Pseudomonas aeruginosa (NCIM 2036). The antibacterial evaluation was carried out at the Department of Biotechnology, Maharaja Ranjeet Singh College, Indore, India.

Composition of Nutrient Agar

- Peptone:10.0g
- Sodium chloride:5.0g
- Beef extract: 10.5g
- Distilled water: upto 1000mL
- pH: 7.4±0.2

Nutrient agar (Hi-Media) was used as the microbiological medium for culturing the test

organisms. The antibacterial potential of the test compounds was assessed against S. aureus and B. subtilis (Gram-positive) as well as E. coli and P. aeruginosa (Gram-negative). Antibacterial activity is generally defined by the ability of a compound to inhibit bacterial growth in a nutrient medium, which was determined using the disk diffusion method. This method is widely employed for evaluating antibacterial efficacy. Culture Medium Nutrient broth was used for the preparation of bacterial inocula, while nutrient agar served as the medium for antibacterial screening.

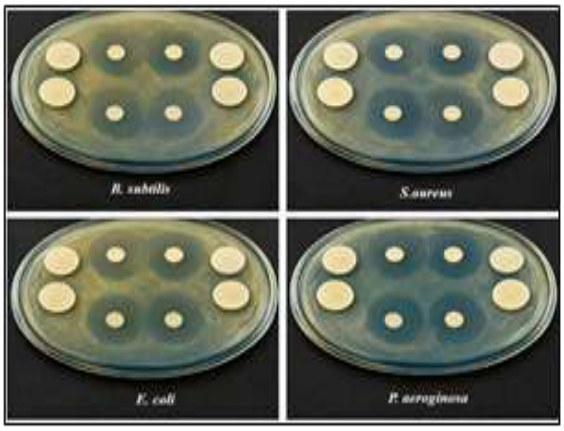


Fig. No.1 Zone of Inhibition

Zoneofinhibition (mm)					
Sr. No.	**Compound**	***B.subtilis***	***S.aureus***	***E. coli***	***P. aeroginosa***
1	III(a)	25.80	20.38	27.56	17.52
2	III(b)	21.68	19.65	24.97	13.66
3	III(c)	24.06	19.56	27.19	14.40
4	III(d)	23.42	20.21	29.16	19.19
5	III(e)	26.88	18.65	26.77	16.35
6	III(f)	25.97	23.87	26.34	14.76
7	Amoxycillin	25.46	28.17	32.56	26.63
8	Strptomycin	34.72	27.22	35.12	30.64

RESULT AND DISCUSSION

The synthesized oxime-based derivatives III (a–f) were evaluated for their in-vitro antibacterial activity using the agar diffusion method against two Gram-positive bacteria (Bacillus subtilis and Staphylococcus aureus) and two Gram-negative bacteria (Escherichia coli and Pseudomonas aeruginosa). The antibacterial efficacy was expressed in terms of zone of inhibition (mm) and compared with the standard antibacterial drugs amoxycillin and streptomycin. The results are summarized in Table. Overall, all the synthesized compounds exhibited moderate to good antibacterial activity, indicating that incorporation of the oxime functional group plays a significant role in enhancing antibacterial potential. Although the activity of the synthesized derivatives was lower than that of streptomycin, several compounds showed comparable or slightly improved activity relative to amoxycillin against selected strains. Activity Against Gram-Positive Bacteria Against Bacillus subtilis, compounds III (a), III (e), and III (f) demonstrated pronounced antibacterial activity, with zones of inhibition measuring 25.80 mm, 26.88 mm, and 25.97 mm, respectively. Notably, compound III (e) exhibited activity comparable to amoxycillin (25.46 mm), suggesting a strong interaction with Gram-positive bacterial targets. Compounds III (c) and III (d) also showed appreciable activity, indicating that structural variations within the oxime framework significantly influence antibacterial efficacy. In the case of Staphylococcus aureus, compound III (f) emerged as the most potent derivative among the test compounds, producing a zone of inhibition of 23.87 mm, which was notably higher than other synthesized analogues. Compounds

III (a) and III (d) also exhibited good activity, while III (e) showed relatively lower inhibition. The enhanced activity of III (f) against S. aureus may be attributed to favorable steric and electronic properties that facilitate stronger binding to bacterial enzymes or improved cell wall penetration. Activity Against Gram-Negative Bacteria All synthesized compounds displayed remarkable activity against Escherichia coli, with zones of inhibition ranging from 24.97 to 29.16 mm. Compound III (d) showed the highest activity (29.16 mm), closely approaching that of amoxycillin (32.56 mm). This observation is particularly significant, as Gram-negative bacteria possess an additional outer membrane that often limits drug penetration. The strong activity of these oxime derivatives suggests enhanced membrane permeability, possibly due to optimized lipophilicity imparted by oxime substitution. Against Pseudomonas aeruginosa, a notoriously resistant Gram-negative pathogen, the compounds exhibited moderate activity. Compound III (d) again demonstrated superior performance with a zone of inhibition of 19.19 mm, followed by III (a) and III (e). Although the activity was lower than the standard drugs, the results are encouraging given the intrinsic resistance mechanisms of P. aeruginosa, including efflux pumps and low membrane permeability. Structure–Activity Relationship (SAR) Discussion A preliminary structure–activity relationship analysis indicates that oxime functionalization significantly enhances antibacterial activity compared to parent carbonyl compounds, as reported in earlier studies. Compounds bearing substituents that balance lipophilicity and hydrogen-bonding capability exhibited improved antibacterial profiles. The consistent activity observed against E. coli implies that oxime derivatives may possess improved penetration across Gram-negative bacterial membranes. Furthermore, variations in activity against S. aureus and P. aeruginosa highlight the influence of steric bulk and electronic effects on target binding and cellular uptake. Comparative Evaluation with Standard Drugs When compared to standard drugs, streptomycin exhibited the highest antibacterial activity across all tested strains, as expected. However, several synthesized compounds showed zones of inhibition comparable to amoxycillin, particularly against B. subtilis and E. coli. This indicates that the synthesized oxime derivatives possess clinically relevant antibacterial potential, especially as lead compounds for further optimization. Overall Interpretation The results clearly demonstrate that oxime-based derivatives III (a–f) possess broad-spectrum antibacterial activity, with notable efficacy against both Gram-positive and Gram-negative bacteria. Among the tested compounds, III (d), III (e), and III (f) emerged as the most promising antibacterial agents. These findings support the hypothesis that oxime incorporation is a viable strategy for developing novel antibacterial agents capable of addressing emerging antimicrobial resistance. A preliminary structure–activity relationship (SAR) analysis suggested that optimal balance between lipophilicity and hydrogen-bonding capability plays a crucial role in determining antibacterial activity. Substituent effects on the oxime scaffold appeared to influence membrane permeability, target binding affinity, and overall antibacterial spectrum. The enhanced activity against Gram-negative bacteria, which are typically more resistant due to outer membrane barriers and efflux mechanisms, highlights the importance of oxime functionalization in improving intracellular drug accumulation. Comparative analysis with standard antibacterial drugs revealed that while streptomycin remained the most potent agent across all tested strains, several synthesized compounds demonstrated encouraging activity relative to amoxycillin. This suggests that oxime-based derivatives possess clinically relevant antibacterial potential and could serve as valuable lead compounds for further structural optimization. Importantly, the moderate activity observed against P. aeruginosa, a notoriously resistant pathogen, underscores the promise of oxime scaffolds in addressing difficult-to-treat infections. Overall, the findings of this study validate the initial hypothesis that oxime functional group modification is an effective strategy for enhancing antibacterial activity. The successful synthesis and biological evaluation of oxime-based derivatives highlight their potential role in the development of new antibacterial agents with improved efficacy and resistance-evasive properties. Although further studies such as minimum inhibitory concentration determination, mechanistic investigations, toxicity profiling, and in-vivo evaluation are required, the present work provides a strong foundation for future research in this area. In conclusion, this project contributes meaningful

insights into oxime-based antibacterial drug design and supports the continued exploration of oxime derivatives as promising candidates in the fight against antimicrobial resistance. The results obtained not only enrich the existing literature but also open new avenues for the rational development of next-generation antibacterial agents.

REFERENCES

1. Davies J, Davies D. Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev. 2010;74(3):417–433.
2. Ventola CL. The antibiotic resistance crisis: part 1—causes and threats. Pharm Ther. 2015;40(4):277–283.
3. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathog Glob Health. 2015;109(7):309–318.
4. Laxminarayan R, Duse A, Wattal C, et al. Antibiotic resistance—the need for global solutions. Lancet Infect Dis. 2013;13(12):1057–1098.
5. Blair JMA, Webber MA, Baylay AJ, Ogbolu DO, Piddock LJV. Molecular mechanisms of antibiotic resistance. Nat Rev Microbiol. 2015;13(1):42–51.
6. Fish DN. Antimicrobial stewardship. Am J Health Syst Pharm. 2011;68(5):401–410.
7. Silver LL. Challenges of antibacterial discovery. Clin Microbiol Rev. 2011;24(1):71 109.
8. Munita JM, Arias CA. Mechanisms of antibiotic resistance. Microbiol Spectr. 2016;4(2): VMBF-0016-2015.
9. Payne DJ, Gwynn MN, Holmes DJ, Pompliano DL. Drugs for bad bugs: confronting the challenges of antibacterial discovery. Nat Rev Drug Discov. 2007;6(1):29–40.
10. World Health Organization (WHO). Antimicrobial resistance: global report on surveillance. Geneva: WHO; 2014.
11. Abid M, Azam A. Synthesis and antibacterial evaluation of steroid oxime-ether derivatives. Bioorg Med Chem Lett. 2006;16(11):2812–2816.
12. Akunuri R, Veerareddy V, Kaul G, et al. Antibacterial evaluation of indole O-benzyl oxime derivatives. Med Chem Lett. 2014;(24)2173–2176.
13. Cui YJ, Rao XP, Shang SB, Song J, Gao YQ. Synthesis and antibacterial activity of oxime ester derivatives from dehydroabietic acid. Lett Drug Des Discov. 2013;10(2)98 100
14. Liu H, Huang J, Wang J, et al. Synthesis, antimycobacterial and antibacterial activity of fluoroquinolone derivatives containing an oxime group. Eur J Med Chem. 2014; 86:628–638.
15. Saleh FT, Netankar PD, Sheikh AA, et al. Synthesis of quinoline oximes and antimicrobial screening. Int J Pharm Sci Drug Res. 2023;15(5):591–596.

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