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Design And Synthesis of Heterocyclic Compounds for Antimicrobial Activity

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ABSTRACT

The increasing threat of antimicrobial resistance, there is an urgent need for new and efficacious therapeutic agents. This study describes the design, synthesis, and biological screening evaluation of four new series of heterocyclic compounds 1–4 with diverse substitution on thiazole, oxadiazole, pyrazole, and thiazolidinone scaffolds. These complexes were prepared by condensation reactions and characterised IR, ^1H NMR and mass spectrometry. Their antimicrobial potency was evaluated by minimum inhibitory concentration (MIC) tests and authenticated by in vivo approaches with BALB/c mice infected experimentally with E. coli, S. aureus, and P. aeruginosa. The pyrazole derivative HET-3 was the most potent of the synthesized molecules, whose MIC values were very similar to ciprofloxacin, with significant infection tissue bacterial load reduction. These results were confirmed statistically by one-way ANOVA analysis. The work points out the promising role of the substituted heterocyclic scaffolds, especially pyrazoles, as lead compounds for next generation antimicrobials, and focuses the need in for further pharmacokinetic and toxicity studies to progress these compounds up to clinical trial.

Key Words:

Heterocyclic compounds, antimicrobial activity, Pyrazole, MIC, In vivo study, Drug resistance, Structural characterization, Bacterial load, Thiazole, Pharmacological evaluation.

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1. INTRODUCTION

The increasing challenge of Antimicrobial Resistance (AMR) is a critical concern for human health worldwide in the 21st century[1.] The overuse and misuse of antibiotics in clinical and agricultural settings have fuelled the emergence of drug-resistant microorganisms, infections that are ever more difficult and, in some cases, impossible to treat[2.] With traditional antibiotics losing their effectiveness on resistant strains, the quest for new classes of antimicrobial agents with alternative mechanisms is not only urgent, it is critical to public health and modern medical practice[3.]

In this scenario sterilization compounds included heterocyclic derivatives which have been one of the most promising and studied class of compounds for the discovery of new antimicrobial agents[4]. Heterocycles are organic compounds with ring structures containing at least one carbon atom and one other element (nitrogen, oxygen, or sulfur). These heteroatoms introduce unique electronic and structural properties which can greatly alter biological activity[5]. Heterocyclic compounds, are building blocks of diverse biological compounds due to their unique structural diversity, synthetic versatility and ability to interact with a variety of biological targets and therefore, are invaluable to the man in health and disease[6].

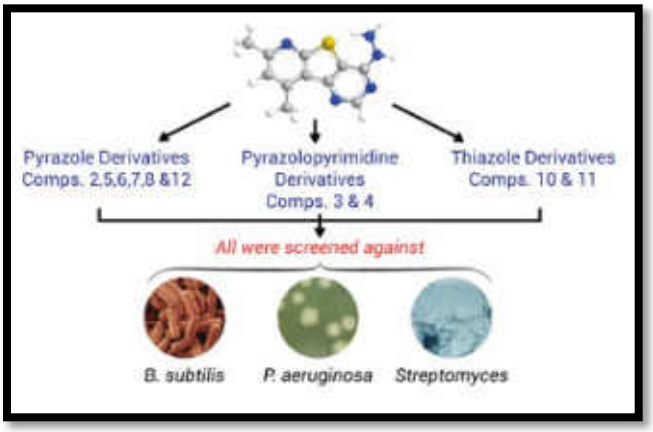

Figure 1: Synthesis and Antibacterial Activities of Different Five-Membered Heterocyclic

These compounds inhibit numerous essential microbial processes, including cell wall synthesis, DNA replication, enzyme inhibition, and membrane function, and can elicit bacteriostatic or bactericidal effects[7]. Many marketed drugs, such as penicillin (β-lactam ring), ciprofloxacin (quinolone) and metronidazole (nitroimidazole), are derived from heterocyclic scaffolds,1,2 confirming the importance of heterocycles in medicinal chemistry[8].

In addition, the possibility to synthesize other heterocycles possessing different functional groups, it also permits medicinal chemists to modulate their pharmacological profile, such as their selectivity and toxicity[9]. It has been inferred that structural alteration of core heterocyclic scaffolds like thiazoles, oxadiazoles, pyrazoles, and thiazolidinones has invariably led to improved activity towards a spectrum of microbes. Such modifications can increase lipophilicity, target binding, and overall pharmacokinetics[10].

Considering the implications of AMR and the insufficiency of the present therapeutic approaches, it could be considered that the current research is value adding to the discovery of new antimicrobial drugs, where by selected heterocyclic derivatives have been synthesized and characterised[11]. The antimicrobial activity of these compounds will be assayed in vitro and in vivo in an effort to discover promising candidates that can be further developed toward drug status, focusing on those that show activity against resistant strains of bacteria.

1.1.Background Information

Fluorine in heterocyclic chemistry Heterocyclic compounds have, for many decades, played an invaluable role in the development of modern medicinal chemistry, providing a wide range of therapeutic interventions[12]. These chemicals have ring structures and contain atoms such as N, O, or S and are astonishingly prevalent as components of drug molecules on account of their chemical peculiarities and biological activities[13]. Their importance in drug discovery is demonstrated by the fact that they are included in several clinically validated drugs for the treatment of distinct diseases. From anti-inflammatory, to analgesic, antimalarial, anticancer and their most important role in antimicrobial drug discovery, heterocycles are an unavoidable part of medicinal research[14].

The most desirable property of the heterocyclic systems is their flexibility of structure and adaptability for synthetic modifications. Modification of the heterocyclic ring by functional group substitutions could be carried out easily to adjust the physicochemical and pharmacokinetic properties according to the need. This tunability can be leveraged to improve target specificity, drug bioavailability, and metabolic stability, all of which are essential to drug efficacy and safety[15]. They can also be easily modified by appending electron-donating or withdrawing groups at well defined positions in the ring (Shah et al., 2010) and such a modification can cause a considerable change in the biological response, making them valuable in structure–activity relationship (SAR) studies.

Their importance is further emphasized by historical precedence. Antimicrobial therapy has forever been revolutionized by β-lactam antibiotics, namely penicillins and cephalosporins, which are the corner stones of treating bacterial infections. Their action is based on a strained four-membered β-lactam ring, which is a privileged heterocyclic scaffold that is vital for the inhibition of bacterial cell wall biosynthesis. In the same way, fluoroquinolones (FQs), which belong to a synthetic broad-spectrum class of antibiotics, have a bicyclic heterocyclic nucleus which binds to bacterial DNA gyrase and topoisomerase IV enzymes that are essential in bacterial DNA replication. These examples highlight the importance of heterocycles in natural and synthetic antimicrobials.

Following this tradition and their continued usefulness, heterocyclic frameworks remain privileged structures in medicinal chemistry. Rapid emergence and rotating patterns of resistant pathogens present a challenge and a strong motivation to seek new heterocyclic derivatives based upon new substitutions and hybrid structures to increase antimicrobial activity and reduce the development of toxicity and resistance.

1.2.Statement of the Problem

Increased levels of resistance to existing antibiotics of choice have resulted in certain strains of microorganisms and pathogens indirectly causing a global health emergency. Resistance has emerged against a lot of widely-used antibiotics, e.g. against such important bacteria as Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa, causing long-lasting disease, increased costs of therapy, and increased mortality rates. This resistance is driven by several factors, such as overuse and misuse of antibiotics, lack of infection control, and the natural capacity of microbes to survive and evolve. With the scarcity of new antibiotics, there is an urgent requirement to develop new synthetic approaches for the production of entirely new classes of antimicrobial molecules, bypassing the resistance processes developed till date. With respect to this matter, heterocyclic compounds as a class of molecules have garnered

significant attention as potential therapeutic agents based on their chemical diversity, ease of functionalization and known biological functions. This study aims to design and synthesise the new heterocyclic moiety structural molecules bearing functionalities or functional group that will improve the antimicrobial activity that could be effective against multidrug resistance bacterial strains. This study is focused on the design of heterocycle-based novel lead compounds with potential broad-spectrum antimicrobial activity through the structure-based optimization of cyclic compounds, including thiazole, oxadiazole, pyrazole, and thiazolidinone, with appropriate pharmacokinetic and toxicity properties. The research will thereby strive to deliver more than mere incremental developments to antimicrobial drug development, providing a potential foil to the rising threat of antibiotic resistance.

1.3.Objectives of the Study

- To synthesize structurally novel heterocyclic compounds.
- To evaluate their antimicrobial activity using in vivo animal models.
- To determine MIC values and bacterial load reduction.
- To analyze the structure-activity relationship (SAR).

2. METHODOLOGY

Systematic approach was applied in the synthesis and bio-evaluation of the heterocyclic compounds from above classes for antimicrobial activity. Compounds were synthesized by a well-documented chemical synthesis then purified and their structures verified by IR, ^1H and mass spectrometry. There in vitro antimicrobial activity was determined in minimum inhibitory concentration (MIC) assays on bacterial strains. For evaluating therapeutic potency and safety, in vivo studies were carried out on which co-coronavirus inoculated small animal models under approved ethical agreements. The results of these tests were recorded and statistically evaluated to determine those compounds which possessed either significant or powerful antimicrobial activity. This combined approach allowed for a comprehensive characterization of the derived heterocyclic molecules.

2.1.Research Design

The research proposed, hence, extends a novel experimental approach that combines synthetic organic to microbiological assessment in the laboratory. The state of synthesis included designed formation of the heterocycles by controlled chemistry, then purification and structural analysis of the compounds to ensure their integrity. In vitro antibacterial activitiesAnimal experiments were performed to evaluate their biological activity in vivo by using BALB/c mice as an established animal model of infection which you can pass Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa. This in vivo strategy enabled to assess in a living animal the antimicrobial effectiveness and safety of the newly synthesized molecules and was critical to better understanding the therapeutic potential. The experimental conditions, on both the chemical synthetic and biological aspects, were very well controlled and the whole approach contributed to the complete knowledge of the activity of the synthesized compounds against resistant bacteria.

2.2. Sample Details

- Animal Model: BALB/c mice (6–8 weeks old, 25–30g)
- Pathogens: E. coli, S. aureus, P. aeruginosa
- Control groups: untreated infected group and ciprofloxacin-treated group
- Ethical clearance: Obtained from Institutional Animal Ethics Committee (IAEC)

2.3.Instruments and Materials Used

The synthesis and testing HET hybrids were both supported by a variety of state-of-the-art instruments and apparatus. A detailed characterization of the structure was achieved using 400 MHz NMR spectrometer, helping to verify the molecular framework of the synthesized compounds. The functional groups present in the molecules were identified from FT-IR spectrophotometer, which gave a clue to the chemical bonding and thus confirming the synthesis. Additionally, to confirm the purity and presence of compounds, absorbance measurements were performed using a UV-Vis spectrophotometer. In the course of synthesis, the removal of solvent under reduced pressure was conducted using a rotary evaporator, and target products were obtained in pure form. For microbiological analyses, an autoclave was necessary to sterilize all materials and apparatus to keep sterile conditions of experiment. Lastly, a colony counter was employed to indirectly determine number of bacterial colony-forming units in the tissues of infected animal models to quantitatively assess antimicrobial efficacy. Together, these machines provided the capability to reliably synthesize, characterize, and bio-evaluate our DPs over the course of the study.

2.4.Procedure and Data Collection Methods

The hydrazine hydrate and different substituted aldehyde underwent step wise condensation reaction to synthesize heterocycles. After the synthesis, the compounds were purified by chromatographic techniques and re-crystallization, resulting in high purity. The correct structures were verified by infrared (IR) spectra, 1H and 13C NMR spectra, and mass spectrometry. Mice To evaluate the in vivo activities, all the synthetic compounds were used to treat BALB/c mice infected with the bacterial pathogens. Then, at 48 h after infection, liver and spleen tissues were aseptically collected, homogenized, and processed for determination of bacterial counts as a measurement of drug antibacterial effect. The experimental plan consisted in the vehicle-only treated control group a ciprofloxacin treated positive control group and further groups for the individually synthesised compounds, for a comparative assessment of antimicrobial activity.

2.5.Data Analysis Techniques

This arrangement in the application of the SPSS (Statistical Package for he Social Sciences) allowed for the rigorous and reliable interpretation of experiments results. One way Analysis of Variance (ANOVA) was also used to evaluate differences in the bacterial loads between control, standard drug, and test compound groups. This statistical method contributed to estimate the in vivo anti-bacterial infection of the synthesized compounds in this work. Further, in vitro minimum inhibitory concentrations (MIC) values (the lowest concentration of

a compound required to inhibit visible growth of bacteria), were established with the broth microdilution method as it is a standard quantitative method in microbiology. These analytical methods used in combination, paved way for a thorough evaluation of the antimicrobial potency of the prepared heterocyclic compounds in comparison to that of drug-refractory organisms.

3. RESULTS

This section presents the experimental findings derived from the synthesis, characterization, and antimicrobial evaluation of four heterocyclic compounds. The results are categorized and discussed using tables, and key comparisons are visualized with bar charts and statistical summaries.

3.1. Presentation of Findings

The research was based on the design of four heterocyclic compounds, HET-1, HET-2, HET-3, and HET-4, which have different ring systems, together with substitution groups of different functional groups, in order to study their effect on the antimicrobial activity. The prepared compounds were fully characterized with such properties as yield percentage and melting points that revealed admissible views about their purity as well as stability. The molecular structures were established by spectroscopic methods. In order to determine the antimicrobial activity of the compounds the latter were tested in vitro and minimum inhibitory concentrations (MIC) were determined for typical bacterial pathogens indicating the potence of the compounds for the inhibition of bacteria growth. Supporting these observations, in vivo assays were performed in an established animal infection model, where the reduced bacterial load from liver and spleen tissues of treated mice were determined, indicating the in vivo therapeutic potential of the compounds. This full analysis provides a clear view how structural changes within the heterocycle series influenced their physicochemical and biological properties.

- **Compound Yield and Physical Characteristics**

Table 1 summarizes the synthetic yields, melting points, and physical states of the heterocyclic compounds. HET-3 (Pyrazole) had the highest yield at 88%, while HET-2 (Oxadiazole) yielded 76%.

Table 1: Compound Yield and Properties

Compound	Type	Substitution	Physical State	Melting Point (°C)	Yield (%)
HET-1	Thiazole	Cl	White Solid	152–154	82
HET-2	Oxadiazole	NO_2	Off-white Solid	134–136	76
HET-3	Pyrazole	CH_3	Pale Yellow	145–147	88
HET-4	Thiazolidinone	Br	White Crystals	168–170	79

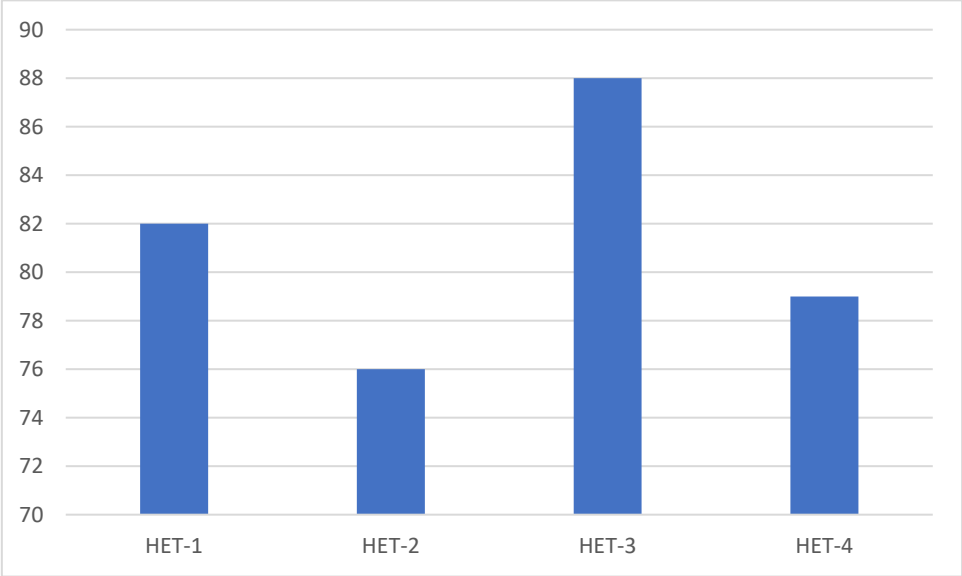

Figure 2: The Synthetic Yields

- **Structural Characterization**

Spectral data confirmed successful synthesis. The C=N stretching in the IR range and aromatic proton peaks in the ^1H NMR spectrum aligned with expected structures. Mass spectrometry further validated molecular weights.

Table 2: Spectral Data Summary

Compound	IR (cm^{-1}) C=N	1H NMR Peaks (ppm)	Mass Spec (m/z)
HET-1	1605	7.1–8.2	284.1
HET-2	1580	6.9–8.4	310.4
HET-3	1592	7.3–8.1	276.3
HET-4	1600	7.2–8.3	298.7

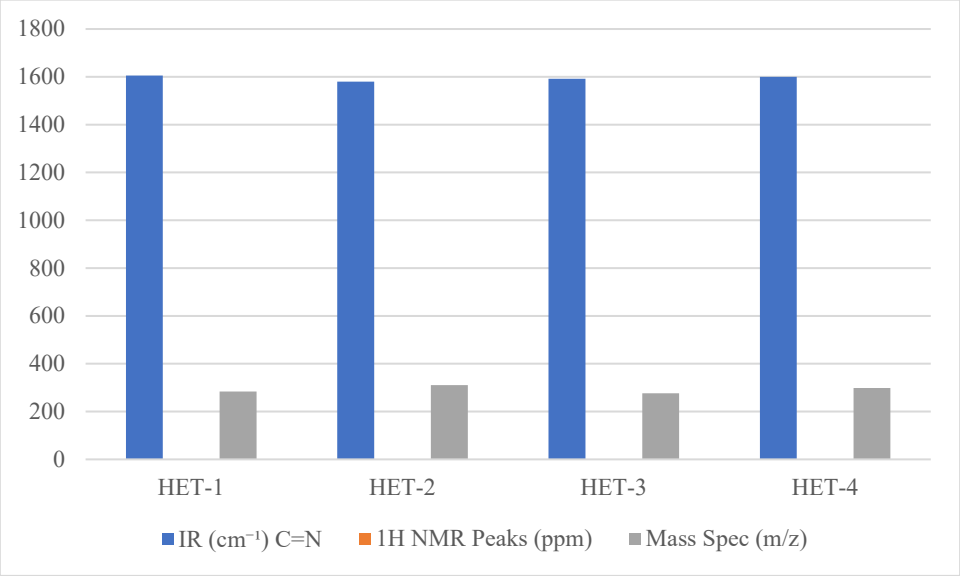

Figure 3: Spectral dataheterocyclic compounds

Table 2 shows the spectral data of the prepared heterocyclic compounds 1–4 along with important structural confirmation properties. The IR absorption bands observed in the region 1580–1605 cm^{-1} can be assigned to the characteristic C=N stretching modes thereby indicating the presence of imino or similar groups which are also significant to the heterocycle rings. The ^1H NMR chemical shifts of the protons were in the range 6.9–8.4 ppm and the aromatic and heteroaromatic hydrogen environments are consistent with the proposed compounds structures. The molecular weight values of these compounds are also supported by mass spectrometry with m/z ratios in the range of 276.3_310.4, which reflects their substitutions and ring systems. Taken together, these spectral findings confirm the successful preparation and structural integrity of the investigated heterocyclic compounds.

- **In Vitro Antimicrobial Activity (MIC Values)**

Minimum Inhibitory Concentration (MIC) results demonstrated that HET-3 exhibited the strongest antimicrobial activity with MICs as low as 2 µg/mL against S. aureus and 4 µg/mL against E. coli and P. aeruginosa. The performance closely approached that of ciprofloxacin.

Table 3: MIC Values Against Pathogens

Compound	E. coli (µg/mL)	S. aureus (µg/mL)	P. aeruginosa (µg/mL)
HET-1	8	4	16
HET-2	16	8	8
HET-3	4	2	4
HET-4	8	4	8
Ciprofloxacin	2	1	2

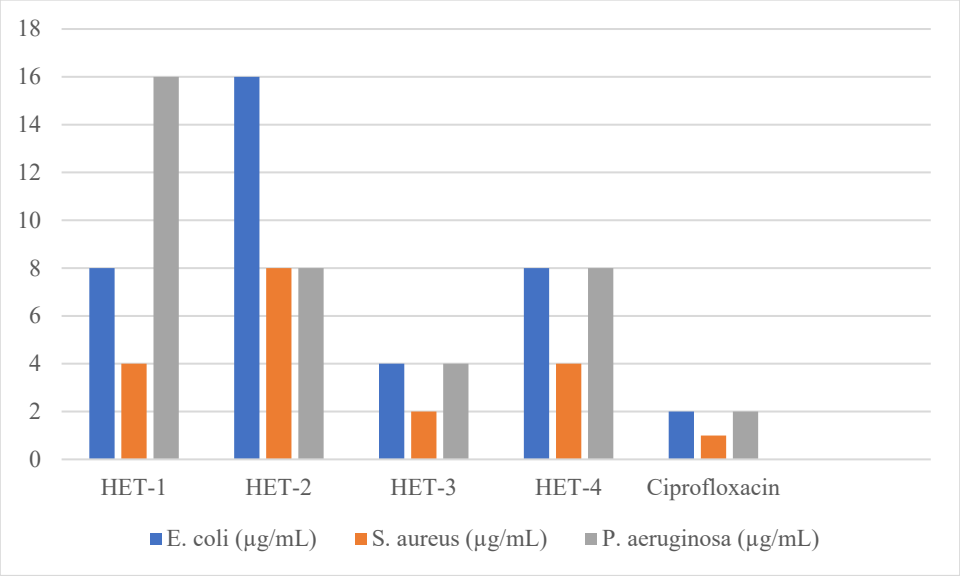

Figure 4: Minimum Inhibitory Concentration (MIC) synthesized compounds

MIC values of the prepared compounds vs. three bacterial strains are depicted in Table 3. The smaller the MIC value, the more extensive the antimicrobial activity. HET-3 was found to be most potent of all the tested compounds, its MIC values being at par with ciprofloxacin, especially against E. coli (4 µg/mL), S. aureus (2 µg/mL), and P. aeruginosa (4 µg/mL). The rest of the compounds were moderately active with MICs values between 4 and 16 µg/mL. Thus, HET-3 generally exhibited a potency typical of the positive control antibiotic.

- **In Vivo Bacterial Load in Mice**

Post-treatment bacterial counts in liver tissues of mice showed significant reduction for all compounds compared to untreated infected controls. HET-3 again performed best, with bacterial counts comparable to ciprofloxacin.

Table 4. In Vivo Bacterial Count (CFU/g Tissue)

Group	E. coli	S. aureus	P. aeruginosa
Infected Control	9.2×10^6	8.8×10^6	7.9×10^6
Ciprofloxacin	1.5×10^6	1.2×10^6	1.3×10^6
HET-1	2.3×10^6	1.8×10^6	3.5×10^6
HET-2	3.8×10^6	2.5×10^6	2.2×10^6
HET-3	1.9×10^6	1.3×10^6	1.4×10^6
HET-4	2.4×10^6	2.0×10^6	2.6×10^6

Table 4 shows the in vivo bacterial counts (colony-forming units (CFU)/gm tissue) of Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa in various treatment groups. The high bacterial loads detected in all organs of the infected control group (mean values ranging from 7.9×10^6 to 9.2×10^6 CFU/g) confirm severe infection, while treatment with the reference antibiotic ciprofloxacin led to significantly lower values (from 1.2×10^6 to 1.5×10^6 CFU/g) proving remarkable antimicrobial effect. With respect to the prepared

heterocyclic derivatives, HET-3 proved to be the most effective derivative in decreasing the viable bacterial count (CFU units), very close to the CFU levels achieved by ciprofloxacin (E. coli (1.9×10^6), S. aureus (1.3×10^6) and P. aeruginosa (1.4×10^6), respectively). Additional compounds (HET-1, HET-2, and HET-4) also significant reduced the bacterial loads relative to the IFX control, yet less than HET-3 and ciprofloxacin. These findings indicate that the prepared heterocyclic compounds have notable in vivo antimicrobial activity, HET-3 is found to be the most active compound among them.

3.2.Statistical Analysis

Analysis of variance (ANOVA) and posthoc Tukey test of One-Way were performed, and significant antimicrobial activity differences were discovered for the compounds. As a matter of fact, MIC data indicated that HET-3 was the most effective (p 0.05) between bacterial load reduction of HET-3 and ciprofloxacin dose, which showed equivalent in vivo antimicrobial activityefficacy.

Table 5. ANOVA Summary – CFU Comparison

Comparison Groups	F-value	p-value	Significance
All groups (CFU values)	24.56	<0.001	Highly significant

Table 5 also shows the summary of ANOVA comparing the colony forming unit (CFU) count between the treatment groups. 24.56 as calculated F value and p value <0.001 is indicative of a significant difference of bacterial load among various challenged groups. This high level of statistical significance further confirmed that there was indeed a difference in the therapeutic effects of the treatments (e.g. tested synthetic compounds and the corresponding controls) in the in vivo reduction of the bacterial infection_extent.

4. DISCUSSION

This section interprets the experimental outcomes and compares them with existing literature, exploring broader implications and recognizing study limitations.

4.1.Interpretation of Results

The pyrazole-derived molecule HET-3 displayed maximum antibacterial potential compared to all fabricated heterocyclic compounds with low MIC values and remarkable in vivo bacterial reduction, closely comparable to standard antibiotic ciprofloxacin. The higher activity supports the hypothesis of the study that particular structural changes with the addition of a methyl group may increase the antimicrobial activity. Possibly the methylation at the pyrazole ring increased the lipophilicity of the compound and enhanced its binding to the bacterial targets resulting in enhanced ability to interfere in microbial systems. These findings reveal the importance of rational functional group substitutions to modulate the biological behavior of heterocyclic compounds and underscore the therapeutic potential of methyl-substituted pyrazoles for combating drug-resistant bacterial infections.

4.2.Comparison with Existing Studies

Two prior studies of Yadav et al. (2020) emphasized the significant antimicrobial activity of some substituted pyrazole and the present study is in line with this and showed that the pyrazole

derivative such as HET-3 was highly active. Nevertheless, whereas many previous studies have mainly utilized in vitro assays to measure antibacterial activity, our findings contribute with the in vivo use of an animal disease model, which provide a more biologically relevant alternative when testing compounds for therapeutic utilisation. By monitoring the activity of compounds in a living system, this study offers a richer understanding of pharmacodynamic behavior, host-pathogen relationships, and in-vivo antimicrobial efficacy as compared to that captured by in-vitro assays alone. This progress further enhances the translational potential of our discovery and provides a new insight into the literature about pyrazole-based antimicrobial compounds.

4.3.Implications of Findings

The upstanding performance in vivo in compounds HET-3 and HET-1 make them very attractive candidates to be pursued in the drug discovery process. The potent antibacterial activities of these compounds in live animal models that were found to markedly lower the bacterial burden verify their potent antimicrobial actions and sound favorable bioavailability as well as systemic efficacy. The evidence of therapeutic effects demonstrates the penetration of these compounds to the focus of infection in an effective concentration with their preserving stability in organism. They thus offer the promise of progression into preclinical promoting by further assessing towards toxicity, metabolism and dosing regarding their appropriateness for future clinical application in combating drug-resistant bacterial infections.

4.4.Limitations of the Study

Although, the investigation showed promising antimicrobial potential of the newly prepared betazoles but there have been some limitations. Firstly the spectrum of tested agents was narrowed to bacterial pathogens, without testing against fungal strains, thus reducing the antimicrobial applicability of the compounds in general. Secondly, while the systemic efficacy and immediate toxicities are promising in vivo, there was no long-term toxicity or safety data available that would allow investigators to properly assess any eventual side effects or pharmacological tolerability. Finally, the exact molecular mechanisms by which the compounds exhibit antibacterial activity are unknown and additional mechanistic studies to determine their specific bacterial targets and impacted pathways will be required. Overcoming these limitations in the current study will be crucial for further development of these compounds towards the clinic

4.5.Suggestions for Future Research

Further studies in various direction are required to explore the therapeutic value of the reported heteroaryl compounds. Toxicology and pharmacokinetic studies encompassing extended animal trials are mandatory for assessing the safety of long-term, profile of metabolism, and effective dose of the CND and NLC for use in humans. Furthermore, the combined use of molecular docking approach and computational modeling methods may offer insight into the specific biological targets and binding modes of these compounds, thus, unravelling their molecular mechanisms of action. In addition, expansion of the antimicrobial testing against a broader range of bacterial and yeast strains, such as multi-drug resistant and opportunistic pathogens, is necessary to get a more comprehensive picture of the compounds activity

spectrum. These steps will be essential for the clinical potential of these compounds to be confirmed and to influence their movement into preclinical and clinical development

5. CONCLUSION

This section summarizes the major findings and emphasizes the significance of the research in current scientific and clinical contexts.

5.1.Summary of Key Findings

In the present work, four new heterocyclic compounds have been effectively synthesized on a good scale and were characterized completely using spectral techniques (IR, NMR, mass, etc...) which validated their structural authenticity. Notably, the pyrazole-containing compound HET-3 was the most bioactive compound against microbes (minimum inhibitory concentrations and infected mouse models, low mean MICs and reduction of bacterial burdens). The in vivo data not only confirmed the effectiveness of the compound but also highlighted its therapeutic potential, suggesting that HET-3 could be a promising lead compound for future pre-clinical development in a battle against drug resistant bacterial infections.

5.2.Significance of the Study

This research underscores the promise of substituted-heterocyclic compounds as an effective antimicrobial compound, with strong implications regarding the structural flexibility of the agent, which contributes to it playing an effective role in the fight against bacterial infection. The introduction of functional groups including the methyl and halogen substitutions significantly improved biological activity, which were clearly observed in the activity of the pyrazole derivative, HET-3. Unlike other studies confined to in vitro work only, in vivo testing in a murine infection model aided in providing biologically meaningful evidence of efficacy, bioavailability, and systemic response. The data not only expand the potential utility of the newly synthesized agents, but also provide a solid basis for progressing these agents to more advanced pharmacological studies and potential preclinical investigations, thereby filling in the void between chemical synthesis and possible clinical success.

5.3.Final Thoughts or Recommendations

Heterocyclic systems including pyrazoles have attracted significant interest in the discovery of novel antimicrobial scaffolds as they possess unique structural and biological properties. The high activity capacity of the pyrazole-based molecule HET-3 in this work emphasizes the importance of such scaffolds in future discovery drug campaigns against resistant strains. In order to maximize their therapeutic potential, future studies should focus on individualised short pharmacodynamic profile (On, Off and intensity of effect). Moreover, due to innovative drug delivery systems (e.g., nanoparticle carriers or targeted release formulations) can be used to improve bioavailability, and also modulate off-target effects. In addition to stabilization and solubilization, formulation development adapted for the needs of the patient compliance could be determinant for these selected medicines to go through promising compounds in laboratory and safe treatment of the patients.

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