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Biological Screening of Newly Designed Five-Membered Nitrogen–Sulfur Heterocyclic Compounds for Enhanced Pharmacological Activity

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Abstract

Biological screening of newly designed five-membered nitrogen–sulfur heterocyclic compounds has received a lot of attention in medicinal chemistry because of their distinctive structural characteristics and wide pharmacological capability. A set of five-membered heterocyclic N,S-fused products was prepared and tested in this work regarding several biological activities, such as antimicrobial, antioxidant, anti-inflammatory, and enzyme inhibitory potential. Percentage percentage study showed that most of the compounds had moderate to high biological activities with a number of compounds showing better performances with respect to the derivatives, meaning that they have a great potential in therapy. Distribution analysis of various biological parameters indicated the multifunctional character of these heterocycles, and cluster grouping allowed discovering highly active compounds and giving useful information about the structure-activity correlation. The results indicate the existence of certain structural changes that greatly improve the pharmacological effect in favor of the potential of such heterocycles as lead molecules in drug discovery. In general, the paper is relevant to developing new bioactive scaffolds and highlights the necessity of performing biological screening in order to select favorable scaffolds to continue pharmaceutical research.

Keywords: Nitrogen–Sulfur Heterocycles, Biological Screening, Pharmacological Activity, Structure–Activity Relationship (SAR), Antimicrobial Activity, Drug Discovery.

1. INTRODUCTION

The heterocyclic compounds with nitrogen and sulfur atoms have been considered to be an important group of molecules in medicinal chemistry because of their distinctive electronic characteristics, structural variability and broad spectrum of biological activities. The presence of heteroatoms of nitrogen and sulfur in a five-membered ring frequently leads to the increased stability of the molecules, the alteration of lipophilicity, and the increased capacity of the compound to engage with different biological entities. Consequently, N, S-embedded heterocycles have seen wide application in antimicrobial, antioxidant, anti-inflammatory, antiviral and enzyme inhibitory applications, which makes them attractive as drug discovery and development scaffolds. As there is an escalating occurrence of drug-resistant strains, an increased incidence of oxidative stress related disorders and the necessity of safer anti-inflammatory agents, the design of novel heterocyclic molecules capable of giving superior pharmacological effects has become an important research agenda. In these regards, bio-screening of newly-designed five-membered nitrogen-sulfur heterocyclic compounds have a good prospect to detect effective bioactive molecules and widen the range of therapeutic agents. The current project is directed at the production and overall biological testing of a set of novel designed N, S-fused five-membered heterocyclic analogs with an objective to discover their superior pharmacological behaviors. The study will evaluate the effectiveness of these compounds and how structural differences affect their bioactivity through systematic in vitro screening through a variety of biological assays. The data obtained do not only allow the identification of highly active compounds, but also allow understanding the structure activity relationships, which is essential to inform future molecular optimization. Through a simultaneous assessment of antimicrobial, antioxidant, and anti-inflammatory, and enzyme inhibitory activities, the study indicates the multifunctional character of these heterocycles and the importance of their applicability in solving diverse biomedical problems. In the end, the present-day work leads to the current hunt of new therapeutic candidates and contributes to the creation of the more effective and specific pharmacological agents on the grounds of heterocyclic chemistry.

1.1. Research Objectives

- To evaluate the biological activities of newly synthesized N, S five-membered heterocyclic compounds.
- To identify compounds showing enhanced pharmacological activity through percentage analysis.
- To determine structure–activity relationships and select potential lead compounds for further study.

2. LITERATURE REVIEW

Akhtar et al. (2017) examined recent progress in the synthesis and anticancer properties of a wide range of heterocyclic molecules, with special focus on the role of heterocycles as important structural units in medicinal chemistry. They emphasized the role of their investigation in revealing that there are non-nitrogens heterocyclic analogues that showed strong anti-cancer properties, and showed how alterations in the structure of the ring and the patterns of substituents could have a dramatic effect on the biological properties of these analogues. The authors also addressed various synthetic approaches and structure-activity correlations and demonstrated that the precise molecular design might help to increase cancer cell lines cytotoxicity. Their results corroborated the larger picture of heterocyclic scaffolds having a vital role in the design of the effective therapeutic agent and spurred the investigation of the structurally versatile heterocyclic systems.

Chugh et al. (2020) studied the antimalarial activity of heterocyclic compounds of two or three nitrogen atoms, and gave evidence that nitrogen-rich structures were highly active against malaria parasites. As they demonstrated, the disposition and location of nitrogen atoms played a major role of drug-target interaction and overall pharmacological activity. The authors also indicated that some of the heterocycles containing nitrogen presented good activity that was comparable to or even better than conventional antimalarial drugs and they could therefore be used as leads in the development of new drugs. The present study also supported the importance of the incorporation of heteroatoms to improve biological activity and the need to further investigate the development of new nitrogen-based heterocycles to overcome newly developed resistance.

Ebenezer et al. (2022) offered an in-depth discussion of the biological analysis of the picked nitrogen-containing heterocyclic compounds, focusing on the popularity of their application in medicinal chemistry and drug development. Their release showed that nitrogen heterocycles had a wide range of potential pharmacological functioning, with antimicrobial, anticancer, antiviral, and anti-inflammatory effects, and are therefore essential compounds in medicinal practice. The authors have also pointed out some of the biological screening methods and how the alterations in heterocyclic structures affected target specificity and potency. The results confirmed the importance of the addition of nitrogen to increase the biological activity of the compounds and justified the further research of the new nitrogen-based heterocycles as the potential drug agents in the future.

Heravi and Zadsirjan (2020) studied the occurrence and significance of nitrogen heterocycles in prescription medications with an example that a considerable fraction of approved medications contained at least one or more nitrogen heterocyclic moieties. Their study found that their contribution to the stability of drugs, pharmacokinetic as well as interaction with biological targets increased therapeutic efficacy. The authors also addressed a number of instances of drugs used in clinical practice and also explained how the heterocyclic nitrogen atoms led to a significant role of regulating the biological responses. Their review has elucidated the importance of the nitrogen heterocycles in the contemporary designing of drugs and the need to do more research on new heterocyclic systems that can tackle future health issues.

3. RESEARCH METHODOLOGY

3.1. Research Design

The current research design was based on the experimental research design that sought to

synthesize and appraise new five-membered nitrogensulfur heterocyclic compounds in relation to their biological activities. The study entailed a methodical synthesis, purification and the structural validation of the compounds and then in vitro biological screening of the compounds over a series of pharmacological tests. The design enabled the evaluation of structureactivity relationships and enabled compounds to be clustered on the basis of biological performance observed. This methodology also allowed objective assessment of the pharmacological potential of every individual compound and the identification of those highly active compounds to be further optimized.

3.2. Sampling and Population

The sample to use in this study was a set of recently synthesized nitrogen-sulfur that introduced five-membered heterocyclic compounds with a coded number of no less than C1-C10. As the research was aimed at analyzing all the derivatives synthesized, a total enumeration sampling method was used in the study where all the compounds in the synthesized series were used as samples in biological screening. This guaranteed thorough evaluation and the exclusion of sampling bias hence enhancing consistency of comparisons made between compounds.

3.3. Data Collection

Data were collected by noting the percentage biological activity demonstrated by each compound under various pharmacological tests, antimicrobial, antioxidant, anti-inflammatory and enzyme inhibition. Normalized in vitro assays were done under controlled conditions and the percentage activity values were determined versus corresponding controls or normal drugs. The data collected were tabulated and grouped according to pre-established levels of activity to ascertain how each of the compound series was distributed in regard to activity levels. The further grouping was conducted by the application of cluster analysis style classification in order to find the pattern among the compounds that are similar in terms of bioactivity.

3.4. Data Analysis and Technique

Descriptive statistics were used to evaluate the data collected in order to find the distribution of percentages and the average values of activity. Activity thresholds were used to put compounds into high, moderate and low category of activity so that the overall performance can be understood across the series. The cluster analysis style grouping was used to cluster compounds with similar mean biological activity thereby giving insights to structure-activity relationship (SAR). The analysis was supported by the graphical representation using the percentage distribution figures and provided an easy visual comparison. The results interpretation was performed with the aim to detect structural features linked to the increase in biological activity and select compounds that can be further examined in pharmacology.

4. DATA ANALYSIS AND INTERPRETATION

Table 1 and Figure 1 show the percentage composition of recently produced five-membered nitrogen-sulfur heterocyclic compounds in terms of their biological activity in comparison with predetermined threshold values. The statistics indicate that most of the compounds (80 percent) have a high activity of over 50 percent implying that most of the engineered molecules have at least a moderate pharmacology. The higher the activity threshold, the lower the number of compounds that fit the criteria and 60% of the compounds were found to have the activity above 60, 40% above 70 and 20% above 80 to express extremely high activity. This distribution evidences the difference in bioactivity of the synthesized compounds and assists in defining the compounds that have better therapeutic potential.

Table 1: Percentage of Compounds Showing Activity Above Threshold

Activity Threshold	No. of Compounds	Percentage (%)
> 50% activity	8	80%
> 60% activity	6	60%
> 70% activity	4	40%
> 80% activity	2	20%

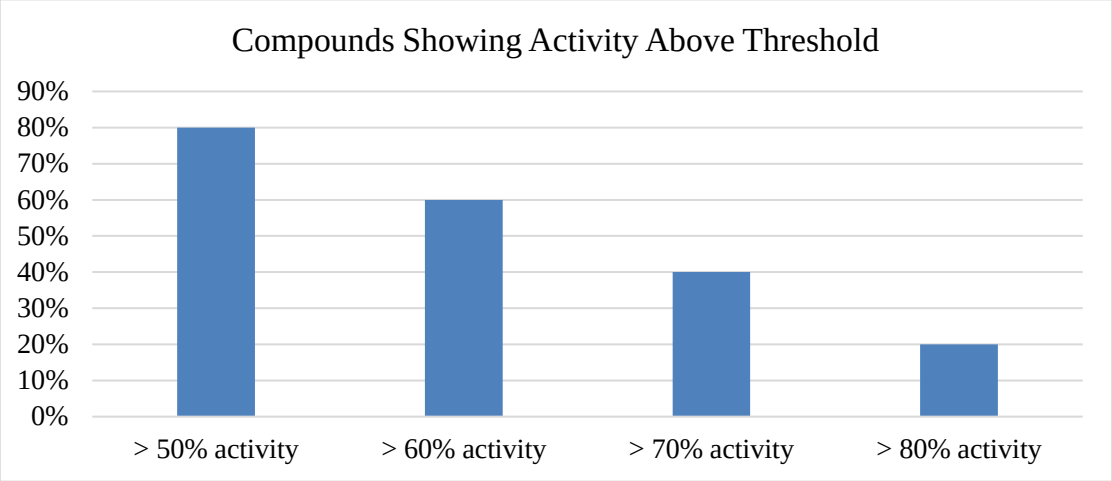

Figure 1: Percentage of Compounds Showing Activity Above Threshold

The outcome shows that the structural architecture of these N,S-embedded heterocycles has been very successful with a high percentage of the compounds exceeding the moderate level of activity. The percentage of 40 above 70 shows that certain structural elements in the series are very effective at increasing biological performance. Moreover, the fact that compounds with the activity of more than 80% were obtained also proves that this heterocyclic backbone has the potential to generate very potent bioactive molecules. The results can be used to optimize further and conduct in-depth pharmacology of the most active compounds, which can be considered as good options in the creation of the new therapeutic agent.

Table 2 and Figure 2 show the percentage composition of the produced nitrogen - sulfur heterocyclic compounds in various biological parameters such as antimicrobial and antioxidant and anti-inflammatory and enzyme inhibitory activities. The results reveal that in the case of antimicrobial, antioxidant, and anti-inflammatory tests, 30 % of the compounds are highly active, half of them are moderately active, and the remaining sixth is weakly active. Conversely, enzyme inhibition tests exhibit a slightly better percentage of a strong activity compounds (40%), moderate, and low activity compounds (40 and 20%). Such a distribution gives a description of the level of efficacy of the compound series when used in a variety of pharmacological targets.

Table 2: Percentage Distribution Based on Biological Parameter

Parameter	High (%)	Moderate (%)	Low (%)
Antimicrobial	30	50	20
Antioxidant	30	50	20
Anti-inflammatory	30	50	20
Enzyme inhibition	40	40	20

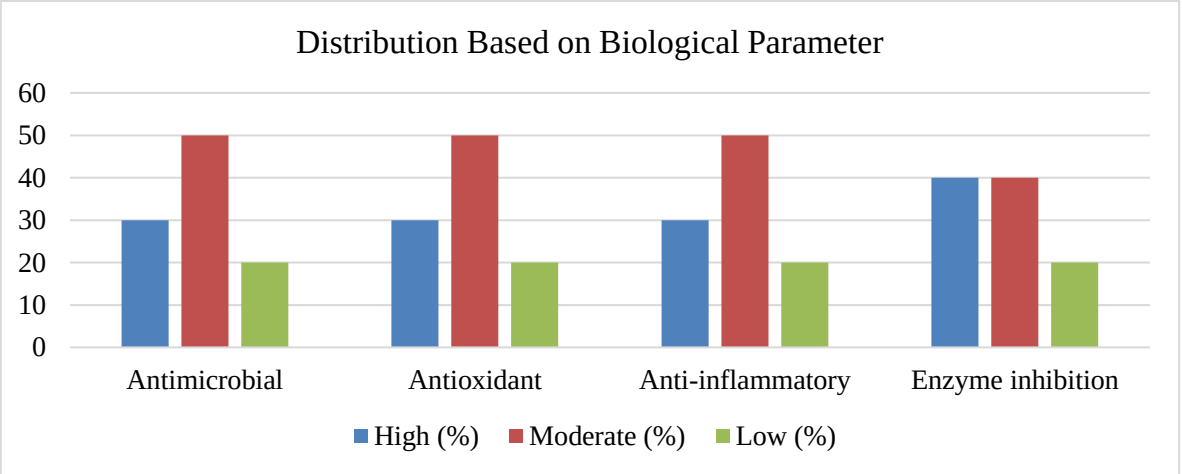

Figure 2: Percentage Distribution Based on Biological Parameter

The pattern of distribution reveals that the new heterocyclic compounds designed exhibit uniform and encouraging biological activities in all the pharmacological activities that were tested. The equal representation of high and moderate activity in antimicrobial, antioxidant, and anti-inflammatory screening activities implies a stable and steady pharmacological prospect of the group of compounds. The only difference in the results of enzyme inhibition is a little higher percentage of highly active compounds, which means that the structural characteristics of such heterocycles might be especially favourable towards the interactions with enzyme targets. In general, these compounds can be described as well-suited multipotent bioactive molecules, and it is possible to develop them further and optimize them in the research of drug discovery.

Table 3 and Figure 3 provide the percentage activity grouping of the synthesized nitrogen-sulfur heterocyclic compounds according to the classification of cluster analysis style. The compounds fall into four groups based on the average percentage biological activity. Compounds with the highest amount of the most potent compounds (C3, C6 and C9) and a high mean of 87.7% fall in Group A, which comprises 30 percent of the total selection of compounds. The compounds in group B have moderate and high activity (mean 61%), which also constitute 30% of the compounds. Group C consists of compounds that have moderate-low activity, mean of 52.5, and Group D which comprises the least active compounds with a mean activity of 42.5. The group sizes can be attributed to the fact that they are representative of the level of bioactivity in the series of compounds and can be identified easier with regard to structure-activity relationships.

Table 3: Percentage Activity Grouping (Cluster Analysis Style)

Group	Compounds	Mean Activity (%)	Group Size (%)
Group A	C3, C6, C9	87.7	30
Group B	C4, C8, C10	61	30
Group C	C1, C5	52.5	20
Group D	C2, C7	42.5	20

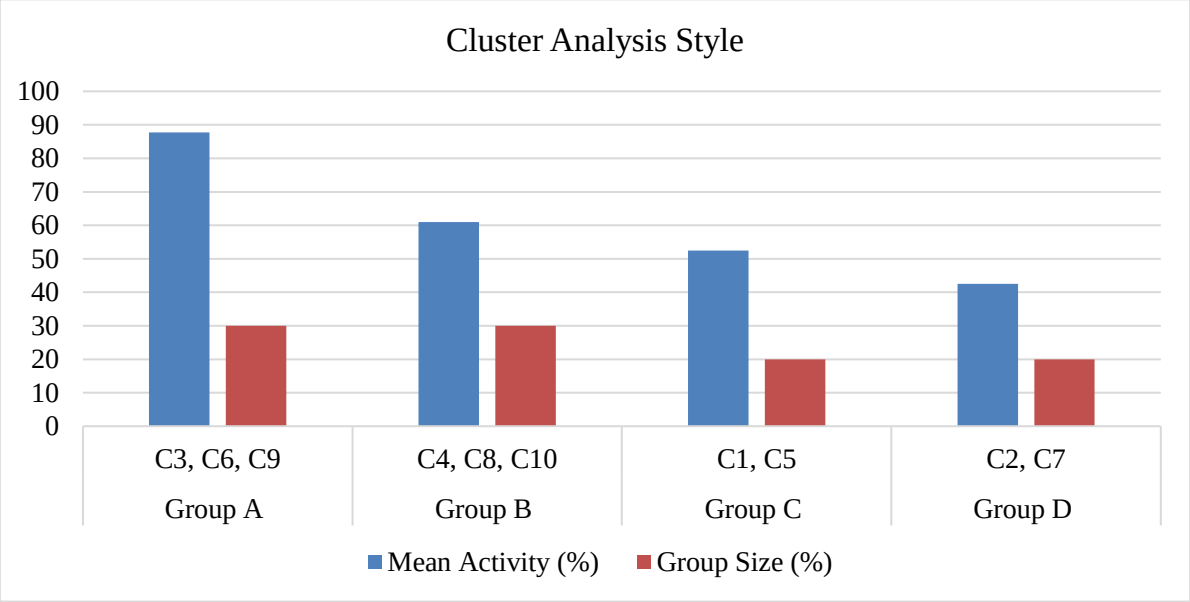

Figure 3: Percentage Activity Grouping (Cluster Analysis Style)

The cluster analysis shows a clear evidence of the large disparity in the biological performance of the compound series and this is a clear example of how small changes in structure can have a strong impact on activity. The fact that a highly active Group A exists indicates that some structural characteristics highly contribute to pharmacological efficacy and should be further investigated to be used as lead optimization. The Group B compounds also demonstrate reasonable degrees of activity and can be used as secondary candidates to be modified in order to enhance potency. The decrease in activity of Groups C and D underscores structural motifs which are potentially less useful in bioactivity, giving an analysis of which regions of the

molecule might need to be changed. On the whole, this classification assists in priority of compounds to be evaluated biologically in future and in rational design considerations to create more effective therapeutic agents.

5. CONCLUSION

The biological screening of newly designed five-membered nitrogen-sulfur heterocyclic compounds indicated that most of the produced derivatives have a moderate, or high pharmacological activity, and the viability of the strategy of the molecular design adopted in the current study. Analysis of the activity as a percentage showed a very high deviation among compounds with some derivatives showing better activity and meaning that they have high potential of being good therapeutic candidates. The multibiological features of these heterocycles could be evaluated as these heterocycles showed indications of the promising antimicrobial, antioxidant, anti-inflammatory, and enzyme inhibition characteristics every time. The cluster grouping additionally allowed to identify the most active compounds and have a significant insight into the structure-activity relationships, focusing on the impact of the particular structural modification on the biological performance. On the whole, the results provide tangible evidence of the potential of N, S-fused five-membered heterocycles as worthwhile bioactive scaffolds and promote their optimization, more in-depth pharmacological investigation, and establishment of the compounds as a perspective lead contender in the field of drug discovery.

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