

CHARACTERIZATION OF NOVEL HETEROCYCLIC MOLECULES CONTAINING NITROGEN

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Abstract. Nitrogen-containing heterocycles remain a cornerstone of medicinal chemistry because they combine structural diversity with tunable intermolecular interactions that govern receptor/enzyme recognition, solubility, and selectivity. Building on this rationale, the present work reports the design and synthesis of a focused series of pyrazole-linked thiazole hydrazones (P25–38), framed as lead-like scaffolds for multi-target bioactivity. The study's strength lies in its emphasis on structure confirmation using complementary analytical platforms (FT-IR, ¹H/¹³C-NMR, LC-MS, and CHNS elemental analysis), which collectively reduce ambiguity in scaffold assignment and support subsequent structure-activity interpretation. Representative spectral signatures: N–H stretching (~3320–3406 cm⁻¹), azomethine C=N bands (~1610–1615 cm⁻¹), diagnostic singlets for pyrazole-NH (~δ 11.8–11.9) and N=CH (~δ 8.1–8.2), and molecular ion consistency in MS; provide a coherent validation chain for the proposed hydrazone–thiazole–pyrazole framework. Biological screening indicates promising antimicrobial (and reported anti-inflammatory/anticancer) potential, with activity trends linked to electron-withdrawing aryl substituents. Notably, chloro/dichloro substitution patterns are repeatedly implicated as potency-enhancing features, suggesting that halogen-driven lipophilicity and electronic effects may improve target engagement and membrane permeability. The SAR discussion, while preliminary, points toward a practical optimisation pathway: systematic substituent modulation on the aryl rings to balance antibacterial efficacy with selectivity, alongside retaining hydrogen-donor motifs (e.g., C=N–NH) associated with antioxidant behaviour. Overall, the work positions these nitrogen-rich heterocycles as credible starting points for lead optimisation, but their translational value will ultimately depend on expanded bioassay panels, potency benchmarking, and mechanistic validation beyond single-point inhibition claims.

Keywords: SAR, antimicrobial, heterocyclic molecules, efficacy, selectivity

Introduction

If a chemical's cyclic ring structure contains at least one heteroatom, it is said to be heterocyclic. The most prevalent heteroatoms are sulfur, oxygen, and nitrogen. Heterocyclic compounds, which are found in a wide variety of plants and animals, make up half of all organic compounds in nature. Natural substances include proteins, enzymes, alkaloids, colors, medicines, and numerous other significant heterocyclic molecules. Electronic structures make it simple to classify heterocyclic molecules. Heterocyclic compounds are mostly composed of unsaturated and saturated groups (Rana et al., 2023; Tupare, 2021; Caiazza et al., 2004). Saturated heterocyclic molecules function similarly to their acyclic equivalents because of modifications in their steric characteristics. Tetrahydrofuran and piperidine are common ethers and amines (Li and Luo, 2002). Due to their unconstrained nature, unsaturated heterocyclic compounds with rings of five or six members have been the subject of extensive research. Unstrained unsaturated heterocyclic compounds include furan, pyridine, thiophene, pyrrole, and their benzo fused derivatives. Among the prominent benzo fused heterocycles are benzothiophene, quinoline, indole, and benzofuran. Heterocyclic

compounds are used in veterinary products, agrochemicals, and pharmaceuticals. Life depends on a large number of heterocyclic compounds. Hormones, alkaloids, antibiotics, and essential elements like proteins, vitamins, hemoglobin, pigments, and dyes are examples of heterocyclic compounds (Du et al., 2016) (Figure 1).

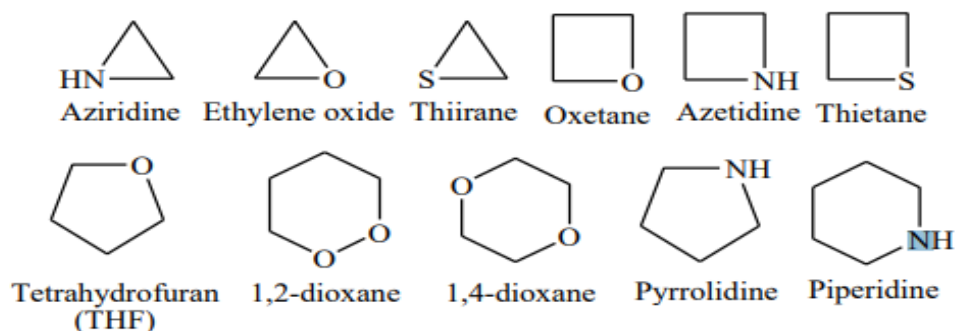


Figure 1. Examples of heterocyclic compounds.

Two separate components make up the ring of heterocyclic molecules. They belong to one of the biggest classes of organic compounds and are very helpful in many different chemical fields. Among these are additional medications, biomass, nucleic acids, artificial coloring, alkaloids, herbicides, vitamins, hormones, antibiotics, and pharmaceuticals. For organic and medicinal chemists, heterocyclic molecules are valuable, yet their synthesis is a constant challenge in both academia and industry (Muralirajan and Cheng, 2016). Diverse biologic functions are provided by heterocyclic systems with a variety of molecular structures. All of these systems have been used to create rare drugs because of their physicochemical characteristics. These compounds have gained popularity recently due to the presence of nitrogen and sulfur atoms. Cancer, stomach ulcers, bacterial and fungal infections, and other illnesses are all commonly treated with these substances (Rana et al., 2023; Tupare, 2021; Majumder et al., 2013; Caiazza et al., 2004). Because of their special properties and uses, these nitrogen-containing heterocyclic compounds have attracted attention from the pharmaceutical sector, medicinal chemistry, and organic chemistry. Furthermore, a number of weak interactions can be produced by the proton-rich nitrogen heterocycle readily taking or giving a proton. Nitrogen compounds have a significant influence on medicinal chemistry due to the intermolecular forces, which include hydrogen bonding, dipole-dipole interactions, hydrophobic effects, van der Waals forces, and π -stacking interactions. Their high solubility in water allows them to establish robust binding contacts with receptors and enzymes. As a result, their progeny exhibit a wide range of bioactivities, and their structural characteristics are beneficial (El Sayed and El Nemr, 2008).

Typical features of compounds with heterocyclic rings

Most Heterocycles are cyclic structures containing either Sulphur, nitrogen, or oxygen atoms, and consist of five or six members. There are six atoms in a pyridine molecule: five carbons and one nitrogen. Pyrrole, furan, and thiophene molecules are characterized by cyclic ring structures that consist of four carbon atoms and one element of either Sulphur, nitrogen, or oxygen atom (Parveen et al., 2017). Ni heterocycles include pyridine and pyrrole with carbon rings. Many biological components include pyridine and pyrrole rings, which release tiny quantities when heated. In the 1850s,

intense bone heating produced an oily combination that included both of these chemicals. Today, pyridine and pyrrole are synthesized. Conversion to dyestuffs and medicines is their main commercial use. Pyridine is a solvent, waterproofed, ingredient for rubber, alcohol denaturant, and food colourant (Muralirajan and Cheng, 2016; El Sayed and El Nemr, 2008). Synthesis of pyrrole and other chemicals is facilitated by furan, an oxygen-containing heterocycle. Oat hulls and corncobs provide furfural, a chemical cousin of furan, used to make nylon intermediates. Thiophene, a sulfur heterocycle, is chemically and physically similar to benzene. It was identified during benzene purification and is a common contaminant of natural benzene. Like other compounds, it is mostly converted. Thiophene and furan were found in the late 19th century (Sal'keeva et al., 2015). Heterocyclic compounds' physical and chemical characteristics are best understood by comparing them to organic molecules without heteroatoms.

History of heterocyclic chemistry

Chemistry remained undivided until 1900, when inorganic, organic, and physical chemistry were needed. Factual content increased separation into subfields. Heterocyclic compounds are the most diverse organic family. Heterocyclic chemistry developed alongside organic chemistry in the 1800s. Some notable 1818 events. Brugnatelli isolates Alloxan from uric acid 1832. By processing starch with sulfuric acid, Dobereiner makes furfural (afuran). 1834: Runge dry distills bones to get pyrrole ("fiery oil") 1906, A major agricultural business is replaced by synthetic chemistry when Friedlander synthesizes indigo dye. 1936: Treibsisolates chlorophyll derivatives from crude oil, explaining petroleum's origin 1951: Chargaff's guidelines emphasize heterocyclic components (purines and pyrimidines) in the genetic code (Li and Luo, 2002). Some important heterocycle breakthroughs include, in general, comparing heterocyclic molecules to organic compounds without heteroatoms to understand their physical and chemical properties. In medical chemistry, heterocyclic molecules are significant. It aids therapeutic drug development. Organic heterocycle chemistry is fascinating. Natural heterocyclic compounds are abundant. Most medications, vitamins, and other natural items are heterocycles (Rana et al., 2023; Tupare, 2021; Yu et al., 2021).

Classifications isocyanide-containing compounds

Various The classification of heterocyclic compounds was done according to the quantity of members and the kind of hetero atoms (N, S, O, Se) that were substituted. Based on structure and electrical arrangement, heterocyclic compounds fall into two types.

Heterocyclic compounds with aliphatic rings

Compounds with heterocyclic aromas

An aliphatic heterocyclic compound is an ether, a thioether, an amide, or a cyclic amine. Without double bonds, saturated heterocycles are aliphatic.. Ring strain mostly affects aliphatic heterocycle characteristics. Figure depicts aliphatic heterocyclic molecules (El Sayed and El Nemr, 2008). But chemicals that are heterocyclic aromatics are similar to benzene. Heterocyclic aromatic compounds follow Huckel's law. Huckel's

rule asserts that because of conjugate double bonds, aromatic compounds must be cyclic, have planar geometry, and contain $(4n+2) \pi$ electrons. Aromatic heterocyclic compounds are shown in *Figure 2*. In a hetero cyclic ring, three or more atoms might be unsaturated or saturated. The heteroatoms that make up a heterocyclic ring might be quite similar or completely dissimilar (Yu et al., 2021; Parveen et al., 2017; Du et al., 2016).

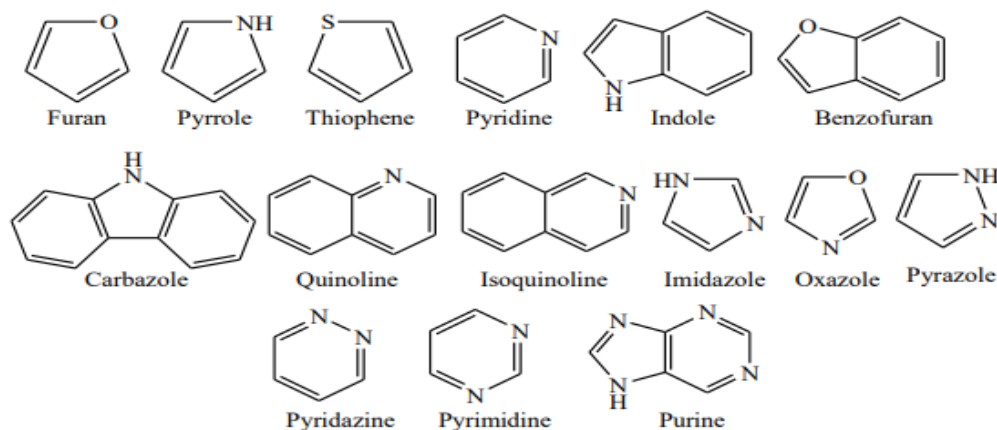


Figure 2. Heterocyclic compounds with aromatic rings.

Characterization bases on schiff and chalcones

Element analysis

There are very few components that make up most organic molecules. Hydrogen, carbon, oxygen, nitrogen, sulfur, chlorine, and so on are among the most crucial. Determining the elemental composition of an organic compound's molecular structure is the primary goal of elementary quantitative organic analysis (Tupare, 2021).

Introduction of spectroscopy

When it comes to studying the structures of systems that are important to chemicals, spectroscopy is the most important and promising method. Spectroscopy is a wonderful tool for extracting structural and other physico-chemical features of molecules, since it explores the phenomena caused by the interaction between matter and electromagnetic radiation. Biological atoms emit electromagnetic radiations when their electric and magnetic dipoles oscillate. Matter absorbs or emits energy in definite quantities termed quanta, which is the most essential consequence of electromagnetic interaction. distinct molecular energy levels have distinct shapes, and this energy gap of individual atoms and molecules may be measured using spectroscopic Techniques (Abed and Ghanem, 2019; Du et al., 2016; Li and Luo, 2002). The molecular structure may be elucidated with the use of several spectroscopy techniques and quantum chemical approaches. The visible and ultraviolet (UV) regions of an electronic spectrum are produced by changes in the energy levels of individual electrons. It reveals details about bonding and molecular orbitals. Organic chemical bond and functional group information is revealed via vibrational transitions that take place in the infrared part of the electromagnetic spectrum. Radioactive decays of nuclear spins may provide light on what is around hydrogen atoms chemically, and how many organic molecules include carbon and hydrogen atoms (Yu et al., 2021). Spectroscopy has been a great asset in the structural

study of biological molecules, polymers, minerals, inorganic and organometallic compounds, and both simple and complex molecules (Yu et al., 2021; Du et al., 2016).

Infrared spectroscopy

Organic chemical identification using infrared spectroscopy is commonplace. The main focus of infrared spectroscopy is the sample's ability to absorb infrared energy. The molecular vibrations caused by the absorption of infrared light give birth to densely packed absorption bands. Qualitative and quantitative analysis may be done using the IR approach in conjunction with intensity measurements. When it comes to revealing the structure of mysterious substances, this method is now dominating the market, even over other scientific techniques, such as electron spin resonance and X-ray diffraction (Sal'keeva et al., 2015).

Infrared activity

Changing the dipole moment is what makes a standard vibration mode infrared active. As the vibration progresses, the electric vector associated with radiation may interact with the alternating electric field produced up by the dipole moment's ongoing variation during a molecule's oscillation. Because of the way it spins or vibrates, the molecule changes its electrical dipole moment and amplitude of vibration, which allows it to absorb infrared light (Majumder et al., 2013).

Materials and Methods

Flushing equimolar quantities of the starting ingredients with thiosemicarbazide in absolute ethanol (*Figure 3*). The method was used to produce substituted phenacyl bromides (9a-c). Refluxing 3-aryl-1H-phenacyl bromides in ethanol with pyrazole-4-carbaldehyde thiosemicarbazones (8a-e) yielded in excellent yield. Scheme 4.1 summarizes the chemical mechanism (Parveen et al., 2017). If R is a group consisting of hydrogen, 4-chloromethyl, 4-fluoromethyl, 4-chloromethyl, and 2,4-chloromethyl, then Ar = C₆H₅, 4-OCH₃-C₆H₄, 4-F-C₆H₄

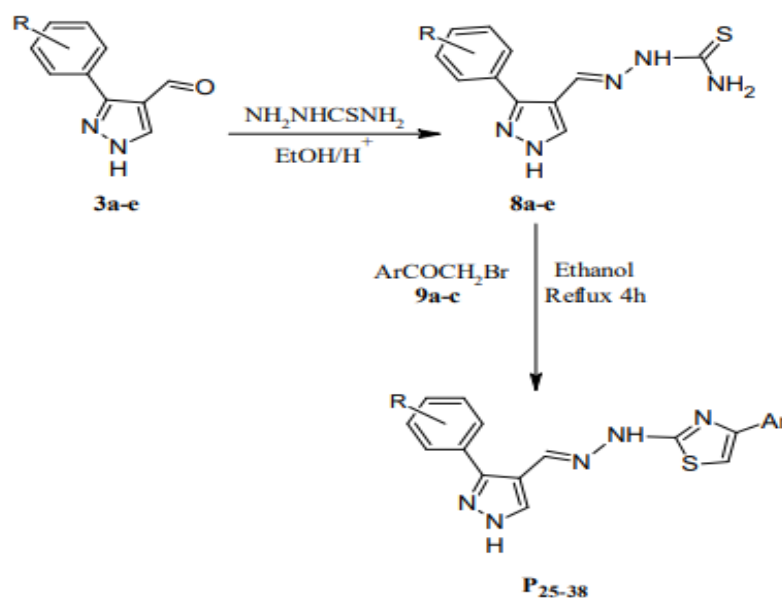


Figure 3. Thiosemicarbazide P25-P28.

A synthesis process for 2,4-disubstituted thiazole analogues P₂₅₋₃₈

Melting points were resolved using open capillary analysis. The infrared spectra were collected using a Thermo Nicolet avatar 330-FT-IR spectrophotometer. A 100 MHz Bruker spectrometer was used to produce the ¹³C NMR spectra, while a 400 MHz Bruker and Varian spectrometer was used to obtain the ¹H-NMR spectra using DMSO-d₆ as the internal standard. Parts per million is the unit of measurement for chemical shift data. The mass spectra were acquired using an Agilent 1100 series LC-MS. In order to examine the parts, we used a Flash EA 1112 CHNS-O Analyser. In thin layer chromatography (TLC), silica gel 60 F254-coated aluminium sheets were used to guarantee reaction completion. Avoiding purification while using commercial solvents and reagents (Rana et al., 2023; Du et al., 2016; El Sayed and El Nemr, 2008).

Results and Discussion

Utilizing nuclear magnetic resonance (NMR), infrared, and elemental spectroscopy, the compounds P25–38 that were synthesized were examined. Spectra and analytical information for every single one of the compounds that were made conformed to the models. There were absorption lines at 3320, 3013, 1610, 1485, and 1085. The N-H proton of the pyrazole compound is seen as a singlet with a chemical shift of δ 11.8 in the ¹H-NMR spectra. P25. At δ 8.1, a singlet resonated from an N=CH proton. The proton of thiazole-5H and the proton of pyrazole-5H did not resonate as a pair at δ 7.29 and 8.0, correspondingly. At $m/z=344$ (M-1), there peaks in the mass spectra of molecular ions at the P25 level, which matches C₁₉H₁₅N₅S experimental component gives spectrum chemistry and C, H, and N analyses.

The hydrazone of compound in a pyrazole ring with three hydrogen atoms attached to a carbamate ring and four phenyl group (P25)

FT-IR (cm^{-1}): 3320 (N-H-str), 3013 (C-H-str), 1610 (C=N), 1485 (C=C) (Figure 4); $^1\text{H-NMR}$ (DMSO- d_6): δ 11.8 (s, 1H, pyrazole-NH), 8.19 (s, 1H, N=CH), 8.04 (s, 1H, pyrazole-5H), 7.3-7.84 (m, 10H, Ar-H), 7.29 (s, 1H, thiazole-5H) (Figure 5); $^{13}\text{C-NMR}$: 168.6, 149.5, 137.22, 134.4, 131.1, 129.2, 129.0, 128.9, 128.6, 128.2, 126.1, 114.2, 103.8 (Figure 6). As seen in Figure 7, $m/z = 344$ (M-1) for MS. C=66.07, H=4.38, and N=20.27 are the results of the analytical calculations for C₁₉H₁₅N₅S. Found: C=66.10, H=4.34, and N= 20.23% (Tupare, 2021).

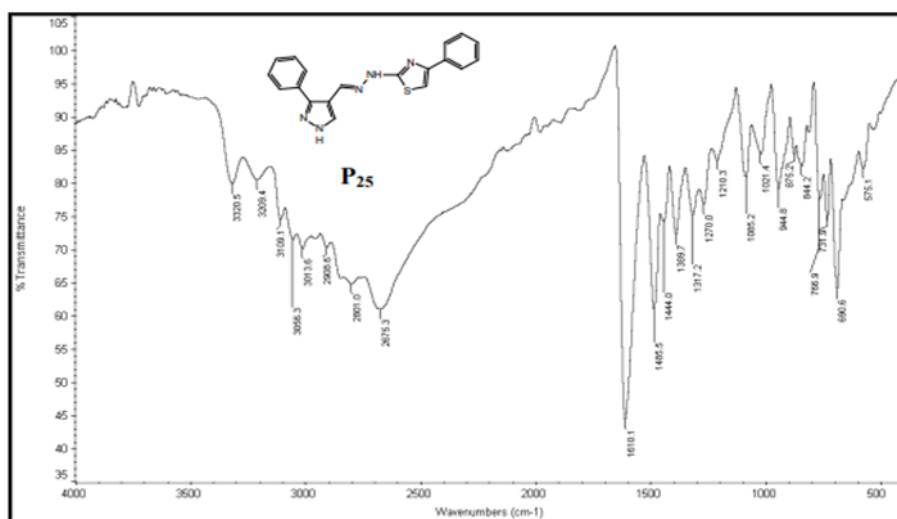


Figure 4. The compound's infrared spectra.

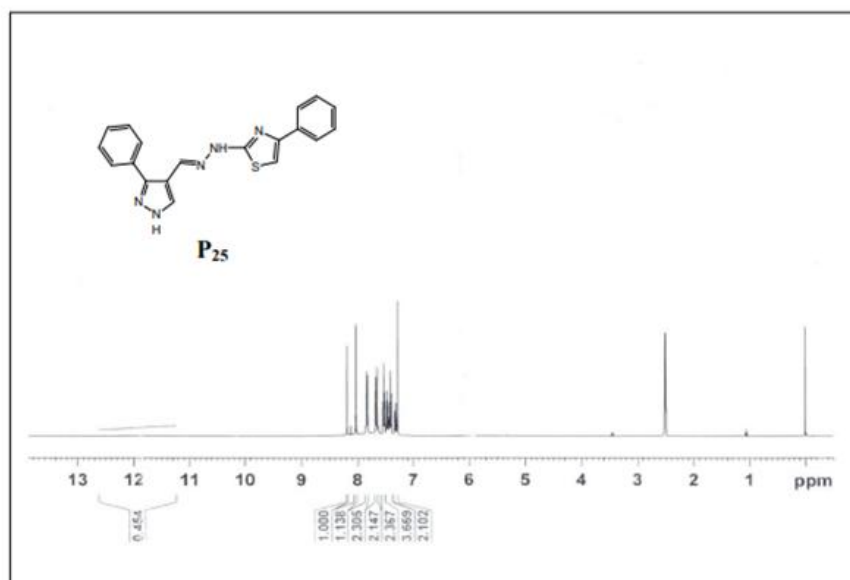


Figure 5. $^1\text{H-NMR}$ spectra of P25-containing substance.

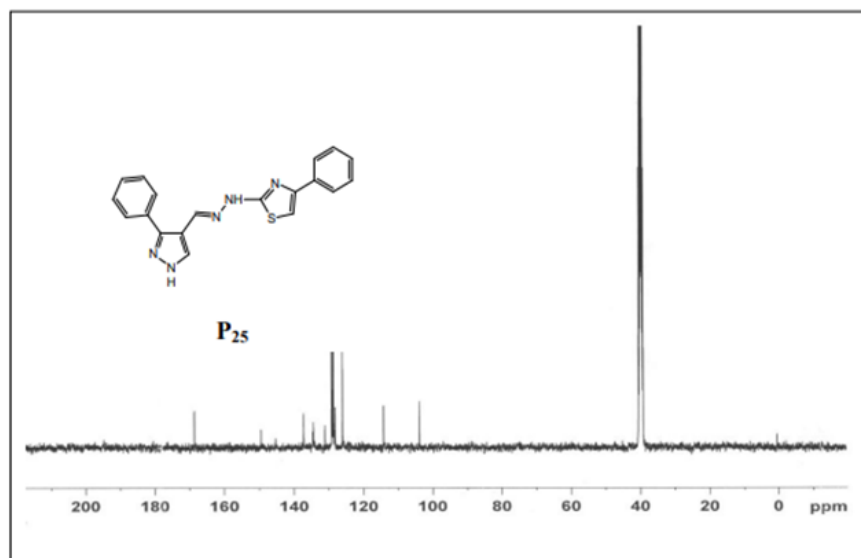


Figure 6. The chemical's ^{13}C NMR spectra P25.

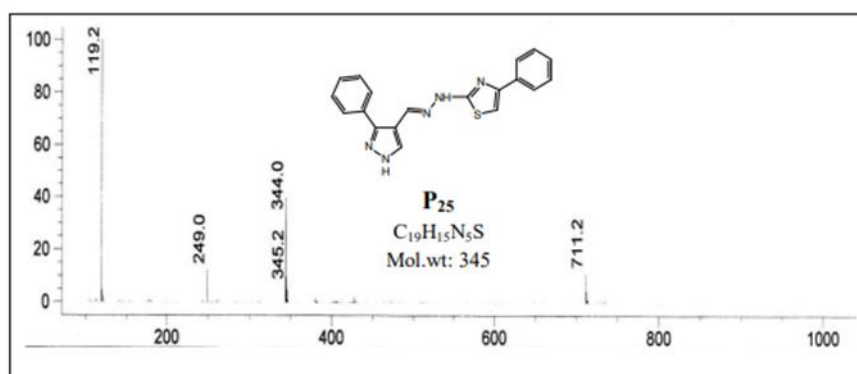


Figure 7. Compound mass spectra P25.

This chemical compound 3-[4-methoxyphenyl]one of its structural components is A-pyrazole-4-carbaldehyde dimer 4-phenyl-1,3-thiazol-2-yl (P26) Hydrazone is an artificial

In cm^{-1} , the following FT-IR values were recorded: 3406 for N-H-str, 3043 for C-H-str, 1615 for C=N, and 1438 for C=C. Additionally, the ^1H -NMR spectrum in DMSO-d_6 reveals the following signals: δ 11.9 (s, 1H, pyrazole-NH), 8.17 (s, 1H, N=CH), 7.99 (s, 1H, pyrazole-5H), 7.08–7.84 (m, 9H, Ar-H), 7.29 (s, 1H, thiazole-5H), and 3.83 (s, 3H, -O [CH₃]). ^{13}C NMR: 168.6, 160.0, 149.2, 144.7, 137.6, 134.3, 130.0, 129.1, 128.7, 128.2, 126.1, 123.1, 114.7, 113.7, 103.8, 55.78. A chemical shift analysis was also performed. The mass-to-charge ratio, abbreviated as MS, is equal to 1 + 376 times the mass. $\text{C}_{20}\text{H}_{17}\text{N}_5\text{OS}$: C, analytical calculations Results: C=63.94, H=4.53, and N= 18.60% determined. H has a value of 63.98 and N has a value of 4.56 (Parveen et al., 2017).

Conclusion

New pyrazole-ringed thiazole synthetic compounds and evaluated their antioxidant and antibacterial capabilities. Six novel pyrazole-containing compounds have been

developed. The compounds include pyrazoline, Triazole Schiff base, triazolothiadiazole, 1,3,4-oxadiazole, and thiazole. were used in the design. Formaldehyde-free FTIR & NMR Elements were analysed, nuclear magnetic resonance (^1H and ^{13}C), mass spectrometry, and MRI were used to clarify the structures of new compounds. Three of the six produced compounds, 1,3,4-oxadiazoles (P₁₁₋₂₄), Thiazoles (P₂₅₋₃₈), and Schiff bases (P₃₉₋₄₈) had remarkable antibacterial activity. Compared to conventional medication, 1,3,4-oxadiazoles P19, P20, thiazoles P29, P38, and Schiff bases P41 and P44 have outstanding antibacterial action. Antimicrobial activity of 1,3,4-oxadiazoles is due to 2-chlorophenyl substituent. Thiazoles with 2,4-dichlorophenyl substituents on pyrazole rings enhance antibacterial action. A chemical must contain hydrogen donor atoms to be antioxidant. The C=N-NH- linker in thiazole family makes them pyrazole rings with phenyl and p-fluorophenyl substituents enhance their antibacterial effect, and they also serve as antioxidants in the Schiff base series. The 1,3,4-thiadiazole series' the triazole ring's propyl chain and the pyrazole ring's p-chlorophenyl substituent are appropriate for anti-inflammatory effects. Because their manner of interaction with the target protein is more successful than others, these chemicals are essential. Pyrazole and other physiologically significant heterocyclic compounds in only one framework exhibit enhanced biological activity. Antimicrobial, anti-inflammatory, and antioxidant chemicals may be made more effectively by modifying them.

Acknowledgement

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Conflict of interest

The authors confirm that there is no conflict of interest involve with any parties in this research study.

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