

Pharmacological activity of Pyrazole and Pyrazoline derivatives: A comprehensive review

Kavya V*, Swathi K, Rakshitha A R, Keerthana M S, C Bindhu Shree, Kempegowda R S, Harish S

Department of Pharmaceutical Chemistry, Bharathi College of Pharmacy, Karnataka, India

Abstract

Heterocyclic compounds constitute an important class of organic molecules in medicinal chemistry due to their diverse biological and pharmacological properties. Among them, pyrazole and pyrazoline derivatives have gained significant attention owing to their broad therapeutic potential and structural versatility. Pyrazole is an aromatic five-membered nitrogen-containing heterocycle, whereas pyrazoline is its partially saturated analogue with enhanced reactivity. Both scaffolds act as key pharmacophores in the design and development of novel therapeutic agents.

This review focuses on the chemistry, structural characteristics, and pharmacological importance of pyrazole and pyrazoline derivatives. It summarizes recent advances in their antimicrobial, anti-inflammatory, antioxidant, and anticancer activities.

Overall, pyrazole and pyrazoline derivatives represent promising molecular frameworks for the development of safer and more effective drugs, highlighting their potential in modern medicinal and pharmaceutical research.

Keywords: Pyrazole, Pyrazoline, pharmacological activity, heterocyclic compounds

Introduction

Pharmaceutical chemistry is devoted to the discovery and development of new agents for treating diseases. The objective of medicinal chemistry is the design and production of compounds that can be used as medicine for the prevention, treatment, and cure of humans or animal diseases. It is concerned with the invention, discovery, design, identification of biologically active compounds, the study of their pharmacokinetic and pharmacodynamic profiles, interpretation of their mode of action at the molecular level and the construction of structure-activity relationship (SAR), the relationship between chemical structure and pharmacological activity for a series of compounds. The five and six membered heterocyclic nitrogen containing systems such as pyrazole, pyrazoline, imidazole, triazoles, thiazolidine.

Heterocyclic compound constitutes one of the most important classes of organic compound and are characterized by the presence of at least one heteroatom, such as nitrogen, oxygen, or sulphur, within a cyclic ring system. These compounds are widely distributed in nature and form the structural backbone of numerous biologically active. Owing to their diverse chemical properties and broad spectrum of considerable attention in pharmaceutical, medicinal, and synthetic chemistry.^[1]

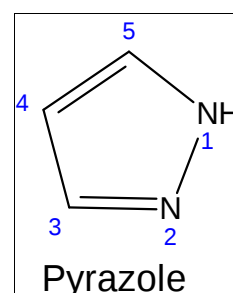
A significant proportion of currently available therapeutic agents contain heterocyclic moieties, highlighting their importance in drug discovery exhibit remarkable pharmacological activity including antimicrobial, antiviral, anti-inflammatory, antidiabetic, antioxidant, anticancer effect. In addition to their pharmaceutical application, heterocyclic compounds are extensively utilized in agrochemicals, dyes, polymers, and, material sciences.

The chemical behaviour of heterocyclic compound is influenced by factor such as ring size, aromaticity, nature of the heteroatom, and substitution pattern. Based on their structural features, they can be classified into aliphatic heterocycles, as well as saturated and unsaturated heterocyclic systems. Common examples include pyrrole,

furan, thiophene, pyridine, quinoline, indole and piperidine derivatives.^[16]

Pyrazole

Pyrazoles constitute an essential class of natural and synthetic products, many of which exhibit flexible biological activity. Antitumor, herbicides, antibacterial, antifungal, hypoglycaemic, antidepressant, analgesic, anti-inflammatory, anticancer, enzyme inhibitor activity are shown among the pyrazoles. As represented by the molecular formula, pyrazole is a five membered ring structure consisting of three carbon atoms and two nitrogen atoms in adjacent positions. The word pyrazole was first coined by Ludwig Knorr 1883. They are known as alkaloids because of their structures and unique alanine.^[2]

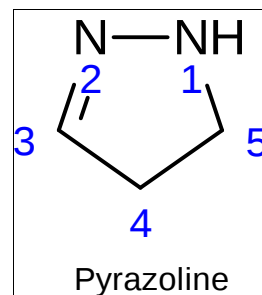


Pyrazole	C ₃ H ₄ N ₂
Molecular weight of pyrazole	68.08g/mol
Density of pyrazole	1.209g/cm ³ at 20°C
Boiling point of pyrazole	187°C
Melting point of pyrazole	66°C - 70°C

One that possesses a cyclic structure with at least one heteroatom in the ring is a heterocyclic compound. The most popular heteroatoms are nitrogen oxygen and Sulphur. In nature, heterocyclic compounds are very widely distributed and important to life in different ways. As is evident from a large number of publications covering their preparation and use, pyrazole constitutes a class of

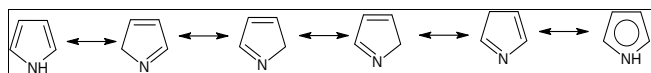
compound synonymous with widespread use in the field of medicine and iatrochemistry.

With a melting point of 70°C, pyrazole is a colorless solid. Pyrazole is a tautomeric substance in pyrazole itself, the presence of a tautomerism cannot be shown but can be inferred by considering pyrazole derivatives. Pyrazole exhibits aromatic properties, e.g., it is readily halogenated, nitrated and sulphonated; the group enters at position 4. The following resonating structures are possible for pyrazole. [5,7]



Aromaticity of Pyrazole

Pyrazole generally does not undergo simple addition reaction like alkenes under ordinary conditions. This behaviour is due to delocalization of the nitrogen atom's lone pair of electrons throughout the ring by conjugation. The electron delocalization increases the stability of the pyrrole ring and its double bonds. Pyrrole is classified as an aromatic heterocyclic compound because it satisfies Hückel's aromatic criterion of $4n+2\pi$ electrons. Its aromatic character is by the presence of several resonance structures. The actual structure of pyrrole is considered a resonance hybrid of all these contributing forms.



The conjugation of the nitrogen lone pair also indicates that pyrrole possesses a planar molecular geometry. This planarity arises because both carbon and nitrogen atoms, three sp^2 -hybridized. In the nitrogen atom, three sp^2 hybrid orbitals participate in sigma bond formation with adjacent carbon atoms. Whereas the third forms a sigma bond with a hydrogen atom. Similarly, each carbon atom uses its sp^2 orbitals to form sigma bonds with neighbouring atoms. The unhybridized p-orbitals of carbon and nitrogen overlap sidewise, creating a continuous delocalized π -electron cloud above and below the five-membered ring. This delocalized electron system is responsible for the aromatic nature and remarkable stability of pyrrole. [2]

Introduction to Pyrazoline

Pyrazoline are five-membered heterocyclic compounds that have attracted considerable attention in pharmaceutical research due to their diverse biological and medicinal properties. These compounds exhibit a broad range of pharmacological activities, including antimicrobial, antioxidant, anti-inflammatory, anticonvulsant, analgesic and anticancer effects. Owing to their therapeutic potential, researchers have focused on modifying the pyrazoline nucleus by incorporating various heterocyclic moieties and functional groups at different positions to develop novel derivatives with enhanced biological activity. The synthesis of pyrazoline derivatives is commonly achieved through the cyclization of α , β -unsaturated ketones (chalcones) with hydrazine hydrates or phenyl hydrazine in the presence of suitable catalyst. In recent years, pyrazoline-based compounds have gained significant interest for their potential applications in drug discovery and development. Therefore, the present study focuses on the synthesis, characterization, biological evaluation, molecular docking and ADMET analysis of newly designed pyrazoline derivatives containing pyridine and benzoisothiazole moieties. [3, 14]

Pyrazoline	$C_3H_6N_2$
Molecular weight of pyrazoline	70.09g/ml
Density of pyrazoline	1.02g/cm ³
Boiling point of pyrazoline	144°C
Melting point of pyrazoline	144°C

Comparison between Pyrazole and Pyrazoline

Pyrazole is a five-membered aromatic heterocyclic ring containing two adjacent nitrogen atoms. Pyrazoline is a five-membered partially saturated heterocyclic ring containing two adjacent nitrogen atoms.

Pyrazole contains two double bonds, making it aromatic and highly stable. Pyrazoline contains one double bond, making it non-aromatic and less rigid than pyrazole.

Pyrazole exhibits high chemical stability because of its aromatic character. Pyrazoline is more chemically reactive due to the absence of complete aromaticity.

Pyrazole derivatives are widely used as anti-inflammatory, analgesic, antimicrobial, anticancer, and antipyretic agents. Pyrazoline derivatives exhibit antioxidant, antimicrobial, anticancer, anti-inflammatory, and antitubercular, anticonvulsant, antidepressant, and many other biological activities.

Pyrazole is commonly used as a core scaffold in medicinal chemistry. Pyrazoline is often used as an intermediate for synthesizing various biologically active compounds.

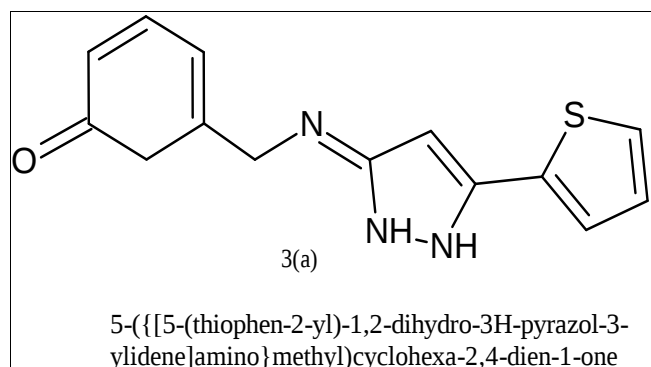
Pyrazoline generally exhibits a broader range of biological activities than pyrazole. Because of its partially saturated structure, pyrazoline derivatives are easier to modify chemically, allowing researchers to introduce different substituents that can enhance pharmacological properties. As a result, pyrazoline compounds have been reported to possess antioxidant, antimicrobial, anti-inflammatory, anticancer, antitubercular, anticonvulsant, antidepressant, antidiabetic, and analgesic activities. [4]

Biological Activity of Pyrazole

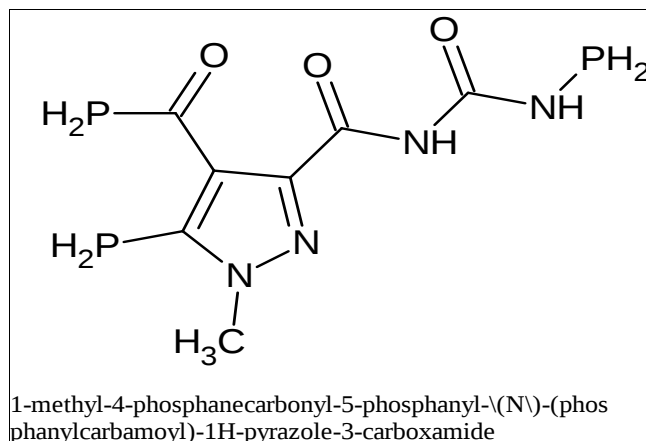
Antimicrobial Activity

Suzan Matar *et al.*, (2026) [5] reported the synthesis of Pyrazole derivatives. Pyrazole derivatives possess the antimicrobial potential of Schiff base pyrazole derivatives was investigated using both the Kirby–Bauer disc diffusion and broth microdilution methods. Although the disc diffusion assay did not show significant antimicrobial activity, the more sensitive broth microdilution method demonstrated that compound 3b possessed promising antibacterial activity against Gram-negative bacteria, including *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. Compound 3b also exhibited strong antifungal activity against *Candida* species, with lower MIC and MFC values than compound 3a,

indicating greater potency. Statistical analysis confirmed that compound 3b was significantly more effective than compound 3a against *Staphylococcus aureus* and *Candida* strains. The enhanced antimicrobial activity of compound 3b may be attributed to its structural characteristics, improved penetration through microbial cell membranes, and its ability to induce reactive oxygen species (ROS). Variations in microbial cell wall composition may also contribute to differences in susceptibility. These findings suggest that Schiff base pyrazole derivatives, particularly compound 3b, are promising antimicrobial agents with potential applications as antibacterial and antifungal drugs. However, further investigations are required to clarify their exact mechanism of action and to evaluate their biological activities in greater detail.^[5]

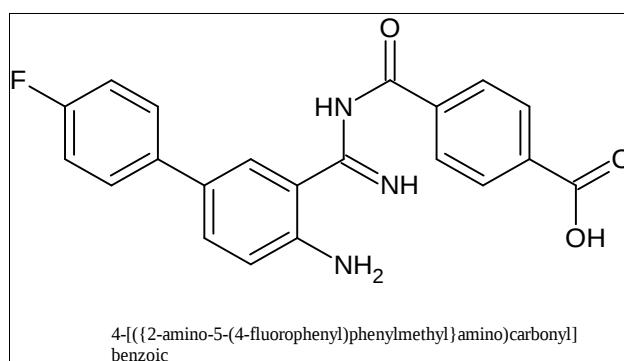


Ahlam S Alqumaya *et al.*, (2025) reported the synthesis of Pyrazole derivatives possess pyrazole derivatives have attracted considerable attention because of their broad-spectrum antimicrobial properties. Several pyrazole-3-carboxylic acid derivatives have been synthesized and evaluated against microorganisms such as *Pseudomonas putida*, *Bacillus cereus*, *Staphylococcus aureus*, and *Escherichia coli*. Among these compounds, compound 278 exhibited the highest antibacterial activity against both Gram-positive and Gram-negative bacteria, making it the most potent derivative in the series. Similarly, pyrazole derivatives containing a quinolinyl chalcone moiety were investigated for their antimicrobial potential, and compound 279 demonstrated remarkable antibacterial and antifungal activity. The antimicrobial effect of these compounds is mainly attributed to the inhibition of bacterial DNA gyrase and topoisomerase IV enzymes. Furthermore, a newly synthesized phosphatized-linked pyrazole derivative (compound 283) showed potent antimicrobial activity with low minimum inhibitory concentration (MIC) values and was effective against clinically isolated Gram-positive bacteria, including quinolone-resistant strains. In another study, N-heterocyclic pyrazole derivatives (compounds 285–291) were screened for antibacterial activity against various pathogenic microorganisms. Additionally, compounds 287 and 288 displayed strong antibacterial activity against Gram-negative bacteria. These findings indicate that pyrazole derivatives possess significant antimicrobial potential and may serve as promising lead molecules for the development of new antimicrobial agents.^[6]



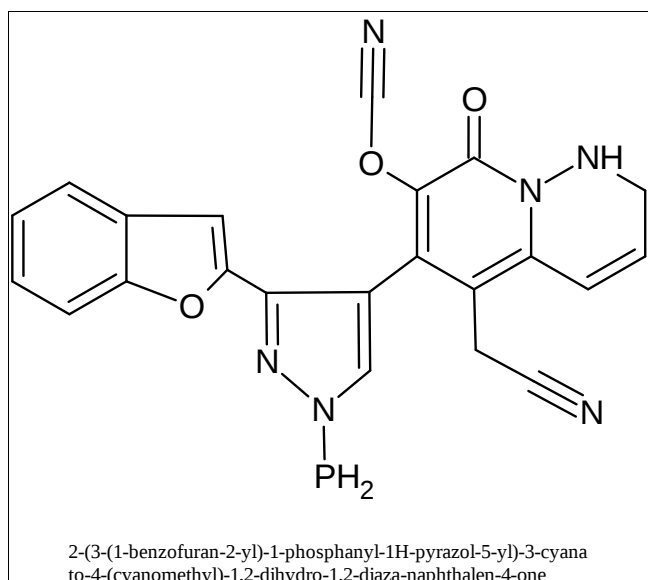
Anti-Inflammatory Activity

Anhar Abdel- Azim *et al.*, (2025)^[8] reported the synthesis of Pyrazole derivatives possess pyrazole derivatives have also demonstrated promising anti-inflammatory activity by inhibiting the production and release of inflammatory mediators responsible for tissue inflammation. These compounds have shown effectiveness against several bacterial strains, including *Streptococcus mutans*, *Klebsiella pneumoniae*, and *Escherichia coli*, under different experimental conditions. In addition to their antimicrobial effects, some pyrazole derivatives possess potential anticancer properties. One of the important therapeutic targets is spleen tyrosine kinase (Syk), whose inhibition is considered an effective strategy for the management of allergic and autoimmune diseases such as rheumatoid arthritis, asthma, and allergic rhinitis. Compound 195 exhibited potent Syk inhibitory activity with an IC_{50} value of 1.2 μ M, which was significantly better than the reference compound (IC_{50} = 3.2 μ M). Furthermore, the incorporation of a meta-benzoic acid substituent into compound 195 markedly enhanced its Syk inhibitory activity. These findings indicate that pyrazole derivatives are promising candidates for the development of novel anti-inflammatory and immunomodulatory agents with potential therapeutic applications in inflammatory, autoimmune, and allergic disorders.^[8]



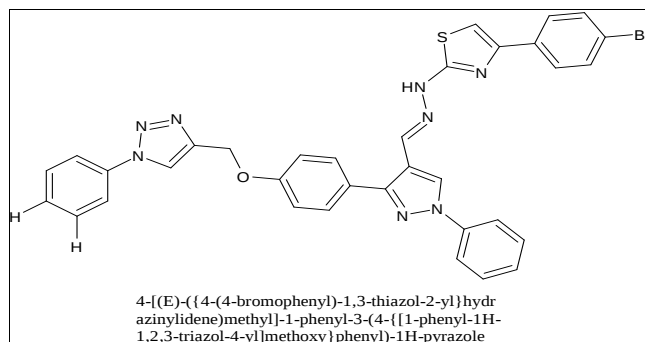
Somaia S. Abd EL-Karim *et.al.*, (2024) reported the synthesis of Pyrazole derivatives possess the newly synthesized compounds were evaluated for their in vitro anti-inflammatory activity using the Human Red Blood Cell (HRBC) membrane stabilization assay. This method

measures the ability of compounds to prevent hypotonicity-induced haemolysis, which reflects stabilization of lysosomal membranes during inflammation. Compounds that protect the HRBC membrane can reduce the release of inflammatory enzymes and help control the inflammatory response. The membrane-stabilizing effect may result from interactions with membrane proteins and changes in cell surface charge. Aspirin and diclofenac sodium were used as standard reference drugs for comparison. Most of the synthesized derivatives showed excellent membrane stabilization, with protection values ranging from $86.70 \pm 0.259\%$ to $99.25 \pm 0.108\%$. In contrast, compounds 10 and 11c exhibited comparatively lower activity. Compound 9 demonstrated promising membrane stabilization ($86.70 \pm 0.259\%$) along with notable antimicrobial activity. Overall, the findings indicate that several synthesized derivatives possess significant anti-inflammatory potential and warrant further pharmacological evaluation.^[9]

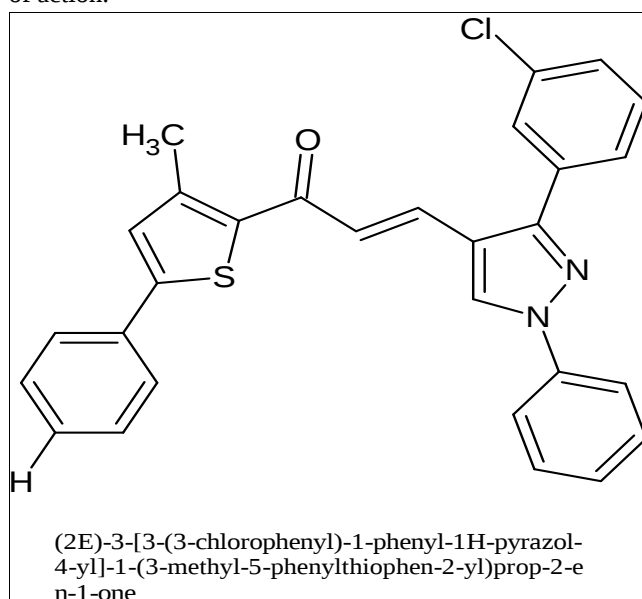


Anti-Oxidant Activity

Raghavendra Matta *et al.*, (2023)^[10] reported the synthesis of Pyrazole derivatives possess the antioxidant potential of the synthesized compounds was assessed using the DPPH free radical scavenging assay. Different concentrations of each compound (10–200 μM) were prepared in sterile Eppendorf tubes, and all experiments were carried out in triplicate to ensure reliable and reproducible results. A freshly prepared DPPH solution (100 μL) was added to each sample, and distilled water was used to adjust the total reaction volume to 1 ml. The reaction mixtures were mixed thoroughly using gentle shaking and vortexing, followed by incubation in the dark at room temperature for 30 minutes. A corresponding blank was prepared using the appropriate diluent with a constant volume of DPPH reagent. After incubation, the absorbance of each sample was measured at 517 nm using a UV–Visible spectrophotometer. The antioxidant activity was then expressed as the percentage of DPPH free radical scavenging based on the recorded absorbance values.^[10]



Dnyaneshwar Sirsat *et al.*, (2019)^[11] reported the synthesis of Pyrazole derivatives possess reactive oxygen species (ROS) and reactive nitrogen species are major contributors to oxidative stress and inflammatory diseases. To evaluate the antioxidant potential of the synthesized compounds (3a–j), DPPH, hydrogen peroxide (H_2O_2), nitric oxide (NO), and superoxide radical (SOR) scavenging assays were performed using ascorbic acid as the standard. Most compounds showed good to moderate activity against DPPH and NO radicals, while moderate to weak activity was observed against H_2O_2 and SOR radicals. Compounds 3j, 3i, 3e, 3h, and 3c exhibited the highest DPPH radical scavenging activity. Compounds 3g, 3j, and 3b also demonstrated significant nitric oxide scavenging effects. The remaining compounds displayed moderate antioxidant activity in both assays. In comparison, all synthesized derivatives showed only moderate to weak inhibition of hydrogen peroxide and superoxide radicals. Overall, the results indicate that these compounds possess promising antioxidant properties. Their ability to scavenge free radicals suggests potential therapeutic value. Further studies are required to confirm their effectiveness and mechanism of action.^[11]

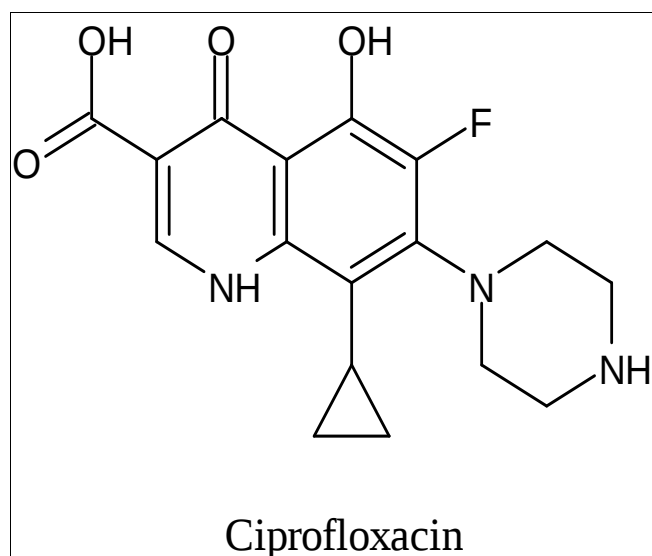


Biological Activity Pyrazoline

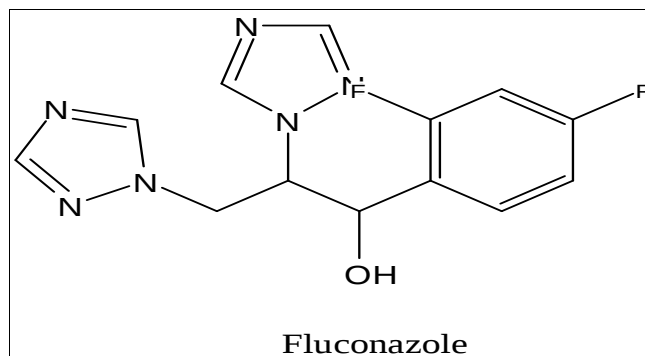
Antimicrobial Activity

SK Sahu *et al.*, (2008) reported the synthesis of pyrazoline derivatives possess the antimicrobial properties of the synthesized compounds were investigated through in vitro

studies using the agar cup plate diffusion technique. Antibacterial activity was evaluated on Mueller–Hinton agar at 37°C for 24 hours with a test concentration of 100 µg/ml. The compounds were screened against *Staphylococcus aureus*, *Staphylococcus faecalis*, *Escherichia coli*, and *Salmonella typhi*. Antifungal activity was examined on Sabouraud dextrose agar at 26°C for 48–72 hours against *Candida albicans* and *Aspergillus niger*. Ciprofloxacin and Clotrimazole were used as the reference drugs for antibacterial and antifungal comparison, while DMF served as the solvent control. The results indicated that derivatives containing halogen, nitro, and hydroxyl substituents on the phenyl ring exhibited superior antimicrobial activity. In comparison, compounds with methoxy, phenyl, and furl groups showed relatively weaker effects.^[12]



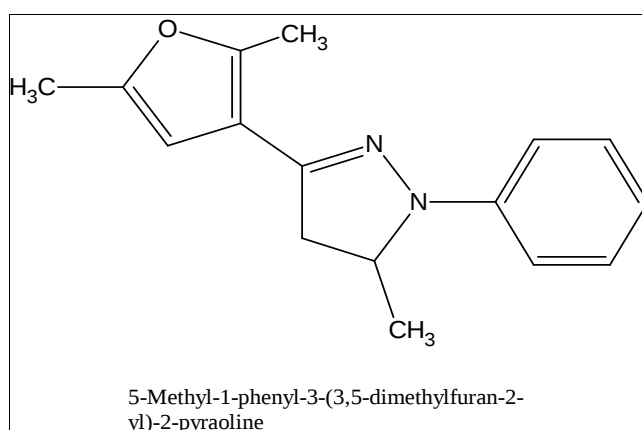
Faith TOK *et al.*, (2022)^[13] reported the synthesis of pyrazoline derivatives possess the synthesized pyrazoline derivatives were evaluated for their in vitro antimicrobial activity against selected bacterial and fungal microorganisms using the minimum inhibitory concentration (MIC) method. The antibacterial study was carried out against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*, while the antifungal activity was assessed against *Candida albicans*, *Candida glabrata*, and *Candida tropicalis*. Ciprofloxacin and fluconazole were used as standard antibacterial and antifungal drugs, respectively. The MIC values of the synthesized compounds ranged from 0.39 to 800 µg/mL, indicating variations in antimicrobial potency. Among the tested derivatives, compounds 7 and 8 exhibited the strongest antibacterial activity with lower MIC values against most bacterial strains. In the antifungal evaluation, compounds 2 and 7 showed promising activity against the tested fungal species. Overall, the synthesized pyrazoline derivatives demonstrated significant antimicrobial potential, suggesting that these molecules may serve as promising candidates for the development of new antimicrobial agents.^[13]



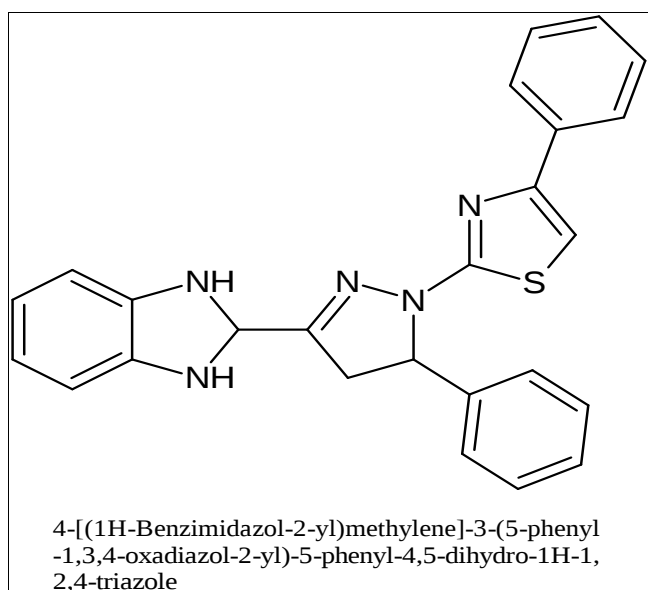
Shailesh H Shah *et al.*, (2021) reported the synthesis of pyrazoline derivatives possess the antimicrobial activity of the synthesized compounds was evaluated using the broth microdilution method to determine their minimum inhibitory concentration (MIC). The compounds were tested against selected bacterial strains (*E. coli*, *S. aureus*, *P. aeruginosa*, and *S. pyogenes*) and fungal strains (*C. albicans*, *A. niger*, and *A. clavatus*). The assay was performed in DMSO using standard laboratory procedures. Gentamicin, ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin, and griseofulvin were used as reference drugs. Among the derivatives, compounds 4a and 4e showed the highest activity against *E. coli*, while 4a and 4f were more effective against *S. pyogenes*. Most of the remaining compounds exhibited moderate antibacterial activity against *S. aureus* and *P. aeruginosa*. Compounds 4e and 4g demonstrated significant antifungal activity against *C. albicans*. However, the other derivatives showed relatively weak activity against *A. niger* and *A. clavatus*.^[14]

Anti-Inflammatory Activity

Zeyad D Najmuldeen *et al.*, (2023)^[15] reported the synthesis of pyrazoline derivatives possess the anti-inflammatory activity of the newly synthesized compounds was assessed in vivo using the egg white-induced paw edema model. The study was conducted to investigate the anti-inflammatory potential of the sulfonamide pyrazoline derivatives, with diclofenac sodium, a well-known cyclooxygenase (COX) inhibitor, used as the standard reference drug. A total of eight groups of albino rats of both sexes, weighing 160 ± 10 g, were obtained from the Animal House of the University of Fallujah, College of Veterinary Medicine and maintained under standardized laboratory conditions. The animals were provided with a standard commercial diet and allowed free access to drinking water throughout the experimental period.^[15]

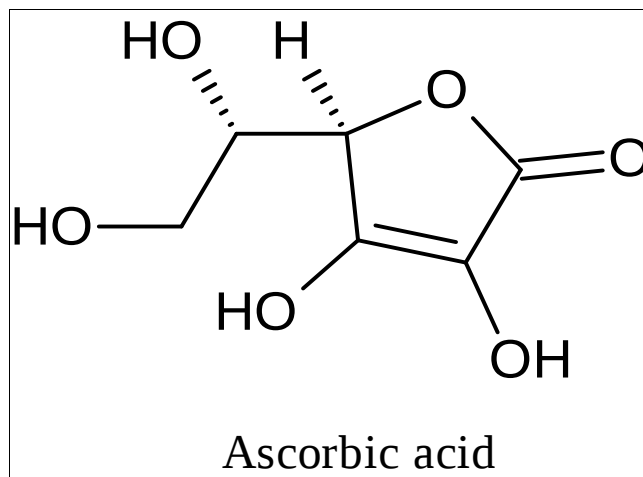


CHANDRA SHEKHAR YADAV *et al.*, (2019) reported the synthesis of pyrazoline derivatives possess successfully reported the synthesis in a series of pyrazoline derivatives from chalcone intermediates (106a–e). The structures of all synthesized compounds were confirmed using different spectroscopic characterization techniques. Their anti-inflammatory potential was subsequently evaluated by determining the concentration required to inhibit 50% of the biological response, including cytokine release, alkaline phosphatase production, or cytotoxicity (IC₅₀). The IC₅₀ values were calculated from dose–response curves obtained using at least five different concentrations of each compound, providing a reliable assessment of their anti-inflammatory activity.^[16]

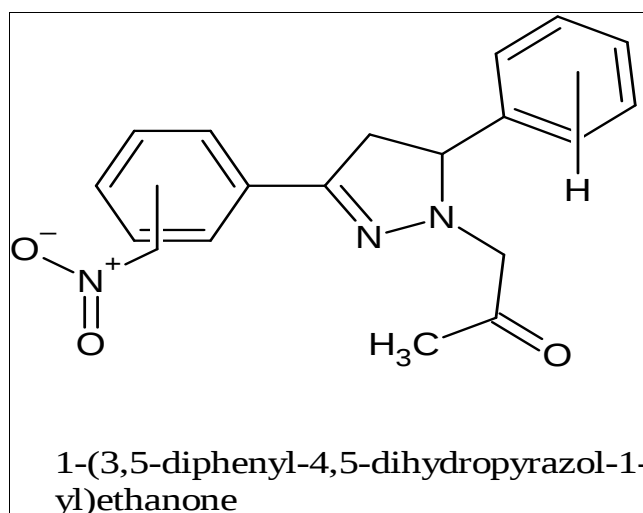


Anti-Oxidant Activity

Er. Manasvi Jain *et al.*, (2024)^[17] reported the synthesis of pyrazoline derivatives possess the DPPH free radical scavenging assay is a simple, rapid, and widely accepted method for evaluating the antioxidant activity of synthesized compounds. In this assay, DPPH, a stable free radical with a deep violet color, is reduced by antioxidant molecules through the donation of hydrogen atoms or electrons, resulting in a color change from violet to pale yellow. The synthesized compounds were dissolved in methanol at an appropriate concentration and mixed with an equal volume of DPPH solution. The reaction mixture was incubated at room temperature for 30 minutes in the dark, after which the absorbance was measured at 517 nm using a UV–Visible spectrophotometer. Ascorbic acid was used as the standard antioxidant for comparison. The antioxidant potential of the compounds was determined by calculating the percentage of DPPH radical inhibition from the absorbance values of the control and test samples. A higher percentage of inhibition indicated stronger free radical scavenging activity, demonstrating the antioxidant efficiency of the synthesized compounds.^[17]



Shivani Sukder Jadev *et al.*, (2025) reported the synthesis of pyrazoline derivatives possess the hydrogen peroxide scavenging assay is a widely used method for evaluating the antioxidant potential of compounds by measuring their ability to neutralize hydrogen peroxide (H₂O₂). The scavenging effect is determined by monitoring the reduction in H₂O₂ absorbance at 230 nm using a UV–Visible spectrophotometer. Hydrogen peroxide is generated in biological systems through the action of various oxidase enzymes and can produce harmful hydroxyl radicals, leading to oxidative damage in cells. Antioxidant compounds reduce hydrogen peroxide to water, thereby minimizing oxidative stress. In this assay, the test compound is incubated with a hydrogen peroxide solution, and the decrease in absorbance at 230 nm indicates its hydrogen peroxide scavenging capacity.^[18]



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