مجلة الدراسات التربوية والعلمية - كلية التربية - الجامعة العراقية
العدد السابع والعشرون - المجلد العاشر - علوم الكيمياء - نيسان 2026 م
doi.org/10.52866/esj.2026.10.27.15

Synthesis of Pyrazole Ring Derivatives through Various Methods and Evaluation of Their Biological Activities : A Review

Baida Hussein Ayada[1] , Raghad khalid khammas[2] , Rasha A.Abdullah[3]
Department of Chemistry, College of Education for Women, University of Anbar[1,2,3]
Email: baedaa.hussien@uoanbar.edu.iq

Abstract:

Pyrazole derivatives are among the most important heterocyclic compounds due to their wide range of pharmacological and biological applications. Numerous recent studies have demonstrated that the incorporation of the pyrazole ring with other heterocyclic systems such as thiazole, imidazole, triazole, and pyrimidine leads to compounds exhibiting high efficacy against various types of bacteria, fungi, and cancer cells. Several newly synthesized metal complexes, azo, and pyrazoline derivatives have shown strong antibacterial and antifungal activities, in addition to antimalarial and anticancer effects particularly iron and cobalt complexes, which exhibited promising cytotoxic properties.Moreover, molecular docking and computational studies revealed that some of these derivatives possess good compatibility with biological receptors and exhibit acceptable pharmacokinetic and drug-like properties. In addition, certain derivatives demonstrated multitarget potential as antioxidants and as antidiabetic, anti-Alzheimer, and anti-arthritic agents, making them strong candidates for the development of multifunctional drugs. These findings confirm that the development of pyrazole derivatives remains a promising field for discovering new drugs with high efficacy and reduced side effects .

Key words : Pyrazole , heterocyclic compound , Cyclocondensation .

تحضير مشتقات حلقة البيرازول من خلال طرق مختلفة وتقييم أنشطتها البيولوجية: مراجعة

بيداء حسين عيادة[1] ، رغد خالد خماس [2] ، رشا عزام عبد الله [3].
جامعة الانبار, كلية التربية للبنات , قسم الكيمياء [3،2،1]

مستخلص:

تعتبر مشتقات البيرازول من بين أهم المركبات الحلقية غير المتجانسة نظرا لمجموعتها الواسعة من التطبيقات الدوائية والبيولوجية. أظهرت العديد من الدراسات الحديثة أن دمج حلقة البيرازول مع أنظمة حلقية غير متجانسة أخرى مثل ثيازول وإيميدازول وتريازول وبيريميدين يؤدي إلى مركبات تظهر فعالية عالية ضد أنواع مختلفة من البكتيريا والفطريات والخلايا السرطانية. أظهرت العديد من المجمعات المعدنية المركبة حديثا ومشتقات الآزو والبيرازولين أنشطة قوية مضادة للبكتيريا والفطريات ، بالإضافة إلى التأثيرات المضادة للملاريا والسرطان وخاصة مجمعات الحديد والكوبالت ، والتي أظهرت خصائص سامة للخلايا واعدة.علاوة على ذلك ، كشفت دراسات الالتحام الجزيئي والحسابية أن بعض هذه المشتقات تمتلك توافقا جيدا مع المستقبلات البيولوجية وتظهر خصائص حركية دوائية وشبيهة بالعقاقير مقبولة. بالإضافة إلى ذلك ، أظهرت بعض المشتقات إمكانات متعددة الأهداف كمضادات للأكسدة وعوامل مضادة لمرض السكر ومضادة لمرض الزهايمر ومضادة لالتهاب المفاصل ، مما يجعلها مرشحة قوية لتطوير عقاقير متعددة الوظائف. تؤكد هذه النتائج أن تطوير مشتقات البيرازول لا يزال مجالا واعدا لاكتشاف أدوية جديدة ذات فعالية عالية وآثار جانبية منخفضة .

الكلمات المفتاحية: بيرازول ، مركب حلقي غير متجانس ، تكثيف حلقي .

1. Introduction

Pyrazole is a heterocyclic five-membered compound containing two adjacent nitrogen atoms as figure 1, which has received wide attention in pharmacochemistry due to the variety of its pharmacological activities and the ease of its structural modification [1]. Since its discovery in 1883 [2], pyrazole has been considered a privileged Scaffold in drug design, as its derivatives exhibit anti-inflammatory, analgesic, antimicrobial, antiviral, tuberculosis, and carcinogenic activities [3,4].

Pharmacological compounds and natural products containing pyrazole nuclei have shown a wide range of important biological activities, which made this heterocyclic ring the focus of great interest in the field of pharmacochemistry [5,6]. In recent decades, the U.S. Food and Drug Administration (FDA) has approved more than forty drugs containing pyrazole nuclei for the treatment of a variety of clinical conditions, including celecoxib as an anti-inflammatory, CDPPB as an antipsychotic agent, difenamizole as a painkiller, along with other drugs with multiple therapeutic applications [7-9]. Such a wide spread of pyrazole-based drugs is due to the unique physicochemical properties of this nucleophile, such as structural stability and the ability to form hydrogen bonds, which contributes to an improvement in pharmacokinetics and pharmacological efficacy compared to drugs with similar heterocyclic rings [10,11].

The combination of pyrazole nuclei with other heterocyclic rings, such as thiazole, furan, pyrimidine and Quinoline, proved its effectiveness in enhancing biological activity and improving pharmacological properties [12,13]. These hybrid compositions show synergistic effects and the ability to overcome drug resistance, with the possibility of adjusting activity and selectivity through structural substitution and structure–efficacy relationship (SAR) studies [14].

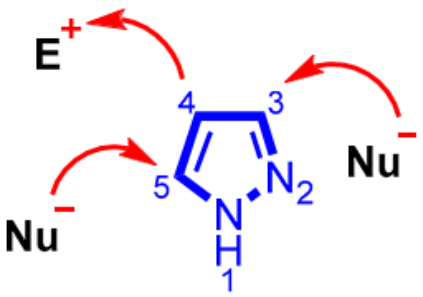


Figure 1. The pyrazole structure.

2. Synthetic Approaches

1.2 Cyclocondensation methods

The formation of substituted pyrazoles is most effectively achieved through a ring-closure (cyclocondensation) reaction between hydrazine or its derivatives—functioning as bifunctional nucleophiles—and 1,3-difunctional carbon frameworks. These frameworks typically comprise 1,3-dicarbonyl compounds (I), α,β-unsaturated carbonyl species (II, III), or β-enaminones and their analogous structures (IV), as shown in Figure 2 .

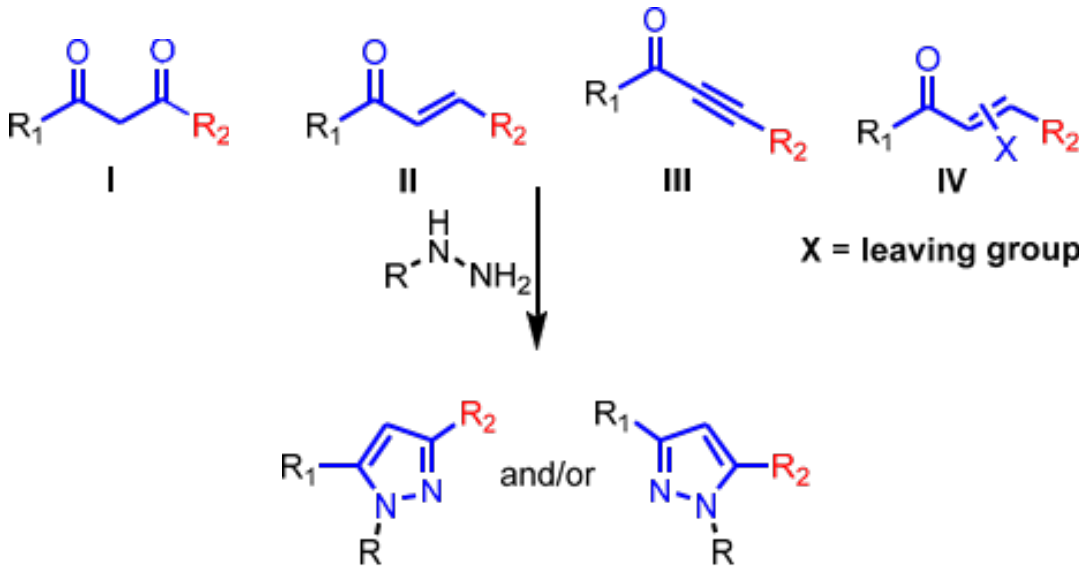
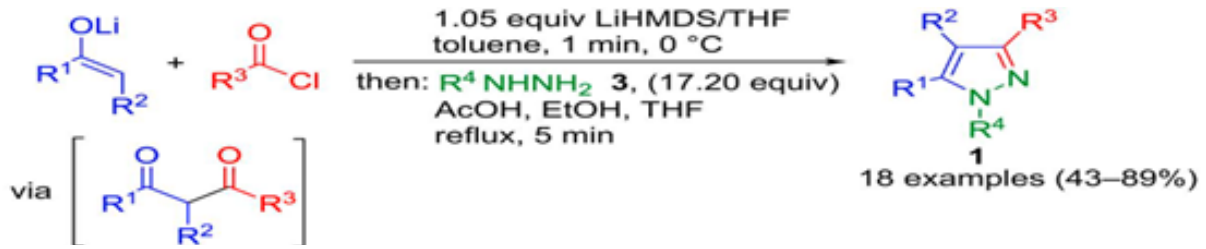


Figure 2 . Examples of α,β-unsaturated carbonyl compounds.

2.2 Metal-catalyzed methods

Pyrazole derivatives were synthesized from the reaction of 1,3-dicarbonyl compounds, which were obtained through the sequential reaction of enolates with acid chlorides, followed by condensation with hydrazines, as illustrated in scheme (1). It should be noted that in the process of selective chemical synthesis, undesired acylation of the predominant 1,3-diketone intermediate does not occur — a complication that was successfully avoided by using LiHMDS as a base [15]. This method provided a good yield and was found to be tolerant to a wide range of functional groups .

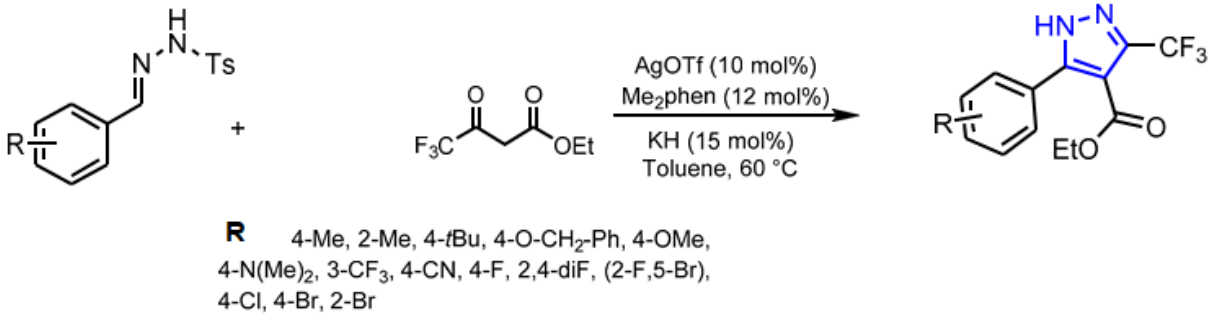


Scheme 1. Preparation of polysubstituted pyrazoles via the reaction of hydrazine derivatives with 1,3-dicarbonyl compoun

The aryl-3-trifluoromethylpyrazoles (9) ,were synthesized using silver as a catalytic agent through the reaction of N-benzylidenetolysulfonohydrazide (7) , with 4,4,4-trifluoro-3-oxobutanoate (8) The reaction involved a sequential nucleophilic addition process leading to the formation of trifluoromethyl-substituted pyrazole derivatives (Scheme 2).

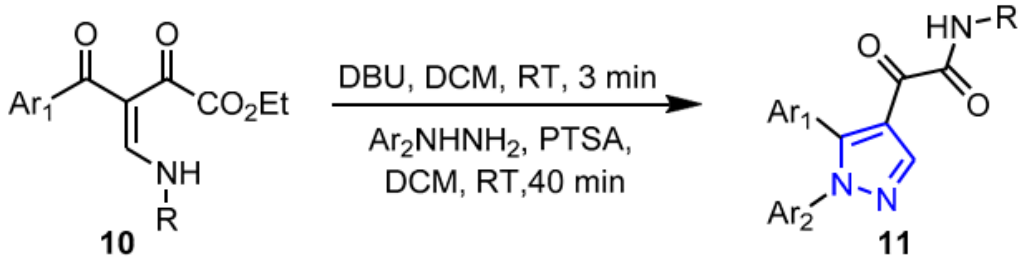
The initial yield was moderate, but optimization by increasing the reaction temperature to 60 °C significantly improved the product yield. However, raising the temperature above 60 °C resulted in a decrease in yield.

Among the catalysts tested, $Cu(OTf)_2$ provided the best yield at 60 °C, whereas $Fe(OTf)_3$ showed no catalytic activity. Regarding solvents, THF gave a higher yield compared to toluene. Similarly, the use of K_2CO_3 as a base produced better results than NaH, KOt-Bu, or NaOt-Bu[16].



Scheme 2 . Silver-Catalyzed Synthesis of 5-Aryl-3-Trifluoromethyl Pyrazoles.

While Poletto and colleagues synthesized high-purity α-ketoamide-N-arylpyrazoles (11) and secondary β-enamine diketones (10) , using aryl hydrazines as substituents, it was observed that the intermediate 4-acyl-5,3-dihydroxy-pyrroline underwent a nucleophilic substitution reaction with aryl hydrazine[17], leading subsequently to the formation of the pyrazole ring (Scheme 3).

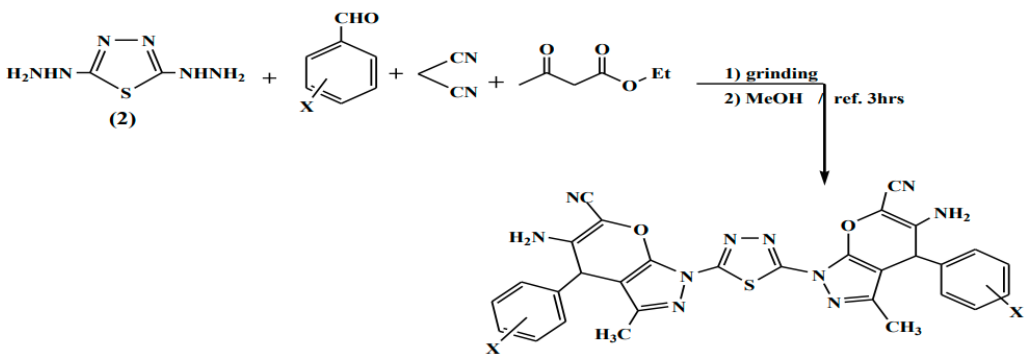


Ar_1 = 4-ClPh, 4-BrPh, 4-FPh, Ph, 4-OMePh, 4-NO_2Ph
Ar_2 = Ph, 4-ClPh
R = Me, Ph

Scheme 4. Preparation of Arylpyrazoles through the Reaction of Secondary β-Enamino Diketones with Arylhydrazines.

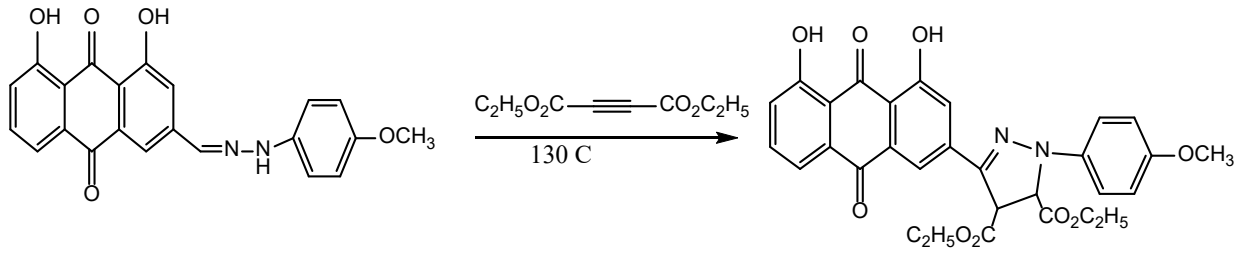
3.2 One-pot and multicomponent reactions

While the two researchers S. Khazaal and S. Y. Ibraheam [18] is prepared from the ring of pyrazole ring derivatives by a multicomponent reaction without a cofactor by benzaldehyde and ethyl acetoacetate compensators as shown in scheme (4).



Scheme 5. Multicomponent synthesis of pyrazoles from benzaldehyde and ethyl acetoacetate.

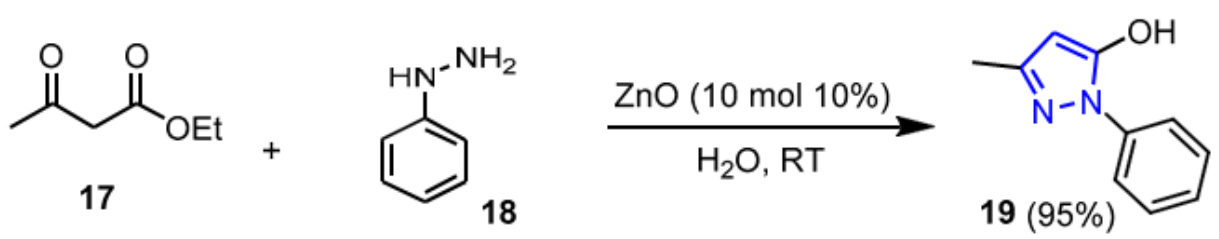
Researcher Kumar and his group [19] prepared pyrazole derivatives through the condensation reaction of an imine group with diethyl butanoate under reflux at 130 °C, yielding a good product as shown in the scheme (6).



Scheme 6. One-Pot Synthesis of Pyrazoles from Arenes and Carboxylic Acids.

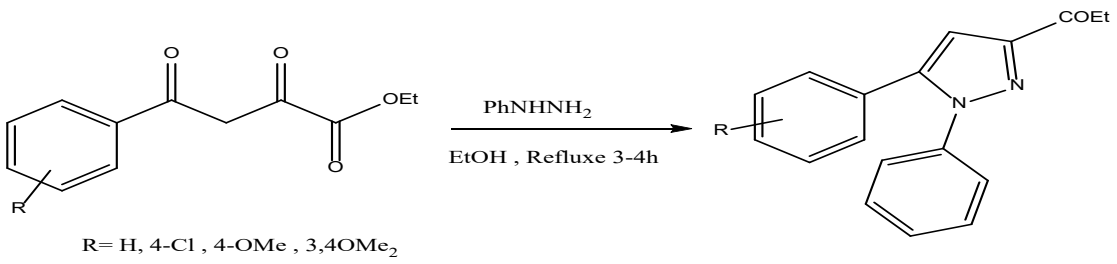
4.2 Novel catalysts/nanomaterials

Girish et al. [20] reported an efficient and environmentally benign strategy for the synthesis of 1,3,5-substituted pyrazole derivatives (19) using a nano-ZnO catalyst. The methodology involves the condensation of phenylhydrazine (18) with ethyl acetoacetate (17) under carefully under controlled (Scheme 7). This approach offers several notable advantages, including high product yield of up to 95%, short reaction time, and a simple post-reaction processing. The combination of these features—excellent efficiency, rapid reaction, and operational simplicity—positions this method as a valuable and practical tool for the preparation of pyrazole derivatives.



Scheme 7. preparation of 3-methyl-5-hydroxe pyrazol by using Nano-ZnO as catalyst.

He researcher Nandurkar, Y [21] and his colleagues synthesized 5-arylphenyl-pyrazole-3-carboxylates through the addition of 1,3-diketoesters to substituted phenylhydrazines in ethanol as a solvent under reflux for 3–5 hours, as shown in the scheme (8).

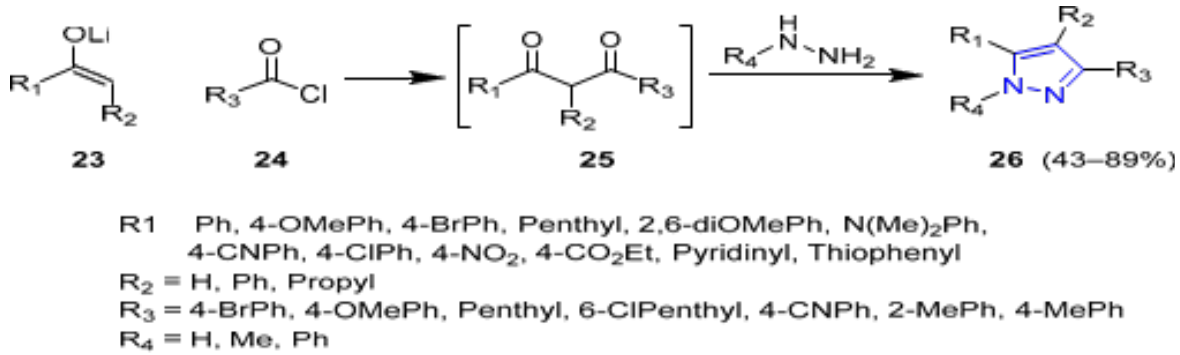


Scheme 8. Preparation of 5-arylphenyl-pyrazole-3-carboxylates from 1,3-diketoesters

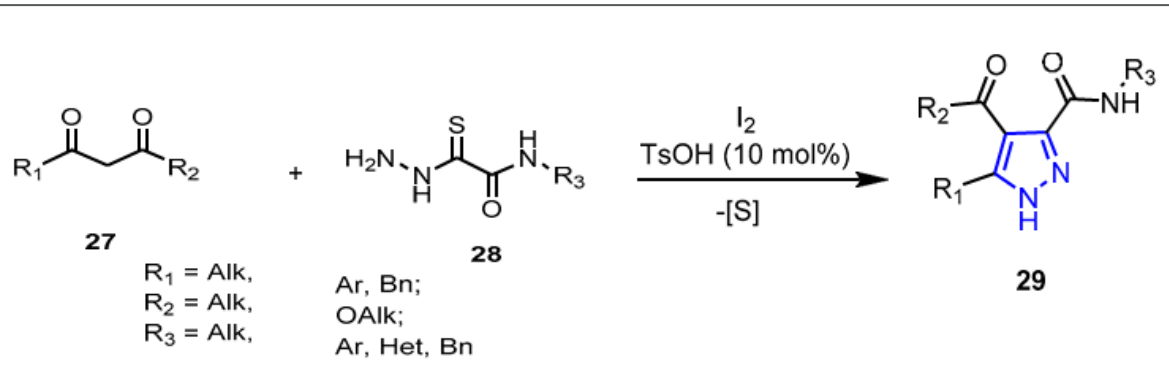
In their research, Heller and Natarajan [22] developed a cutting-edge in situ method for pyrazole synthesis. The strategy involves the direct formation of 1,3-diketones (25) from ketones (23) and acid chlorides (24), which are subsequently converted into pyrazoles (26) through reaction with hydrazine, affording products a excellent yields (Scheme 9). This methodology is distinguished by its rapid reaction rate, broad applicability, and high chemoselectivity, enabling access to pyrazoles that were previously challenging to synthesize, including fused pyrazole-containing ring systems. The combination of speed, versatility, and selectivity makes this approach a valuable tool for synthetic chemists, facilitating the generation of various pyrazole-based compounds with increased molecular complexity.

Similarly, Komendantova and colleagues [23] reported an efficient strategy for the preparation of substituted pyrazoles (29). This method employs a wide variety of 1,3-dicarbonyl compounds (27) and oxamic acid thiohydrazides (28) in an iodine-promoted cascade sequence involving conversion to imines, cyclization, and ring contraction, catalyzed by small amounts of TsOH, with concurrent elimination of sulfur (Scheme 10). The procedure

provides a straightforward and highly effective route to functionalized pyrazoles, utilizing readily accessible starting materials under mild reaction conditions.

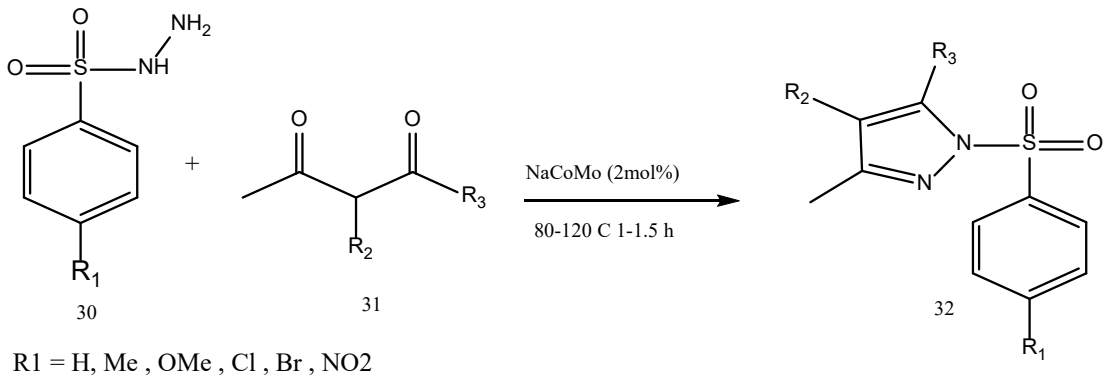


Scheme 9. Preparation of Substituted Pyrazoles through the Reaction of 1,3-Diketones with hydrazone derivatives.



Scheme 10. Preparation of Substituted Pyrazoles through Reactions of 1,3-Diketones with Hydrazine Derivatives.

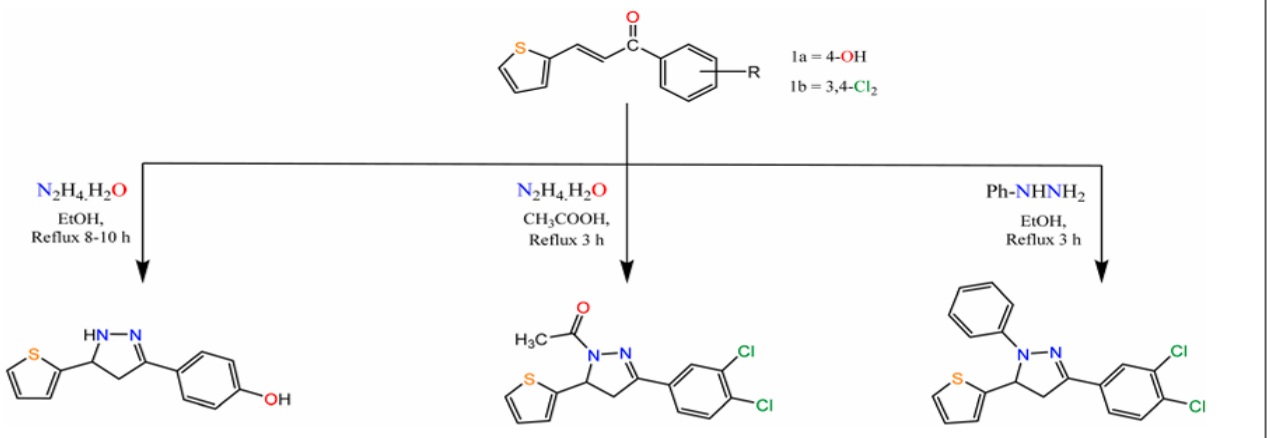
Yan et al. [24] reported the development of a novel inorganic framework, termed the "3D platelike ternary-oxo-cluster" (NaCoMo), based on metal-oxo clusters. This framework functions as a highly effective catalyst for the synthesis of pyrazole derivatives. Notably, it demonstrates exceptional catalytic efficiency .Through the condensation and subsequent cyclization of sulfonyl hydrazides (30) with 1,3-diketones (31), producing the corresponding pyrazoles (32) in yields of up to 99% (Scheme 11). The achieved preparation of NaCoMo represents overview of a new class of unconventional polyoxometalates with promising applications in catalytic transformations.



Scheme 11.
Preparation of Substituted Pyrazoles via NaCoMo-Catalyzed Reactions.

5.2 Preparation of Pyrazoles from α,β-unsaturated ketone

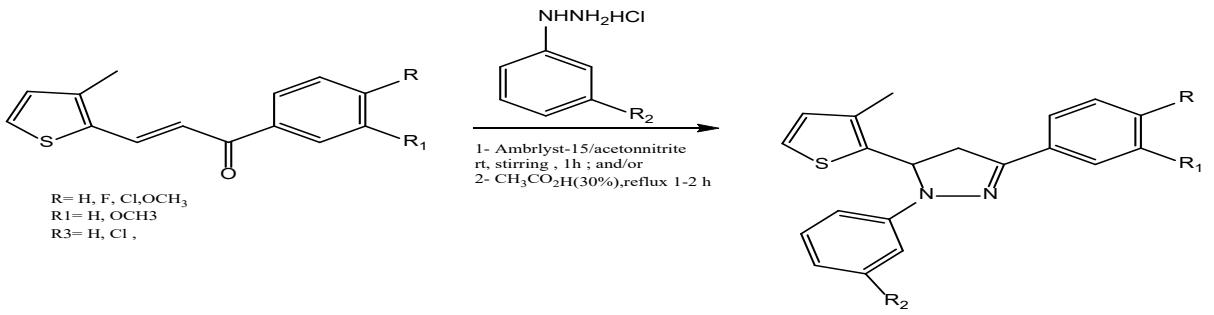
Pyrazole derivatives were synthesized from α,β-unsaturated ketone compounds with hydrazine hydrate and its derivatives, in the presence of a catalyst such as glacial acetic acid or using a solvent such as ethanol [25], as shown in the Scheme(12).



Scheme 12. The synthetic pathway
to pyrazole derivatives reaction of α,β- unsaturated ketone,.

Meanwhile, the researcher Kumara [26]. synthesized substituted pyrazoline derivatives via the reaction of substituted chalcones with substituted phenylhydrazines in the presence of the Amberlyst catalyst for 30–60 min-

utes. The obtained product was then washed with ethyl acetate, stirred, and triturated with diethyl ether, as shown in the scheme (13).

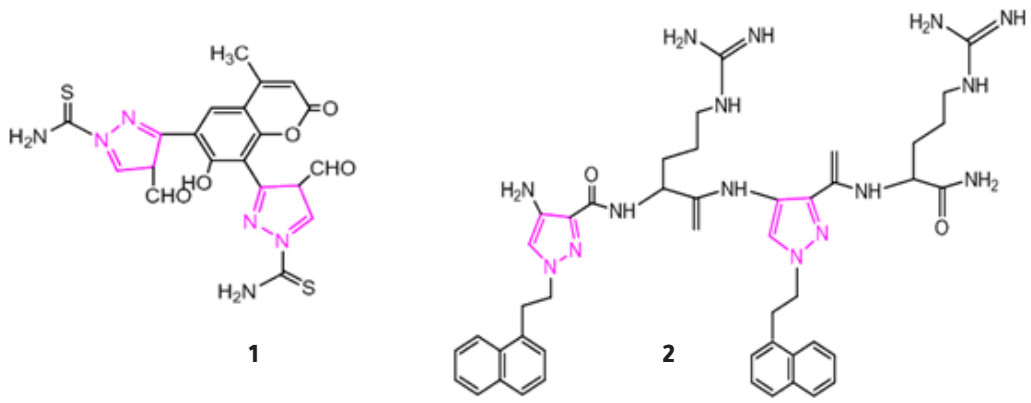


Scheme 13. Preparation of Pyrazole Derivatives from chalcones .

3. Biological and pharmacological activities

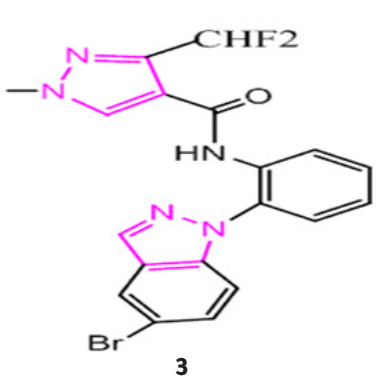
1.3 Antimycobacterial .

In contrast compound 1 exhibited strong antibacterial and antifungal effects, showing high efficacy against sepsis-related microorganisms [27]. Additionally, compound 2 displayed notable activity against Escherichia coli, Pseudomonas aeruginosa, Staphylococcus epidermidis, and Staphylococcus aureus [28].



2.3 ANTIFUNGAL .

N-(2-(5-Bromo-1H-indazole-1-yl)-phenyl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (compound 3) demonstrated significant antifungal activity against seven phytopathogenic strains [29], compound 4 also showed good effectiveness for fungal[30].

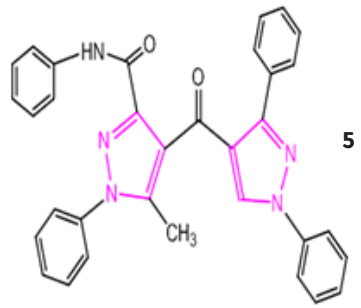


3

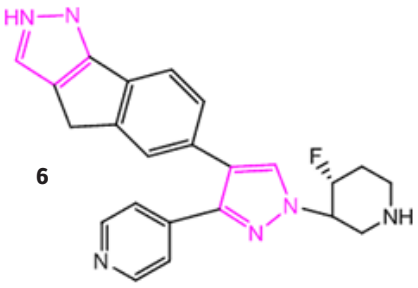
4

3.3 Antitumor Activity

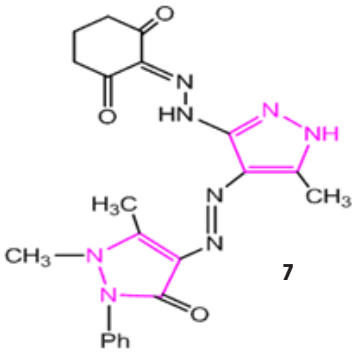
A novel series of bis-pyrazole derivatives has been investigated for their anticancer potential. Compound 5 displayed moderate activity against B-Raf enzyme inhibition [31]. Compound 6 demonstrated antitumor effects against Ehrlich ascites carcinoma cells [32], while compound 7 was identified as a potent anticancer agent [33]. Furthermore, a series of bis-pyrazole analogs, including compound 8, showed promising anticancer activity, highlighting the potential of this scaffold for the development of rapid-acting anticancer agents [34].



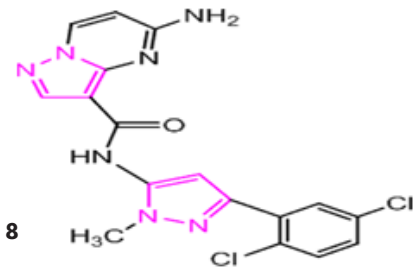
5



6



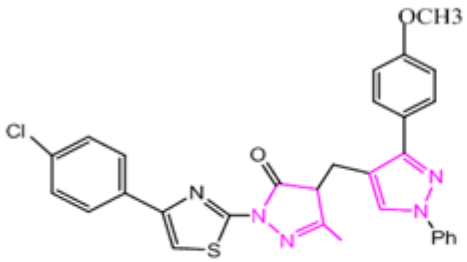
7



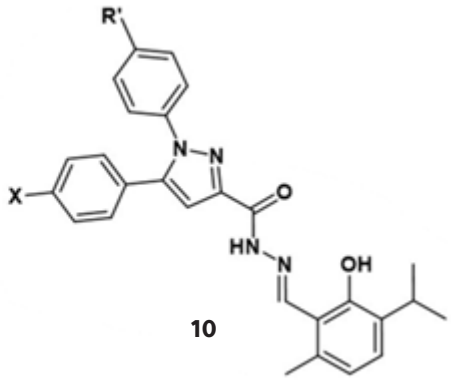
8

4.3 Anti inflammatory .

Several bis-pyrazole derivatives have been synthesized and evaluated for their anti-inflammatory activity, with compounds 9 and 10 showing notable effects [35,36].



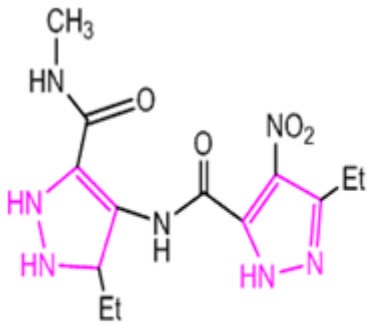
9



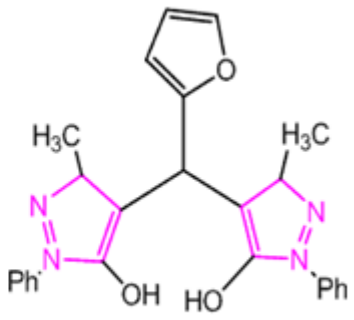
10

5.3 **Antiviral activity .**

Additionally, many of these derivatives, including compounds 11 and12, exhibited excellent antiviral activity [37,38].



11



12

4. Structure–Activity Relationship (SAR) Trends .

Studies of the structure–efficacy relationship (SAR) have shown that the pyrazole ring is a privileged scaffold in pharmacochemistry, where the nature of the substitution and its location on the ring play a decisive role in determining the biological activity of compounds [39,40]. Studies have shown

that substitution at the C-3, C-4 and C-5 positions of the pyrazole ring directly affects the potency and selectivity towards various biological targets [41] , for example, the following pyrazole derivatives showed a difference in their effectiveness against fungi with different functional group [42], as in the figure (3) .

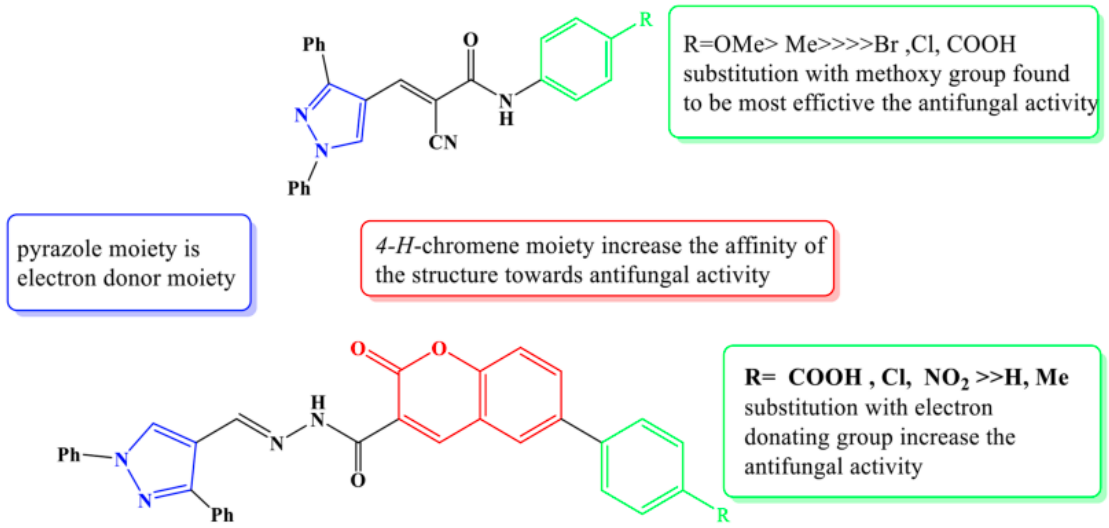


Figure 3. Structure-activity relationship SAR studies of tested compounds against antifungal activities

5. Conclusions and future perspectives

Pyrazoles represent an important group of five-membered heterocyclic compounds characterized by the presence of two nitrogen atoms within their ring system , these compounds have gained considerable attention due to their significant role in pharmaceutical research and drug discovery , they serve as key structural frameworks for the design of novel therapeutic agents capable of addressing a wide spectrum of clinically relevant diseases , the wide-ranging pharmacological potential of pyrazole derivatives has greatly stimulated advances in their synthetic methodologies , over the past decade, remarkable progress has been made through the development of efficient and adaptable synthetic strategies. These include the utilization of transition-metal cataly-

sis, photoredox processes, and one-pot multicomponent reactions, in addition to the introduction of novel reactants and reaction pathways, collectively, these innovations have enhanced both the preparation and functional diversification of pyrazole-based compounds , the information compiled in this review provides a significant foundation useful to researchers seeking to further explore the chemistry of pyrazoles and their derivatives , such knowledge can guide future investigations aimed at developing new derivatization routes and expanding the library of pyrazole-containing molecules, nevertheless, there remains a substantial need for continued research—particularly in understanding how the pyrazole ring directly influences biological activity and in identifying cases where it primarily functions as a structural scaffold , further exploration of these aspects will deepen the scientific understanding of pyrazole chemistry and its diverse applications. Considering the ongoing growth of interest in this field, it is anticipated that the discovery of novel synthetic routes—such as those involving condensation, cycloaddition, and other innovative transformations—will significantly advance the scope and utility of pyrazole derivatives in the future.

5. References

[1] M. Lusardi, A. Spallarossa, and C. Brullo, "Amino-pyrazoles in medicinal chemistry: A review," *Int. J. Mol. Sci.*, vol. 24, no. 9, p. 7834, 2023.

[2] L. Knorr, "Einwirkung von acetessigester auf phenylhydrazin," *Berichte der Dtsch. Chem. Gesellschaft*, vol. 16, no. 2, pp. 2597–2599, 1883.

[3] H. Brahmbhatt, M. Molnar, and V. Pavić, "Pyrazole nucleus fused tri-substituted imidazole derivatives as antioxidant and antibacterial agents," *Karbala Int. J. Mod. Sci.*, vol. 4, no. 2, pp. 200–206, 2018.

[4] I. Saleh *et al.*, "Design, synthesis, and antibacterial activity of N-(trifluoromethyl) phenyl substituted pyrazole derivatives," *RSC Med. Chem.*, vol. 12, no. 10, pp. 1690–1697, 2021.

[5] L. Aroua, A. S. Alqumaya, T. Alresheedi, F. A. S. Al-Yusufy, and W. A. El-Sayed, "Pyrazole Derivatives: A New Synthesis, Biological Importance, and Recent Practical Applica-

tions: Pyrazole Derivatives: A New Synthesis, Biological Importance," *J. Qassim Univ. Sci.*, vol. 4, no. 1, 2025.

[6] H. Kumar, K. K. Bansal, and A. Goyal, "An insight into pyrazole-containing compounds: synthesis and pharmacological activities," *Anti-Infective Agents*, vol. 20, no. 5, pp. 1–26, 2022.

[7] A. A. Bekhit *et al.*, "Investigation of the anti-inflammatory and analgesic activities of promising pyrazole derivative," *Eur. J. Pharm. Sci.*, vol. 168, p. 106080, 2022.

[8] G. Li, Y. Cheng, C. Han, C. Song, N. Huang, and Y. Du, "Pyrazole-containing pharmaceuticals: target, pharmacological activity, and their SAR studies," *RSC Med. Chem.*, vol. 13, no. 11, pp. 1300–1321, 2022.

[9] M. Premalatha *et al.*, "Molecular Structure, Vibrational Analysis, and Pharmacokinetic Evaluation of a Novel Pyrazole Derivative: Experimental and Computational Study," *Indian J. Sci. Technol.*, vol. 18, no. 21, pp. 1662–1680, 2025.

[10] H. A. Hofny, M. F. A. Mohamed, H. A. Hassan, E. M. N. Abdelhafez, and G. E. A. Abuo-Rahma, "A review of recent advances in anticancer activity and SAR of pyrazole derivatives," *Arch. Pharm. (Weinheim).*, vol. 358, no. 3, p. e2400470, 2025.

[11] R. Kumar, R. Sharma, and D. K. Sharma, "Pyrazole; a privileged scaffold of medicinal chemistry: A comprehensive review," *Curr. Top. Med. Chem.*, vol. 23, no. 22, pp. 2097–2115, 2023.

[12] A. Ansari, A. Ali, and M. Asif, "Biologically active pyrazole derivatives," *New J. Chem.*, vol. 41, no. 1, pp. 16–41, 2017.

[13] D. Wanode, D. Nandurkar, M. Ambatkar, N. Rarokar, and P. Khedekar, "A Review of Research from 2012 to 2024 on Pyrazole-based Anticancer Agents with SAR Study," *Curr. Top. Med. Chem.*, 2025.

[14] S. T. Heller and S. R. Natarajan, "1, 3-Diketones from acid chlorides and ketones: a rapid and general one-pot synthesis of pyrazoles," *Org. Lett.*, vol. 8, no. 13, pp. 2675–2678, 2006.

[15] Y. Xu, Q. Chen, Y. Tian, W. Wu, Y. You, and Z. Weng, "Silver-catalyzed synthesis of 5-aryl-3-trifluoromethyl pyrazoles," *Tetrahedron Lett.*, vol. 61, no. 5, p. 151455, 2020.

[16] J. Poletto *et al.*, "One-pot highly regioselective synthesis of α-ketoamide N-arylpyrazoles from secondary β-enamino diketones," *Org. Lett.*, vol. 21, no. 16, pp. 6325–6328, 2019.

[17] G. D. Kumar, B. Siva, S. Vadlamudi, S. R. Bathula, H. Dutta, and K. S. Babu, "Design, synthesis, and biological evaluation of pyrazole-linked aloe emodin derivatives as potential anticancer agents," *RSC Med. Chem.*, vol. 12, no. 5, pp. 791–796, 2021.

[18] S. Khazaal and S. Y. Ibraheam, "One-pot synthesis of new pyranopyrazoles via domino multicomponent reaction," *Egypt. J. Chem.*, vol. 65, no. 10, pp. 259–265, 2022.

[19] Y. R. Girish, K. S. S. Kumar, H. S. Manasa, and S. Shashikanth, "ZnO: An Ecofriendly, Green Nano-catalyst for the Synthesis of Pyrazole Derivatives under Aqueous Media," *J. Chinese Chem. Soc.*, vol. 61, no. 11, pp. 1175–1179, 2014.

[20] M. Ahn *et al.*, "Pyrazole derived ultra-short antimicrobial peptidomimetics with potent anti-biofilm activity," *Eur. J. Med. Chem.*, vol. 125, pp. 551–564, 2017.

[21] Y. Nandurkar, A. Shinde, M. R. Bhoye, S. Jagadale, and P. C. Mhaske, "Synthesis and biological screening of new 2-(5-aryl-1-phenyl-1 H-pyrazol-3-yl)-4-aryl thiazole derivatives as potential antimicrobial agents," *ACS omega*, vol. 8, no. 9, pp. 8743–8754, 2023.

[22] A. S. Komendantova, K. A. Lyssenko, I. V Zavarzin, and Y. A. Volkova, "Iodine-promoted synthesis of pyrazoles from 1, 3-dicarbonyl compounds and oxamic acid thiohydrazides," *Org. Chem. Front.*, vol. 7, no. 13, pp. 1640–1646, 2020.

[23] G. Yang, Y. Liu, X. Lin, B. Ming, K. Li, and C. Hu, "Self-assembly of a new 3D platelike ternary-oxo-cluster: An efficient catalyst for the synthesis of pyrazoles," *Chinese Chem. Lett.*, vol. 33, no. 1, pp. 354–357, 2022.

[24] S. M. Al-Muntaser, A. A. Al-Karmalawy, A. M. El-Naggar, A. K. Ali, N. E. A. Abd El-Sattar, and E. M. Abbass, "Novel 4-thiophenyl-pyrazole, pyridine, and pyrimidine derivatives as potential antitumor candidates targeting both EGFR and VEGFR-2; design, synthesis, biological evaluations, and in silico studies," *RSC Adv.*, vol. 13, no. 18, pp. 12184–12203, 2023.

[25] K. Kumara *et al.*, "Design, synthesis, characterization, and antioxidant activity studies of novel thienyl-pyrazoles," *Heliyon*, vol. 7, no. 7, 2021.

[26] W. F. Rodhan *et al.*, "Chemistry and synthesis of Bis Pyrazole derivatives and their biological activity : a review," vol. 1853, pp. 1–12, 2021, doi: 10.1088/1742-6596/1853/1/012059.

[27] R. Nagamallu, B. Srinivasan, M. B. Ningappa, and A. K. Kariyappa, "Synthesis of novel coumarin appended bis (formylpyrazole) derivatives: Studies on their antimicrobial and antioxidant activities," *Bioorg. Med. Chem. Lett.*, vol. 26, no. 2, pp. 690–694, 2016.

[28] A. Ragab, S. A. Fouad, Y. A. Ammar, D. S. Aboul-Magd, and M. S. Abusaif, "Antibiofilm and anti-quorum-sensing activities of novel pyrazole and pyrazolo [1, 5-a] pyrimidine derivatives as carbonic anhydrase I and II inhibitors: design, synthesis, radiosterilization, and molecular docking studies," *Antibiotics*, vol. 12, no. 1, p. 128, 2023.

[29] S. Du *et al.*, "Synthesis, antifungal activity and structure-activity relationships of novel 3-(difluoromethyl)-1-methyl-1 H-pyrazole-4-carboxylic acid amides," *Molecules*, vol. 20, no. 5, pp. 8395–8408, 2015.

[30] Z. Liang *et al.*, "Design, synthesis and antifungal activity of novel pyrazole amides derivates," *J. Mol. Struct.*, vol. 1277, p. 134881, 2023.

[31] A. M. Farag, A. S. Mayhoub, S. E. Barakat, and A. H. Bayomi, "Regioselective synthesis and antitumor screening of some novel N-phenylpyrazole derivatives," *Bioorg. Med. Chem.*, vol. 16, no. 2, pp. 881–889, 2008.

[32] B. J. Newhouse *et al.*, "Non-oxime pyrazole based inhibitors of B-Raf kinase," *Bioorg. Med. Chem. Lett.*, vol. 21, no. 11, pp. 3488–3492, 2011.

[33] E. J. Hanan *et al.*, "Discovery of potent and selective pyrazolopyrimidine janus kinase 2 inhibitors," *J. Med. Chem.*, vol. 55, no. 22, pp. 10090–10107, 2012.

[34] M. A. Metwally, M. A. Gouda, A. N. Harmal, and A. M. Khalil, "Synthesis, antitumor, cytotoxic and antioxidant evaluation of some new pyrazolotriazines attached to antipyrine moiety," *Eur. J. Med. Chem.*, vol. 56, pp. 254–262, 2012.

[35] R. D. Kamble *et al.*, "Synthesis

and in silico investigation of thiazoles bearing pyrazoles derivatives as anti-inflammatory agents," *Comput. Biol. Chem.*, vol. 61, pp. 86–96, 2016.

[36] M. M. M. El-Miligy, A. K. Al-Kubeisi, M. G. Bekhit, S. R. El-Zemity, R. A. Nassra, and A. A. Hazzaa, "Towards safer anti-inflammatory therapy: synthesis of new thymol–pyrazole hybrids as dual COX-2/5-LOX inhibitors," *J. Enzyme Inhib. Med. Chem.*, vol. 38, no. 1, pp. 294–308, 2023.

[37] S.-R. Shih *et al.*, "Pyrazole compound BPR1P0034 with potent and selective anti-influenza virus activity," *J. Biomed. Sci.*, vol. 17, no. 1, p. 13, 2010.

[38] D. Q. Zhang, G. F. Xu, Z. J. Fan, D. Q. Wang, X. L. Yang, and D. K. Yuan, "Synthesis and anti-TMV activity of novel N-(3-alkyl-1H-pyrazol-4-yl)-3-alkyl-4-substituted-1H-pyrazole-5-carboxamides," *Chinese Chem. Lett.*, vol. 23, no. 6, pp. 669–672, 2012.

[39] M. Abdel-Aziz, G. E.-D. A. Abuo-Rahma, and A. A. Hassan, "Synthesis of novel pyrazole derivatives and evaluation of their antidepressant and anticonvulsant activities," *Eur. J. Med. Chem.*, vol. 44, no. 9, pp. 3480–3487, 2009.

[40] S. P. O'Connor *et al.*, "Synthesis, SAR, and atropisomerism of imidazolopyrimidine DPP4 inhibitors," *Bioorg. Med. Chem. Lett.*, vol. 20, no. 21, pp. 6273–6276, 2010.

[41] M. Purohit, V. V. S. R. Prasad, and Y. C. Mayur, "Synthesis and Cytotoxicity of Bis-1, 3, 4-oxadiazoles and Bis-pyrazoles Derived from 1, 4-Bis [5-thio-4-substituted-1, 2, 4-triazol-3-Yl]-butane and Their DNA Binding Studies," *Arch. Pharm. (Weinheim).*, vol. 344, no. 4, pp. 248–254, 2011.

[42] B. T. Abd-Elhalim, G. G. El-Bana, A. F. El-Sayed, and G. E. Abdel-Ghani, "Antifungal activity and biocompatibility assessment with molecular docking and dynamic simulations of new pyrazole derivatives," *BMC Biotechnol.*, vol. 25, no. 1, p. 15, 2025.