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A Review: Synthesis, Methodology and biological evolution of pyrazole moiety

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Abstract
Pyrazole and its derivatives are significant nitrogen-containing heterocyclic compounds with diverse chemical and biological properties. This review summarizes recent advances in the synthesis and methodology of pyrazole derivatives using conventional, catalytic, microwave-assisted, multicomponent, solvent-free, and green synthetic approaches. Different strategies for structural modification of the pyrazole nucleus are discussed in relation to their biological performance. Pyrazole derivatives exhibit promising antibacterial, antifungal, antioxidant, anti-inflammatory, antitubercular, antiviral, and anticancer activities. The review highlights important synthetic methodologies, biological evaluation, structure–activity relationships, and potential medicinal applications of pyrazole-based compounds.
Keywords: *Pyrazole; Pyrazole derivatives; Heterocyclic compounds; Synthesis; Biological evaluation; Pharmacological activity; Medicinal chemistry.*

Introduction

Heterocyclic compounds constitute one of the most important classes of organic compounds because of their remarkable structural diversity and wide range of applications in medicinal chemistry, pharmaceuticals, agrochemicals, and materials science. Among nitrogen-containing heterocycles, pyrazole and its derivatives have attracted considerable attention because of their versatile chemical properties and broad spectrum of biological activities. Pyrazole is a five-membered aromatic heterocycle containing two adjacent nitrogen atoms and three carbon atoms. The presence of two nitrogen atoms provides distinctive electronic and coordination properties and allows diverse substitution patterns, making the pyrazole nucleus an important structural motif in the design and development of biologically active molecules[1-2].

The synthesis of pyrazole derivatives has been extensively investigated, and numerous synthetic methodologies have been developed to obtain structurally diverse compounds with improved biological properties. Classical approaches generally involve the condensation of hydrazines or substituted hydrazines with 1,3-dicarbonyl compounds, α,β-unsaturated carbonyl compounds, β-ketoesters, and related precursors. In particular, cyclocondensation reactions of hydrazines with chalcones and other carbonyl compounds provide convenient routes to substituted pyrazoles and pyrazolines. More recently, microwave-assisted synthesis, multicomponent reactions, catalytic methodologies, solvent-free reactions, ionic-liquid-mediated reactions, and other green synthetic approaches have been explored to improve reaction efficiency, reduce reaction time, and minimize environmental impac[2]. These developments have considerably expanded the structural diversity accessible within the pyrazole family.

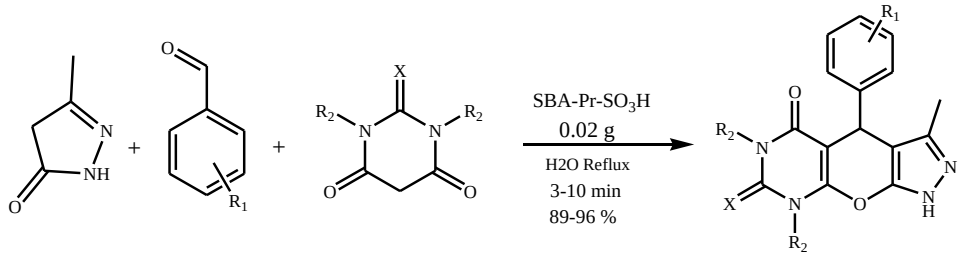
The biological significance of pyrazole derivatives is equally extensive. Structural modification of the pyrazole ring can produce compounds possessing antibacterial, antifungal, antitubercular, antiviral, antioxidant, anti-inflammatory, analgesic, antidiabetic, antiparasitic and anticancer activities.[3-4] Several biologically important drugs contain a pyrazole or substituted-pyrazole pharmacophore, demonstrating the medicinal value of this heterocyclic system. For example, celecoxib contains a substituted pyrazole nucleus and exhibits selective cyclooxygenase-2 inhibitory activity. Other pyrazole-based compounds have been investigated as inhibitors of enzymes, receptors, kinases, and microbial targets. Consequently, pyrazole has become an important scaffold for structure–activity relationship (SAR) studies and rational drug design.

Recent research has increasingly focused on combining pyrazole with other pharmacologically relevant heterocyclic systems to generate hybrid molecules with enhanced or complementary biological properties. Pyrazole-containing hybrids incorporating benzimidazole, pyrimidine,

isoxazole, thiadiazole, thiazole and other heterocyclic moieties have been reported with promising antimicrobial, anticancer and enzyme-inhibitory activities. Computational techniques such as molecular docking, molecular dynamics, density functional theory (DFT), pharmacophore modelling and ADMET prediction are also increasingly being integrated with experimental synthesis and biological evaluation to understand molecular interactions and guide the development of new derivatives.[5-6]

Despite substantial progress, there remains considerable scope for developing new pyrazole derivatives with improved potency, selectivity, physicochemical properties and reduced toxicity. Therefore, systematic investigation of synthetic strategies, structural characterization, biological evaluation and structure–activity relationships is essential for identifying promising pyrazole-based compounds. This review therefore focuses on the major synthetic methodologies used for the preparation of pyrazole and its derivatives, diverse biological activities, structure–activity relationships, recent medicinal-chemistry developments, and emerging strategies for the design of novel pyrazole-based bioactive molecules.

Tanitame et al.[7] DNA gyrase inhibitors Tanitame the authors synthesized a series of pyrazole derivatives designed as antibacterial agents targeting bacterial DNA gyrase and topoisomerase IV. Several derivatives showed strong antibacterial activity, including activity against Gram-positive strains resistant to quinolones or coumarins. One vinyl-substituted pyrazole showed particularly strong activity and selective inhibition of bacterial topoisomerases. The study established pyrazole as a useful scaffold for developing DNA-gyrase/topoisomerase inhibitors and demonstrated that structural modification can produce compounds active against resistant bacterial strains.(Scheme 1)



Scheme 1

Bekhit et al.[8] Antimalarial pyrazoles Bekhit Novel pyrazole derivatives were synthesized and evaluated for antimalarial activity using a *Plasmodium berghei* mouse model. The most active compounds were subsequently tested against a chloroquine-resistant *P. falciparum* strain. The investigation demonstrated that appropriately substituted pyrazoles can possess meaningful antimalarial activity and provide leads for further optimization against resistant malaria parasites. (Fig. 1)

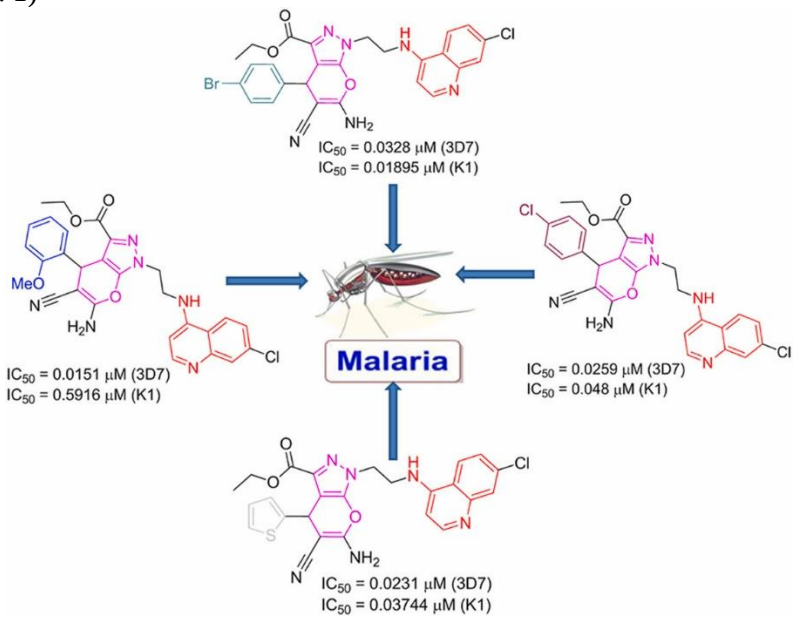
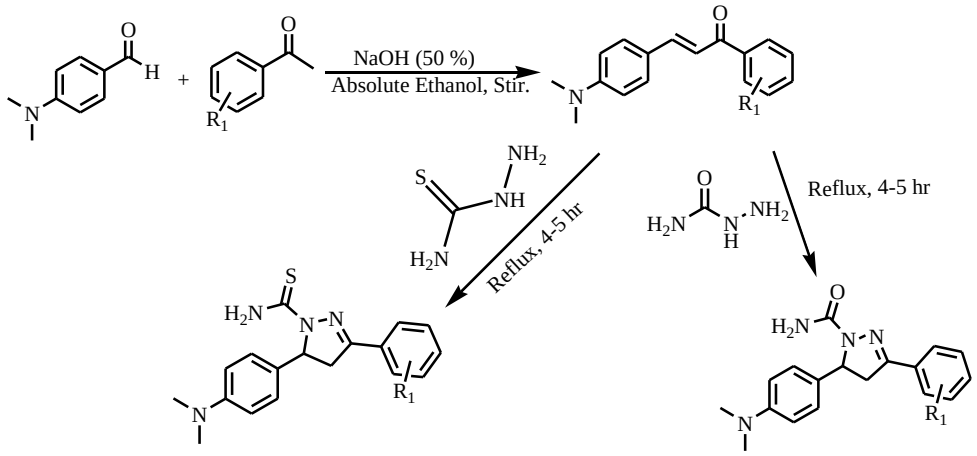


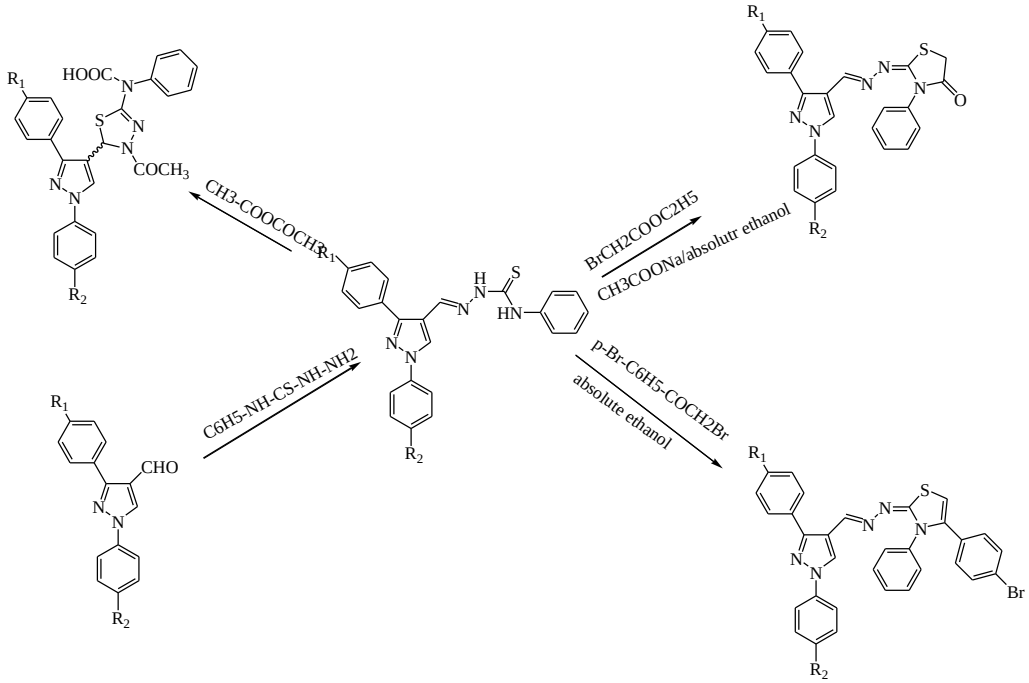
Fig 1

Alam et al. [9] Anticancer pyrazoles A series of pyrazle derivatives was designed and synthesized to investigate anticancer activity. Cytotoxicity assays, human topoisomerase IIα inhibition and molecular docking were used to establish biological activity and possible molecular interactions. The study identified pyrazole derivatives capable of inhibiting cancer-related targets and demonstrated that molecular modification of the pyrazole nucleus can generate potential anticancer leads. (Scheme 2)



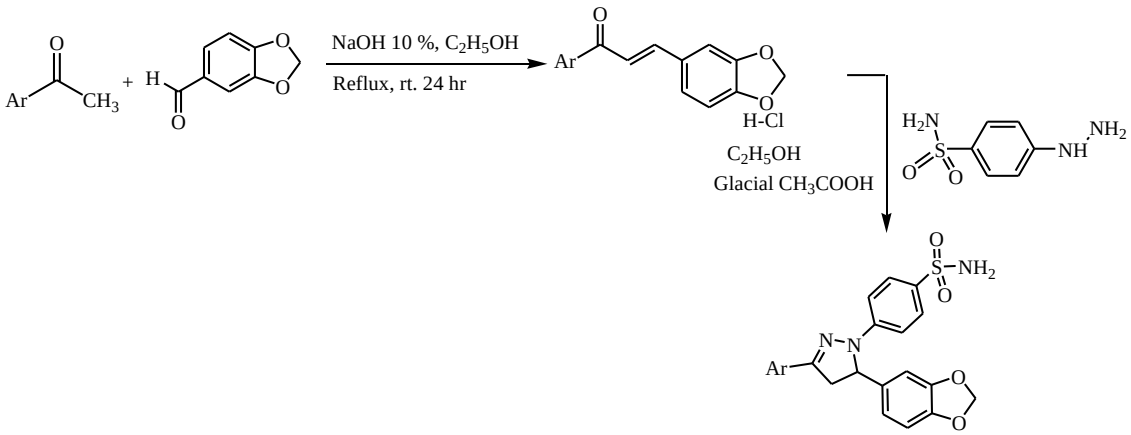
Scheme 2

Bekhit et al. [10] Pyrazole hybrids against malaria ad leishmaniasis Pyrazole-based heterocyclic hybrids were designed and synthesized with the objective of obtaining compounds active against both malaria and leishmaniasis. The derivatives were evaluated through appropriate parasitic assays. The hybridization strategy demonstrated that pyrazole can be incorporated into multifunctional antiparasitic scaffolds and provided candidates for further structural optimization. (Scheme 3)



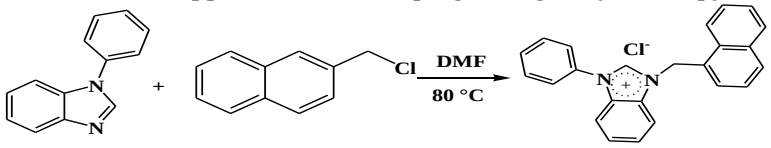
Scheme 3

Turkan et al.[11] Carbonic anhydrase and AChE inhibition, New pyrazole derivatives were synthesized and investigated for inhibition of carbonic anhydrase isoenzymes and acetylcholinesterase. Enzyme inhibition assays were complemented by molecular docking to investigate ligand–enzyme interactions. The synthesized pyrazoles demonstrated inhibitory potential toward the investigated enzymes, supporting the pyrazole scaffold as a useful pharmacophore for enzyme-targeted drug design. (Scheme 4)



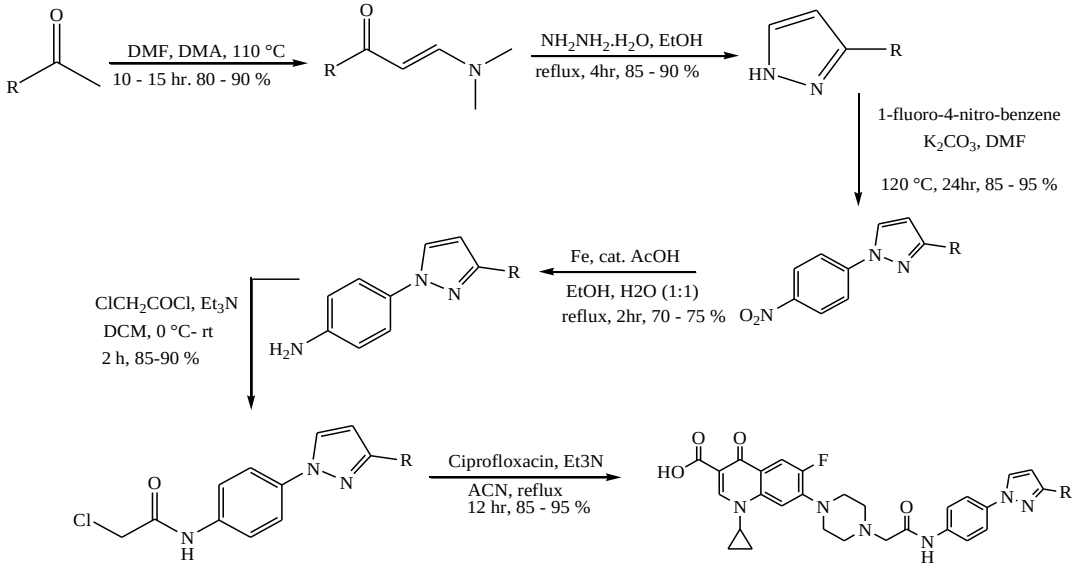
Scheme 4

Sivarama karthikeyan et al.[12] Benzimidazole–pyraole hybrids Benzimidazole-ornamented pyrazoles were synthesized through a multistep route. The compounds were evaluated for anti-inflammatory, antioxidant and anticancer properties, followed by molecular docking studies. Different substituents strongly influenced biological performance. Selected derivatives demonstrated promising anti-inflammatory, antioxidant and anticancer properties, supporting molecular hybridization as an approach for developing biologically active pyrazoles. (Scheme 5)



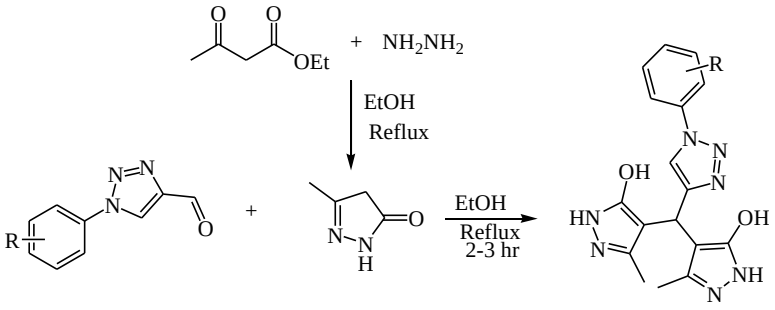
Scheme 5

Desai et al.[13] Pyrazole–oxadiazole hybrids Pyrazole–oxadiazole hybrids were prepared using conventional and microwave-assisted synthetic methods. Microwave irradiation reduced reaction time and generally improved synthetic efficiency. The compounds were evaluated against *Mycobacterium tuberculosis* strains and investigated by molecular docking.Microwave synthesis provided an efficient alternative to conventional synthesis, while several derivatives showed promising antitubercular activity and favorable docking interactions with the mycobacterial InhA target. (Scheme 6)



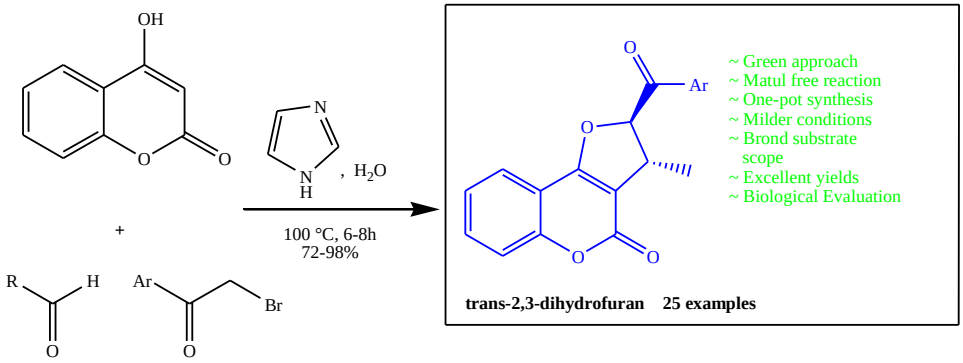
Scheme 6

Danne et al. [14] Bis-pyrazoles A series of triazole-apended bis-pyrazoles was synthesized and characterized. Biological screening and molecular docking were performed to determine their potential as bioactive heterocyclic compounds.The incorporation of two pyrazole units with a triazole linker produced compounds with promising biological properties, illustrating the usefulness of heterocyclic hybridization in medicinal chemistry. (Scheme 7)



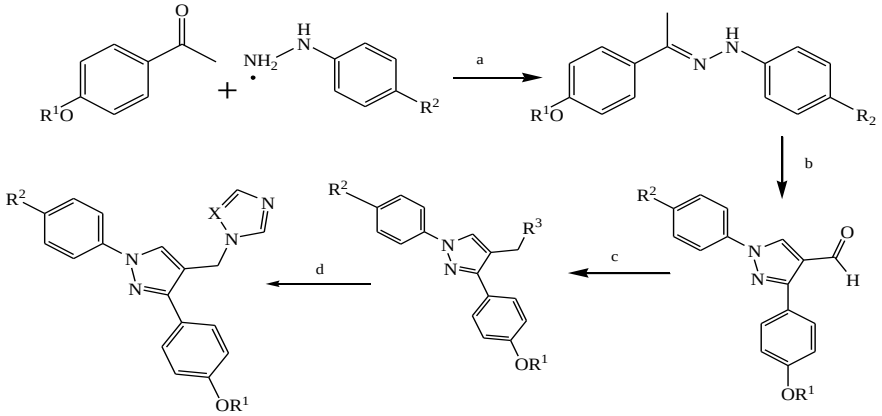
Scheme 7

Mali et al.[15] Pyranopyrazoles A taurine-catalyzed green multicomponent reaction was developed for synthesizing densely substituted dihydropyrano[2,3-*c*]pyrazoles. The products contained isonicotinamide, spirooxindole and indole substituents. Molecular docking was used to investigate interactions with wild-type and resistant *S. aureus* dihydrofolate reductase. The work established a green multicomponent method for accessing complex pyrazole-containing scaffolds and identified compounds with potential for further antistaphylococcal development. (Scheme 8)



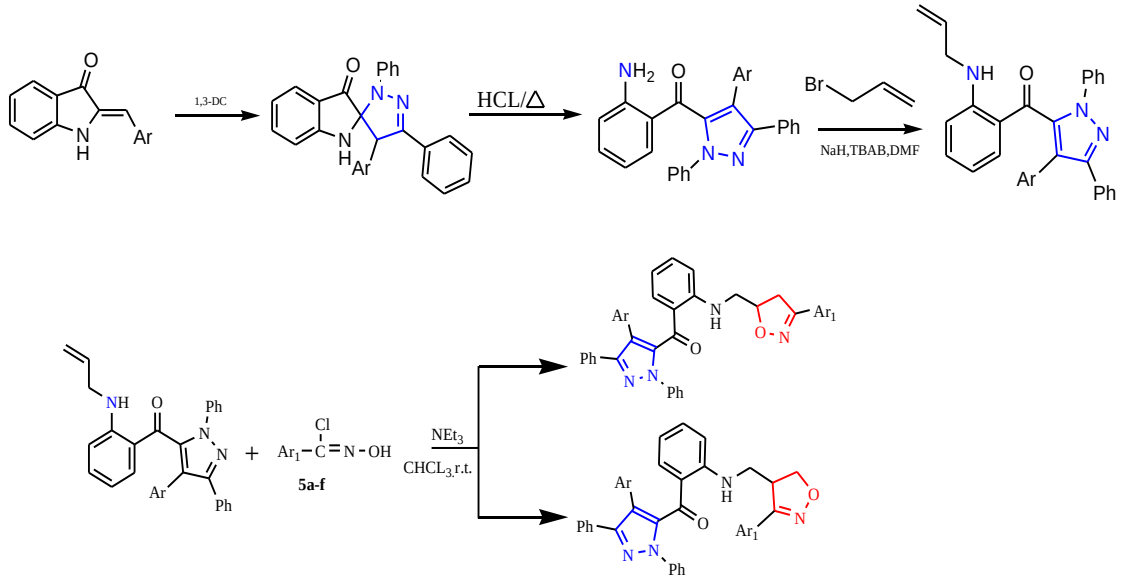
Scheme 8

Alshabani et al.[16] Antitubercular pyrazoles Pyazole derivatives were synthesized and investigated as inhibitors of CYP121A1, an enzyme associated with *M. tuberculosis*. Biological assays were combined with computational and structural investigations. The study identified pyrazole-based compounds capable of interacting with CYP121A1 and demonstrated the potential of this scaffold for developing new antitubercular agents. (Scheme 9)



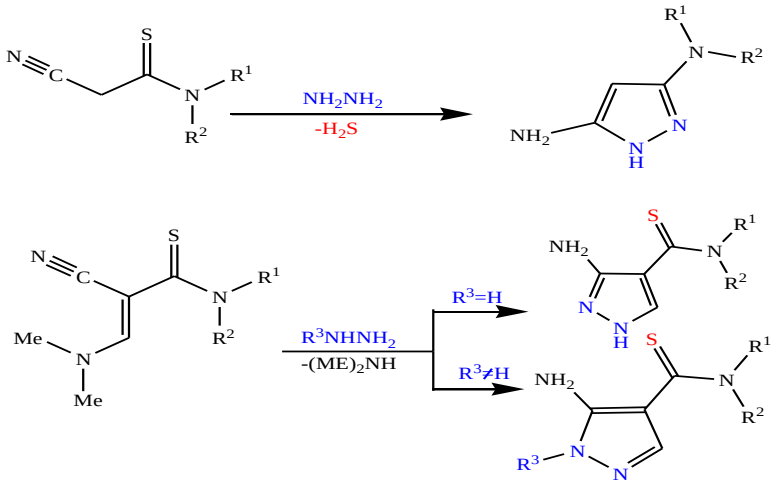
Scheme 9

Chalkha et al.[17] Pyrazole–isoxazoline hybrids Pyrazole–isoxazoline hybrids were synthesized using N-alkylation and 1,3-dipolar cycloaddition. Their structures were established using IR, NMR and HRMS. DFT calculations investigated reaction regioselectivity, while antimicrobial testing, molecular docking and ADMET studies assessed biological potential.The compounds showed variable antimicrobial activity dependent on substitution. The authors attributed enhanced activity to the combined effects of the pyrazole and isoxazoline pharmacophores. (Scheme 10)



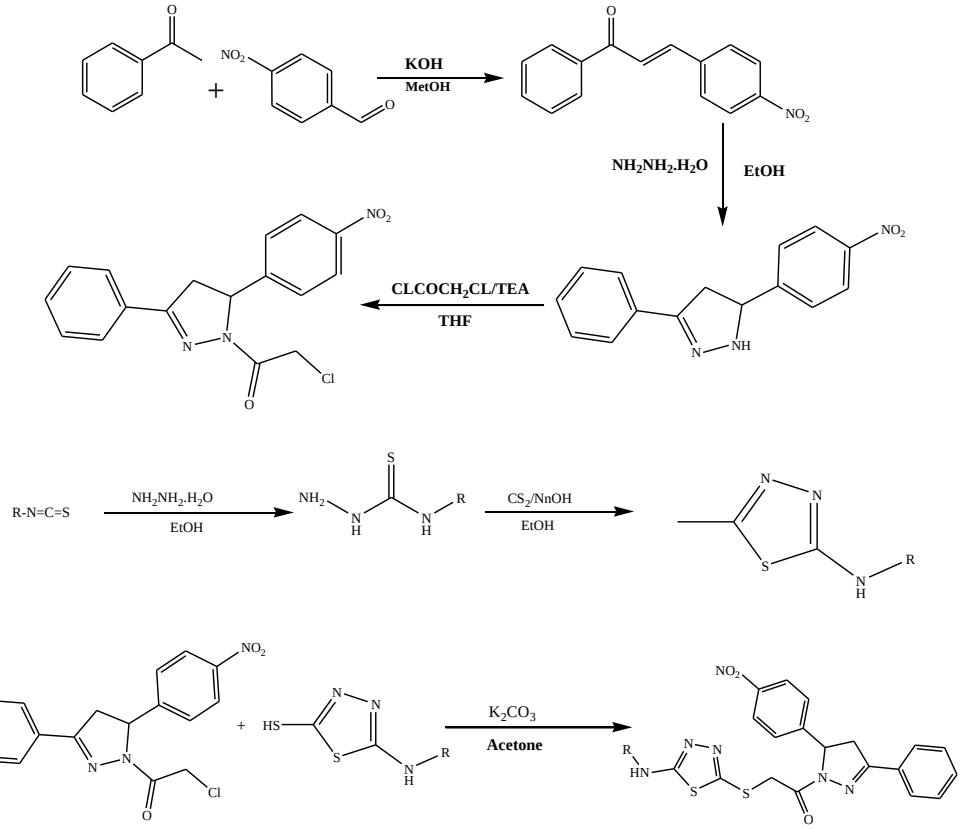
Scheme 10

Mahesh et al.[18] Pyrazole-4-sulfonamides Two seriescontaining nineteen pyrazole-4-sulfonamide derivatives were synthesized under relatively mild conditions and evaluated for antiproliferative and cytotoxic properties.The synthetic methodology provided access to pyrazole-4-sulfonamides under mild conditions. The biological screening demonstrated that this structural class deserves further investigation for antiproliferative applications. (Scheme 11)



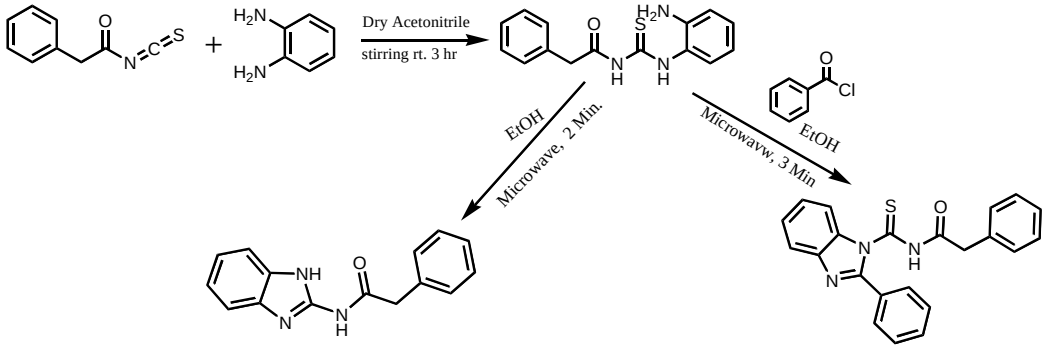
Scheme 11

Kurban et al.[19] Pyrazole–thiadiazole EGFR inhibitors New pyrazole–thiadiazole derivatives were developed as potential EGFR inhibitors. Cytotoxicity, mitochondrial membrane potential and EGFR inhibition were investigated, with molecular docking and molecular dynamics used to explore binding. Several derivatives displayed substantial antiproliferative and EGFR inhibitory activity. The study identified pyrazole–thiadiazole structures as candidates for further optimization against EGFR-associated cancer. (Scheme 12)



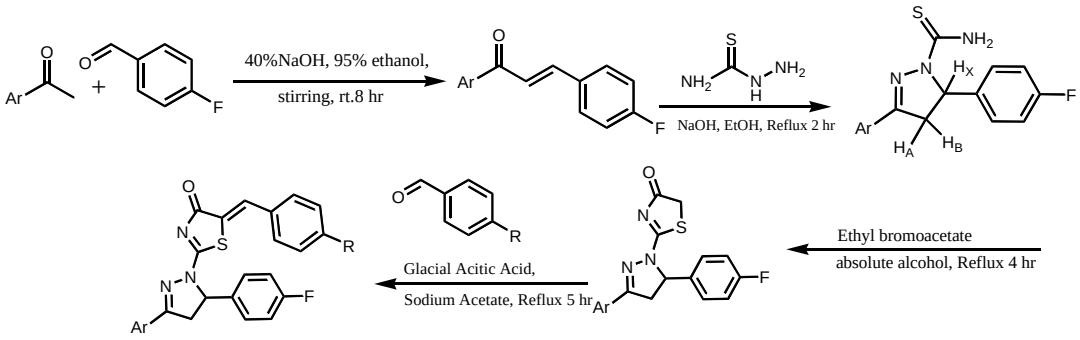
Scheme 12

Othman et al[20] Pyrazole / pyrimidine EGFR inhibitos New pyrazole and pyrimidine derivatives were synthesized as ATP-mimicking EGFR inhibitors. Anticancer activity was tested against MCF-7 and HepG-2 cells, while antimicrobial assays and molecular docking were also conducted. The compounds showed combined anticancer and antimicrobial potential, while computational studies supported their interaction with EGFR. The results provide a basis for further development of pyrazole-containing kinase inhibitors. (Scheme 13)



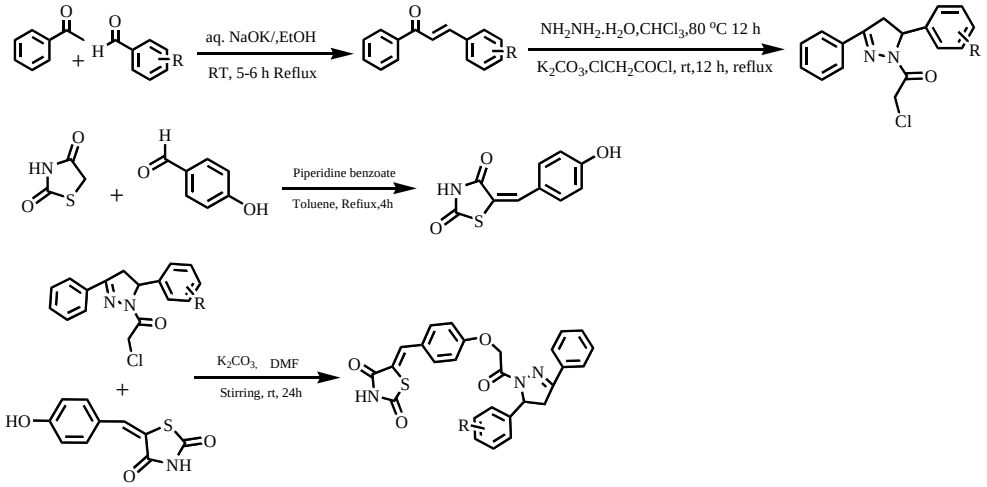
Scheme 13

George et al.[21] Trisubstituted pyrazolines. A variety of trisubstituted pyrazolines were synthesized through condensation of chalcones with hydrazine derivatives. Cytotoxicity against MCF-7 cells, toxicity toward normal fibroblasts and EGFR inhibition were investigated. Several pyrazoline derivatives showed promising anticancer activity with acceptable selectivity toward cancer cells, and selected compounds demonstrated EGFR inhibition supported by docking studies. (Scheme 14)



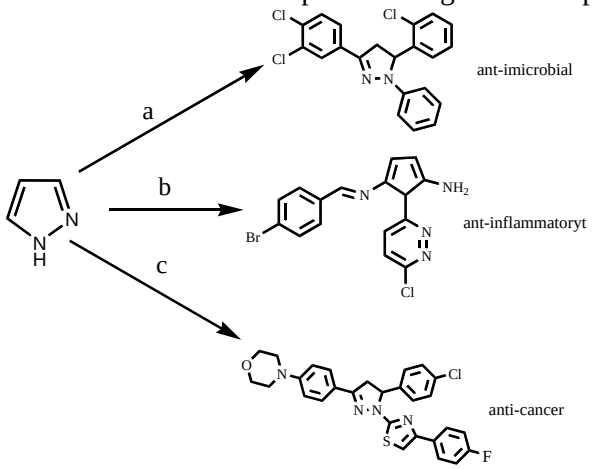
Scheme 14

Tok et al [22] 2-Pyrazoline anticancer derivative New pyrazoline derivatives were prepared from chalcone precursors and characterized using IR, ^{1}H NMR, ^{13}C NMR and elemental analysis. Their antiproliferative effects were investigated against HeLa, MCF-7 and MKN-45 cancer cells and a normal fibroblast cell line.Selected compounds exhibited significant cytotoxicity toward cancer cells without comparable toxicity toward normal cells. Biological investigations indicated involvement of apoptotic pathways involving Bax, Bcl-2 and caspase-3. (Scheme 15)



Scheme 15

Tilekar et al[23] Pyrazoline–pyrrolidinedione **hybrids** Pyrazoline–pyrrolidine-2,5-dione hybrids were designed and synthesized as potential anticancer agents. The compounds underwent computational, in vitro and in vivo evaluation.The study demonstrated that combining pyrazoline with a pyrrolidine-dione pharmacophore can generate compounds with antitumor potential and provided candidates for additional pharmacological development. (Scheme 16)



Scheme 16

Rasal et al[24] Pyrazoline–pyrrole carboxylic acid derivatives Twenty-four novel pyrazoline-conjugated pyrrole carboxylic acid and amide derivatives were synthesized and screened for antimicrobial activity. Molecular modeling was also employed to investigate possible biological

interactions. Several derivatives showed measurable antimicrobial activity, demonstrating that molecular hybridization between pyrrole and pyrazoline can provide useful scaffolds for further antimicrobial optimization. (fig 2)

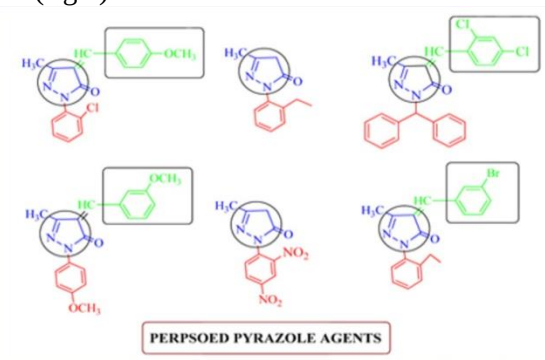
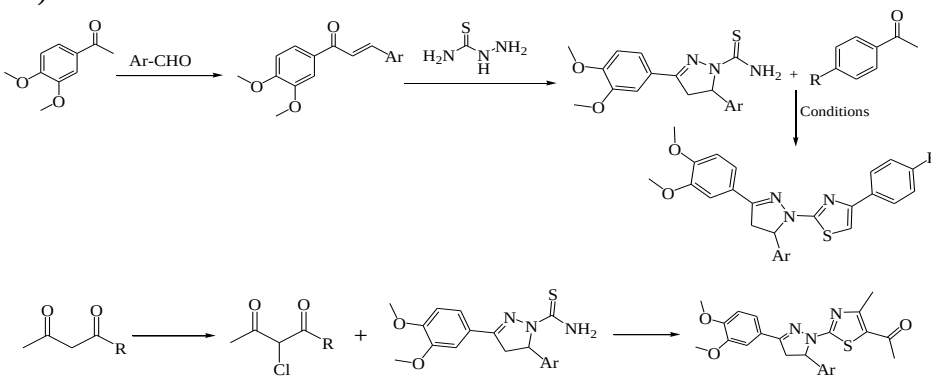


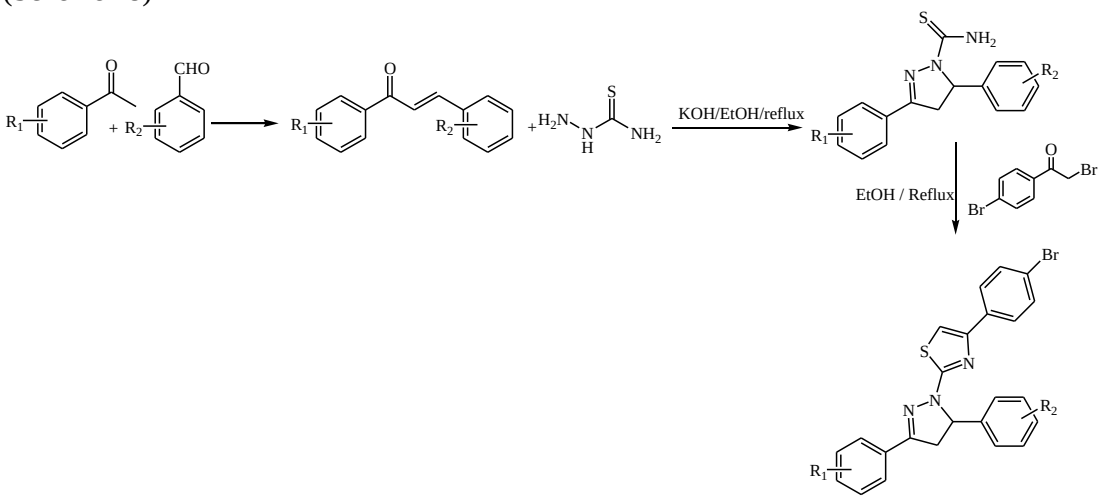
Fig 2

Fakhry et al [25] Pyrazoline antiproliferative agents Novel pyrazoline-based compounds were rationally designed and synthesized and evaluated against MCF-7 breast cancer cells. Molecular modeling and structure–activity relationships were used to understand their antiproliferative properties. The investigation identified pyrazoline derivatives with promising antiproliferative activity and provided structural information useful for designing more active analogues. (Scheme 17)



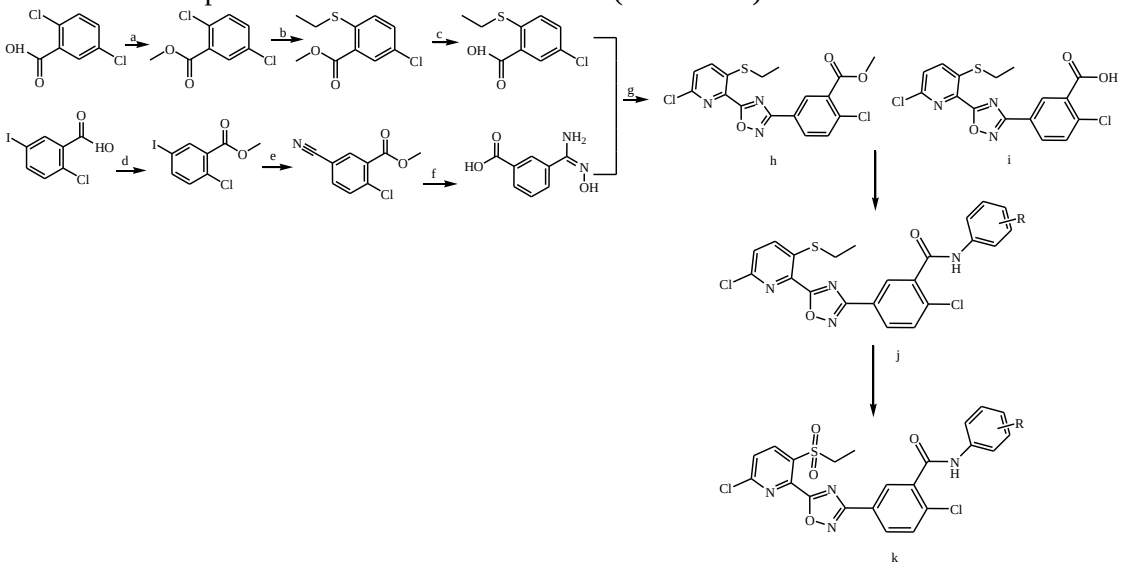
Scheme 17

Hosseini Nasab et al [26] Eleven thiazolyl-pyrazoline derivatives were synthesized and tested against A549 lung carcinoma and A375 melanoma cells. Selected active compounds were further examined for effects on MMP-2, MMP-9 and COX-2. Several derivatives showed antiproliferative activity and selected compounds also demonstrated anti-metastatic and anti-inflammatory potential, supporting thiazole–pyrazoline hybridization as a useful strategy. (Scheme 18)



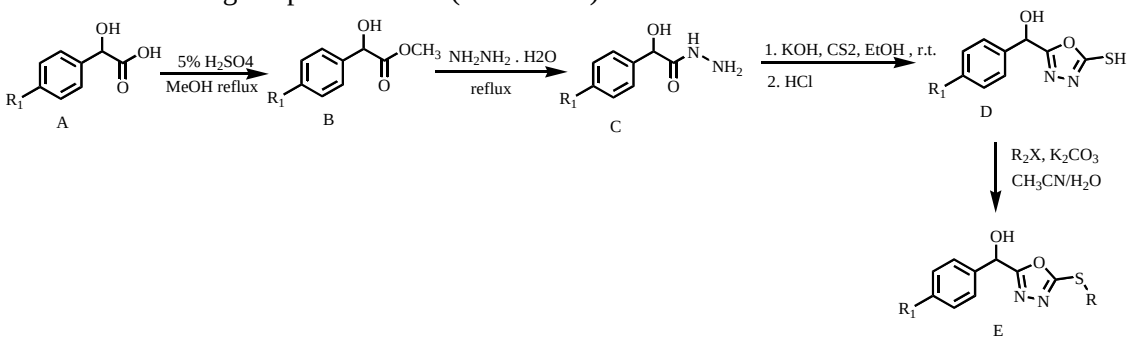
Scheme 18

Zhang et al [27] Pyrazole carboxamides as fungicides Novel pyrazole carboxamides incorporating diarylamine structural features were synthesized as potential succinate dehydrogenase inhibitors. Their antifungal activities were assessed against pathogenic fungi. The study demonstrated that pyrazole carboxamide derivatives can act as potent fungicidal scaffolds through SDH-related mechanisms and provided useful SAR information. (Scheme 19)



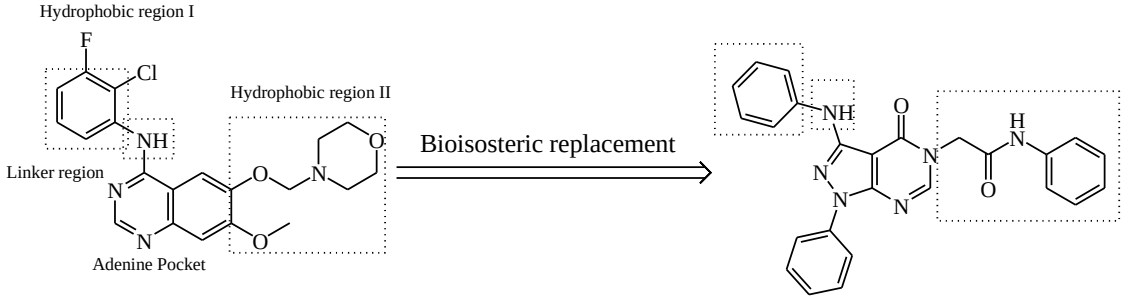
Scheme 19

Zhao et al [28] The work investigated how a pyrazole carboxamide containing a diarylamine scaffold acts against *R. solani*. Biological experiments were combined with mechanistic studies to determine the basis of antifungal activity. The research provided mechanistic evidence supporting pyrazole carboxamides as potential fungicidal agents and helped connect structural features with biological performance. (Scheme 20)



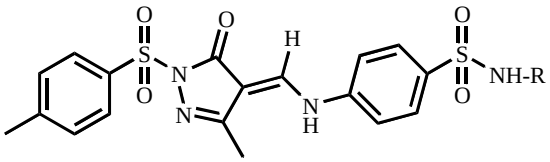
Scheme 20

Farag F. Sherbiny et al[29] Othman-related pyrazolo[3,4-d]pyrimidine derivatives Novel fused pyrazolo[3,4-d]pyrimidine derivatives were synthesized and evaluated against several human cancer cell lines. Selected compounds were examined for EGFR inhibition and apoptosis induction. The study demonstrated that fused pyrazolo-pyrimidine systems can provide biologically active kinase-targeting scaffolds and identified candidates for further anticancer optimization. (Scheme 21)



Scheme 21

Gad-Elkareem, M. A. et al[30] Pyrazolone and dipyrazolotriazine derivatives New pyrazolone and dipyrazolotriazine derivatives were synthesized and characterized. Antimicrobial and antioxidant assays were combined with molecular docking, SAR and drug-likeness studies.The work identified structural features associated with antimicrobial and antioxidant effects and suggested these compounds as potential dual-function bioactive scaffolds. (Fig 3)

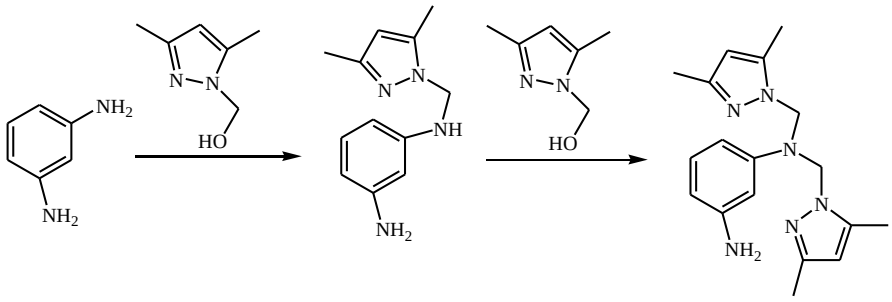


5a:R=H,
5b:R=Pyrimidinyl

5a-Peroxiredoxinr
5b-tyrosyl-t RNA Synthetase

Fig 3

Kaddouri, Y et al[31] Pyrazole derivatives against Fusarium oxysporum Mono-, bis- and tetrakis-pyrazole-containing heterocycles were synthesized in good yields and characterized. Their antifungal activity against *F. oxysporum* was studied alongside DFT calculations, reaction-mechanism analysis and molecular docking. The research demonstrated a relationship between molecular structure, calculated electronic properties and antifungal activity, providing useful information for designing antifungal pyrazole derivatives. (Scheme 22)



Scheme 22

Chalkha, M. et al[32] Pyrazole–isoxazoline hybrids — ACS Omega The study developed hybrid molecules containing pyrazole and isoxazoline rings. N-alkylation and cycloaddition were used for synthesis, followed by spectroscopic and HRMS characterization, antimicrobial assays, DFT analysis, docking and ADMET assessment. The authors concluded that substitution significantly controls antimicrobial activity and that the combination of two pharmacophores can provide synergistic biological effects. (Fig 4)

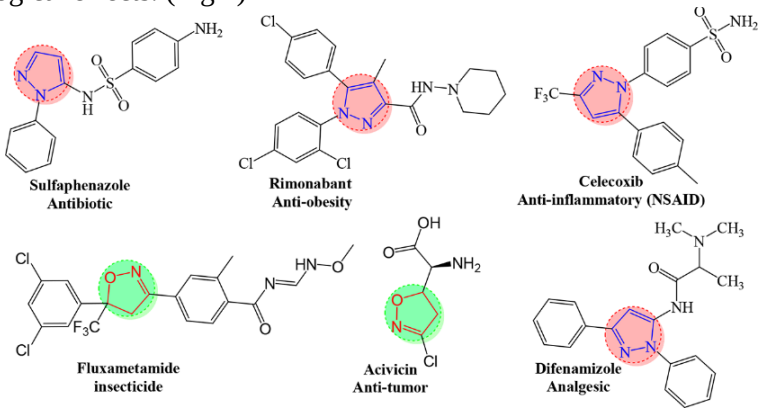


Fig 4

Singh, S. et al[33] New pyrazole derivatives antimicrobial, antioxidant and anti-inflammatory studies A new series of pyrazoles was synthesized and characterized using physicochemical and spectroscopic methods. The compounds were evaluated for antimicrobial, antioxidant, antidiabetic and anti-inflammatory activities, with molecular docking and DFT studies providing additional mechanistic information. Different pyrazole substituents produced distinct biological

responses. The study identified derivatives with promising antimicrobial, antioxidant, antidiabetic and anti-inflammatory profiles and provided SAR information for future design. (Fig 5)

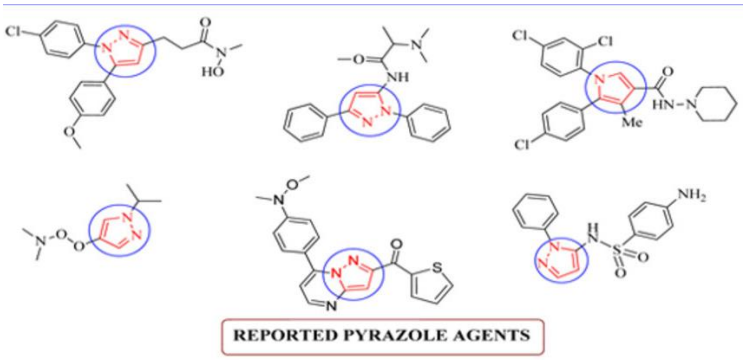
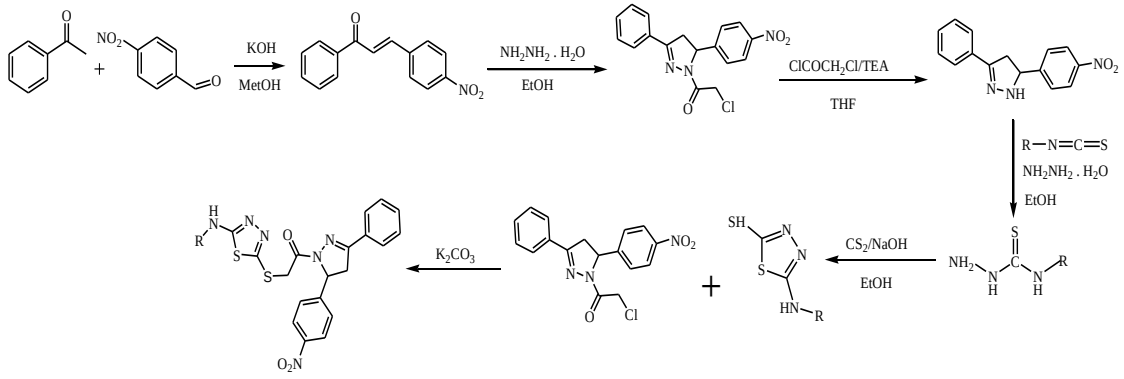


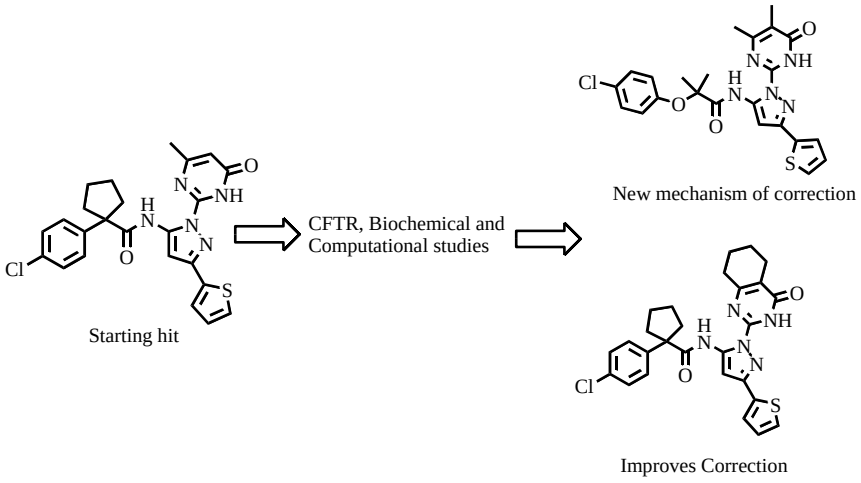
Fig 5

Kurban, B.[34] Pyrazole–thiadiazole EGFR inhibitors Pyrazole–thiadiazole hybrids were synthesized and evaluated using cellular cytotoxicity, mitochondrial membrane-potential assays and EGFR inhibition. Molecular docking and molecular dynamics were used to support the experimental observations. Selected compounds displayed substantial activity against lung cancer cells and EGFR, demonstrating the potential of this hybrid scaffold for further anticancer research. (Scheme 23)



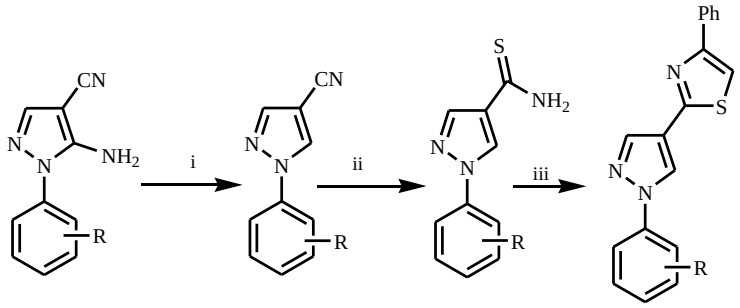
Scheme 23

Vaccarin, C. et al[35] Pyrazole pyrimidone derivatives New pyrazole–pyrimidone compounds were designed from an earlier CFTR-corrector scaffold. The compounds were evaluated for their ability to improve folding, trafficking and function of mutant CFTR proteins, including variants that respond poorly to existing correctors. The study identified optimized pyrazole–pyrimidone correctors with improved activity and demonstrated that pyrazole-containing scaffolds can be useful for addressing rare CFTR mutations and combination therapies. (Scheme 24)



Scheme 24

Pereira, C, et al[36] Pyrazole thiazole hybrids recent ACS Omega study Pyrazole–thiazole hybrids were synthesized and fully characterized and then evaluated against *T. cruzi* and *M. tuberculosis*. Physicochemical profiling and computational studies were used alongside biological assays. Halogenated derivatives showed notable activity. The study demonstrated that halogen substitution can substantially influence the biological performance of pyrazole–thiazole hybrids and identified compounds suitable for further optimization against neglected infectious diseases. (Scheme 25)



i) t-butyl nitrilr,THF,Reflux:, ii) Lawesson reagent, ethanol, 24 h, Reflux i
ii) bromoacetophenone, DMF, 1-4h. 70^{o}C

Scheme 25

Conclusion

Pyrazole and its derivatives represent an important class of nitrogen-containing heterocyclic compounds with remarkable synthetic versatility and broad biological potential. This review highlights the major synthetic methodologies used for the preparation of pyrazole derivatives, including conventional cyclocondensation, multicomponent reactions, microwave-assisted synthesis, solvent-free protocols, and green catalytic approaches. Structural modification of the pyrazole nucleus through appropriate substitution has enabled the development of compounds with diverse pharmacological properties, including antimicrobial, antifungal, anti-inflammatory, anticancer, antioxidant, antitubercular, antimalarial, and analgesic activities. Advances in modern characterization techniques such as FT-IR, NMR, mass spectrometry, and X-ray crystallography have facilitated reliable structural elucidation and structure–activity relationship studies. Recent developments in green chemistry and biologically oriented molecular design have further expanded the scope of pyrazole chemistry. Future research should focus on environmentally sustainable synthetic methodologies, computationally guided drug design, detailed mechanistic investigations, toxicity evaluation, and optimization of pharmacokinetic properties. Overall, continued exploration of the pyrazole scaffold is expected to provide valuable new molecules with improved biological efficacy and potential applications in medicinal and pharmaceutical chemistry.

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References

1. Karrouchi, K.; Radi, S.; Ramli, Y.; Taoufik, J.; Mabkhot, Y. N.; Al-Aizari, F. A.; Ansar, M. *Molecules* **2018**, *23*, 134. DOI: 10.3390/molecules23010134.
2. Dwivedi, J.; Sharma, S.; Jain, S.; Singh, A. *Mini-Rev. Med. Chem.* **2018**, *18*, 918–947. DOI: 10.2174/1389557517666170927160919.
3. Ebenezer, O.; Shapi, M.; Tuszynski, J. A.*Biomedicines* **2022**, *10*, 1124. DOI: 10.3390/biomedicines10051124.
4. Kumar, R.; Sharma, R.; Sharma, D. K. *Curr. Top. Med. Chem.* **2023**, *23*, 2097–2115. DOI: 10.2174/1568026623666230714161726.
5. Moussa, Z.; Ramanathan, M.; Alharmoozi, S. M. *Heliyon* **2024**, *10*, e38894. DOI: 10.1016/j.heliyon.2024.e38894.

6. Menezes, R. A.; Bhat, K. S. *Discover Applied Sciences* **2025**, *7*, 137. DOI: 10.1007/s42452-025-06528-x.
7. Tanitame, A.; Oyamada, Y.; Ofuji, K.; Fujimoto, M.; Iwai, N.; Hiyama, Y.; Suzuki, K.; Ito, H.; Terauchi, H.; Kawasaki, M.; Nagai, K.; Wachi, M.; Yamagishi, J.-i. *J. Med. Chem.* **2004**, *47*, 3693–3696. DOI: 10.1021/jm030394f.
8. Bekhit, A. A.; Hymete, A.; Asfaw, H.; Bekhit, A.-D. A. *Arch. Pharm.* **2012**, *345*, 147–154. DOI: 10.1002/ardp.201100078.
9. Alam, R.; Wahi, D.; Singh, R.; Sinha, D.; Tandon, V.; Grover, A.; Rahisuddin. *Bioorg. Chem.* **2016**, *69*, 77–90. DOI: 10.1016/j.bioorg.2016.10.001.
10. Bekhit, A. A.; Hassan, A. M. M.; Abd El Razik, H. A.; El-Miligy, M. M. M.; El-Agroudy, E. J.; Bekhit, A. E.-D. A. *Eur. J. Med. Chem.* **2015**, *94*, 30–44. DOI: 10.1016/j.ejmech.2015.02.038.
11. Turkan, F.; Cetin, A.; Taslimi, P.; Karaman, M.; Gulçin, İ. *Bioorg. Chem.* **2019**, *86*, 420–427. DOI: 10.1016/j.bioorg.2019.02.013.
12. Sivaramakarthikeyan, R.; Iniyaval, S.; Saravanan, V.; Lim, W.-M.; Mai, C.-W.; Ramalingan, C. *ACS Omega* **2020**, *5*, 10089–10098. DOI: 10.1021/acsomega.0c00630.
13. Desai, N. C.; Bhatt, K.; Monapara, J.; Pandit, U.; Khedkar, V. M. *ACS Omega* **2021**, *6*, 28270–28284. DOI: 10.1021/acsomega.1c04411.
14. Danne, A. B.; Deshpande, M. V.; Sangshetti, J. N.; Khedkar, V. M.; Shingate, B. B. *ACS Omega* **2021**, *6*, 24879–24890. DOI: 10.1021/acsomega.1c03734.
15. Mali, G.; Shaikh, B. A.; Garg, S.; Kumar, A.; Bhattacharyya, S.; Erande, R. D.; Chate, A. V. *ACS Omega* **2021**, *6*, 30734–30742. DOI: 10.1021/acsomega.1c04773.
16. Alshabani, L. A.; Kumar, A.; Willcocks, S. J.; Srithiran, G.; Bhakta, S.; Estrada, D. F.; Simons, C. *RSC Med. Chem.* **2022**, *13*, 1350–1360. DOI: 10.1039/D2MD00155A.
17. Chalkha, M.; Nour, H.; Chebbac, K.; et al. *ACS Omega* **2022**, *7*, 46731–46744. DOI: 10.1021/acsomega.2c05788.
18. Mahesh, P.; Akshinthala, P.; Katari, N. K.; Gupta, L. K.; Panwar, D.; Sharma, M. K.; Jonnalagadda, S. B.; Gundla, R. *ACS Omega* **2023**, *8*, 25698–25709. DOI: 10.1021/acsomega.2c07539.
19. Kurban, B.; Sağlık, B. N.; Osmaniye, D.; Levent, S.; Özkay, Y.; Kaplancıklı, Z. A. *ACS Omega* **2023**, *8*, 31500–31509. DOI: 10.1021/acsomega.3c04635.
20. Othman, I. M. M.; Alamshany, Z. M.; Tashkandi, N. Y.; Gad-Elkareem, M. A. M.; Anwar, M. M.; Nossier, E. S. Bioorg. Chem. **2021**, *114*, 105078. DOI: 10.1016/j.bioorg.2021.105078.
21. George, R. F.; Kandeel, M.; El-Ansary, D. Y.; El Kerdawy, A. M. *Bioorg. Chem.* **2020**, *99*, 103780. DOI: 10.1016/j.bioorg.2020.103780.
22. Tok, F.; Abas, B. I.; Cevik, O.; Kaymakcioglu, B. K. *Bioorg.* Chem. **2020**, *102*, 104063. DOI: 10.1016/j.bioorg.2020.104063.
23. Tilekar, K.; Upadhyay, N.; Meyer-Almes, F.-J.; et al. Chem Med Chem **2020**, *15*, 1813–1825. DOI: 10.1002/cmdc.202000458.
24. Rasal, N. K.; Sonawane, R. B.; Jagtap, S. V. Arch. Pharm. **2021**, *354*, e2000267. DOI: 10.1002/ardp.202000267.
25. Fakhry, M. M.; Mahmoud, K.; Nafie, M. S.; et al. Pharmaceuticals **2022**, *15*, 1245. DOI: 10.3390/ph15101245.
26. Hosseini Nasab, N.; Azimian, F.; Shim, R. S.; Eom, Y. S.; Shah, F. H.; Kim, S. J. *Bioorg. Med. Chem. Lett.* **2023**, *80*, 129105. DOI: 10.1016/j.bmcl.2022.129105.
27. Zhang, A.; Zhou, J.; Tao, K.; et al. Bioorg. Med. Chem. *Lett.* **2018**, *28*, 3042–3045. DOI: 10.1016/j.bmcl.2018.08.001.
28. Zhao, Y.; Yang, N.; Deng, Y.; et al. J. Agric. Food Chem. **2020**, *68*, 11068–11076. DOI: 10.1021/acs.jafc.9b06937.
29. *Bioorg. Chem.* **2021**, *116*, 105325. DOI: 10.1016/j.bioorg.2021.105325.
30. *Bioorg. Chem.* **2021**, *109*, 104704. DOI: 10.1016/j.bioorg.2021.104704.
31. *Bioorg. Chem.* **2021**, *110*, 104696. DOI: 10.1016/j.bioorg.2021.104696.
32. Chalkha, M.; Nour, H.; Chebbac, K.; et al. *ACS Omega* **2022**, *7*, 46731–46744. DOI: 10.1021/acsomega.2c05788.

33. Singh, S.; Tahlan, S.; Singh, K.; Verma, P. K. J. Mol. Struct. **2024**, *1310*, 138186. DOI: 10.1016/j.molstruc.2024.138186.
34. Kurban, B.; Sağlık, B. N.; Osmaniye, D.; Levent, S.; Özkay, Y.; Kaplancıklı, Z. A. *ACS Omega* **2023**, *8*, 31500–31509. DOI: 10.1021/acsomega.3c04635.
35. Vaccarin, C.; Veit, G.; Hegedus, T.; Torres, O.; Chilin, A.; Lukacs, G. L.; Marzaro, G. J. Med. Chem. **2024**, *67*, 13891–13908. DOI: 10.1021/acs.jmedchem.4c00685.
36. Pereira, C. N.; et al. ACS Omega **2026**, *11*, 21890–21902. DOI: 10.1021/acsomega.5c12469.