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Pyrazole: a versatile therapeutic agent with diverse biological activities

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ABSTRACT

Pyrazole and its derivatives has received enormous attention due to their pharmacological properties and are active constituent of pharmaceutical drug molecules. Due to their structural modification they offered a high degree of diversity that has proven useful for the development of therapeutic agents with improved potency and reduced toxicity. In the present article we have studied the pyrazole derivatives for pharmacological activities with highlighting their active compound.

Keywords: Pyrazole Derivatives, Antimicrobial, Antioxidant, Antiinflammatory, Anticonvulsant, Antitubercular

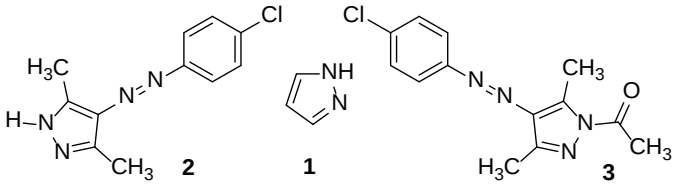
INTRODUCTION

Pyrazole is one of the most important five membered heterocyclic compound containing three carbon atom and two nitrogen atom in the adjacent position ring structure.[1] Pyrazole moiety and its reduced form pyrazoline are well known nitrogen containing compounds and various procedures have been deployed for their synthesis.[2] Pyrazole derivatives remain of great interest due to their wide applications in the pharmaceutical and agrochemical industry.[3] The pyrazole scaffold are found to exhibit a wide range of pharmacological activities; the most important activities such as anti-inflammatory,[4] anti-depressant,[5] antitubercular activity,[6] anti-viral,[7] antimicrobial,[8] anti-convulsant,[9] anti-cancer activity[10] and antiepileptic.[11] In addition, some pyrazole derivatives are widely used as fungicides, antiviral agents, analgesic agents, insecticides and herbicides[12] and many more.

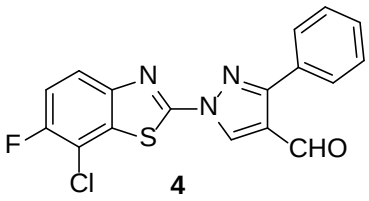
Biological activities of pyrazole derivatives:

1. Antimicrobial activity

In 2013, Kale *et al*[13] synthesized 3,5-dimethyl azopyrazole derivatives and evaluated for their antimicrobial activity against different strains of bacteria such as *S. aureus*, *B. subtilis*, *E. coli* and *S. paratyphi* by using agar diffusion method. Out of all the newly synthesized compounds 2 & 3 indicated better activity than ciprofloxacin (reference drug).



Lokapure *et al*[14] reported synthesis of 3-aryl-1-(7-chloro-6-fluoro-1 benzothiazole-2yl) pyrazole derivative and evaluated them for anti-bacterial activity against *S.aureus* ATCC 29213, *E.coli* ATCC 25922, *Pseudomonas aeruginosa* MTCC 741 and anti-fungal activity against *Aspergilus niger* ATCC 1015, *Candida albicans* ATCC 9025 by cup plate method. Ciprofloxacin and Ketoconazole were used as standard drugs. All the compounds exhibited significant to moderate antimicrobial activity.



R= C6H5, 3-OCH3-C6H4, 2-NH2-C6H4, 4-Br-C6H4, 2-C6H4 4-Cl-C6H4

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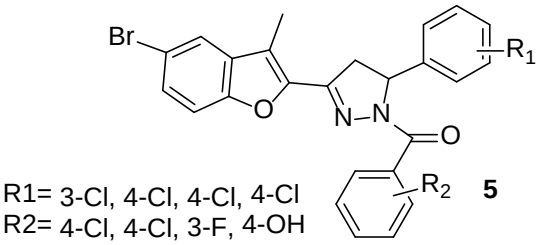
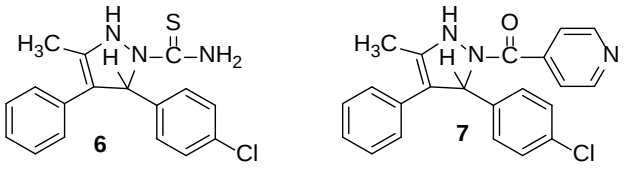
Patil *et al*[15] synthesized5-Aryl-3-(5-Bromo-3-Benzofuran-2-yl)-1-Pyrazole. Antimicrobial screening of compounds for their in-vitro anti-microbial activity against *Staphylococcus aureus*ATCC3750, *Salmonella typhi* NCTC786, *Candida albicans* ATCC10233 and *Aspergillus niger* ATCC 16404 using tube dilution method was done. The tested compounds showed significant activity.



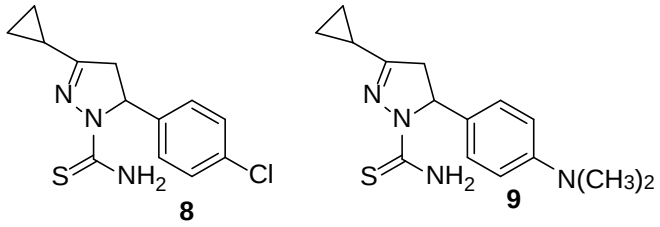
R1= 3-Cl, 4-Cl, 4-Cl, 4-Cl
R2= 4-Cl, 4-Cl, 3-F, 4-OH

Sharshira *et al*[16] synthesized some some pyrazole derivatives. The antimicrobial activity of the newly isolated heterocyclic compounds was evaluated against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*. Rifampicin was used as standard antimicrobial drugs, compounds 6 and 7 i.e. chloro derivatives exhibits good activities

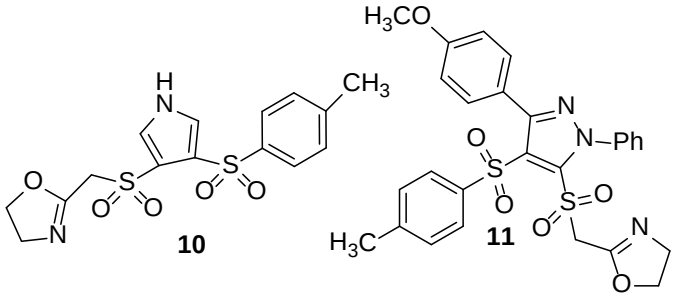


2. Antioxidant activity

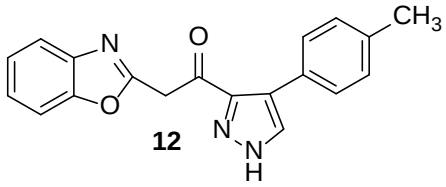
Khalil *et al*[17] synthesized a series of novel 5-aryl-3-cyclopropyl-4,5 dihydropyrazole derivatives and evaluated for their antioxidant activity using Superoxide radical scavenging. The results demonstrated that compound 8 and 9 having highest activity when compared with rutin, taken as a reference standard.



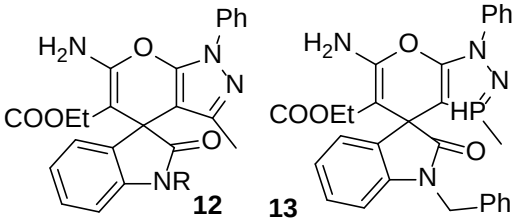
Padmaja *et al*[18] synthesized pyrazolyl derivatives and the antioxidant activity evaluation of the synthesized compounds was done using DPPH method. Compounds 10, 11 showed high antioxidant activity when compared with the reference ascorbic acid.



Durgamma *et al*[19] (2013) synthesized amido-linked pyrazoles and synthesized compounds were evaluated for their antioxidant property by 2,2,-diphenyl-1-picrylhydrazyl (DPPH), taking ascorbic acid as standard. Results showed that compound 12 displayed greater antioxidant activity when compared with the standard drug ascorbic acid.

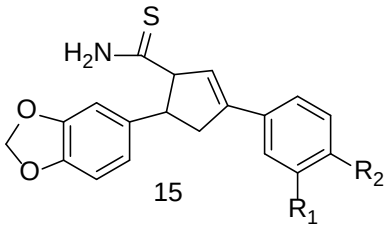


Dandia *et al*[20] (2013) synthesized spiro[indoline3,40-pyrano[2,3-c]pyrazole] derivatives and their antioxidant activities using three model systems were used namely DPPH•, ABTS• and NO scavenging activity. Compounds 13, 14 were found to be most potent antioxidant compounds.



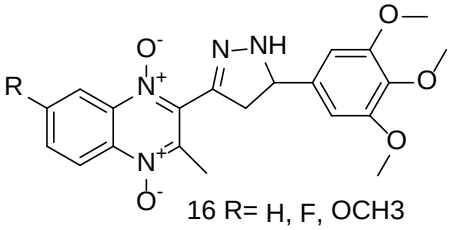
3. Anti-inflammatory Activity

Mathew *et al*[21]synthesized a series of pyrazole analogues of natural piperine. The anti inflammatory activity of the synthesized compounds was determined by Human Red BloodCell (HRBC) membrane stabilization method taking diclofenacsodium as standard drug. Compound 15 showed significant anti-inflammatory activity when compare to that of standard drug diclofenac.



Burguete *et al*[22]synthesized and evaluated the anti-inflammatory activity of substituted 3-phenyl-1-(1,4-di-N-oxidequinoxalin-2-yl)-2-propen-1-one derivatives and of their 4,5-

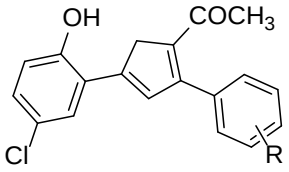
dihydro-(1H)-pyrazole analogues. The synthesized compounds were tested for their anti-inflammatory activity by their potential to inhibit carrageenin-induced rat paw edema while the reference drug used was indomethacin. It was observed that prescence of the pyrazolyl ring decreases the biological response as in compound 16.



16 R= H, F, OCH3

4. Analgesic activity

Rajasekaran *et al*[23]novel [1-(3-(5-chloro-2-hydroxy phenyl)-5-aryl-4,5-dihydro pyrazol-1-yl] ethanone derivatives have been synthesized and were screened for analgesic activity by Acetic Acid Induced Writhing Inhibition Method. Results showed that all the synthesized compounds shown significant activity when compared with that of standard drug.



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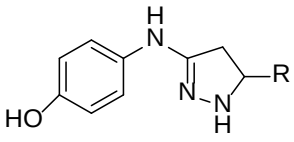

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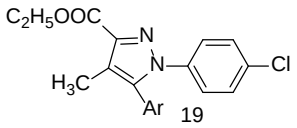
R=C_6H_5, 2-furyl, 4-$NO_2C_6H_5$, 4-OCH_3-C_6H_4, 2-OH-C_6H_5, 4-Cl-C_6H_5

Sahu *et al*[24] synthesized a series of novel4-(5-substituted aryl-4,5-dihydropyrazole-3-yl-amino) phenols. The synthesized compounds were evaluated for their analgesic activities, in some cases their activities are equally potent than the standard drugs.

Gawad *et al*[25]synthesized some of pyrazole derivatives. Analgesic activity of the target compounds as well as celecoxib were tested for their analgesic activity using the *p*-benzoquinone-induced writhing test. The results revealed that only compound 19 exhibited analgesic activity showed that substitution of pyrazole ring with aryl moiety was found to be essential for analgesic activities.



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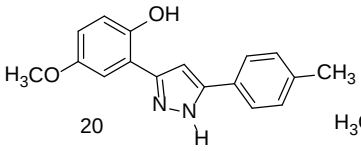

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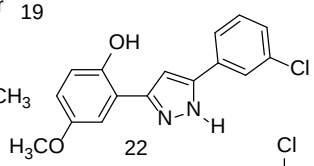

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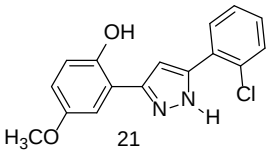

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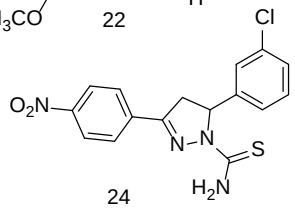

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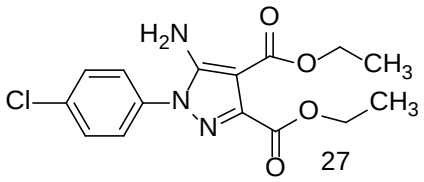
5. Anticonvulsant activity

Patel *et al*[26] reported the synthesis of novel 3, 5-diarylpyrazole derivatives and were evaluated for their anticonvulsant activity by maximal electro shock (MES) method. Out of all the newly synthesized derivatives the compounds 20, 21 & 22 was found to be the have good activity while compared with standard drug phenytoin. It was observed that prescence of -CH_3, Cl favours anticonvulsant activity.

Singh *et al*[27]synthesized pyrazole derivatives containing thiourea biological evaluated for their anticonvulsant activity using Pentylenetetrazole-Induced Convulsions model. Compound 23 revealed significant activity then rest of the compounds.

6. Cytotoxic activity

Sekkak *et al*[28]synthesized a series of novel pyrazole-3,4-dicarboxylates and tested for their cytotoxic activity against the murine P815 mastocytoma cell line. Compound 27, having chlorine atom substitution on pyrazole-3,4-carboxylate at para position of benzene group found to have promosing anticancer activity.



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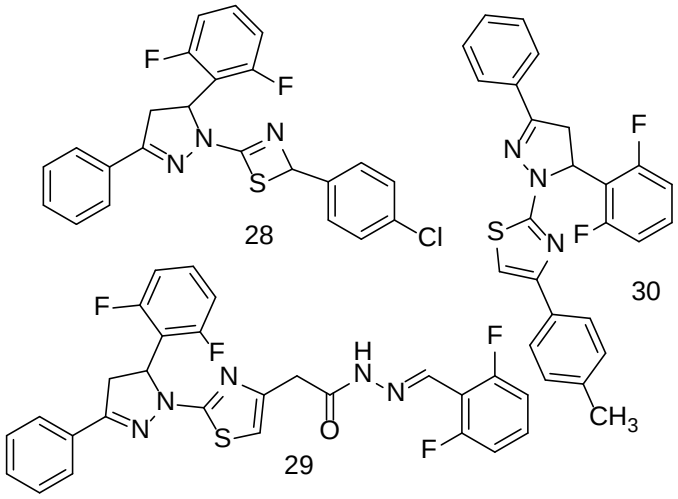
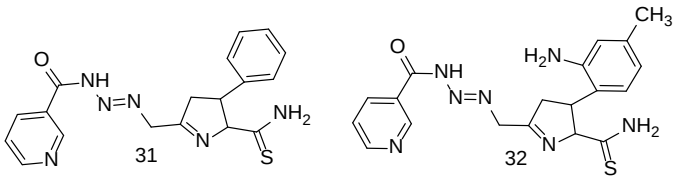
Prasad *et al*[29] (2013) synthesized a series of 4,5-dihydropyrazole derivatives and were evaluated for their in vitro anticancer activity against Hela (human cervixcarcinoma cell line), A549 (human lungadenocarcinoma cell line), MCF-7 (human breast adenocarcinoma cell line), A2780 (human ovarian cancer cell line), and BGC-823 (human gastric cancer cell line) by using MTT assay Mosmann's method. Results showed that compounds 28, 29 and 30 with most potent compounds in comparison to reference standard cisplatin.



28 30 29

7. Anti-tubercular activity

Koduru *et al*[30] (2012) synthesized pyrazoline derivatives and all the compounds tested for antitubercular activity by REMA(Resazurin microtiter assay) plate method. The compounds 31 and 32 showed decrease in inflammation comparable to that of standard Indomethacin.

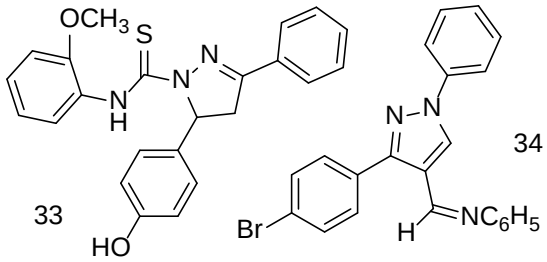


31 32

Patel *et al*[31] (2010) synthesized some pyrazole derivatives and the evaluation of their anti-tubercular activity was determined using and ethambutol as Standard strain. Compound 33 found to have good activity.

8. Acetylcholinesterase inhibitors:

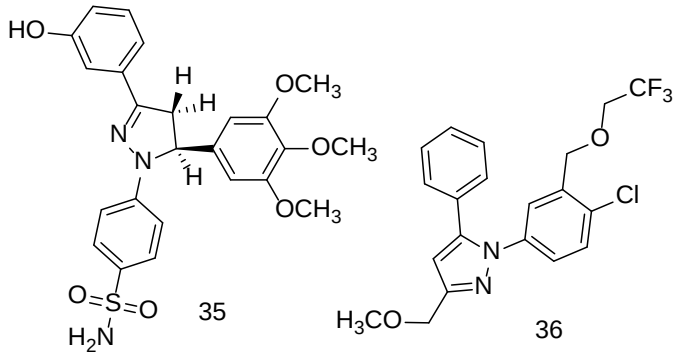
Kumar*et al*[32] synthesized a series of 3-aryl-1-phenyl-1H-pyrazole derivatives. The synthesized compounds were analyzed for their ability to inhibit acetylcholinesterase by Ellman's method. Compound 34was found to be the most potent inhibitor when compared with standard drug Donepezil.



33 34

9. Pyrazole as hypoglycemic agents

Ovais *et al*[33] synthesized a series of novel pyrazolines bearing Benzenesulfonamide moiety. The synthesized compounds were screened for their blood glucose lowering activity. Out of all tested compounds only compound 35 was found to lowering the blood glucose level when compared to the standard drug gliclazide.



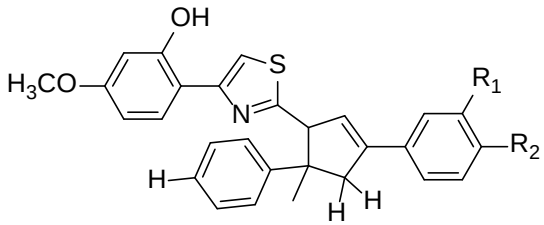
35 36

10. Herbicidal activity

Kudo *et al*[34] synthesized a series of 1, 5 diarylpyrazole derivatives. The synthesized compounds were tested for herbicidal activities against various kinds of weeds. The synthesized compound, 36 exhibited good activity.

11. Hypotensive activity

Turan *et al*[35]synthesized some 1-(4-Arylthiazol-2-yl)-3,5-diaryl-2–pyrazoline derivatives. The synthesized compounds were evaluated for their hypotensive activity by tail-cuff method using clonidine as reference standard. All examined compounds shows appreciable hypotensive activities.



37

a: $R_1=R_2=R_3=H$, b: $R_1=R_2=R_3=OCH_3$

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