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ANTIMICROBIAL ACTIVITIES OF PYRAZOLE DERIVATIVES: A REVIEW OF THE LITERATURE

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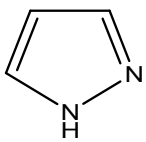
ABSTRACT

The Pyrole ring is an ubiquitous structural feature of many synthetic compounds with diversified therapeutic efficacy. A large volume of published literature over the last few decades preludes a comphrehensive review. The major activities exhibited by the pyrrole derivatives are insecticidal, antibacterial, antiviral, sedative, hypnotic, anticonvulsant and antiinflammatory activity. The article presents a comphrehensive review on the antimicrobial activities of some novel derivatives of pyrrole ring.

KEYWORDS: Pyrazole, Antimicrobial activity.

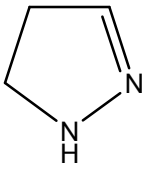
INTRODUCTION

The term Pyrazole was given by Ludwig Knorr in 1883. Pyrazole refers to the class of simple aromatic ring organic compounds of the heterocyclic series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions. Being so composed and having pharmacological effects on humans, they are classified as alkaloids, although they are rare in nature. In 1959, the first natural pyrazole, 1-pyrazolyl-alanine, was isolated from seeds of watermelons.



Pyrazole

Pyrazoline is basic in nature. An intermolecular conjugated charge transfer process has been reported to exist in it in excited state. The conjugated part (-N1-N2-C3-) of the ring, the nitrogen atom at the 3 position is, respectively electron donating and withdrawing moieties. The carbon atoms at 4- and 5- position do not conjugated with remaining part of the ring.

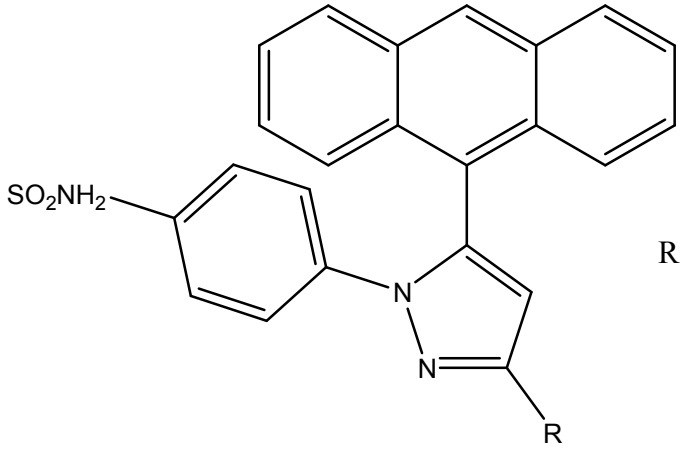


Pyrazoline/ 4,5-dihydropyrazole

Pyrazoles and their substituted derivatives are important biological agents. These are used as antitumor, antibacterial and antifungal, antiviral, antiparasitic, anti-tubercular and insecticidal agents. Some of these compounds have also shown anti-inflammatory, anti-diabetic, anesthetic and analgesic properties. This research article highlights the recent work that has been carried out on pyrazole derivatives reporting the anti-microbial properties of the pyrazole derivatives.

Pyrazoles as Anti-microbial Agents

Salem.A.Basaif *et al*[1] (1997) reported the synthesis and biological activity of new pyrazoline and pyrazolidine derivatives. The pyrazole derivatives such as 5- Anthracen-9-yl-3-aryl-1-(p-sulfamylphenyl)pyrazoles were synthesized from p-sulfanyl phenylhydrazine and chalcones. All the synthesized pyrazole analogues were evaluated for antimicrobial activity.

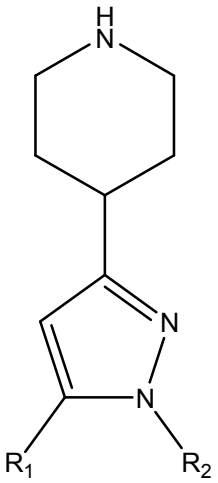


R = C_6H_5, p-$CH_3C_6H_4$, p-BrC_6H_4

5-anthracene-9-yl-3-aryl-1-(p-sulphanylphenyl)pyrazoles

Tanitame.A. *et al* [2] (2004) synthesised some novel pyrazole derivatives and screened for their antibacterial activity.They showed inhibitory activity against DNA gyrase and

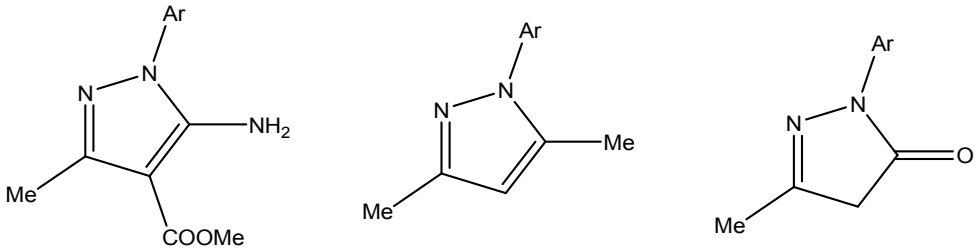
Topoisomerase IV.The derivative 5-[(E)-2-(5-chloroindol-3-yl)vinyl]pyrazole showed potent antibacterial activity and inhibitory activity against Topoisomerase IV.



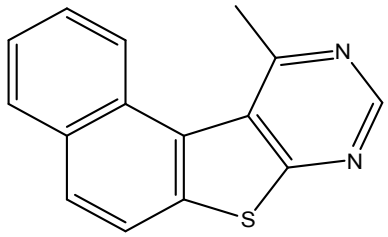
R_1 = 4-$PhCH_2OPh$, 4-MeOPh, 2-naphthyl

R_2 = H, Me, 3-ClPh, $PhCl_2$

Aymn El-sayed Rashad *et al* [3] (2005) synthesized some biologically active pyrazoles and were tested for antimicrobial activity. The new derivatives of pyrazoles i.e., 1-(5,6-dihydronaphtol[1,2':4,5]thieno[2,3-d]pyrimidin-11-yl)-pyrazole were synthesized from (5,6-dihydronaphtol[1,2':4,5]thieno[2,3-d]pyrimidin-11-yl)-hydrazine.Some of the synthesized compounds showed potent antimicrobial activity.



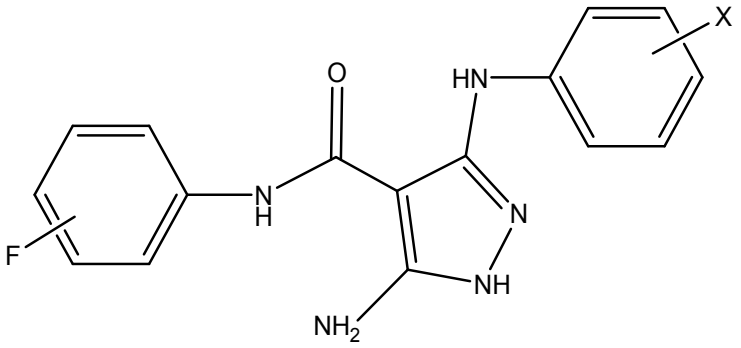
Ar =



1-(5,6-dihydrnapthol[1,2':4,5]thieno[2,3-d]pyrimidin-11yl)-pyrazole

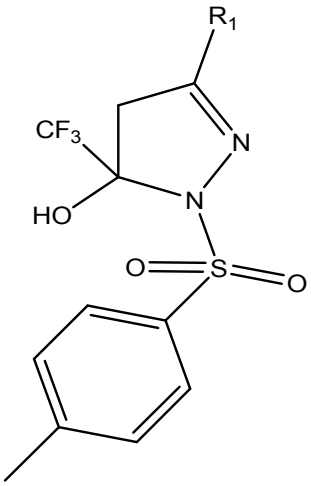
Kurz T. *et al* [4] (2006) reported synthesis of fluoro substituted derivatives of pyrazoles. The fluoro substituted cyanoacetamide derivatives with aryl isothiocyanate afforded fluorinated ketene N, S-acetals. The pyrazole derivatives were prepared from fluorinated ketene N, S-

acetals and hydrazine. The synthesized compounds were screened for their anti microbial activity.



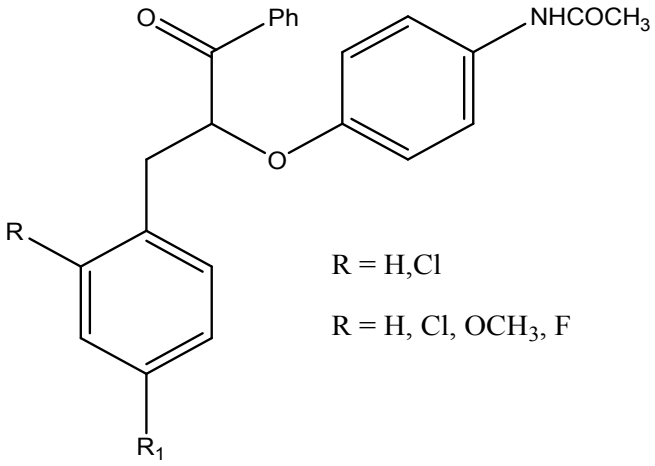
X = H, 2-F, 4-F,Cl

Bonacorso H.G. *et al* [5] (2006) reported the synthesis of some novel pyrazole derivatives containing sulfone and trifluoromethyl groups and were screened for antimicrobial activity against gram-positive, gram-negative and fungi. All the synthesized derivatives showed good activity when compared to the standard drugs.

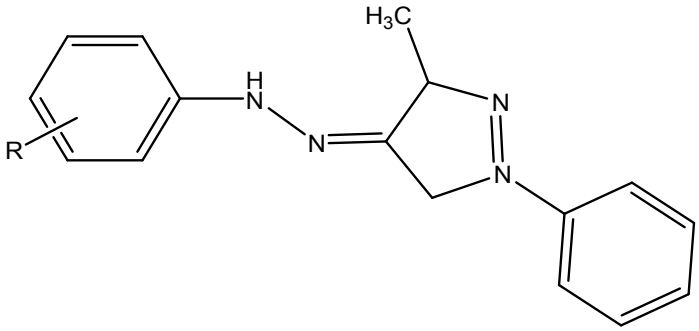


R_1 = H, 4FPh, 4-MeOPh, 4-BrPh, Ph, Me

Chandanam Sreedhar *et al* [6] (2008) reported the synthesis and antibacterial screening of 2-(p- Acetamido phenoxy) -1- aryl-3- phenyl -3-oxo –prop -1-ene(substituted) pyrazoles. The synthesized compounds were screened for antibacterial activity (by measuring zone of inhibition) against B. subtilis, P. vulgareus, E. coli, S. aureus and they showed moderate antibacterial activity.

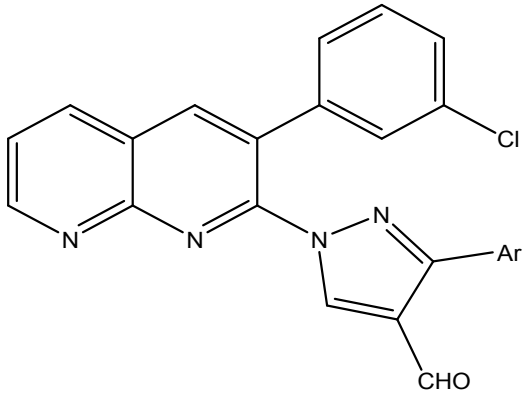


Yuvaraj S. *et al* [7] (2009) reported the synthesis, analysis and biological evaluation of pyrazole derivative. Pyrazole derivatives were prepared from benzenediazonium chloride and ethyl acetoacetate.The resulting compound was condensed with phenylhydrazine to afford pyrazole derivative. All the synthesized compounds were screened for antibacterial activity against gram-positive and gram.negative microorganisms by Cup and Plate method and they showed good activity against Staphylococcus aureus (gram-positive).



R = H, CH_3, OCH_3, F, NH_2, NO_2

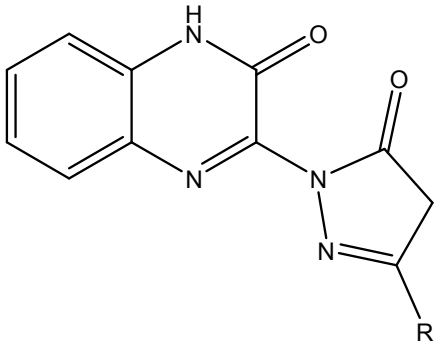
K. Mogilaiah *et al* [8] (2009) synthesized 3-aryl-4-formyl-1-(3-(3-chlorophenyl)-1,8-naphthyridin-2-yl]pyrazoles by condensing 2-hydrazino-3-(3-chlorophenyl)-1,8-naphthyridin with different acetophenones in methanol containing a catalytic amount of glacial acetic acid followed by vilsmeier-Haack reaction The compounds thus obtained were screened for their antibacterial activity.



Ar = p-$CH_3OC_6H_4$, p-$CH_3C_6H_4$, p-ClC_6H_4, pBrC_6H_4

3-aryl-4-formyl-1-[(3-(3-chlorophenyl)-1,8-napthyridin-2-yl]pyrazoles

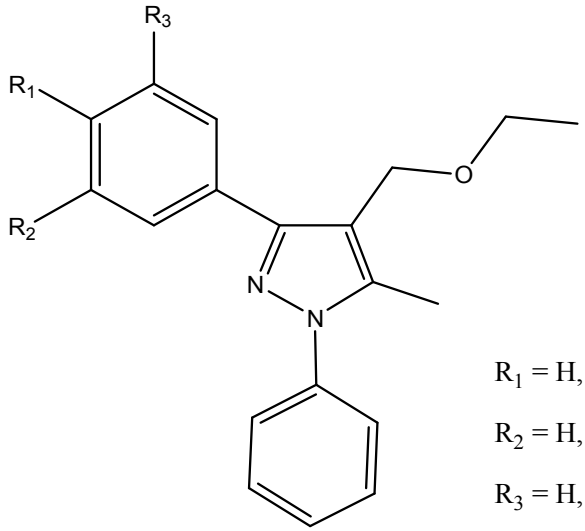
Olayinka O.Ajani *et al* [9] (2009) reported microwave assisted synthesis and antibacterial activity of some pyrazol-1-yl quinoxalin-2(1H)-one derivatives.All the compounds were screened for antibacterial activity on nine gram-positive and five gram negative bacterial strains using agar well diffusion method.



R = Me, Et, CF_3, NH_2

Substituted pyrazol-1-yl quinoxalin-2(1H)-one

K.B.Umesha and K.M.L.Rai *et al* [10] (2010) reported the synthesis and antimicrobial activity of pyrazole derivatives via 1,3-dipolar cycloaddition of nitrile imines with ethylacetoacetate.All the synthesized compounds were screened for their antibacterial and antifungal activities.

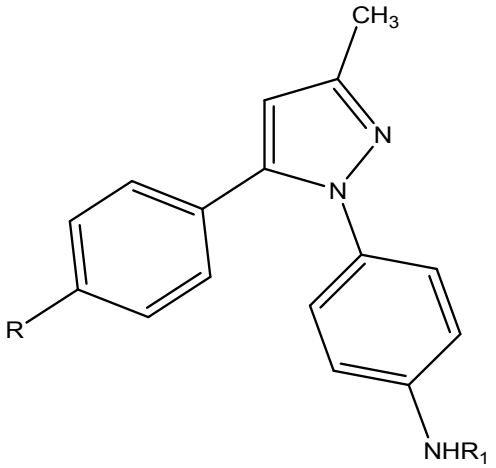


R_1 = H, OCH_3, Cl, $N(CH_3)_2$, CH_3

R_2 = H, OCH_3

R_3 = H, OCH_3, CH_3

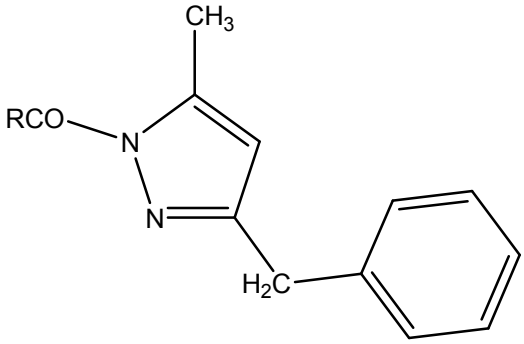
Vertika Gautam *et al* [11] (2010) reported the synthesis, characterization, and antimicrobial evaluation of some 1,3,5-trisubstituted pyrazole derivatives. All the derivatives(5-(4-substituted) -3-methyl-1-(4-nitrophenyl)-1H-pyrazole) synthesized were screened for antibacterial and antifungal activities. The newly synthesized compounds showed promising activity against gram- positive, gram-negative and fungal strains.



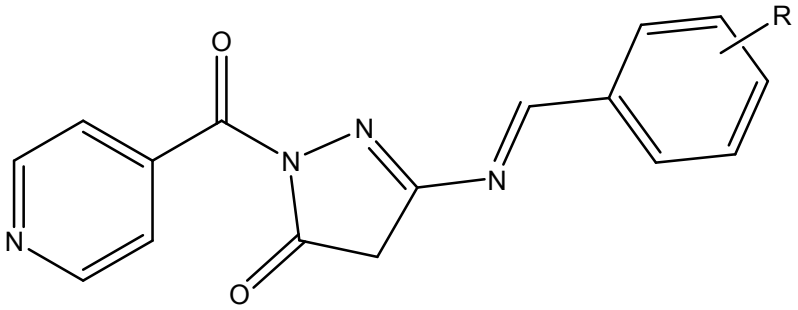
R = CH_3, C_2H_5, Cl

5-(4-substituted)-3-phenyl-1-(4-nitrophenyl)-1H-pyrazole

D.P. Gupta *et al* [12] (2010) reported the synthesis and antimicrobial activity of N-substituted pyrazole derivatives. N-substituted 3-benzyl-5-phenylpyrazole derivatives were obtained from substituted benzohydrazide. All the synthesized compounds were screened for their antimicrobial activity against different bacterial strains such as Bacillus subtilis, Bacillus aureus, E.coli. Standard drugs like ampicilin, amoxicillin were used.



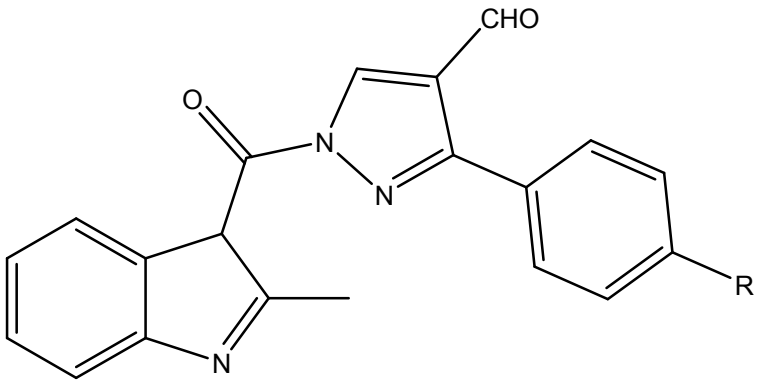
Bharat Parashar *et al* [13] (2010) reported the microwave assisted synthesis and antimicrobial activity of some novel isonicotinoyl-pyrazole derivatives. The derivatives(substituted 3-(benzylidene amino)-1- isonicotinoyl-1H-pyrazole-5(4H)-one were prepared from the condensation of isonicotinohydrazide with ethyl-2-cyanoacetate.All the newly synthesized compounds were screened for their anti microbial activity against E.coli, S.aureus, P.aeruginosa and fungi such as C.albicans and they showed promising antifungal and antibacterial activities.



R = OCH_3, OH, CH_3, F

Substituted-3-(benzylamino)-1-isnicotinoyl-1H-pyrazole-5(4H)-one

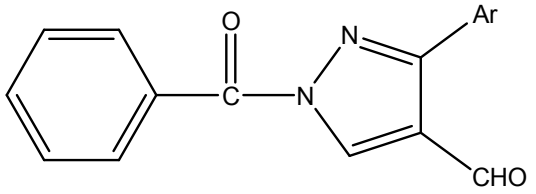
P. Bharath Rathna Kumar *et al* [14] (2011) synthesized some novel 1H-pyrazole derivatives from ethyl-2-indole-3-carboxylate and hydrazine hydrate. The hydrazides formed were treated with different acetophenones in methanol followed by Vilsmeier-Haack reaction furnishes pyrazole derivatives(1-[(2-methyl-1H-indol-3-yl)carbonyl]-3-substituted phenyl-1-Hpyrazole-4-carbaldehyde derivatives) and these synthesized compounds were screened for antibacterial studies.

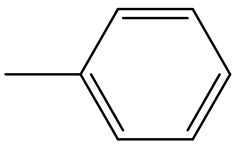
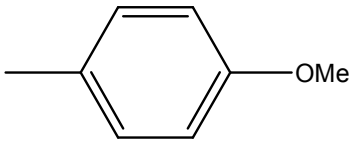
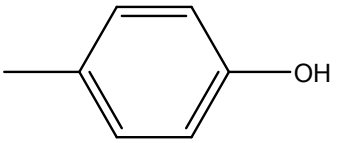


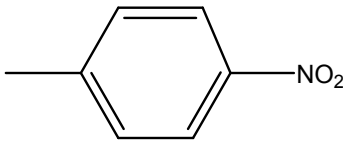
R = H, Br, NO_2, NH_2, OH

1-[(2-methyl-1H-indol-3-yl)carbonyl]-3-substituted phenyl-1H-pyrazole-4-carbaldehyde

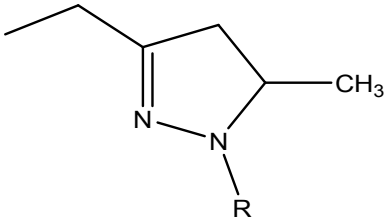
A.P.Rajput and S.S.Rajput *et al* [15] (2011) synthesized formyl pyrazoles using Vilsmeier-Haack reaction.The pyrazole derivatives were prepared by the formylation of a series of acetophenone substituted phenyl carbonyl hydrazones. All the newly synthesized derivatives were screened for their antibacterial activities.



Ar =  ,  ,  ,.

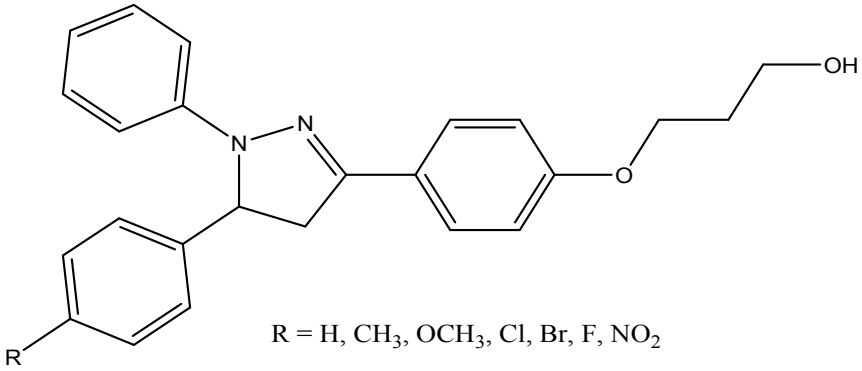


Vishnuvardan Rao *et al* [16] (2011) reported the design, synthesis and biological activity of a new series of 1-(5-methyl-4H-pyrazol-3-yl) methanamine and they were synthesized by reacting phthalimide with chloroacetylchloride.The synthesized compounds were screened for antibacterial activity.The derivatives showed promising anti-bacterial activity when compared with the standard drugs.



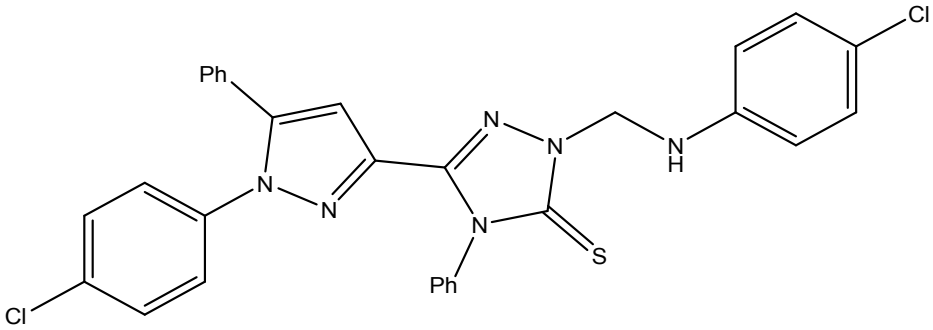
1-(5-methyl-4H-pyrazol-3-yl)methanamine

Sandeep Jain *et al* [17] (2012) synthesized 1-phenyl-3-(4-(3-propanoloxy)phenyl)-5-aryl-1H-pyrazoles from chalcones i.e.,3-aryl-1-(4-hydroxyphenyl) prop-2-en-1-ones and the synthesized compounds were screened for their antibacterial activity against two gram positive and gram negative strains and determined their minimum inhibitory concentration.



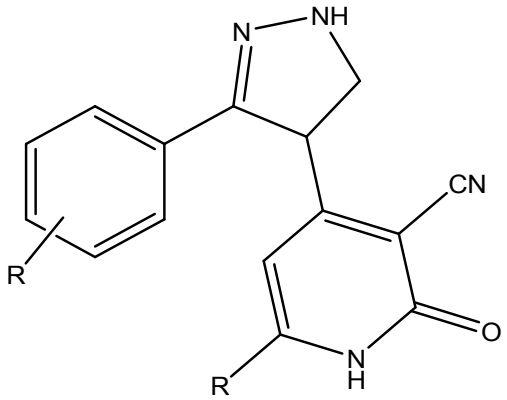
R = H, CH_3, OCH_3, Cl, Br, F, NO_2

Eman M. Flefel *et al* [18] (2012) synthesized some triazolopyrazole derivatives i.e, 2-{(4-chlorophenylamino)methyl}-5-{1-(4-chlorophenyl)-5-phenyl-1H-pyrazole-3-yl}-4-phenyl-2H-[1,2,4]triazole-3(4)H-thione, 2-{(4-chloro phenyl amino) methyl}- 5-{1-(4- chloro phenyl)-5-phenyl-1H-pyrazole-3-yl}-4-phenyl-2-{(piperidin-1-yl)methyl}-2H-[1,2,4]triazole-3(4)H-thione etc. All the synthesized compounds were tested for their antibacterial and antifungal activities and they showed high activity compared with the standard drugs like ciprofloxacin and fusidic acid.



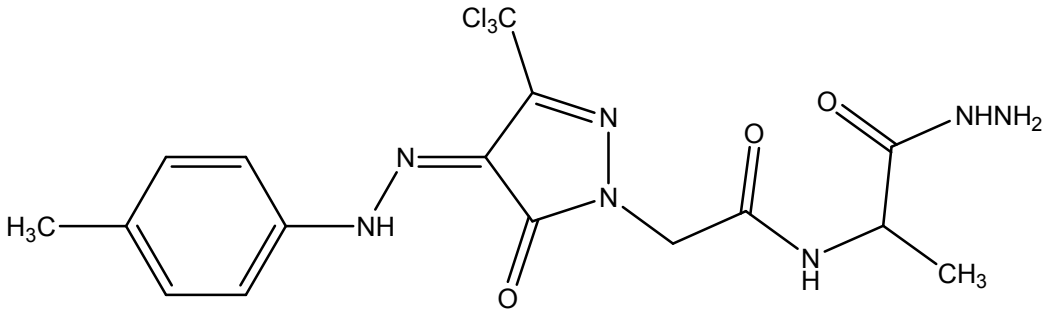
2-{(4-chlorophenyl amino)methyl}-5-{1-(4-chlorophenyl)-5-phenyl-1H-pyrazole-3-yl}-4-phenyl-2-{(piperidin-1-yl)methyl}-2H-[1,2,4]-triazole-3-(4H)-thione

Arun M. Isloor *et al* [19] (2012) synthesized pyrazole containing cyanopyridone derivatives i.e,4, 6-disubstituted-3-cyano-2-pyridone and these compounds were screened for antibacterial and antifungal activity and they showed significant activity when compared with standard drug streptomycin. They showed good antibacterial activity against the bacterial strain (E.coli ,Staphylococcus aureus and Pseudomonas aeruginosa) and antifungal activity against Aspergillus flavus.

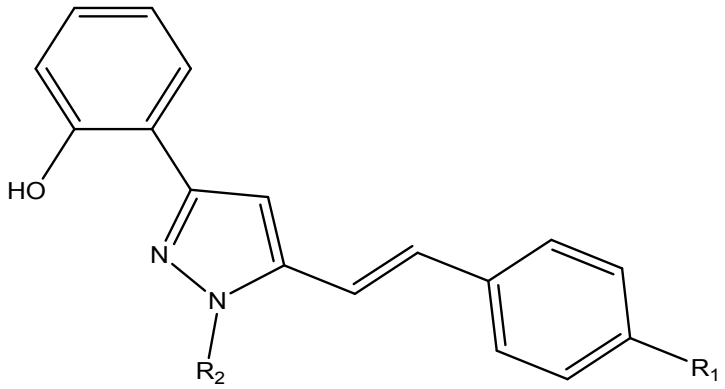


R = thienyl, 1-naphthyl, 5-Chlorothienyl,
R_1 = H, 4-F; 4-Cl; 2,4-Cl_2, 4-CH_3

L.K. Ravindranath *et al* [20] (2012) synthesized a series of substituted phenyl hydrazono pyrazolyl derivatives. All the synthesized compounds were screened for their antibacterial, antifungal activities and showed significant activity against gram positive, gram negative bacteria and fungus strain.



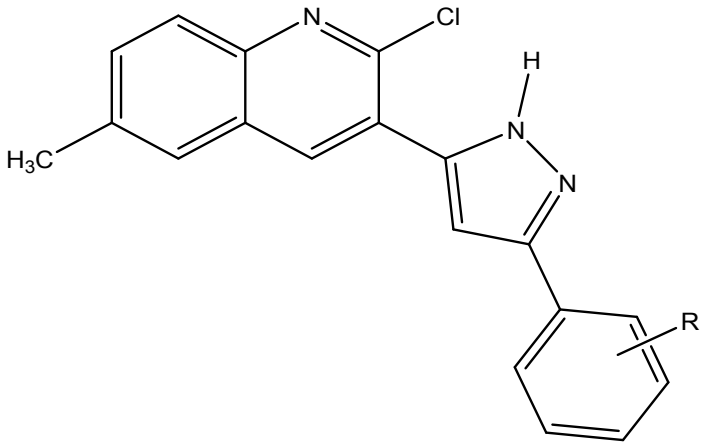
Madhava Rao *et al* [21] (2012) synthesized some novel pyrazole derivatives i.e. 3-(2-hydroxy phenyl) -5- (4- chloro styryl) -1-phenyl pyrazole; 3-(2- hydroxy phenyl) -5-(4-methoxystyryl)-1-phenylpyrazole etc and were screened for antimicrobial activity by agar cup method and filter paper disc method. Chloro substituted pyrazole was found to be more efficient against Xanthomonas campestris and Aspergillus niger.



R_1 = H, Cl, OCH_3; R_2 = Ph, H

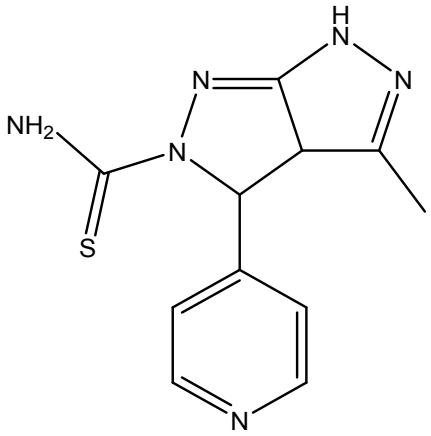
3-(2-hydroxyphenyl)-5-(4-chlorostyryl)-1-phenylpyrazole

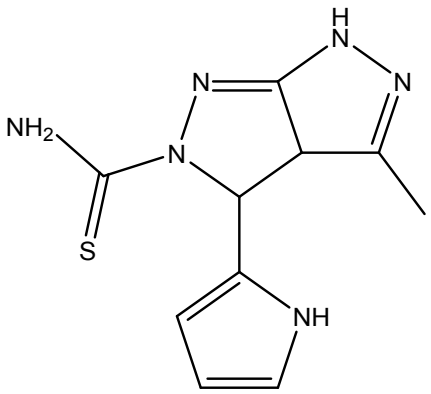
B.D. Mistry *et al* [22] (2012) reported the conventional and microwave assisted synthesis of pyrazole derivatives. The compounds were evaluated for their antibacterial and antifungal activities against a varieties of bacterial and fungal strains.



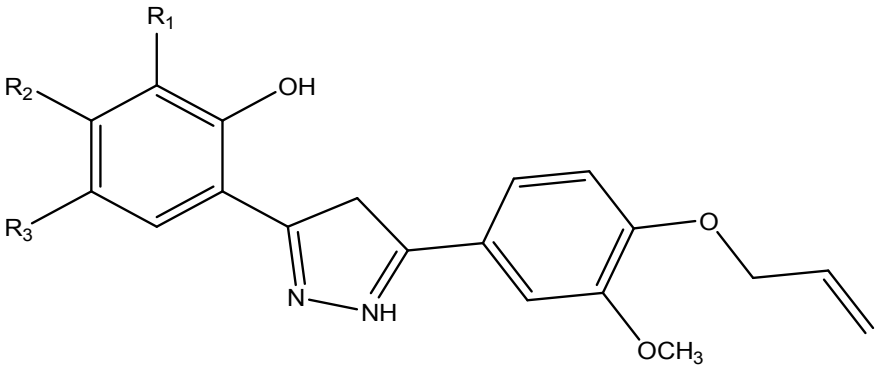
R = H, 4-Br, 4-Cl, 4-CH_3, 4-OH, 4-NO_2

R. Mallikarjuna Rao *et al* [23] (2012) reported the synthesis and biological screening of some pyridine and pyrrole derivatives of pyrazolo [3, 4-c] pyrazoles. These derivatives were prepared by the reaction of chalcones of pyrazolone with hydrazinehydrate, thiosemicarbazide, and phenyl hydrazine in presence of NaOH/EtOH or AcONa/AcOH. The synthesized compounds were evaluated for their antibacterial activity against gram-positive and gram-negative bacteria and antifungal activity against Aspergillus niger and Candida albicans.





Asha V.Chate *et al* [24] (2012) reported the synthesis and antimicrobial screening of novel2-(5- (4-(allyloxy)-3- methoxy phenyl) -1H- pyrazol -3-yl) phenol analogues. These derivatives were prepared from 2-(4-(allyloxy)-3-methoxyphenyl)-4H-chromen-4-ones and hydrazine hydrate. All the synthesized compounds were screened for antibacterial and antifungal activities and they showed significant activity when compared to the standard drugs.



R_1 = H,Cl, CH_3
R_2 = H, CH_3
R_3 = H, Cl, F, CH_3

2-(5-(4-(allyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)phenyl analogues

CONCLUSION

The plethora of research subscribed in this review indicates that the pyrazole analogues possess anti-microbial activity. The biological profiles of these new generations of pyrazoles would represent a fruitful matrix for further development of better medicinal agents.

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