

Review Article

A REVIEW ON PYRAZOLINE DERIVATIVES AS ANTIMICROBIAL AGENT

SARAS KUMAR JAIN*, ROHIT SINGHAL

LBS College of Pharmacy, Jabalpur (M. P.), Department of Pharmacy, Oriental University, Indore (M. P.)
Email: saras.jain1@gmail.com

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ABSTRACT

At present, there is a lot of research about the pyrazoline heterocyclic compound, its ring structure is being changed and new derivatives are being made, many of which have antimicrobial activity over the derivatives. Pyrazoline is the five-member heterocyclic ring which have two N atoms in nearby position and contains two endocyclic double bonds. Noteworthy consideration has been concentrated on pyrazolines and pyrazoline derivative due to their important pharmacological action. Some replaced pyrazolines have been stated near retain particular important pharmacological actions as antimicrobial, antifungal, antineoplastic, antidepressant, insecticidal, anticonvulsant, anti-inflammatory, antibacterial and antitumor properties.

Keywords: Antimicrobial Activity, Pyrazoline, Heterocyclic Compound

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INTRODUCTION

Microbial Infections (fungal and bacterial) have been informed to rise affected globally in present days and main causes are toward the block resistance. Both hospitalized and ambulatory patients are very needful of antimicrobials widespread. It is described that 24% to 40.8% of hospitalized persons accept them [1]. Destruction of resistance owing to several causes such as distortion, operations, immunosuppressive treatments, old age, HIV infection, is a reasonable sources that seats patients at great risk for transmittable contagious contaminations. This condition is exacerbated through growing rate of microbial conflict to the general antibiotics existing nowadays [2]. Antimicrobial alteration is a main anxiety, the threat to the community health in addition permits improvement and development of new and active antibiotics to challenge drug quarrel. To reveal these matters, there is a essential to develop new insignificant, harmless and effective drugs with a wide range of antimicrobial action [3]. There are several heterocyclic ring compounds having nitrogen atom such as pyrazole, pyrrolones, pyridazinones, pyrazolines have been considered generally used for the improvement of essential antimicrobial action. The powerful new drugs must be displayed to save lives when used to give some severe infections and to reduce the trouble of illness when used prophylactically in certain clinical situation. For the synthesis of new antibiotics, researcher effort lots on chemical compounds and pyrazoline derivatives are valuable as antimicrobial agents. Pyrazolines are enormously valuable nitrogen-containing heterocyclic compounds that occur in a diversity of chemical and biological agents and improve their activities. N–N bond of the pyrazoline ring is restrained to be the important cause in their biological activities [4]. Pyrazoline can be defined as dihydro pyrazole having only one endocyclic double bond. On the basis of the position of the double bond three types of pyrazoline are possible: (i) 1-pyrazoline (ii) 2-pyrazoline and (iii) 1, 3-pyrazoline, 2-pyrazoline is most attractive and important among all type of pyrazolines for frequent studies.

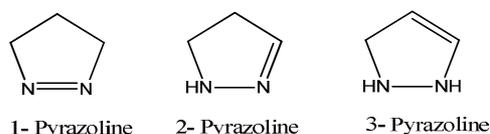


Fig. 1: Types of pyrazoline

Actually, pyrazolines are the reduced forms of pyrazoles, while pyrazolidine is a completely reduced form of pyrazole.

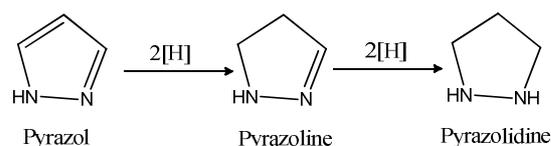


Fig. 2: Hydrogenation of pyrazole to pyrazoline then pyrazolidine

Pyrazoline derivatives have been found in natural products in the form of vitamins, alkaloids, and pigments.

Pyrazoline end products were stated to retain a number of evident pharmacological activities, antimoebic, antimicrobial, antibacterial, antidepressant, antitubercular, antifungal, antiviral, anticancer, anticonvulsant. Some of the modern drugs of the pyrazoline nucleus include Phenazone, Metamizole, Aminopyrine, Phenylbutazone, Sulfinpyrazone, Oxyphenbutazone and Celecoxib. The literature search was steered using accessible databases, including ScienceDirect, PubMed, Scopus and Google Scholar. The dissertations, thesis, books and technical reports were also combed. The objective of this review is to provide all the literature of approximately fifteen years.

Antimicrobial activity of pyrazoline derivatives

Chimenti *et al.* (2005) prepared N-substituted 3, 5-diphenyl pyrazoline derivatives and then screened for antibacterial activity. All pyrazoline derivatives displayed minute activity or no activity against different bacteria and fungus. The similar derivatives displayed a substantial activity against *H. pylori* strains. Between the synthesized derivatives, which containing the N-acetyl group and methoxy group at position 4 on the phenyl ring exhibited the greatest potential against metronidazole resistant *H. pylori* strains at the 1–4 µg/ml [5].

Shivarama *et al.* (2005) reflux aryl furfurals with different acetophenones then condensate Aryl furyl propenones. Cyclo-condensation provided 1H-pyrazoline derivatives and N-phenylpyrazoline derivatives, respectively, when arylfuryl propenones react with hydrazine hydrate and phenylhydrazine. We

found deliberated antibacterial activity of the new pyrazoline derivatives [6].

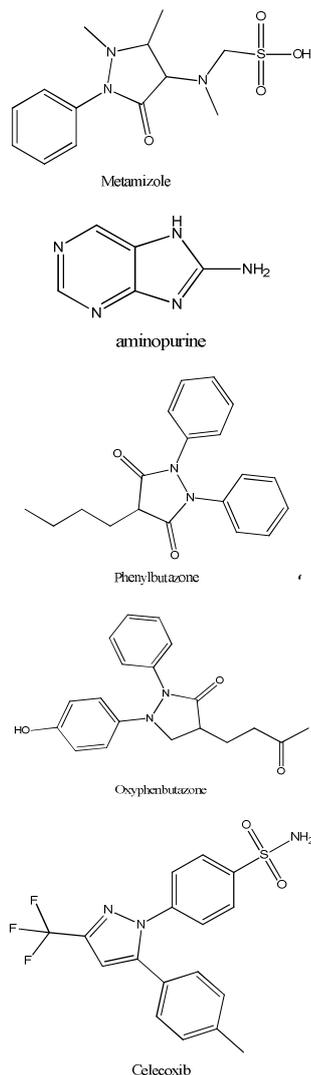


Fig. 3: Some of the modern drugs having pyrazoline nucleus

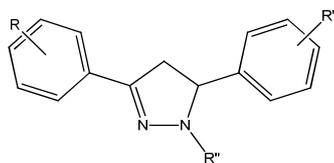


Fig. 4: N-substituted 3,5-diphenyl pyrazoline derivatives

Ozdemir *et al.* (2007) synthesized 1-(4-aryl-2-thiazolyl)-3-(2-thienyl)-5-aryl-2-pyrazoline derivatives from phenacyl bromides in ethanol. All manufactured derivatives evaluated against *E. coli*, *S. typhimurium*, *S. aureus*, *S. faecalis*, *B. cereus*, *A. hydrophila*, *C. albicans*, *C. glabrata* for antimicrobial activity [7].

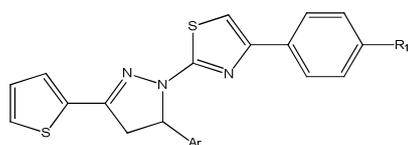


Fig. 5: Substituted 1-(4-aryl-2-thiazolyl)-3-(2-thienyl)-5-aryl-2-pyrazoline

Kaplanciki *et al.* (2007) synthesized the substituted pyrazoline derivatives. For this, when phenacyl bromides react with different 3-(2-thienyl)-5-aryl-1-thiocarbamoyl-2-pyrazolines in ethanol results 1-(4-aryl-2-thiazolyl)-3-(2-thienyl)-5-aryl-2-pyrazoline derivatives. The antimicrobial activity of synthesized compound was evaluated in contrast to *S. typhimurium*, *E. coli*, *B. cereus*, *A. hydrophila*, *L. monocytogenes*, *S. aureus*, *C. albicans*, and *C. glabrata* [8].

Kaplanciki *et al.* (2007) reported the newly prepared 1-(4-aryl-2-thiazolyl)-3-(2-thienyl)-5-aryl-2-pyrazoline derivatives by substituted 3-(2-thienyl)-5-aryl-1-thiocarbamoyl-2-pyrazolines. The antimicrobial activity of synthesized pyrazoline derivatives was screened against bacterial strains *E. coli*, *S. aureus*, *S. typhimurium*, *B. cereus*, *L. monocytogenes*, *A. hydrophila*, *C. albicans*, and *C. glabrata* [9].

Shaharyar *et al.* (2007) synthesized the pyrazoline derivatives by 4-hydroxy-3-methylacetophenone condensed with different aromatic aldehydes in methanolic KOH results chalcones. These chalcones react with the hydrazine hydrate in ethanol to results pyrazoline derivatives. All synthesized derivatives were evaluated against *Mycobacterium tuberculosis* H₃₇Rv for their anti-tubercular activity. The novel heterocyclic compound displayed favorable anti-tubercular activity against *Mycobacterium tuberculosis* drug-sensitive and drug-resistant strains of *Mycobacterium tuberculosis* [10].

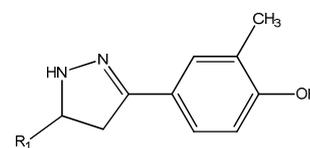


Fig. 6: 4-hydroxy phenyl pyrazoline derivatives

Munawar *et al.* (2008) explained the quinolinyl chalcones react with phenyl hydrazine to obtain a series of 2-pyrazoline derivatives under both conventional and microwave-induced method. All synthesized compounds were evaluated for antimicrobial activity against bacteria *S. aureus*, *S. typhi*, *E. coli*, and *Shigella* dysentery. All synthesized derivatives have displayed antimicrobial activity. The compounds which containing a chloro group as a substituent has been more potent antimicrobial activity [11].

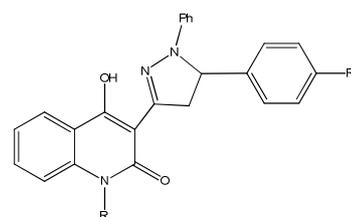


Fig. 7: Quinolinyl 2-pyrazoline derivatives

Kiniet *et al.* (2008) reacting isoniazid with substituted diaryl chalcones in N, N-DMF to synthesize the 1,3,5-trisubstituted-2-pyrazoline derivatives. All the synthesized derivatives screened for *in vitro* antimicrobial activity against *E. coli*, *P. aeruginosa*, *B. subtilis*, *S. aureus* and *A. niger* at different concentrations, compounds show significant antimicrobial activity [12].

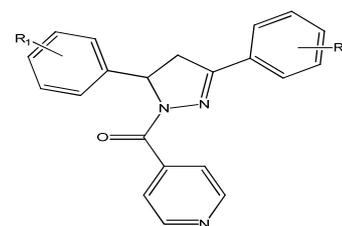


Fig. 8: 1,3,5-trisubstituted-2-pyrazoline

Kini *et al.* (2008) reported when the isoniazid reflux with different substituted diaryl chalcones in N,N-dimethyl formamide at 120-140 ° results 1,3,5-trisubstituted-2-pyrazolines. For antimicrobial activity, the synthesized compounds were screened against *B. subtilis*, *S. aureus*, *P. aeruginosa*, *A. niger* and *E. coli*. Also the quinoliny chalcones react with phenyl hydrazine to obtain series of 2-pyrazolines under both conventional and microwave-induced warming method. All synthesized compounds were evaluated for antimicrobial activity against *S. aureus*, *S. typhi*, *E. coli*, and *Shigella* dysentery. All synthesized derivatives have displayed antimicrobial activity. The compounds containing chloro group as a substituent have been more potent antimicrobial activity [13].

Ramesh *et al.* (2009) prepared the chalcones of 2-acetyl thiophene reflux with phenylhydrazine hydrochloride in alkaline alcohol outcomes new pyrazoline derivatives. Some of these derivatives exhibited moderate to considerable antimicrobial activity. The results are showing that the compounds 1 and 2 showed significant antibacterial activity at conc. of 0.05-0.1 ml concentration levels as compared through standard drug sparfloxacin. The other compounds 3, 4 and 5 displayed adequate activity [14].

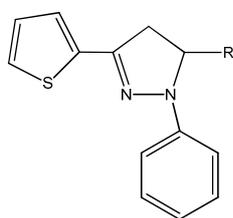


Fig. 9: Thiophene pyrazoline derivatives

Manna *et al.* (2009) reported a series of 2-[1-(5,8-Dihydroquinoxalino[2,3-*b*]indoloacetyl)-3-(1-benzofuran-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl] phenyl derivatives which is synthesized by reacting the 2-(5,8-dihydro quinoxalino[2,3-*b*]indol-5-yl) aceto-hydrazide with (2*E*)-1-(1-benzofuran-2-yl)-4-phenylbut-2-en-1-ones derivatives by microwave-assisted method. Some compounds were show decent antibacterial activity against *S. aureus*, *P. aeruginosa* and *E. coli*, compared with standard drugs sparfloxacin and norfloxacin at the conc. of 10 µg/ml [15].

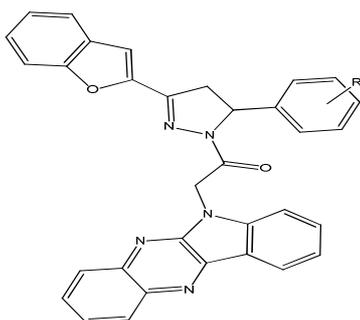


Fig. 8: 2-[1-(5, 8-Dihydroquinoxalino [2, 3-*b*] indoloacetyl)-3-(1-benzofuran-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl] phenyl derivatives

Chawla *et al.* (2010) synthesized substituted [3-(4-phenyl)-5-phenyl-4, 5-dihydropyrazol-1-yl](pyridine-4-yl)methanone and 3-substituted phenyl-5-substituted phenyl-4,5-dihydro-pyrazole-1-carbothioamides by microwave techniques. All the derivatives were evaluated for antibacterial activity against *B. subtilis*, *E. coli*, *P. aeruginosa* and *S. aureus* and antifungal activity beside *C. albicans*, *A. niger*. The derivatives showed adequate antibacterial and respectable antifungal actions [16].

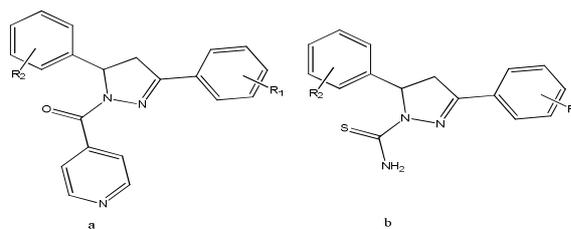


Fig. 11: (a) substituted [3-(4-phenyl)-5-phenyl-4,5-dihydropyrazol-1-yl](pyridine-4-yl)methanones, (b) 3-substituted phenyl-5-substituted phenyl-4,5-dihydro-pyrazole-1-carbothioamides

Sivakumar *et al.* (2010) manufactured novel 1, 3, 5-triphenyl-2-pyrazoline derivatives and two-fold dilution method using resazurin (indicator dye) is used for screening of antibacterial activity against *S. aureus*, *S. typhi*, *B. subtilis*, *E. aerogenes*, *P. aeruginosa* and *Proteus vulgaris* by SAR study concluded that 1,3,5-triphenyl-2-pyrazoline derivatives. Chlorine replacement in the ring A, is the positive discrimination for antibacterial activity. Hydrophilic/lipophilic balance of the derivatives are important parameters [17].

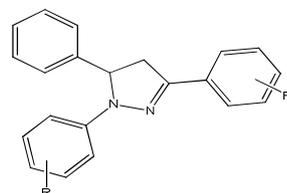


Fig. 12: Novel 1, 3, 5-triphenyl-2-pyrazoline derivatives

Venkataraman *et al.* (2010) synthesized some new pyrazoline derivatives from Chalcones. Which may be synthesized by different acetophenones react with different benzaldehydes to give chalcone, which on condensed with hydrazine hydrate in ethanol to acquire pyrazoline derivatives. All derivatives were tested for *in vitro* antibacterial and anti-inflammatory activities. All synthesized derivatives were confirmed activity against *S. aureus*, *B. subtilis*, *E. coli*, *P. aureginosa*. Some of the new derivatives exhibited promising anti-inflammatory activities [18].

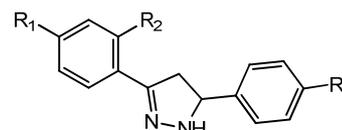


Fig. 13: 3, 5 diphenyl pyrazoline

Sakthinathan *et al.* (2012), reported that when 2-naphthyl chalcones in the presence of phenylhydrazine hydrochloride and sodium acetate by the cyclization reaction results 2-naphthyl pyrazoline derivatives. 2-naphthyl pyrazoline derivatives subjected for antimicrobial activity [19].

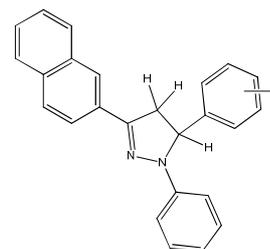


Fig. 14: 2-naphthyl pyrazoline derivatives

Shah *et al.* (2012) synthesized 4-(4-hydroxyphenyl)-3-chloro-1-{4-[5-(substituted phenyl)-1-phenyl-4,5-dihydro-pyrazol-3-yl]phenyl} azetidin-2-one by 3-chloro-1-{4-[3-(substituted-phenyl)prop-2-enoyl]phenyl}-4-(4-hydroxyphenyl) azetidin-2-one (0.01M) and phenylhydrazine (0.01 M) in presence of glacial acetic acid. All the synthesized derivatives were screened for antimicrobial activity through broth dilution method. The compound containing chloro substitution in the phenyl ring has shown respectable antibacterial activity [20].

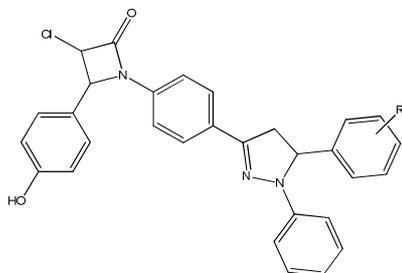


Fig. 15: 4-(4-hydroxyphenyl)-3-chloro-1-{4-[5-(substituted phenyl)-1-phenyl-4,5-dihydro-pyrazol-3-yl]phenyl} azetidin-2-one

Rani *et al.* (2012) prepared alkoxy a series of N-substituted cyclized pyrazoline equivalents [5-(furan-2-yl)-3-[2-(alkoxy phenyl)-4, 5-dihydro-1H-pyrazole-1-carbothioamide] by cyclization of [1-[2-(alkoxy phenyl)-5-(furan-2-yl)-prop-2-en-1-one] chalcone with thiosemicarbazide in the presence of alkaline ethanol. By the disc diffusion method, *in vitro* antibacterial activity of newly prepared derivatives were screened and the minimum inhibitory concentration (MIC) was calculated against microorganism such as *A. hydrophila*, *Y. enterocolitica*, *L. monocytogenes*, and *S. aureus*. Between all the compounds, alkoxy [5-(furan-2-yl)-2-(benzyloxy)phenyl]-4,5-dihydro-1H-pyrazole-1-carbothioamide and 5-(furan-2-yl)-1-[2-(naphthalen-2-ylmethoxy) phenyl]-4,5-dihydro-1H-pyrazole-1-carbothioamide exhibited the greatest favorable antibacterial activity as compared to standard gentamycin and tetracycline [21].

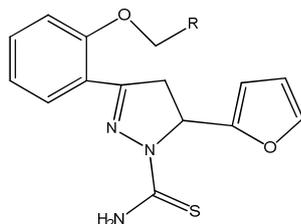


Fig. 16: N-substituted cyclized pyrazoline

Dipankar *et al.* (2012) synthesized twelve 2-pyrazoline derivatives and evaluated the antimicrobial activity against *A. niger* and *S. aureus*. For this, 2 types of acetophenone reacted with 3 types of substituted benzimidazole derivatives to acquire 6 chalcone derivatives, which undergo condensation and cyclisation with isoniazid and 1-(2-naphthoxy acetate) hydrazine to acquire the 2-pyrazoline derivatives. The synthesized derivatives were established to have good antimicrobial activity at the conc. of 20-70 µg/ml [22].

S Y Hassan (2013) has reported a series of new 2-pyrazoline derivative carrying benzene sulfonamide moieties were produced by reaction of suitable chalcones with 4-hydrazinyl benzene sulfonamide HCl. Besides the reaction of chalcones with the hydrazine derivative produces pyrazole compounds. All the synthesized compounds have been categorized by physical and spectral fig. Antimicrobial activity of synthesized compounds were tested against *S. aureus*, *P. aeruginosa*, *E. coli* and antifungal activity in contrast to *C. albicans* must be considered by the nutrient agar and saboraud dextrose agar diffusion procedures [23].

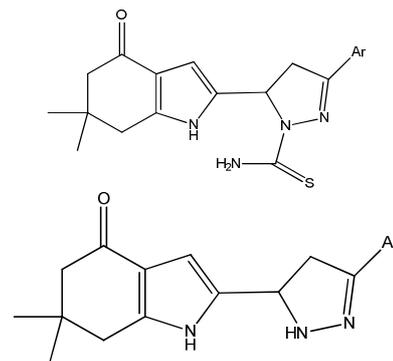


Fig. 17: Pyrazoline derivative carrying benzene sulfonamide

Nosrat *et al.* (2013) prepared novel 2-(3, 5-diphenyl-4, 5-dihydro-1H-pyrazol-1-yl)-4-phenylthiazoles via cyclo-condensation of several chalcones, phenacyl bromide and thiosemicarbazide. The reaction was efficiently conducted under reflux through a few drops of HCl in Ethanol. The antibacterial action of compounds was observed, Certain compounds display satisfactory actions [24].

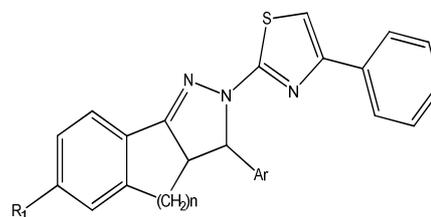


Fig. 18: Substituted 2-(3, 5-diphenyl-4, 5-dihydro-1H-pyrazol-1-yl)-4-phenylthiazoles

Rani *et al.* (2014) synthesized the sequence of new pyrazoline derivative as well as antimicrobial activity of certain pyrazoline derivatives and the structures were identified by spectral fig. Certain derivatives exhibited analogous results after tested against *Y. enterocolitica*, *A. hydrophila*, *S. aureus* and *L. monocytogene*. Some derivatives display additional action as compared to the standard drugs tetracycline (30 µg) and gentamicin (10 µg) [25].

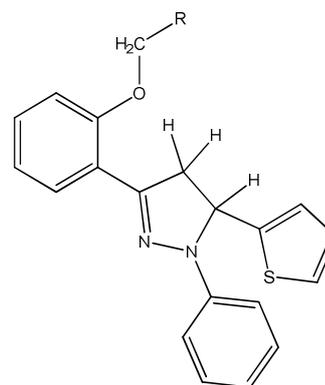


Fig. 19: Tricyclic pyrazoline derivative

Vidya *et al.* (2014) have reported a modest, well-organized method for the synthesis of novel 2-pyrazolines. In this, the chalcones condense with hydrazine hydrate/isoniazid/tolylsulfonfyl hydrazide results pyrazoline derivatives. The synthesized derivatives have been tested for antimicrobial activity in several types of microorganisms. An important level of activity was noticed [26].

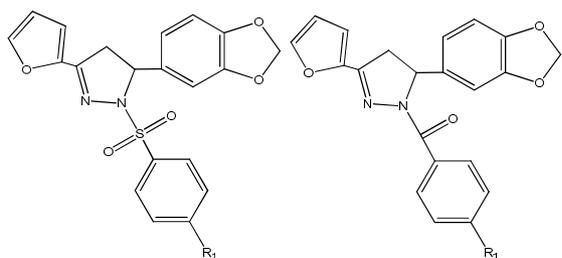


Fig. 20: Novel 2-pyrazolines

Desai *et al.* (2014) synthesized quinazoliny-2-pyrazoline derivatives series and screened for the *in vitro* antibacterial potency against gram-positive strains (*S. Aureus*, *B. Subtilis*) and gram negative strains (*E. coli*, *P. aeruginosa*) comparing with the standard drugs ampicillin, amoxycillin and penicillin and antifungal activity against *C. Albicans* and *C. Krusei*. as compared with fluconazole by disc diffusion method [27].

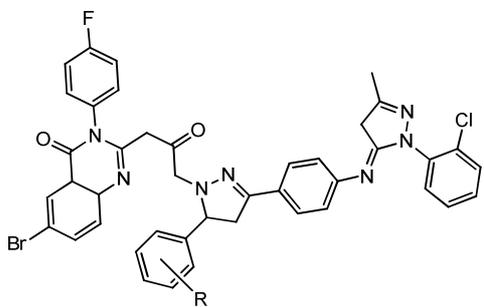


Fig. 21: Quinazoliny 2-pyrazolines

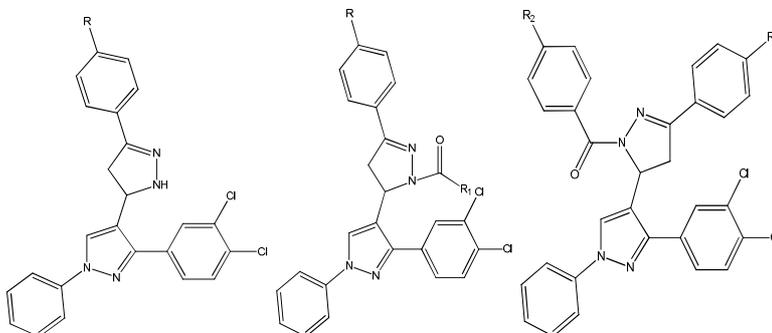


Fig. 23: Newly synthesis of pyrazolines

Alam *et al.* (2015) synthesized a series of pyrazoline derivatives and structural identification done by ^1H NMR, ^{13}C NMR, IR and Mass spectrum. All newly synthesized derivatives were evaluated against two bacterial and four fungal strain (*C. Albicans*, *A. Flavus*, *A. Fumigatus*, *A. versicolor*) at the conc. of $12.5\mu\text{g/ml}$ compared with standard drug fluconazole. All compounds display moderate to potent antifungal activity [30].

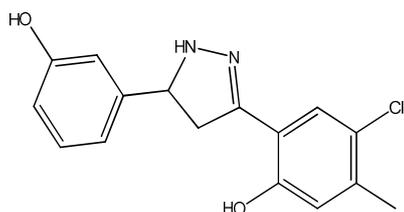


Fig. 24: Disubstituted pyrazoline derivatives

Ishwar Bhat *et al.* (2014) were reported that the reactions of chalcones with aryloxy acetyl hydrazines yield (70-80%) 1, 3, 5 substituted pyrazoline derivatives in the presence of glacial acetic acid. Synthesized compounds were screened for antibacterial, antifungal and antitubercular activity studies. Synthesized compounds showed significant activity against ampicillin and moderate to significant antifungal activity against griseofulvin. Antibacterial activity studies reveals that good antitubercular activities against isoniazid as a standard drug [28].

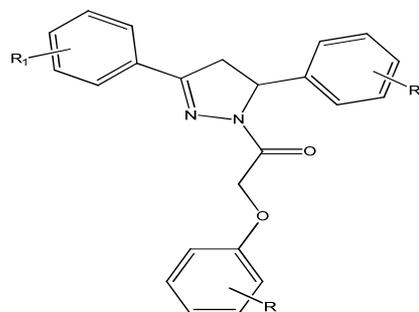


Fig. 22: 1, 3, 5 Substituted pyrazoline derivatives

Viveka *et al.* (2015) reported substituted pyrazole skeleton linked newly synthesis of pyrazolines. The reaction was accomplished by a multistep procedure. They were tested these novel derivatives for antibacterial, analgesic and anti-inflammatory activities. The derivatives which contain halogen atom at phenyl ring on 3rd position of the pyrazoline ring were establish to be active in contrast to bacteria at the conc. of 0.2-0.4 mg/ml. Derivatives those containing *N*-propionyl pyrazolyl-pyrazoline recognized as, having dual activity, anti-inflammatory and antibacterial activity [29].

Parajuli *et al.* (2015) reported that the reaction of chalcones with phenylhydrazine results a novel 3-phenyl-5-(4-dimethylaminophenyl)-1-phenyl-pyrazolone. The synthesized compounds were tested against *S. faecalis*, *S. aureus* and *E. coli* for their antibacterial activity by disc diffusion method. The researcher concluded on the basis of antibacterial evaluation data that the synthesized new compounds showed sufficient antibacterial activity towards *S. aureus* [31].

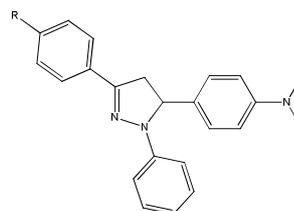


Fig. 25: Novel 3-phenyl-5-(4-dimethylaminophenyl)-1-phenyl-pyrazoline

Sulthana *et al.* (2015) reported a research paper on design and synthesis a new series of thiophene and benzodioxole appended thiazolyl-pyrazoline derivatives by the microwave-assisted method and screened for antimicrobial potency against different bacteria and fungi. Few compounds show good antimicrobial potency [32].

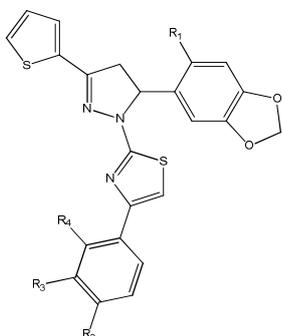


Fig. 26: Thiazolyl-pyrazoline derivatives

Alnitop *et al.* (2015) synthesized Thiazolyl-pyrazoline derivatives and subjected to evaluate for antifungal potency against the pathogenic yeast and mold by broth microdilution method as compared to standard drug ketoconazole at the MIC conc. of 250 µg/ml [33].

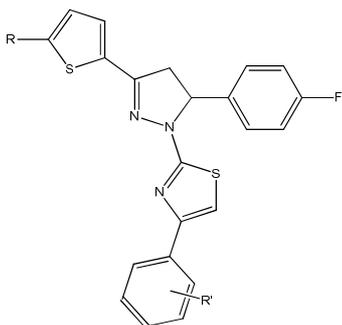


Fig. 27: Thiazolyl-pyrazoline derivatives

Indorkar *et al.* (2015) published a research paper on newly synthesized 1-acetyl/acetophenyl-3-(4-nitrophenyl)-5-(substituted phenyl) pyrazoline derivative. They tested them for antimicrobial potency against the pathogenic bacterial strains such as *B. subtilis*, *E. coli*, *K. pneumonia* and *S. aureus*. Further tested against a pathogenic panel of fungal strains like *A. niger*, *A. flavus*, *T. viride* and *C. albicans* for antifungal activity. On the basis of obtained results, it is concluded that almost all the synthesized new pyrazoline derivatives had displayed variable growth inhibitory effects [34].

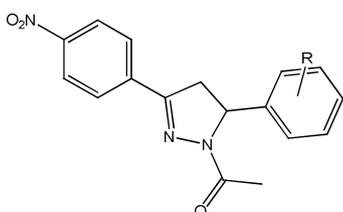


Fig. 28: 1-acetyl/acetophenyl-3-(4-nitrophenyl)-5-(substituted phenyl) pyrazoline derivative

Karangiya *et al.* (2016) reported a series of newly synthesized 3-(Aryl)-5-[4-(2,4-Dichlorophenylmethoxy)-3-methoxyphenyl]-4,5-

dihydro pyrazoline and 3-(Aryl)-5-[4-(2,4-Dichlorophenylmethoxy)-3-methoxyphenyl]-4,5-dihydroacetyl pyrazoline derivatives. The chalcones were synthesized by Claisen-Schmidt condensation. The synthesized compounds were subjected for antimicrobial activity [35].

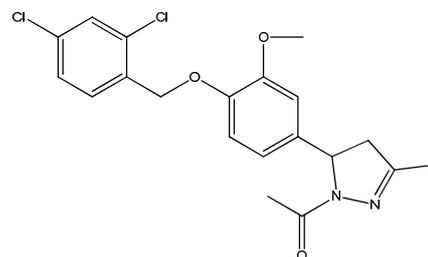


Fig. 29: 3-(Aryl)-5-[4-(2,4-Dichlorophenylmethoxy)-3-methoxyphenyl]-4,5-dihydro pyrazoline

Ahmed *et al.* (2016) reported the synthesis of two series of pyrazoline derivatives beginning from p-acetamidophenol (paracetamol) and screened for antimicrobial activity. Chalcones were prepared by reacting 3-acetyl-4-hydroxyphenyl acetamide with different aromatic aldehydes. These chalcones were further reacted with phenylhydrazine and isoniazid to get phenyl-pyrazolines and isoniazid-pyrazolines. New pyrazoline derivatives displayed important antibacterial potency against *E. coli*, *S. aureus*, and *P. aeruginosa* compared using the standard antibiotic ciprofloxacin. In the conclusion found that some derivatives possesses powerful antibacterial activity against *S. aureus*, *P. aeruginosa* and at the conc. of 3.12 mg/ml [36].

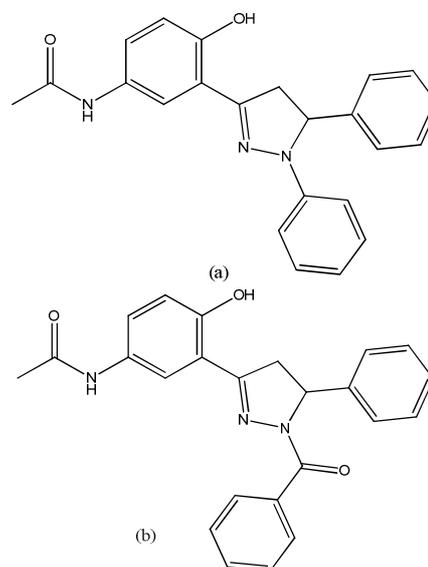


Fig. 30: (a) phenyl-pyrazolines and (b) isoniazid-pyrazolines

Muneera *et al.* (2016) synthesized biologically active pyrazoline derivatives by the reaction of imidazole-2-carboxaldehyde with 1-acetyl-2-hydroxynaphthalene using Claisen-Schmidt condensation reaction. Metal acetates ligands further formed from the metal complexes with Ni(II), Co(II), Cu(II) and Zn(II) metals, respectively. All metal complexes structures were analytically confirmed by IR, NMR, Mass, ESR spectroscopy and elemental analysis. All synthesized derivatives were screened against bacterial strains *E. coli*, *S. aureus*, *K. pneumoniae*, *Proteus mirabilis* and *S. typhi* as compared to the standard drug streptomycin. All compounds also were estimated for *in vitro* antimycobacterial activity against *Mycobacterium tuberculosis* [37].

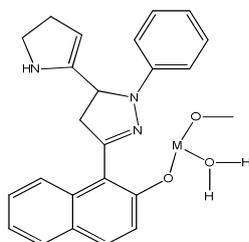


Fig. 31: Metal complex of pyrazoline derivatives

Sid *et al.* (2016) synthesized the 1-formyl-3-phenyl-5-(4-isopropylphenyl)-2-pyrazoline as pure crystal and their structure was confirmed by spectral analysis like FT-IR, NMR, XRD. Compound was screened for anti-microbial activity and the compound shows favorable activity [38].

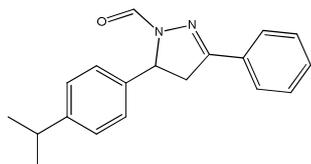


Fig. 32: 1-formyl-3-phenyl-5-(4-isopropylphenyl)-2-pyrazoline

Patel *et al.* (2016) reported the synthesis of 2-pyrazolines from chalcones by conventional and microwave-assisted techniques. All new compounds have been confirmed by The ^1H NMR, $[13]\text{C}$ NMR, IR and Mass spectroscopy. All the synthesized compounds were screened for antibacterial potency against gram-positive bacteria (*S. Aureus*, *S. Pyrogens*) at the conc. of 200 $\mu\text{g}/\text{ml}$, and gram-negative bacteria (*P. Aeruginosa*, *E. coli*) at the conc. of 500 $\mu\text{g}/\text{ml}$ as compared to standard ampicillin and for the antifungal potency against *A. niger*, *C. Albicans*, *A. Clavatus* at conc. of 250,500, 1000 $\mu\text{g}/\text{ml}$ as compared with the standard griseofulvin and nystatin [39].

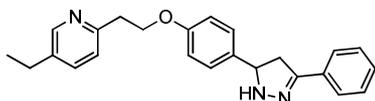


Fig. 33: 2-pyrazolines derivatives

Shamsuzzaman *et al.* (2016) synthesized a new steroidal pyrazoline derivatives series by the reaction between α , β unsaturated ketone in DMSO and 2,4 dinitrophenyl hydrazine with few drops of acetic acid. The structures of synthesized new derivatives were elucidated by ^1H NMR, $[13]\text{C}$ NMR, IR, Mass spectra and analytical data. The synthesized compound were evaluated for antimicrobial potency against *Coryne bacterium xerosis*, *S. epidermidis*, *E. coli* by disc diffusion method as compared to the gentamicin and anti fungal activity against *M. azygosporus*, *A. niger* *C. purpurea*, as compared with the standard drug ketoconazole [40].

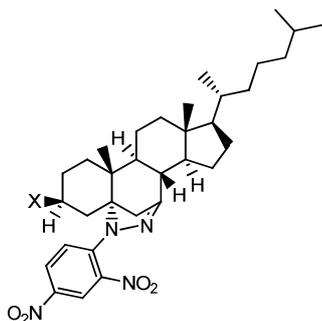


Fig. 34: New steroidal pyrazoline derivatives

Karad *et al.* (2016) synthesized a novel morpholino quinoline based conjugates with pyrazoline moiety by microwave irradiation technique. The new compounds were evaluated for *in vitro* antibacterial activity against pathogenic strains of bacteria and fungi comparing with standard drugs ampicillin, chloramphenicol, ciprofloxacin and griseofulvin [41].

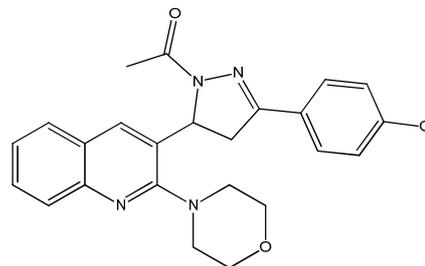


Fig. 35: Morpholino quinoline based pyrazoline

Tejas J. Shah *et al.* (2016) prepared a series of 3-[3'-(2'',4''-dichloro-5''-fluorophenyl)-5'-(2''-furyl)-4', 5'-dihydro-1H-pyrazol-1'-yl]-5-substituted phenyl-2-pyrazolines and 1-Nitroso-3-[3'-(2'',4''-dichloro-5''-fluorophenyl)-5'-(2''-furyl)-4',5'-dihydro-1H-pyrazol-1'-yl]-5-substituted phenyl-2-pyrazolines. Some compounds exhibited antimicrobial activity against some Gram (+) and Gram (-) bacteria [42].

Desai *et al.* (2017) synthesized few novel derivatives of (5-(2-chloroquinoline-3-yl)-3-(aryl)-4,5-dihydro-1H-pyrazol-1-yl)(pyridin-4-yl) methanones moieties embedded in different biologically active heterocyclic compounds e. g. pyrazoline quinoline and pyridine derivatives. Reported compounds were analytically determined by spectrometric methods like IR, ^1H NMR, $[13]\text{C}$ NMR, Mass spectra. These compounds were screened for antimicrobial activity on four strains of bacteria (*S. aureus*, *S. pyogenes*, *E. coli*, *P. aeruginosa*) and three strains of fungi (*C. albicans*, *A. niger*, *A. clavatus*) using griseofulvin and ampicillin as the standard drugs [43].

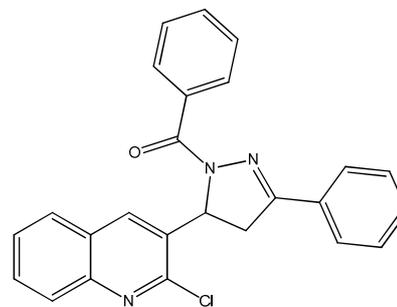


Fig. 36: (5-(2-chloroquinolin-3-yl)-3-(aryl)-4,5-dihydro-1H-pyrazol-1-yl)(pyridin-4-yl) pyrazoline

Mishra *et al.* (2017) prepared a novel series of 1, 3, 5-trisubstituted pyrazoline derivatives by reacting chalcones and nicotinic acid hydrazide in two steps. 1st step is the preparation of chalcones by treatment of substituted benzaldehyde with 4-hydroxy acetophenone by Claisen-Schmidt Condensation. 2nd step is the reflux condensation of isoniazid with chalcones in alkaline ethanol results in various pyrazoline derivatives. The newly manufactured compounds were structurally confirmed by spectral analysis (IR, ^1H NMR, $[13]\text{C}$ NMR) and elemental analysis. The pyrazoline derivatives were screened for antibacterial and antimalarial activity as compared to the standard drugs ciprofloxacin. The compounds were tested on bacteria *S. aureus*, *B. Subtilis*, *E. coli* and *P. aeruginosa*, and fungus against *A. niger* at the MIC-3.25 $\mu\text{g}/\text{ml}$ and *C. albicans* at MIC-6.5 $\mu\text{g}/\text{ml}$ as compared with the standard drug fluconazole. For antimalarial activity, the pyrazoline derivatives were tested against

chloroquine-sensitive and chloroquine-resistant *P. falciparum* strains [44].

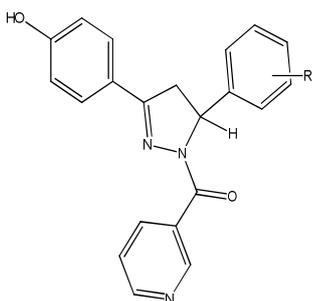


Fig. 37: Novel series of 1, 3, 5-trisubstituted pyrazolines

Rashmi *et al.* (2017) synthesized a novel series of four 1-thiocarbamoyl-3, 5-diphenyl-2-pyrazoline derivatives by microwave irradiation method in a modified domestic microwave oven. The synthesized new compounds were evaluated for their antibacterial activity by well diffusion method against two gram-positive strains (*Staphylococcus aureus* MRSA, *Pseudomonas* spp.) and two gram-negative strains (*Escherichia coli*, *Bacillus cereus*). The synthesized compounds 1-thiocarbamoyl-3,5-diphenyl-2-pyrazoline and 1-thiocarbamoyl-3-(4'-chlorophenyl)-5-(4-chlorophenyl)-2-pyrazoline showed potent activity against both the gram-positive strains *Staphylococcus aureus* MRSA and *Pseudomonas* spp [45].

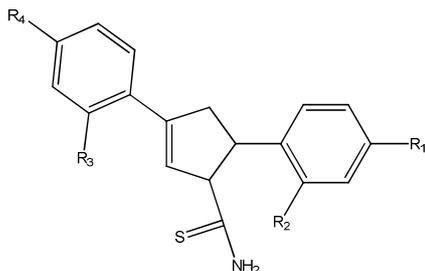


Fig. 38: 1-thiocarbamoyl-3,5-diphenyl-2-pyrazoline derivatives

Sadashiva *et al.* (2017) published a research paper on the design and synthesis of 2, 4 disubstituted 1,3-thiazoles linked pyrazoline moiety series. The structural elucidation of synthesized new compounds was done by UV-Vis, IR, NMR, Mass spectroscopy and elemental analysis. The new compounds were screened for *in vitro*, antimicrobial activity against some pathogenic microbial strains [46].

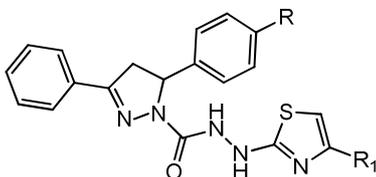


Fig. 39: 2, 4 disubstituted 1,3-thiazoles linked pyrazolines

R Umadevi (2017) synthesized some novel pyrazoline derivatives from chalcones which are prepared by the treating 2-acetyl-5-bromothiophene with various aromatic aldehydes. These chalcones further condensate with phenylhydrazine HCL, pyridine as a catalyst results 3-(5-bromo thiophene-2-yl)1-phenyl-1-pyrazole derivatives. The synthesized compounds have been identified by their melting point, TLC, IR and NMR spectral data. All the synthesized compounds have been evaluated for antibacterial potential against gram-positive

bacterial strains, *B. subtilis* and *B. pumilus* and gram-negative bacterial strains *E. coli* and *P. vulgaris* and antifungal activity against fungal strains, *A. niger* and *p. crysogenium* [47].

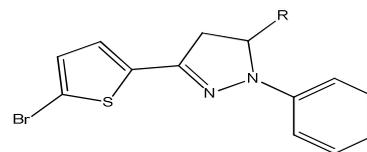


Fig. 40: 3-(5-bromo thiophene-2-yl)1-phenyl-1-pyrazole derivatives

Kumarswami *et al.* (2017) synthesized some new pyrazoline derivatives from chalcones and the hydrazine hydrate in alkaline ethanol. The chalcones have been prepared by the reaction of acetophenone with various benzaldehyde. The synthesized new compounds were characterized by NMR, IR and mass spectroscopy. All the compounds were evaluated for antibacterial activity against gram-positive strains (*S. Aureus*, *B. Subtilis*) and gram negative strains (*E. coli*, *K. Pneuminoae*) at suitable conc. as compared to standard drug ciprofloxacin. All the compounds showed moderate to potent antibacterial activity [48].

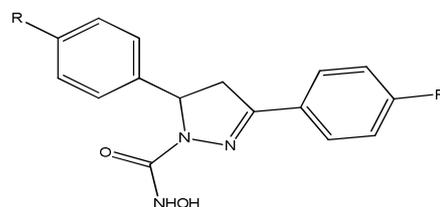


Fig. 41: New pyrazoline derivatives

Yusuf *et al.* (2017) synthesized a series of bispyrazolines from the cyclization of bischalcone with phenylhydrazine by reflux in dry acidic ethanol medium. According to Claisen-Schmidt condensation reaction, chalcone obtained by reacting p-hydroxy acetophenone with 2-furfuraldehyde. The bischalcones and bispyrazolines structures were confirmed by ¹H NMR, ¹³C NMR, IR and Mass spectroscopy. Newly synthesized compounds were screened for their antimicrobial potency against seven strains of bacteria (*E. coli*, *K. pneumonia*, *P. fluorescens*, *S. aureus*, *P. aeruginosa*, *B. subtilis*, *S. pyrogen*) and five strains of fungus (*A. sclerotium*, *Penicillium glabrum*, *A. niger*, *A. janus*, *Fusarium oxysporum*) by using serial tube dilution method as compared to the standard drug amoxicillin and fluconazole [49].

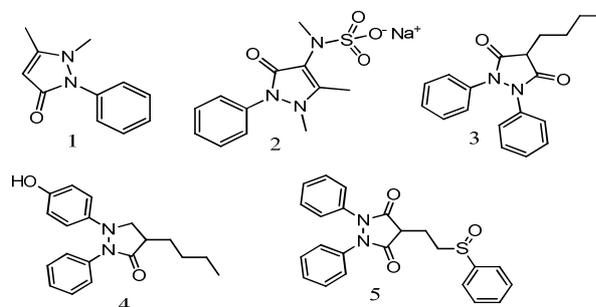


Fig. 42: Bispyrazolines

Burmizda *et al.* (2018) synthesized a series of ferrocenyl ketones by the reaction of ferrocene with substituted acryloyl chlorides. The reaction of ferrocenyl ketones with hydrazine in acidic medium prepares new pyrazoline derivatives. 12 strains of microbes

(bacteria and fungi) were taken for antimicrobial activities of synthesized compounds as compared to standard drugs streptomycin and ketoconazole at the MIC conc. from 0.039-0.312 mg/ml [50].

Silveri et al. (2019) reported the design and synthesis of pyrazoline incorporated 1,2,3 triazole benzene sulphonamides and all the synthesized compounds were characterized by FT IR, HNMR, ¹³CNMR and Mass spectra. The synthesized compounds were evaluated for cytotoxic activity through using 3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay and anti-gout activity by potassium oxonate induced assay [51].

Asad et al. (2020) synthesized a series of N-propionyl 2-pyrazolines from the chalcones by reacting propionic acid with hydrazine hydrate. The atomic structure of new pyrazoline derivatives were confirmed by FT-IR, NMR spectroscopy, crystal structure, X-ray diffraction techniques. All new compounds were evaluated for antibacterial activity against gram-positive bacterial strain (*B. Subtilis*, *S. Aureus*) and gram-negative bacterial strain (*E. Coli*, *P. Peli*). All new compounds display significant activity against bacteria [52].

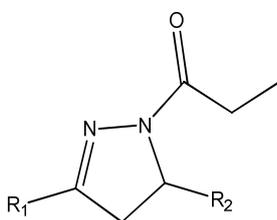


Fig. 43: N-propionyl 2-pyrazolines

CONCLUSION

The objective of this review is to provide a platform for researcher, academician, chemist and industrialists to have all the information regarding the antimicrobial activity of pyrazoline. Various synthetic routes were discussed with its chemistry. The literature eliciting the antimicrobial activity were discussed. As the literature shows that there is always demand of novel antimicrobial agents due to the pathogen resistance. So, this literature would be fruitful to the society as well. This would provide the researcher a lead that they may come with a new and potent pyrazoline bearing derivative.

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AUTHORS CONTRIBUTIONS

The complete review work was suggested and designed by Saras Kumar Jain. Literature collection and written works were carried out by R Singhal.

CONFLICT OF INTERESTS

Authors declare no conflict of interest.

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