ORIGINAL RESEARCH PAPER

Chemistry

AN OVERVIEW ON THE BIOLOGICAL ACTIVITIES OF PYRAZOLE

KEY WORDS: Pyrazole, Derivatives, Biological functions, Pharmacological activities

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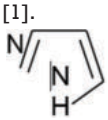
ABSTRACT

The purpose of this study is to provide a summary of the various pyrazole moieties' pharmacological actions. Pyrazole is a well-known and essential nitrogen-containing 5-membered heterocyclic compound, and different techniques for synthesis have been developed. Pyrazole, also known chemically as 1, 2-diazole, has become a prominent subject due to its numerous applications. Numerous pyrazole derivatives have been discovered to have a wide range of biological functions, which has fueled study in this area. Pyrazoles and their variants are among the most powerful groups of chemicals, with anti-bacterial, anti-convulsant, analgesic, anti-microbial, anti-inflammatory, anti-diabetic, sedative, anti-rheumatic, anticancer, and anti-tubercular properties. The goal of this study was to compile literary work on pyrazole for its different pharmacological activities, as well as to report on new efforts made on this moiety.

INTRODUCTION

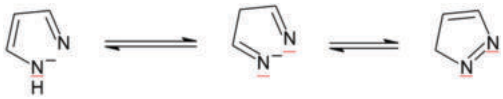
Pyrazole chemistry has been widely researched in the past. Pyrazoles are five-member ring heterocyclic compounds that have two nitrogen elements in neighbouring positions and are also known as azoles. [1].



Individual atoms' effects can describe the pyrazole molecule's chemical reaction. Because the N-atom in position 2 has two electrons, it is basic and interacts with electrophiles. The unreactive N-atom in position 1 loses its proton in the presence of base. The merged two N-atoms decrease the charge density at C3 and C5, allowing C4 to be attacked electrophilically.

In the presence of a powerful base, deprotonation at C3 can occur, resulting in ring opening. Pyrazole protonation produces pyrazolium cations that are less apt to be electrophilically attacked at C4, but attack at C3 is promoted. The pyrazole anion is much less reactive towards nucleophiles, but it is more reactive towards electrophiles [2].

Because of their planar conjugated ring geometries with six delocalized electrons, pyrazoles are aromatic compounds. As a result, many significant characteristics of these molecules were investigated by comparing them to those of benzene derivatives [3]. Pyrazoles, like other nitrogen-containing heterocycles, can have a variety of tautomeric forms. Unsubstituted pyrazole exists in three tautomeric forms [4].

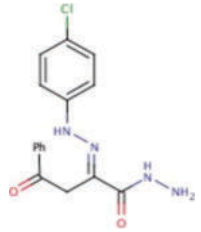


Unsubstituted Pyrazole Tautomers

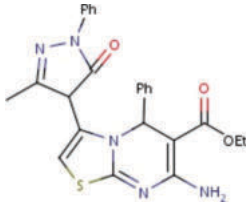
Nowadays, a large number of molecules with pyrazole nuclei have been found to exhibit a wide range of biological action, including. Antibiotic [5, 6], antiviral [7, 8], anti-tumor [9, 10], anti-depressant [11], pesticides [11], and fungicides [11]. The pyrazoles ring is an important synthetic route in the pharmaceutical business due to its broad spectrum of biological action. In fact, a heterocyclic moiety like this is the fundamental composition of many medicines.

Literature Rivew:

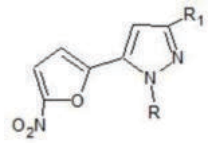
Eman M. Flefel et al. reported the synthesis of novel substituted pyrazole, thiazole, and 1, 2, 4- triazole derivatives. Sugar hydrazones, acetylated derivatives, derived acyclic C-nucleoside analogues, and thioglycosides of 1, 2, 4-traizole derivatives were also synthesized. Some of the synthesized compounds were evaluated for antitumor activity, and a number of them exhibited considerable activity [12].



Mohamed salahk youssef and colleagues synthesized 7 - amino - 3 - (3 - methyl - 5 - oxo - 1 - phenyl – 2 – pyrazoline – 4 - yl) - 5 - aryl - 5H - hiazolo[3,2 - a] ethyl 7 - amino-3 - (3 -methyl - 5 - oxo - 1-phenyl - 2 – pyrazoline - 4 -yl The reaction of 4 - (2 – aminothiazole - 4 - yl) - 3 – methyl - 5 – oxo - 1 – phenyl - 2 - pyrazoline with arylidene ethyl cyanoacetate produced pyrimidine-6-carboxylate, which was then converted to related fused heterocyclic systems via reaction with different reagents [13]

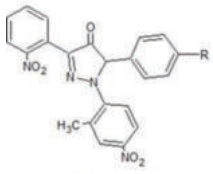


Rao Jyothi et al. created a novel sequence of 1, 3, 5-trisubstituted pyrazoles through the cyclo condensation reaction of chalcones and substituted hydrazides using microwave energy as well as a conventional technique. Compound 3g was effective against E. coli and P.aeruginosa. Compound 3j was found to be effective against the pathogen A.fumigatus [14].

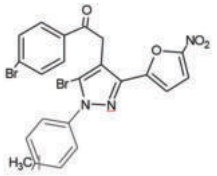


R	R_1
3i) P-Chloro Phenyl	Nicoinyl
3i) P-Chloro Phenyl	2Methyl 5,nitro-1 imidazoacetyl

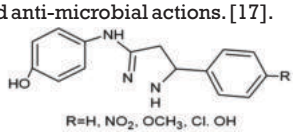
Sagar K. Mishra et al. synthesised a sequence of 1 - (2, 4 - dinitrophenyl) - 3 - (3-nitrophenyl) - 5 -(4 - substituted phenyl) - 2-pyrazolins. - 4-ones are formed through the oxidation of 1 - (2, 4 -dinitrophenyl) - 3 - (3 - nitrophenyl) - 5 - (4 - substituted phenyl) - 4 - bromo - 2 - pyrazolines were combined with dimethyl-sulfoxide and tested for antibacterial action in vitro. The majority of the synthesised substances lacked substantial inhibitory action against the examined strains [15].



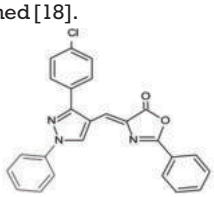
SatheeshaRai N and Balakrishna Kalluraya et al. published a new set of nitro furans having 1,3,4,5 tetra substituted pyrazole derivatives. Compound 3b outperformed all other chemicals in terms of antibacterial and antifungal action [16].



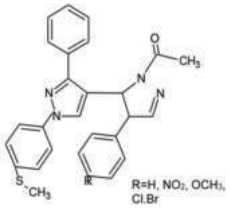
By treating substituted aryl-N-chalconyl amino phenols with hydrazine hydrate, Sahu SK et al. made a sequence of new 4-(5-substituted aryl-4, 5-dihydropyrazole-3-yl-amino) phenols. The existence of 4-NO2, 2-OH, and 4-Cl in the phenyl ring at the 5-position of the pyrazoline ring of synthesised substances was found to enhance analgesic, anti-inflammatory, and anti-microbial actions. [17].



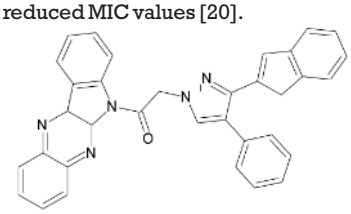
The standard microwave help Synthesis of pyrazole having 2, 4-disubstituted oxazol-5-one as a novel family of antimicrobial agents was reported by Argade N. D et al. Microwave-assisted synthesis has several benefits over traditional methods in terms of reaction time and total yield. Compounds containing electron removing groups demonstrated antimicrobial and antifungal activity. Compound (3d) demonstrated the greatest action of the compounds examined [18].



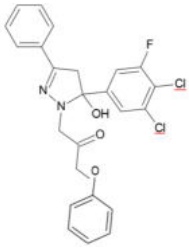
Chovatia P. T et al. made derivatives and evaluated them in vitro for anti-tubercular and antimicrobial activity [19].



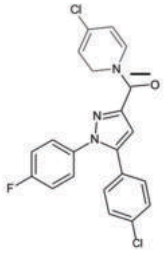
Kuntal Manna et al. found that microwave-assisted synthesis of pyrazoline incorporating benzofuran with indo phenazine ring is more regioselective and saves time. Because of their potency and selectivity, these molecules are promising candidates for the synthesis of novel compounds with higher activity and reduced MIC values [20].



Mari Sithambaram Karthikeya et al. made hydroxypyrazolines containing chlorofluorine from chlorofluorine chalcones. The bromination of chalcones at ambient temperature yielded chalconedibromides. When chalconedibromides were treated with aryloxy acid hydrazides in the presence of triethylamine, chloro-fluorine containing hydroxyl pyrazolines were formed (6). Some substances demonstrated extremely potent antibacterial and antifungal action [21].

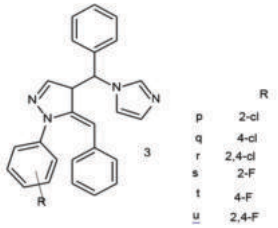


Venkat Ragavan R et al. created a new class of 1,5-diaryl pyrazoles by modifying the active portion (amide bond) and testing them for biological activity. The findings of our current research indicate that the aliphatic amide pharmacophore is essential for the antimicrobial activities of the investigated pyrazoles, with the presence of the 4-piperidine moiety enhancing the activities. Antibacterial and antifungal action was demonstrated by the compounds[22].



1,5 Diaryl pyrazoles with amide pharmacopho

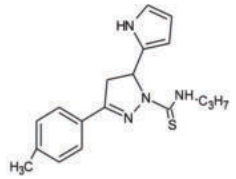
During their research in the azole antifungal field, Giulia Menozzi et al. created a number of 1, 5-disubstituted-1Hpyrazoles, counterparts of bifonazole. In vitro, 1, 5-diphenyl-1H-pyrazole 3 demonstrated moderate antimycotic and antimicrobial activity. They produced a number of fluoro and chloro derivatives of 3 to improve these characteristics, given that the halo substitution was discovered to be capable of boosting antifungal effects. Some dichloro and trichloro compounds demonstrated antibacterial activity [23].



Nesrin Gokhan-Kelekci et al. examined the capacity of 1-thiocarbomyl-3-substituted phenyl -5-(2-pyrole)-4, 5-dihydro-(1H)-derivatives to inhibit MAO.

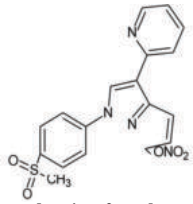
The majority of the chemicals were highly active against MAO. Anti-inflammatory and analgesic activity was also determined.

Compound (3k) demonstrated antiinflammatory and analgesic action similar to indomethacin while having no ulcerogenic impact [24].

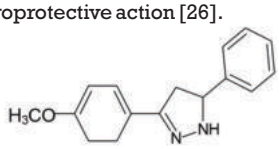


Ezawa M et al. created 4-3-[(1Z)-4-(nitrooxy) but-1-enyl] The COX-2 inhibiting efficacy of -5-(3-pyridyl) pyrazolyl-1- (4-

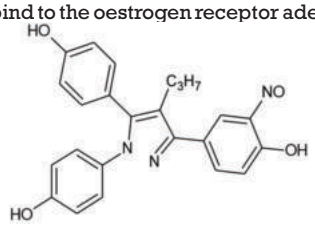
methylsulfonyl) benzene (9). A pyrazole ring with a nitric oxide (NO)-donating group at the 3-position was synthesised and tested for its capacity to suppress COX isozymes in human whole blood. They discovered that 3-pyridyl modified 1, 5-disubstituted pyrazole compound 9 havingaNO - donating group at the 3-position of the pyrazole ring showed significant COX-2 potency and selectivity in the pyrazole family of COX-2 selectiveinhibitors [25].



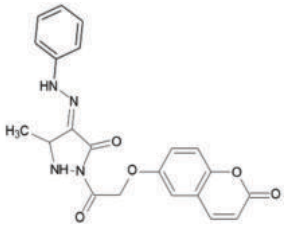
The simultaneous synthesis of aryl azoles has been reported by Giuseppe Cocconcelli et al. The reaction of modified phenyl hydrazine with,-unsaturated ketones results in the regioselective production of 4, 5-dihydro-1-H-pyrazole, with acetic acid acting as a catalyst. Substances (3a and 2g) show promising neuroprotective action [26].



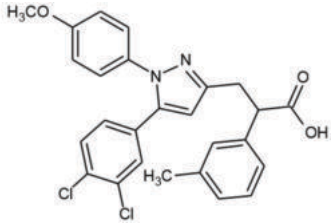
FotiniNaoum et al. created new tetra substituted pyrazole compounds with nitro substituents on the phenol ring. Among the compounds examined, 2-nitro phenolderivatives (5c) were found to bind to the oestrogen receptor adequately [27].



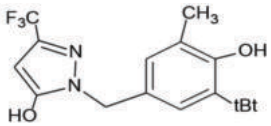
To investigate the possible function of coumarin derivatives containing pyrazole as antioxidants and cytotoxicagents against Dalton's lymphoma ascites tumour cells (DLA) and Ehrlich ascites carcinoma cells, Parameswaran Manojkumar et al. synthesised coumarin derivatives containing pyrazole (EAC). Compound (5a) demonstrated potential antioxidant and cytotoxic action against DLA and EAC cells in vitro [28].



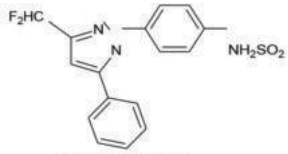
Laurent Gomez et al. reported the synthesis and SAR studies of 1, 5-diarylpyrazole analogues with various structural modifications of the molecule's alkane side chain, concluding that compound (19) demonstrated good oral bioavailability and could be used for the potential treatment of IBS and other GI disorders [29].



VasileDinoiu, Jian-Ming, and colleagues created modern fluorine-containing organic molecules. The pyrazoles with trifluromethyl and/or methyl substituents were formed by reacting 3, 5-dialkyl-4-hydroxybenzylhydrazine with hexafluroacetyl acetone and trifluroacetylacetone. The pyrazole-5-ones withtrifluroacetoacetic acid ethyl ester were synthesised using the same hydrazine derivatives. When lead was oxidised in dichloromethane, tetraacetate and aroxyls were produced [30].

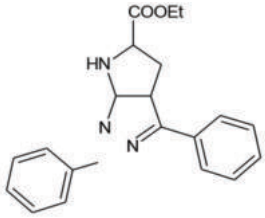


Sunil Singh K et al. investigated the microwave promoted condition and optimised it to obtain a1,5-diaryl-pyrazole, which they then applied to the parallel synthesis of various compounds, and they concluded that this was an excellent method for the rapid generation of 1,5-diarylpyrazole using microwave inaqueous medium under normal laboratory conditions [31].



1, 5 diaryl pyrazole

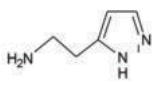
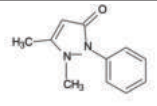
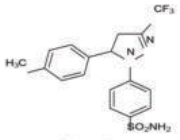
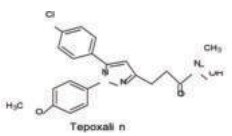
El-Saied Aly A et al. demonstrated an unique synthetic method for the production of novel pyrazole derivatives. They created some new pyrazole derivatives by reacting 3-aryl-1-phenyl-1H-pyrazolecarbaldehydes with acylglycine, benzamidine HCl, and azidoacetate, yielding pyrrolopyrazole derivatives [32].

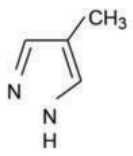


Pyrrolo pyrazole derivative

Some Of The Marketed Products Of Pyrazole Nucleus Are Listed Below [33].

Table 1: Marketed products containing Pyrazole moiety

MARKETED DRUG	STRUCTURE
Betazole functions as an H2 receptor ligand. It is used in therapeutic settings to assess stomach secretory function.	
Analgesic and antipyretic phenazone (INN), phenazon, antipyrine (USAN), or painkiller.	 Phenazone
Celecoxib is a nonsteroidal anti-inflammatory medication (NSAID) that is used to treat osteoarthritis, rheumatoid arthritis, acute pain, uncomfortable periods, and menstrual complaints.	 Celecoxib
Lonazolac is an anti-inflammatory medication that is not steroidal.	 Lonazolac
Tepoxalin is a nonsteroidal anti-inflammatory drug that has been authorised for use in animal medicine in the United States and the European Union.	 Tepoxali n

Fipronil is a broad-spectrum pesticide that affects the insect central nervous system by preventing chloride ions from passing through the GABA receptor and glutamate-gated chloride channels (Glu Cl), both of which are central nervous system components.	 Fibronil
The antidote fomepizole or 4-methylpyrazole is recommended for use in verified or suspected methanol or ethylene glycol poisoning. Aside from its medicinal applications, 4-methylpyrazole has been investigated for its function in coordination chemistry.	 Fomepizole

CONCLUSION

The examined Pyrazole is a one-of-a-kind template that is linked to a variety of cellular processes. Antibacterial, anticonvulsant, analgesic, antifungal, anti-inflammatory, anti-diabetic, calming antirheumatic, antitumor, and antitubercular actions are exhibited by different substituted pyridines. This piece highlighted the study efforts of many researchers who were published in the literature for various purposes.

Synthesized pyrazole molecules have pharmacological effects. The study provided thorough information about pyrazole analogues, potent compounds described for specific pharmacological action, and the method or technique used in the assessment process. More research is needed to assess pyrazole's additional activities for a variety of illnesses.

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