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# A Comprehensive Review on Pyrazole and It's Pharmacological Properties

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Abstract: Heterocyclic chemistry is very important aspects in organic chemistry. Heterocyclic system consists of one or more heteroatoms like nitrogen, oxygen, sulphur, etc with hydrogen atoms. The system can be classified as saturated as well as non saturated system or hydrocarbons. Another classification of this ring system is divided in some categories like three-membered, four-membered, five-membered, six-memebered, seven-membered, fused heterocyclics etc. Some compounds under this cklassification are acidic or basic in nature. Examples of heterocyclic compounds are Pyrole, Furan, Thiophene, Pyridine, Quinoline, Isoquinoline, Indole, Purine, Pyrazole, etc. Pyrazole is very important under this heterocyclic ring sysyem. Pyrazole is five membered heterocyclics. Pyrazole is basic and unsaturated in nature due to presence of double bonds in their ring structure. When two nitrogen atoms are associated with five menbered heterocyclic ring in 1,2 positions called as Pyrazole structure. It is also known as 1,2-diazole. It is present in many drugs as well as organic compounds and Pharmaceutical compounds. The review study shown that the structure, physical and chemical properties, nomenclature, synthetic approaches, biological activities of Pyrazole heterocyclic ring structure.

Keywords: Pyrazole, Physical & chemical properties, Structure, Nomenclature, Tautomerism, Biological activities.

## I. INTRODUCTION

Pyrazole is an one of the most important five membered heterocyclic compound contain three carbon atom and two adjacent nitrogen atoms which are ortho substitution. German chemist Ludwig Knorr use the term Pyrazole to identify to this class of compounds in 1883 [1] but it was firstly synthesized from acetylene and diazomethane by the German chemist Hans Von Pechmann in the year 1898 [2].

Now a day's derivatives of different compounds have huge application in medicine and industry [3] and engaged a huge area of interest for researcher in the field of medicinal chemistry[4]. Pyrazole ring is very important to develop a new class of drugs and present in large number of medicinal compounds[5-7]. Nitrogen containing heterocyclic core of pyrazole moiety shows different types of biological effects in different binding sites [8-11].

Pyrazole moiety shows a broad spectrum of biological activities like Antimicrobial, antiviral, antitumor, anti-histaminic, anti-depressant, insecticides and fungicides, due to this reasons many pharmaceutical industry synthesize vast number of compounds containing pyrazole nucleus using different synthetic routes.





# PHYSICAL & CHEMICAL PROPERTIES

A. Physical Properties of Pyrazole

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Property Name	Property Value
Colour	White to yellow
Chemical formula	C (52.93%), H (5.92%), N (41.15%)
Molar Mass	68.079 g mol <sup>-1</sup>
Composition	C (52.93%), H (5.92%), N (41.15%)
Density	1.4088
Refractive index	1.4203
Melting point	$66 - 70^{\circ} \mathrm{C}$
Boiling point	$186 - 188^{\circ} C$
$pK_a$	2.48 at 25 <sup>°</sup> C
Solubility	Water, Chloroform, Methanol
Sensitivity	Hygroscopic

Table 1: Physical properties of Pyrazole [12]

#### B. Chemical Properties of Pyrazole

Types of reaction	Reaction	Structure	Reference
Basic Character	Presence of inorganic acid like HCl Pyrazole form pyrazole hydrochloride salts.	N H.HCI	13
Acylation	During acylation pyrazole nucleus is replaced by an acyl group, to give N-acetyl pyrazole.	COCH <sub>3</sub> N-acetyl Pyrazole	13
Oxidation	Presence of alkaline KMnO4 Pyrazoles are oxidized and form corresponding carboxylic acid pyrazole.	HOOC N C 6H 5 1-phenyl-4-pyrazole carboxylic acid	14
Reduction	Presence of sodium-ethanol, N-phenyl derivative may be reduced to corresponding pyrazoline.	NH N C <sub>6</sub> H <sub>5</sub> N-Phenyl Pyrazoline	15
Halogenation	Under controlled condition pyrazole gives 4- mono halo pyrazoles	CI N H 4- Chloro Pryazole	16



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Nitration	Presecce of Concentrated nitric acid Pyrazole undergo straight nitration at C-4, it gives 1-nitro- pyrazole	NO2 1-Nitro-1H-Pyrazole	17
Sulphonation	When Pyrazole reacts with fuming sulphuric acid to yield pyrazole 4–sulphonic acid.	HO3S N H Pyrazole-4-sulphonic acid	18

Table 2: Chemical properties of Pyrazole

### III. AROMATICITY

Pyrazole contains six delocalized  $\pi$ -electrons and due to planner conjugated ring structure pyrazole shows aromaticity. Pyrazole shows many same properties when comparing with different benzene derivatives [19]. Pryazoles shows three different tautomeric structure likely as other heterocyclic molecule contain nitrogen atom [20]. Pyrazoline, pyrazolidine and pyrazolone are reduce or oxidized form of pyrazole but they are not aromatic compounds due to the lack of delocalized  $\pi$  electrons and conjugation [21].

One of the two nitrogen atom of pyrazole molecule is pyrrole types and another one is pyridine types and between two nitrogen's one is basic in nature and another one is neutral. It is observed that bond length between position 3 and 4 atom has high value[22]. 2-Pyrazolines are most commonly examined pyrazoline-type heterocyclic systems[23] are observed among the three reduce form of pyrazole such as 1-pyrazoline, 2-pyrazoline and 3-pyrazoline[24].



#### IV. CHEMICAL REACTIVITY

The chemical reactivity of the pyrazole moiety depends on the effect of individual atoms presence in ring system. Nitrogen atom at second position is basic in nature due to the presence of two electrons and hence react with electrofiles but nitrogen atom posit in one is unreactive but reduce or loses its proton in the presence of base. In pyrazole ring system C4 position is available for electriphilic attack due to the both nitrogen atom reduce charge density at C3 and C5 position. Presence of strong base C3 carbon leading to ring opening due to deprotonation. Electrophilic attack less likely occour at C4 position due to the protonation of pyrazole C3 position is also facilitated. Pyrazole anion shows more reactivity towards electrophiles rather than nucleophiles [25].



Three Tautomeric structure of pyrazole



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#### V. NOMENCLATURE

The nomenclature is started from the hydrogen attached with the nitrogen atoms in the Pyrazole ring. It is known as 1,2-diazole as because two nitrogen atoms attached with this ring. As per the heterocyclic criteria, nitrogen atom is called as aza as prefix. In this structure, two nitrogen atoms are present so the structure can be noted as 1,2-diazole. Due to presence of double bond in ring structure it can be classified under unsaturated derivative [12].



#### VI. SYNTHETIC METHODOLOGIES

Pyrazole can be synthesized from  $\alpha,\beta$ -unsaturated aldehyde or ketones with hydrazines. Through dehydrogenation mechanism, Pyrazole was synthesized. 1,3-diketone is condensed with hydrazine to form pyrazoles. This condensation organic reaction is known as Knorr-pyrazole [26] condensation reactions. The mechanism of reaction is based upon some steps like attacking of entire hydrazine molecules on the carbonyl carbons of diketones and the imine derivatives formation to yield ultimately Pyrazole [27].



Figure: Synthetic scheme of Pyrazole [27]

#### VII. STANDARD DRUGS CONTAINING THE PYRAZOLE RING

Sl. No.	Drug	Activity	References
1	Pyrazofurin	Anticancer	
2	Crizotinib	Cytoprotective	
3	Celecoxib and Lonazolac	Antiinflammatory	28 - 35
4	Difenamizole	Analgesic	
5	Rimonabant	Antiobesity	
6	Sildenafil	Vasodilator	
7	Fezolamide	Antidepressant	
8	Floxan	Anti-inflammatory	36 37
9	Pyrazomycin	Anticancer	
10	Deramaxx	NSAID	

 Table 3: Standard drugs containing the Pyrazole ring



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Sl. No.	Biological activity	References
1	Antitubercular	38
2	Anti AIDS	39
3	Anti malarial	40
4	Anti microbial	41
5	Anti tumer	42,43
6	Anticancer	44
7	Antifungal	45
8	antihyperglycemic	46
9	antidepressent	47
10	anticonvalsant	48
11	antipyretic	49
12	antianxiety	50,51
13	insecticidal	52
14	Diuretic	50
15	Cytotoxic	
16	Cardiovascular agent	

#### VIII. BIOLOGICAL ACTIVITY OF PYRAZOLE

 Table 4: Biological Activity of Pyrazole

#### IX. CONCLUSION

Pyrazole is known as 1,2-diazole a five-membered heterocyclic compounds. It is basic and unsaturated. It is having very significant structure in modern heterocyclic organic chemistry as this structure is present in so many drugs containing antimalarials, antimicrobials, anticancer, antifungal, antidepressant, anticonvulant, antipyretic, antianxiety, diuretic, antihyperglycemic, etc. This ring is showing very safe, stable and potent activities to improve the various efficacies against different diseases. Conflict of Interest: Nil

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