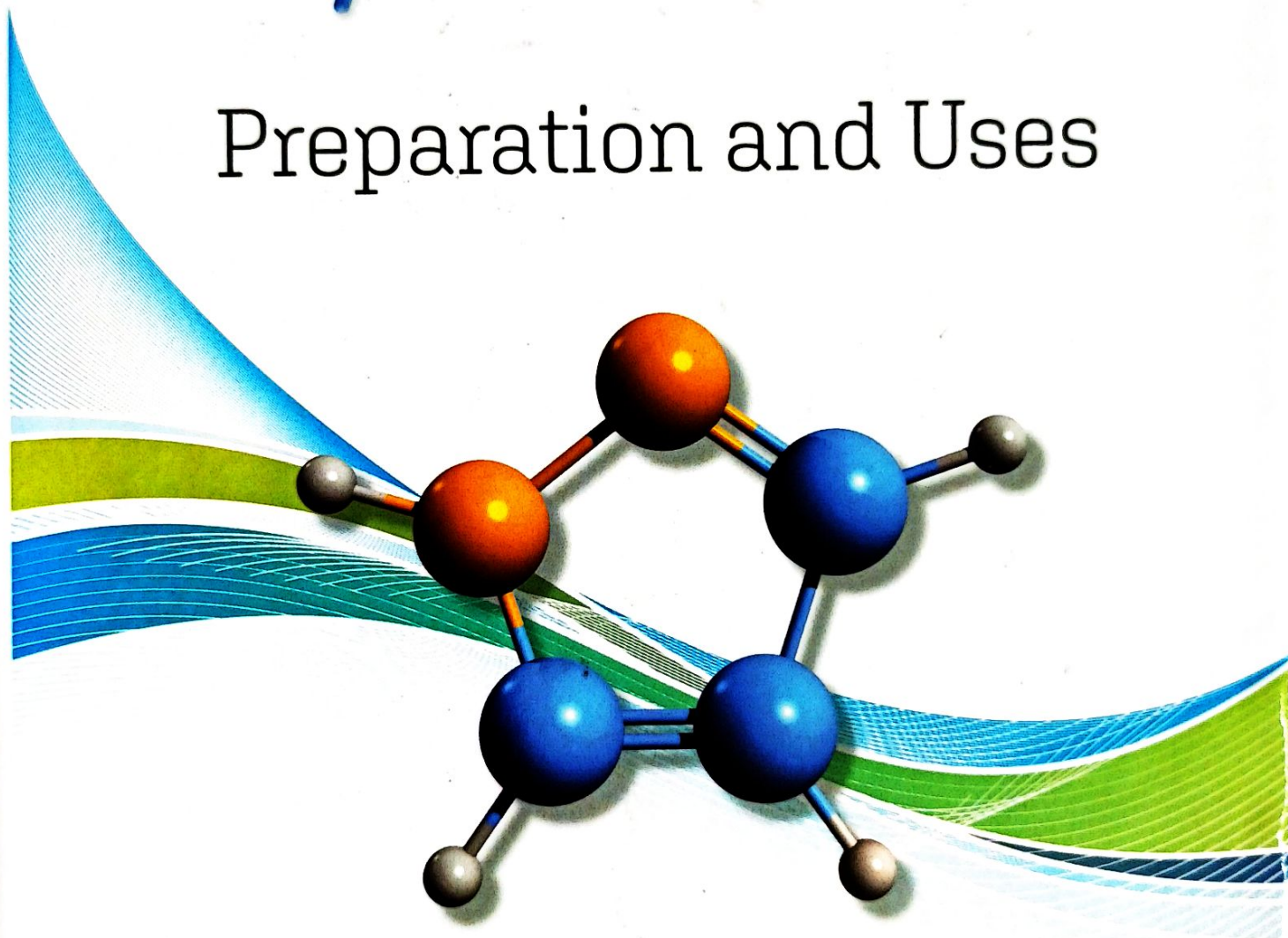


CHEMISTRY RESEARCH AND APPLICATIONS

# Pyrazole

Preparation and Uses



Dilipkumar Pal

Editor

NOVA

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## ROLE OF PYRAZOLE RING IN NEUROLOGICAL DRUG DISCOVERY

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### ABSTRACT

Pyrazole is one of the 5-membered heterocyclic ring systems with two consecutive nitrogens. The molecular formula of the ring system is  $C_3H_3N_2H$  with the systematic name of 1, 2-Diazacyclopenta-2,4-diene. Substituted/fused/linked pyrazole molecules are observed with the greater neuroprotective property. Various pyrazole derivatives such as: 3-substituted-N-aryl-6,7-dimethoxy-3a,4-dihydro-3H-indeno[1,2-c] pyrazole-2-carboxamide was observed with protection against maximal electroshock seizure; 3,5-Diaryl-N-substituted-4,5-dihydro-1H-pyrazole-1-carbothioamide, 3-(4-Fluorophenyl)-5-aryl-N-substituted-4,5-dihydro-(1H)-pyrazole-1-carbothioamide,  $N_1$ -propanoyl-3,5-diphenyl-4,5-dihydro-(1H)-pyrazole were observed with remarkable inhibition against human monoamine oxidase enzyme; 5-(furan-2-yl)-3-(4-methylphenyl)-N-(propan-2-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide showed dual inhibition of monoamine oxidase and acetylcholinesterase enzymes; 3-(3-(ethoxycarbonyl)-1-phenyl-1H-pyrazol-5-yl)phenyl cyclohexylcarbamate showed greater inhibition of human fatty acid amide hydrolase; curcumin fused pyrazole showed proper inhibition of fibrils aggregation fibrils and modulate toxicity due to  $\alpha$ -Synuclein; tricyclic pyrazole carboxamides observed with cannabinoid-2 receptor inhibition; another pyrazole moiety JNJ-28583113 observed with Transient receptor potential melastatin type 2 inhibitor; another set of pyrazole derivatives were observed with  $\beta/\gamma$  secretase inhibition; newer pyrazole derivative as 2-

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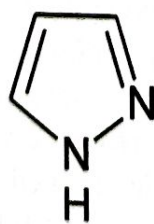
MBAPA showed inhibition of microglial formation, so in a collective manner, these data reflected the importance of pyrazole derivatives to act against convulsion, seizure, Parkinson, Alzheimer and deposition of amyloid- $\beta$  peptide and microtubule-binding tau protein.

**Keywords:** Pyrazole, Alzheimer disease, Tau protein,  $\beta$ -amyloid peptide, Monoamine oxidase.

## 1. INTRODUCTION

Pyrazole is a five-membered ring with two consecutive nitrogens among them one is basic another one is neutral in nature (Figure 1). The structure consists of four pi electrons and a pair of a nonbonding electron with three tautomeric structures (Figure 2) [1, 2].

When pyrazole is reduced by sodium hydride, it transfers into pyrazoline and pyrazolidine. The molecular formula of pyrazole is  $C_3H_4N_2$ , the molecular weight of pyrazole is 68.08 g/mol, partition co-efficient, LogP, and XLogP3 value are 0.26, 0.26 and 0.3, hydrogen bond donor and acceptor are 1 each, the molecular mass of pyrazole is 68.037 g/mol, the topological surface area of pyrazole is  $28.7 \text{ \AA}^2$  [3,4], the boiling and melting points of pyrazole are  $187^\circ\text{C}$  and  $67^\circ\text{C}$ , acid dissociation co-efficient at  $25^\circ\text{C}$  is 2.48, molar refractivity, molar volume, parachor value, surface tension, the polarizability of pyrazole were 18.77 cc, 60.9 cc, 161, 48.6 dyne/cm,  $7.44 \times 10^{-24}$  cc, respectively [5-7]. The melting point of, hydrochloride salt, nitrate, and oxalate of pyrazole showed  $234^\circ\text{C}$ ,  $148^\circ\text{C}$ ,  $192^\circ\text{C}$ , respectively. A group of Japanese scientists named as Kosuge and Okeda, first isolated natural pyrazole from *Houttuynia cordata* (Piperaceae Family) in the form of 3-n-nonylpyrazole (Figure 3) with microbial inhibition property. A chemist named Ludwig Knorr luckily developed a pyrazole derivative antipyrine (Figure 4) for minimization of pain sensation and lowering the manifestation of rheumatoid arthritis [8].



Pyrazole

Figure 1. Structure of Pyrazole.