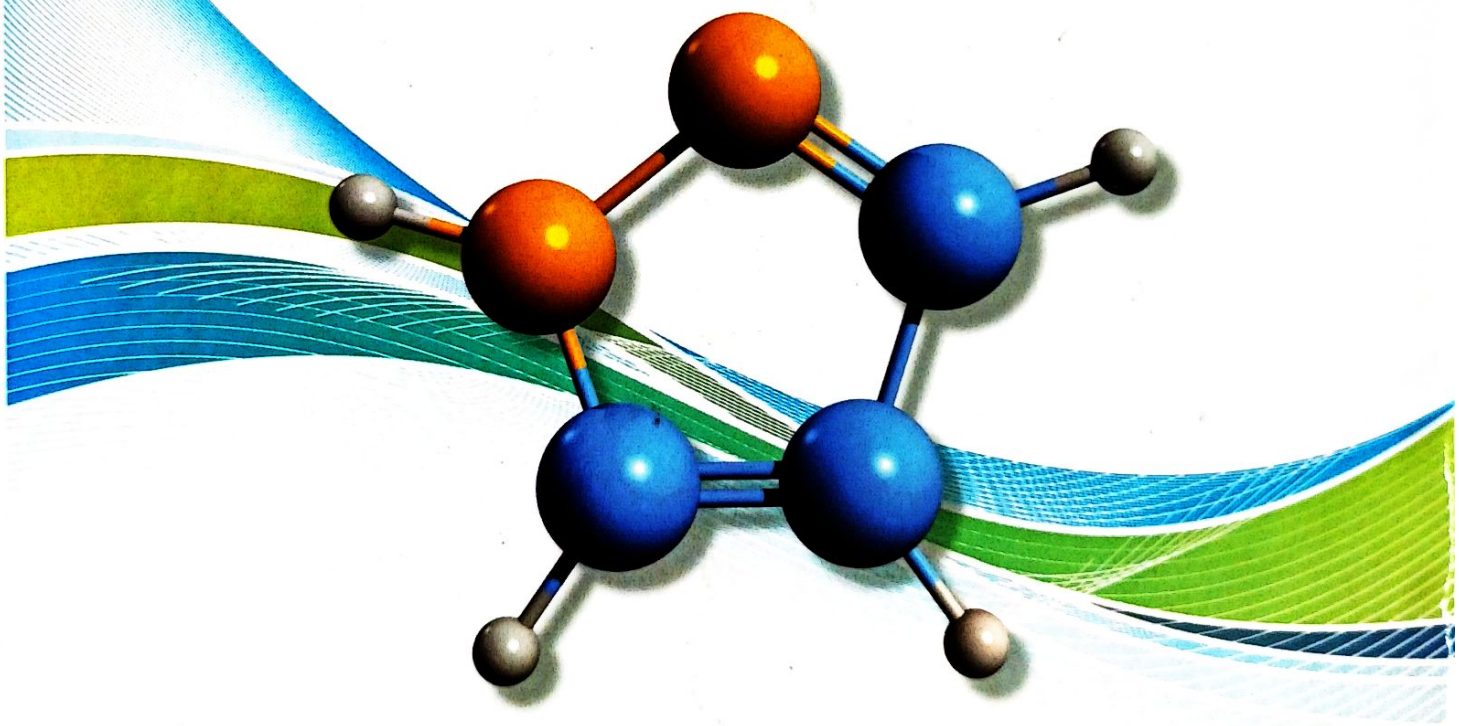
CHEMISTRY RESEARCH AND APPLICATIONS

Pyrazole

Preparation and Uses



Dilipkumar Pal
Editor

NOVA

Library of Congress Cataloging-in-Publication Data

Names: Pal, Dilipkumar, 1971- editor. Title: Pyrazole : preparation and uses / Dilipkumar Pal (editor), Associate Professor, Department of Pharmaceutical Sciences, GURU GHASIDASH VISHWAVIDYALAYA (A Central University), Koni, Bilashpur, India.
Description: New York : Nova Science Publishers, [2020] | Series: Chemistry research and applications | Includes bibliographical references and index. | Summary: "This book has comprehensively reviewed the latest information on pyrazoles, their preparations and uses. It provides extended ideas on pyrazole and its derivatives including their synthesis, chemistry, structure activity relationship (SAR) and therapeutic applications. The health promoting properties of these pyrazoles are discussed in this book with different therapeutic applications of pyrazole scaffold. Topics related to pyrazole and its analogues as potential anticancer, anti-angiogenesis, antiviral, antioxidative, anti-convulsive, anthelmintic, anti-inflammatory, antidiabetic agents are described in this book in detail. Furthermore, current status and future prospects of pyrazole moiety in drug discovery, importance of it in plant systems, its relevance in neurological drug discovery, its potency as herbicidal and antimicrobial agents have been enumerated through different chapters. In a summary, this book is a valuable resource for research scholars, academics, students, industrialists and subject experts working in the multidisciplinary fields like medicinal chemistry, synthetic chemistry, biochemistry, pharmacology, natural product chemistry and other related areas in the field of pyrazole derivatives drug discovery and research"-- Provided by publisher. Identifiers: LCCN 2020031403 (print) | LCCN 2020031404 (ebook) | ISBN 9781536182507 (hardcover) | ISBN 9781536183801 (adobe pdf)
Subjects: LCSH: Pyrazoles. Classification: LCC QD401 .P9918 2020 (print) | LCC QD401 (ebook) | DDC 547/.593--dc23
LC record available at https://lccn.loc.gov/2020031403
LC ebook record available at https://lccn.loc.gov/2020031404

Published by Nova Science Publishers, Inc. † New York

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In: Pyrazole: Preparation and Uses
Editor: Dilipkumar Pal

ISBN: 978-1-53618-250-7

Chapter 10

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 α-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 β/γ secretase inhibition; newer pyrazole derivative as 2-

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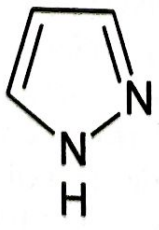
MBAPA showed inhibition of microglial formation, so in a collective manner, these data reflected the importance of pyrazole derivatives to act against convulsion, seizure, Parkinson, Alzheimer and deposition of amyloid-β peptide and microtubule-binding tau protein.

Keywords: Pyrazole, Alzheimer disease, Tau protein, β-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 C3H4N2, the molecular weight of pyrazole is 68.08 g/mol, partition co-efficient, LogP, and XLogP3 value are 0.26, 0.25 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 $Å^2$ [3,4], the boiling and melting points of pyrazole are 187°C and 67°C, acid dissociation co-efficient at 25°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, 7.44×10^{-24} cc, respectively [5-7]. The melting point of, hydrochloride salt, nitrate, and oxalate of pyrazole showed 234°C,148°C, 192°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.