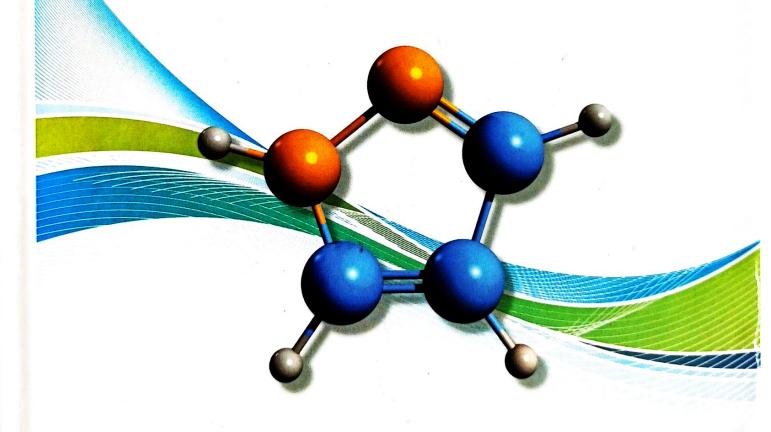
# Pyrazole

Preparation and Uses



Dilipkumar Pal Editor



# Copyright © 2020 by Nova Science Publishers, Inc.

All rights reserved. No part of this book may be reproduced, stored in a retrieval system or transmitted in any form or by any means: electronic, electrostatic, magnetic, tape, mechanical photocopying, recording or otherwise without the written permission of the Publisher.

We have partnered with Copyright Clearance Center to make it easy for you to obtain permissions to reuse content from this publication. Simply navigate to this publication's page on Nova's website and locate the "Get Permission" button below the title description. This button is linked directly to the title's permission page on copyright.com. Alternatively, you can visit copyright.com and search by title, ISBN, or ISSN.

For further questions about using the service on copyright.com, please contact:

Copyright Clearance Center

Phone: +1-(978) 750-8400

Fax: +1-(978) 750-4470

E-mail: info@copyright.com.

### NOTICE TO THE READER

The Publisher has taken reasonable care in the preparation of this book, but makes no expressed or implied warranty of any kind and assumes no responsibility for any errors or omissions. No liability is assumed for incidental or consequential damages in connection with or arising out of information contained in this book. The Publisher shall not be liable for any special, consequential, or exemplary damages resulting, in whole or in part, from the readers' use of, or reliance upon, this material. Any parts of this book based on government reports are so indicated and copyright is claimed for those parts to the extent applicable to compilations of such works.

Independent verification should be sought for any data, advice or recommendations contained in this book. In addition, no responsibility is assumed by the Publisher for any injury and/or damage to persons or property arising from any methods, products, instructions, ideas or otherwise contained in this publication.

This publication is designed to provide accurate and authoritative information with regard to the subject matter covered herein. It is sold with the clear understanding that the Publisher is not engaged in rendering legal or any other professional services. If legal or any other expert assistance is required, the services of a competent person should be sought. FROM A DECLARATION OF PARTICIPANTS JOINTLY ADOPTED BY A COMMITTEE OF THE AMERICAN BAR ASSOCIATION AND A COMMITTEE OF PUBLISHERS.

Additional color graphics may be available in the e-book version of this book.

## 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

# **CONTENTS**

Preface		
Chapter 1	Current Status of Pyrazolo Moiety in Drug Discovery (Synthetic vs. Natural)	xi
	Chandi Charan Kandar and D <mark>ilipkumar Pal</mark>	1
Chapter 2	Synthesis and Therapeutic Applications of Pyrazole Scaffold Roli Mishra and Satyendra Mishra	27
Chapter 3	Pyrazole Based Ligands: Versatile Building Blocks Preeti Oswal, Aayushi Arora, Gyandshwar Kumar Rao, Sushil Kumar, Arun Kumar and Ajai Kumar Singh	49
Chapter 4	Pyrazole and Its Analogues as	
	Potential Anti-Angiogenesis Agents  Dilipkumar Pal and Souvik Mukherjee	91
Chapter 5	Green Chemistry Methods in Pyrazole Synthesis  Maja Molnar and Mario Komar	107
Chapter 6	Pyrazoles as Antiviral Agents  Jeanne Fichez and Patricia Busca	145
Chapter 7	Recent Research Advances in Aqueous Phase Synthesis of Pyrazoles Venkata Durga Nageswar Yadavalli, Nelson L. C. Domingues, Ramesh Katla and Rakhi Katla	179
Chapter 8	Pyrazole Moiety as a Source of Natural Products Dilipkumar Pal, Souvik Mukherjee, Om Prakash Panda, Sitansu Sekhar Nanda and Dong Kee Yi	195

Chapter 9	Pyrazole and Its Derivatives, Preparation, 57 He and Uses as Antioxidative Agent Supriyo Saha and Dilipkumar Pal	211
Chapter 10	Role of Pyrazole Ring in Neurological Drug Discovery Supriyo Saha and Dilipkumar Pal	245
Chapter 11	Pyrano[2,3-c]pyrazole Derivatives: Synthesis and Application Devendra Dewangan, Trimurti L. Lambat, Sami H. Mahmood and Subhash Banerjee	ns 265
Chapter 12	Pyrazole and Pyrazole Derivatives: A Versatile Platform in Anti-Convulsive Drug Discovery Dilipkumar Pal, Suvadeep Mal and Souvik Mukherjee	301
Chapter 13	Pyrazole Affixed Heterocycles: Synthesis and Their Herbicidal Activity Shridevi Doddamani and Srikantamurthy Ningaiah	323
Chapter 14	Development in Chemistry and Synthesis of Pyrazole Derivatives as Potential Anticancer Agents Ashish D. Patel, Vinod Kumar Gurjar and Dilipkumar Pal	347
Chapter 15	Recent Advances in Chemistry and Synthesis of Pyrazole Derivatives as Potential Promising Antimicrobial Agents Vinod Kumar Gurjar, Dilipkumar Pal and Ashish D. Patel	377
Chapter 16	Scaffold of Pyrazole Derivatives for Enzyme Inhibition Neetu Sachan, Phool Chandra and Dilipkumar Pal	411
Chapter 17	Role of Pyrazolo Ring in Plant System  Chandi Charan Kandar	447
Chapter 18	Pyrazole and Its Derivatives: Preparation, SAR and Anthelmintic Activity  Arindam Maity	471
Chapter 19	Pyrazole and Its Derivatives, Preparation, SAR and Anti-Inflammatory Activity Kiran Gangarapu, Gouthami Thumma, Niveditha Nakka, Krishna Prasad Devarakonda, Dilipkumar Pal and Arivarasan Vishnu Kirthi	485
Chapter 20	Pyrazole and Its Derivatives as Anti-Diabetic Agents  Dilipkumar Pal and Khushboo Pai	505

	Contents	ix
Chapter 21	Future Prospects of Pyrazole Ring in Drug Discovery	523
	Sajal Kumar Jha and Tanmoy Guria	
About the Editor		533
List of Contributors		535
		539
Index		

In: Pyrazole: Preparation and Uses ISBN: 978-1-53618-250-7

Editor: Dilipkumar Pal © 2020 Nova Science Publishers, Inc.

Chapter 1

# CURRENT STATUS OF PYRAZOLO MOIETY IN DRUG DISCOVERY (SYNTHETIC VS. NATURAL)

### Chandi Charan Kandar<sup>1,\*</sup> and Dilipkumar Pal<sup>2</sup>

<sup>1</sup>Department of Pharmaceutical Chemistry, Institute of Pharmacy, Jalpaiguri,
Government of West Bengal, West Bengal, India

<sup>2</sup>Department of Pharmaceutical Sciences, Guru Ghasidas Vishwavidyalaya
(A Central University), Bilaspur, Chhattisgarh, India

#### **ABSTRACT**

Drug discovery is an ongoing process to search the best formulation that relieves from illness using a small amount of drug molecule causing fewer hazards in the administration of drug formulation and to overcome side effects of synthetic compounds. Phytomedicine or natural medicine is the science, art, and exploration of using botanical remedies to treat illness. Herbalists believe that the body is a self-healing organism and that herbs should be used to enhance wellness, not simply relieve symptoms or treat disease. The pharmaceutical industry specialized in as well as relied on natural products aimed at optimizing the quality of herbal drugs by standardization and scientific basic research. This development was paralleled by an intensified evaluation of herbal drugs and a search for the active principles of phytopreparations. Besides this, nowadays pyrazole compounds have taken an important role in the platform of new drug discovery. Due to a lack of abundance of pyrazolo ring containing compounds in the natural system, scientists are trying to develop various synthetic compounds by addition or fusion of pyrazole ring to the existing molecule to explore and develop a new class of drug having an alteration of bioactivity as well as a potent drug. The scientists throughout the world have prepared various pyrazolo-compounds that are useful in psychiatric disorder, anxiety, depression and also as anthelmintic. The main objective of this chapter is to

<sup>\*</sup>Corresponding Author's Email: cckandar@rediffmail.com.

highlight the present scenario of biologically active synthetic pyrazole derivatives and natural products containing pyrazole ring obtained from various fields and their comparison.

Keywords: drug discovery, synthetic pyrazolo compounds, natural products

### INTRODUCTION

The new drug development program for the different compounds is initiated because there is a disease or clinical condition without suitable pharmacotherapeutic products available. New drug development can proceed along various pathways for different compounds. Drug invention programs result in the synthesis of compounds that are tested in assays and animal models. The drug development process involves rigorous testing and optimization of selected compounds to identify the most effective drug. This testing is done in cells (*in vitro*) and animals (*in vivo*) to study the metabolism and to produce a product that is safe and has passed all regulatory requirements.

Among the organic compounds, the heterocyclic moiety is abundant in the different pharmacological classes of drug molecules. As a consequence, the heterocyclic compound has become important as well as the unparalleled class of compounds. The plant is the source of phytoconstituents containing various heterocyclic rings. Therefore, heterocyclic compounds like as pyrrole, pyrazole, pyridine, etc. are available in nature and take part in metabolism process to produce different secondary metabolites of plants which are regarded as drugs of various kinds such as alkaloids, glycosides, tannins, vitamins, hormones, minerals, antibiotics, etc. [1, 2, 3].

Amongst naturally occurring heterocyclic compounds, most of the drugs and natural products such as narcotic analgesic, anti-psychotic, anti-depressant, anti-anxiety, CNS stimulants, cardiovascular drugs, gastrointestinal agents and antihistaminics, etc. contain heterocycles having one or more nitrogen atoms. As a result, such compounds have taken an important place in the field of natural science and widely distributed in natural products like as alkaloids, glycosides, hormones, antibiotics, and vitamins, etc. [4, 5].

The scientists are attempting to prepare a new drug molecule that contains a pyrazole ring structure in the center for a long time. It is published in different journals that pyrazole compounds have created a new opportunity in the field agrochemical industry to manufacture herbicides or pesticides, pharmaceutical industry to synthesize new drug molecules as well as chemical industry to prepare pyrazole based chemicals [6, 7].

Pyrazole or pyrazole derivatives have created immense importance in the synthetic field of medicinal chemistry. The development in the synthesis of pyrazole having compounds by chemical architects have been generated a lot of compounds which show different biological activities in various systems like as antimicrobials, against hormone-related disease, diabetes, CNS activities i.e., analgesic, antipyretic, anti-inflammatory,

highlight the present scenario of biologically active synthetic pyrazole derivatives and natural products containing pyrazole ring obtained from various fields and their comparison.

Keywords: drug discovery, synthetic pyrazolo compounds, natural products

### Introduction

The new drug development program for the different compounds is initiated because there is a disease or clinical condition without suitable pharmacotherapeutic products available. New drug development can proceed along various pathways for different compounds. Drug invention programs result in the synthesis of compounds that are tested in assays and animal models. The drug development process involves rigorous testing and optimization of selected compounds to identify the most effective drug. This testing is done in cells (*in vitro*) and animals (*in vivo*) to study the metabolism and to produce a product that is safe and has passed all regulatory requirements.

Among the organic compounds, the heterocyclic moiety is abundant in the different pharmacological classes of drug molecules. As a consequence, the heterocyclic compound has become important as well as the unparalleled class of compounds. The plant is the source of phytoconstituents containing various heterocyclic rings. Therefore, heterocyclic compounds like as pyrrole, pyrazole, pyridine, etc. are available in nature and take part in metabolism process to produce different secondary metabolites of plants which are regarded as drugs of various kinds such as alkaloids, glycosides, tannins, vitamins, hormones, minerals, antibiotics, etc. [1, 2, 3].

Amongst naturally occurring heterocyclic compounds, most of the drugs and natural products such as narcotic analgesic, anti-psychotic, anti-depressant, anti-anxiety, CNS stimulants, cardiovascular drugs, gastrointestinal agents and antihistaminics, etc. contain heterocycles having one or more nitrogen atoms. As a result, such compounds have taken an important place in the field of natural science and widely distributed in natural products like as alkaloids, glycosides, hormones, antibiotics, and vitamins, etc. [4, 5].

The scientists are attempting to prepare a new drug molecule that contains a pyrazole ring structure in the center for a long time. It is published in different journals that pyrazole compounds have created a new opportunity in the field agrochemical industry to manufacture herbicides or pesticides, pharmaceutical industry to synthesize new drug molecules as well as chemical industry to prepare pyrazole based chemicals [6, 7].

Pyrazole or pyrazole derivatives have created immense importance in the synthetic field of medicinal chemistry. The development in the synthesis of pyrazole having compounds by chemical architects have been generated a lot of compounds which show different biological activities in various systems like as antimicrobials, against hormone-related disease, diabetes, CNS activities i.e., analgesic, antipyretic, anti-inflammatory,