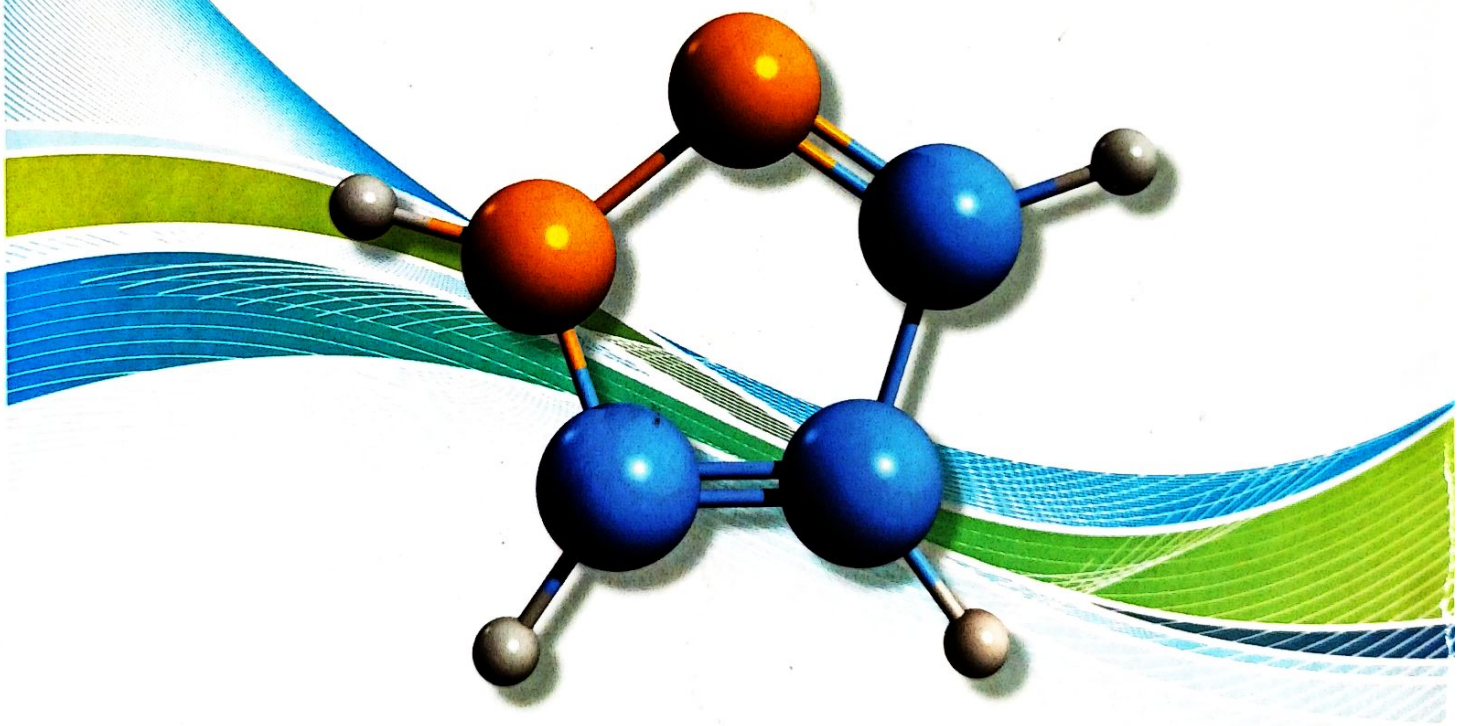
CHEMISTRY RESEARCH AND APPLICATIONS

Pyrazole

Preparation and Uses



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Chapter 16

SCAFFOLD OF PYRAZOLE DERIVATIVES FOR ENZYME INHIBITION

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ABSTRACT

Pyrazole, a five membered heterocyclic ring containing two nitrogen atoms, has unique place in medicinal chemistry. It is an indispensable core scaffold present in many natural (1-pyrazolyl-alanine) and synthetic biologically important compounds. In 1883, first time Ludwig Knorr coined the term 'Pyrazole' in the field of heterocyclic chemistry. Pyrazole derivatives have displayed broad spectrum of pharmacological and biological activities such as anti-microbial, anti-fungal, antitumor, anti-tubercular, antiviral, anti-inflammatory, antidepressant, anticonvulsant, antihyperglycemic, cholecystokinin-1 receptor antagonist, estrogen receptor (ER) ligand activity, and enzymes inhibitory activities. This chapter features an important synthesis of pyrazole derivatives as the enzyme inhibitors with an emphasis on recent developments. Enzyme inhibition includes carbonic anhydrase, acetylcholine esterase, Plasmodium falciparum dihydroorotate dehydrogenase, cyclooxygenase, tyrosinase, α-glucosidase, etc.

Keywords: pyrazole derivatives, scaffold, enzyme inhibitors

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INTRODUCTION

Pyrazole, a five membered heterocyclic ring containing two nitrogen atoms, has unique place in medicinal chemistry [1].

Pyrazole

It is an indispensable core scaffold present in many natural (1-pyrazolyl-alanine) and synthetic biologically important compounds. In 1883, first time Ludwig Knorr coined the term 'Pyrazole' in the field of heterocyclic chemistry [2]. Pyrazole derivatives have displayed broad spectrum of pharmacological and biological activities such as anti-microbial, anti-fungal, antitumor, anti-tubercular, antiviral, anti-inflammatory, antidepressant, anticonvulsant, antihyperglycemic, cholecystokinin-1 receptor antagonist, estrogen receptor (ER) ligand activity, and enzymes inhibitory activities [3].

In this chapter authors presented the important synthesis of pyrazole derivatives as the enzyme inhibitors with an emphasis on recent developments. Enzyme inhibition includes carbonic anhydrase, acetylcholine esterase, Plasmodium falciparum dihydroorotate dehydrogenase, cyclooxygenase, tyrosinase, α-glucosidase, phospholipase A-2 and serine hydrolase.

CARBONIC ANHYDRASE INHIBITORS

Two genetically distinguished human carbonic anhydrase (hCA) isoforms designated hCA I, and II isoenzymes are present in RBC cells. Both isoforms exhibit 60% sequence homology, several particular activities and several immunologic specificities [4]. While, CA II isoform is expressed in an extensive diversity of tissues and cells, CA I isoform has a more restricted cellular expression. Also, hCA II isoform can produce NO molecule, owing to the structural similarity between nitrite and bicarbonate [5]. The hCA II isoform is a zinc ion (Zn^{2+}) and catalysis reversible interconversion of carbon dioxide (CO_2) and bicarbonate (HCO_3^-). It is found in platelets, vascular smooth muscle, and erythrocytes. Also, hCA II isoenzyme contributes to vascular adjustment and could be a source of good hCA II-mediated generation of nitric oxide (NO) from nitrite [6]. Since nitrite exhibits similar to sp^2 geometry as HCO_3^-, it is hypothesized that hCA II isoform acts as a nitrous anhydrase factor, wherein nitrite binds hCA II active site and is dehydrated, analogously to HCO_3^- [7, 8]. CA isoforms are zinc-containing metallocatalists that perform the