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Biological Significance of Pyrazolone: A Review

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ABSTRACT:

Pyrazolone is a five membered lactum ring containing two Nitrogens and one ketonic group in its structure. During the discovery of pyrazolone, they were only known as NSAIDs but in recent time they play versatile role in several complications like cerebral ischaemia and cardiovascular diseases. The chemistry of pyrazolone has gained increasing attention due to its diverse pharmacological properties such as cytotoxic, anti-inflammatory, antimicrobial, antioxidant, antifungal, antiviral, oral hypoglycaemic activity, etc. Pyrazolones are believed to be involved in various biochemical and physiological reactions and thus scientific research programs are continuously pouring in with respect to improvised synthetic techniques to prepare numerous pyrazolone derivatives. From a last decade a lot of work is going on the pyrazolone nucleus. Scientists have developed large number of new compounds related to this moiety and screened them for their different pharmacological activities to get a molecule of desired pharmacological activity. Although earlier many of pyrazolone derivatives were associated with adverse effect such as agranulocytosis, skin rashes and blood dyscariasis, etc. that may have haulted peer progress for sometime but peer extensive and versatile profile have made the pyrazolones favorites for newer drug development. Keeping in view the increasing importance of these derivatives, a need to review the progress regarding pyrazolone was felt.

KEYWORDS: Pyrazolone, Cytotoxic, Anti-inflammatory, Hypoglycaemic, SARS.

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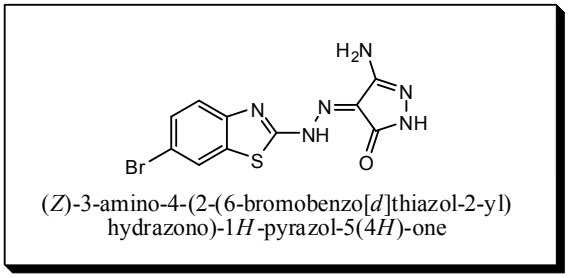
1. INTRODUCTION:

Heterocyclic compounds are acquiring more importance in recent years because of broad pharmacological activities. Pyrazolone have a particular value due to both their broad spectrum of biological activity and their wide ranging utility as synthetic tools in the design of various bioactive molecules. Pyrazolone is a five membered lactum ring containing two Nitrogens and one ketonic group in its structure. The chemistry of pyrazolone was started by Knorr in 1883 and reported the first pyrazolone derivative[1]. Antipyrine was the first pyrazolone derivative for clinical use and was synthesized in 1883[2]. It was used as the first agent to reduce fever and also for arthritis. Many other NSAIDs like phenylbutazone, oxyphenbutazone, aminophenazone, propyphenazone, etc. contains pyrazolone as the basic nucleus and widely used as analgesic, antipyretic and anti-inflammatory drugs. Although clinical use of pyrazolones is surrounded by controversies because of their association with serious side effects like gastrointenstinal irritation, ulceration,[3] etc. but their benefits and wide range of clinical applications have kept the interest of research community alive.

2. PHARMACOLOGICAL ACTIVITIES OF PYRAZOLONE DERIVATIVES:

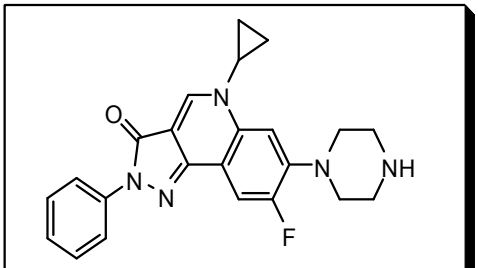
2.1 CYTOTOXIC ACTIVITY:

- **Kumar Siva**[4] ***et al*** synthesized a series of 5-amino-4-[2-(6-bromo-1,3-benzothiazol-2-yl)hydrazinylidene]-2,4-dihydro-3H-pyrazol-3-one derivatives and were screened for their cytotoxic activity. These compounds had shown prominent cytotoxic activity.



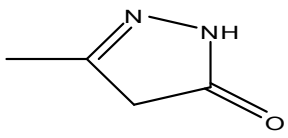
(*Z*)-3-amino-4-(2-(6-bromobenzo[*d*]thiazol-2-yl) hydrazono)-1*H*-pyrazol-5(4*H*)-one

- **Devnath H.P.**[5] ***et al*** synthesized some pyrazolone derivatives from ciprofloxacin and were evaluated for their cytotoxic activity and it was found that these compounds had shown potential cytotoxic activity against brine shrimp nauplii than ciprofloxacin**.**



5-Cyclopropyl-8-fluoro-2-phenyl-7-piperazin-1 -yl-2,5-dihydro-pyrazolo [4,3-c]quinolin-3-one

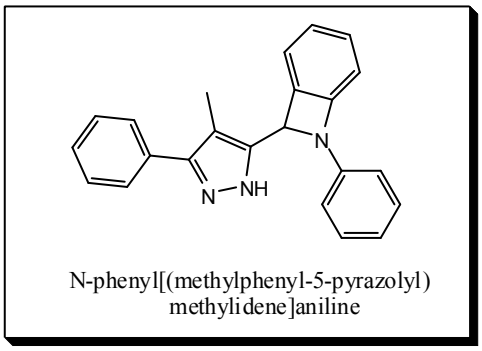
- **Khan Rahat** [6] ***et al*** synthesized brominated 5-methyl-2,4-dihydropyrazol-3-one and its derivatives. All of these derivatives had shown significant cytotoxic activity.



5-methyl-2,4-dihydropyrazol-3-one

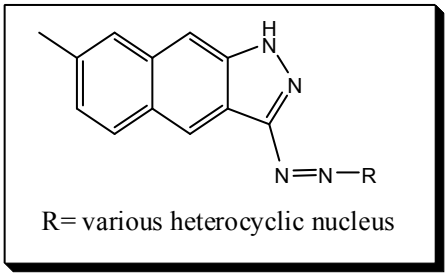
2.2 ANTIMICROBIAL ACTIVITY:

- **Sunitha S.**[7] ***et al*** synthesized a series of N-phenyl[(methylphenyl-5-pyrazolyl)methylidene]aniline compounds. These compounds were screened for their *in vitro* antimicrobial activity against various gram +ve and gram –ve bacteria and they had shown prominent antimicrobial activity.



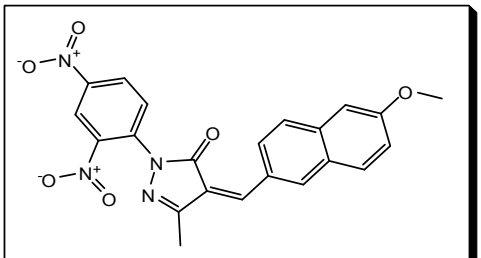
N-phenyl[(methylphenyl-5-pyrazolyl) methylidene]aniline

- **Thakor S.F.**[8] ***et al*** synthesized 3-Amino-6-methyl-1*H*-pyrazolo[3,4-*b*]quinoline. These compounds were screened for their antibacterial activity. These compounds had shown significant antibacterial activity.

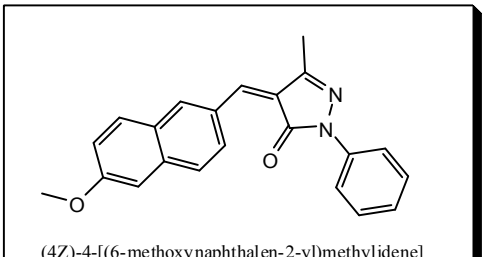


R= various heterocyclic nucleus

- **Isloor A.M.**[9] ***et al*** synthesized (4Z)-2-(2,4-dinitrophenyl)-4-[(6-methoxynaphthalen-2-yl)methylidene]-5-methyl-2,4-dihydro-3H-pyrazol-3-one and (4Z)-4-[(6-methoxynaphthalen-2-yl)methylidene]-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one and were screened for their antimicrobial activity. These compounds had shown potent antimicrobial activity.



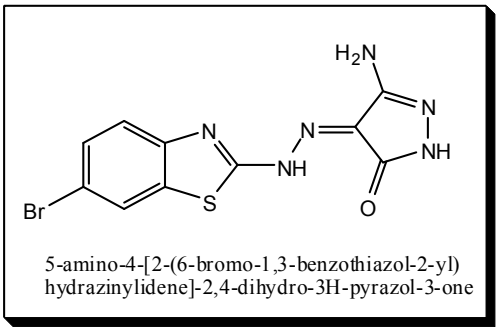
(4Z)-2-(2,4-dinitrophenyl)-4-[(6-methoxynaphthalen-2-yl) methylidene]-5-methyl-2,4-dihydro-3H-pyrazol-3-one



(4Z)-4-[(6-methoxynaphthalen-2-yl)methylidene] -5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one

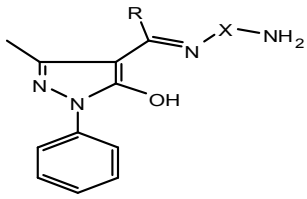
2.3 ANTIOXIDANT ACTIVITY:

- **Kumar Siva**[10] ***et al*** synthesized 5-amino-4-[2-(6-bromo-1,3-benzothiazol-2-yl) hydrazinylidene]-2,4-dihydro-3H–pyrazol-3-one derivatives and were screened for their antioxidant activity. These compounds had shown good antioxidant activity.



5-amino-4-[2-(6-bromo-1,3-benzothiazol-2-yl) hydrazinylidene]-2,4-dihydro-3H-pyrazol-3-one

- **Parmar N.**[11] ***et al*** synthesized some novel 5-pyrazolone based schiff bases by the condensation of 4-acylpyrazolone with different aromatic diamines and it was observed that all of the compounds showed significant antioxidant activity.

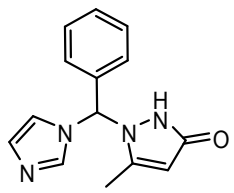


X=-C_6H_4 R=-CH_3, Ph

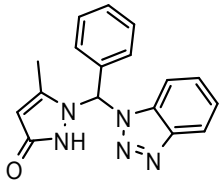
5-pyrazolone Schiff bases

2.4 ANTI-INFLAMMATORY ACTIVITY:

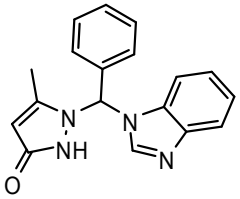
- **Soni J.P.**[12] ***et al*** synthesized series of pyrazolone derivatives with imidazol, benzimidazol and benzotriazol moiety and were screened for their anti-inflammatory activity and it was observed that the pyrazolone derivatives with benzimidazol had shown significant anti-inflammatory activity. .



1-[1H-imidazol-1-yl(phenyl)methyl]-5-methyl-1,2-dihydro-3H-pyrazol-3-one

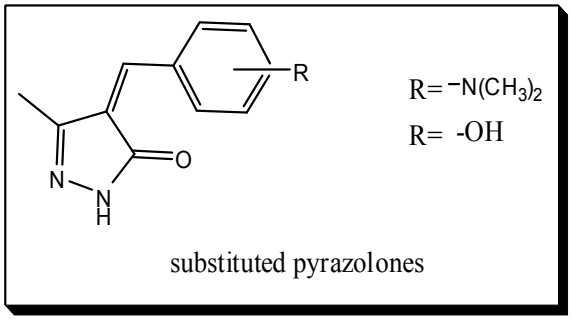


1-[1H-benzotriazol-1-yl(phenyl)methyl] -5-methyl-1,2-dihydro-3H-pyrazol-3-one



1-[1H-benzimidazol-1-yl(phenyl)methyl] -5-methyl-1,2-dihydro-3H-pyrazol-3-one

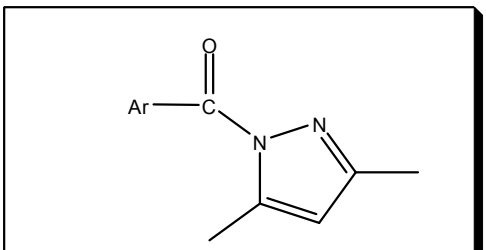
- **Mariappan G.**[13] ***et al*** synthesized 3-methyl-4-substitutedbenzylidene-pyrazol-5-one derivatives. These compounds were screened for their anti-inflammatory activity. These compounds had shown good anti-inflammatory activity.



substituted pyrazolones

2.5 ANALGESIC ACTIVITY:

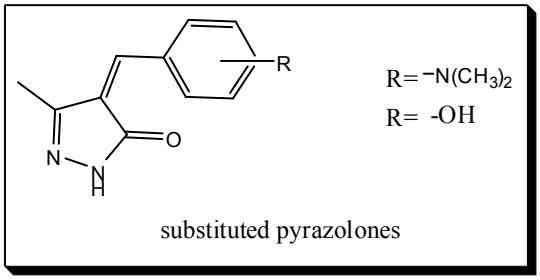
- **Amir M.**[14] ***et al*** synthesized 3 methyl pyrazol-5-one derivatives diclofenac, ibuprofen, flurbiprofen and it was found that the most of the compounds were screened for their analgesic activity. These compounds had shown potent analgesic activity.



Ar=Diclofenac, Ibuprofen, Flurbiprofen

3-methyl pyrazol-5-one derivatives

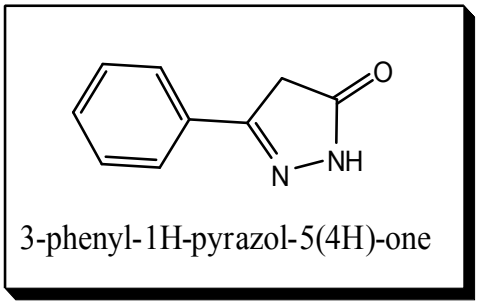
- **Mariappan G.**[15] ***et al*** synthesized 3-methyl-4-substitutedbenzylidene-pyrazol-5-one derivatives and these were screened for their analgesic activity. These compounds had shown prominent analgesic activity.



substituted pyrazolones

2.6 ANTIFUNGAL ACTIVITY:

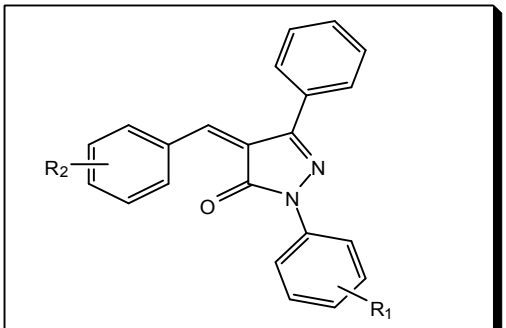
- **Mohmoud M.**[16] ***et al*** synthesized various pyrazolone derivatives which had shown fungicidal activity.



3-phenyl-1H-pyrazol-5(4H)-one

2.7 SARS-CORONAVIRUS 3C-LIKE PROTEASE INHIBITORS:

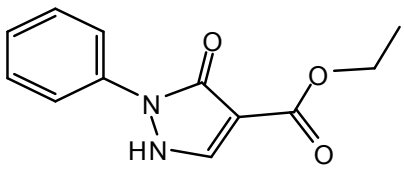
- **Liang P.H.** [17] ***et al*** synthesized series of pyrazolone compounds and evaluated by in vitro protease assay using fluorogenic substrate peptide. It was observed that several compounds showed potent inhibition against the 3C-Like protease and one of the inhibitors was also active against 3C protease.



pyrazolone derivatives

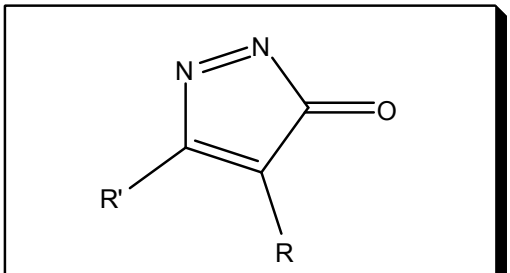
2.8 HYPOGLYCEMIC ACTIVITY:

- **Das**[18] ***et al*** synthesized Ethyl 2-phenyl-1H-pyrazol-3-one-4-carboxylate derivatives and were screened for their hypoglycemic activity. These compounds had shown potent hypoglycemic activity.



Ethyl-2-phenyl-1*H*-pyrazol-3-one
-4-carboxylate

- **Kees K.L.**[19] ***et al*** synthesized group of 4-(arylmethyl and heteroarylmethyl)-5-subsituted-3-pyrazolone derivatives and was evaluated for its antihyperglycaemic activity. It was observed that it showed significant antihyperglycaemic activity which is useful in NIDDM.

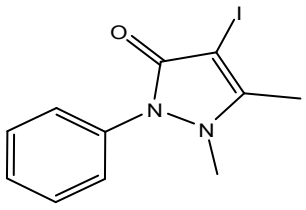


R= aryl/ heteroaryl rings

R'= substituted groups

2.9 ANTIVIRAL ACTIVITY:

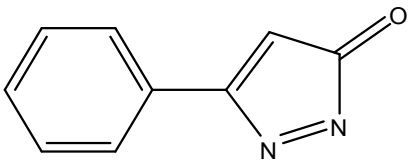
Evstropov A.N. [20] ***et al*** synthesized 4-iodo-1,5-dimethyl-2-phenyl-pyrazol-3-one (iodoantipyrine) and was evaluated its antiviral activity against different varieties of viruses. These derivatives had shown potent antiviral activity against tick borne encephalitis virus, hantavirus, HBV or HCV, coxsackie A and B enteroviruses, Rift valley fever viruses and influenza type A viruses.



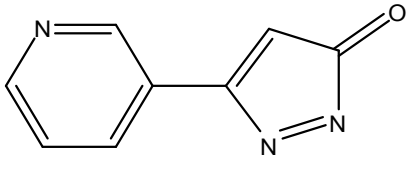
4-iodo-1,5-dimethyl-2-phenyl-pyrazol-3-one

2.10 CARDIOVASCULAR ACTIVITY:

Kuçukguze G.[21] ***et al*** synthesized a series of 3-phenyl or pyridyl-5-pyrazolone derivatives which was useful in improving cardiac contractibility.



3-phenyl-5-pyrazolone



3-pyridyl-5-pyrazolone

3. CONCLUSION:

For more than a century, heterocyclic compounds have constituted one of the largest area of research in organic chemistry. Pyrazolones are the versatile active heterocyclic which are of immense importance biologically and industrially. Pyrazolone nucleus is present as a core structural component in array of drug categories such as antimicrobial, antiviral, etc. This review reflects the contribution of pyrazolone heterocycle to the development of society from a biological point of view as well as to the understanding of life processes. This article may also enlighten the medicinal chemists who are aspiring to discover a versatile drug candidate for the benefit of mankind.

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