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Synthesis and Biological Significance of Pyrazolones: A Review

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***Abstract*— Heterocyclic compounds are acquiring more importance in recent years because of their pharmacological activities. Pyrazolones have a particular value due to 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 lactam ring, containing two nitrogen and one ketonic group in its structure. In addition, pyrazolones possess antimicrobial, antifungal, antimycobacterial, antibacterial, anti-inflammatory, antitumor, gastric secretion stimulatory, antidepressant and antifilarial activities. They also serve as precursors for dyes, pigments, pesticides and chelating agents, besides finding applications in the extraction and separation of various metal ions. The high therapeutic properties of the pyrazolone-related drugs have encouraged medicinal chemists to synthesize a large number of novel chemotherapeutic agents. Numerous methods for the synthesis of pyrazolone and also their various structure reactions offer enormous scope in the field of medicinal chemistry. This article aims to review the work reported, their chemistry and biological activities of pyrazolone during past years.**

Index Terms*— *Pyrazolone, Heterocyclic, Antibacterial, Antifungal and Antitumor.

I. INTRODUCTION

Since the last two decades, a rapid progress in synthetic organic chemistry is associated with a search for new compounds with desired properties. Such compounds are widely used in pharmaceutical industries. Among these, the heterocycles form the largest of the classical division of organic chemistry and are of immense biological and industrial importance. The majority of biologically active compounds are heterocycles, also applicable as additives and modifiers used in industries of cosmetics, photography, information storage and plastics. Heterocyclic compounds are also used in pharmacy and agriculture.

Analysis of scientific papers in the last two decades revealed that there is a general trend in research for new drugs involving modification of existing biologically active matrices and molecular design of the structures of compounds. In the recent years much attention has been focused on the synthesis of heterocycles containing nitrogen atom because of their biological and medicinal importance including ontological research.

Pyrazolones is a five member heterocyclic compound containing one ketonic group and two nitrogen atoms adjacent to each other. In 1883, Knorr et al. gave the generic name pyrazole to above class of the compounds, which is a five member unsaturated ring compound with two adjacent nitrogen atoms. Antipyrine was the first pyrazolone derivative for clinical use and was synthesized in 1883. It was used as the first agent to reduce fever and also for arthritis.

Pyrazolone derivatives are an important class of heterocyclic compounds that occur in many drugs and synthetic products. These compounds exhibit remarkable analgesic, antitubercular, antifungal, antibacterial, anti-inflammatory, antioxidant and antitumor activities. Due to their easier preparation and rich biological activity, pyrazolone framework plays an essential role and represents an interesting template for combinatorial and medicinal chemistry.

II. SYNTHESIS OF PYRAZOLONE DERIVATIVES

A. By Refluxing Methods

Sujatha et al. reported the preparation of 4,4'-(arylmethylene)bis(1H-pyrazol-5-ols) by tandem Knoevenagel-Michael reaction of two equivalents of 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one with various aromatic aldehydes catalyzed by ceric ammonium nitrate (CAN) in water.

Liu et al. reported a novel solid-state reversible fluorescence photo switching system (FPS) based on photochromism of photochromic pyrazolones developed by employing phosphor Sr2P2O7 co-doped with europium ion and chlorine ion. Baciu-Atudosie et al. reported a simple one-pot approach for the synthesis of new 5-substituted pyrazolones containing a phenothiazine unit by reaction of N-chloroacetyl compound, ethyl acetoacetate with hydrazine hydrate.

Kumar et al. reported the synthesis of 1-(4-methylcoumarinyl-7-oxyacetyl)-3,5-dimethyl-4-(arylazo)pyrazoles by reaction of 1,3-diketo-1,3-dimethyl-2-(arylazo)propane and 4-methylcoumarinyl-7-oxyacetic acid hydrazide in glacial acetic acid refluxed for 10 hours.

Mosaddegh et al. reported the synthesis of 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) performed effectively by the reaction of aryl aldehydes and 1-phenyl-3-methyl-5-pyrazolone in the presence of a catalytic amount of Ce(SO4)2.4H2O as reusable and environmentally friendly catalyst in water/ethanol solution. The method has advantages of high yields, short reaction time, simple work-up and reusability of catalyst.

Shamsuzzaman et al. reported a convenient synthesis of nano steroidal pyrazolones by adding cyanoacetohydrazide in equimolar ratio to a solution of steroidal ketones in acetic acid under refluxing for 7 hours. Laufersweiler et al. reported novel substituted [5,5]-bicyclic pyrazolones prepared in multisteps involving reaction of t-Boc and benzyl carbazate followed by ring closure via intramolecular cyclocondensation.

B. By Microwave Irradiation

Tu et al. synthesized C-tethered bispyrazol-5-ols via multicomponent domino reactions of acetylenedicarboxylates, phenylhydrazine and aromatic aldehydes under microwave irradiation. Sivakumar et al. reported an efficient synthesis of Mannich base of 5-methyl-2-[(2-oxo-2H-chromen-3-yl)carbonyl]-2,4-dihydro-3H-pyrazol-3-one using multicomponent approach with microwave techniques showing shorter reaction time and good yield.

Antre et al. reported various 4-(2-amino-6-(substituted)pyrimidin-4-yl)-3-methyl-1-(substituted)-1H-pyrazol-5(4H)-one derivatives and their Schiff bases synthesized by microwave assisted method. Zang et al. reported synthesis of 4-[(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)-phenyl-methyl]-5-methyl-2-phenyl-1,2-dihydro-pyrazol-3-ones using ionic liquid [HMIM]HSO4 catalyst under ultrasonic irradiation.

C. Green Synthesis Methods

Ghosh et al. reported a glacial acetic acid catalyzed reaction for the combinatorial synthesis of highly functionalized benzylpyrazolyl coumarin prepared by a green one-pot four-component reaction between aryl hydrazine, ethyl acetoacetate, aromatic aldehydes and 4-hydroxycoumarin in water medium under refluxing conditions.

III. PHARMACOLOGICAL PROPERTIES

A. Antibacterial Activity

Pyrazolone derivatives exhibit significant antibacterial activity. (4Z)-4-(1H-indol-3-ylmethylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one shows anti-bacterial activity. Methyl (5-oxo-1-phenyl-2,5-dihydro-1H-pyrazol-3-yl)acetate also possesses antibacterial activity. 3-amino-5-hydroxy-4-phenyl-1H-pyrazole-1-carboxamide exhibits antibacterial properties. 4-[(3-chloro-2-oxoazetidin-1-yl)methyl]-5-methyl-2,4-dihydro-3H-pyrazol-3-one demonstrates antibacterial activity against multiple strains.

B. Anticancer and Antitumor Activity

Several pyrazolone derivatives exhibit anticancer activity. 2-phenyl-2,10-dihydro-3H-[1]benzoxepino[3,4-c]pyrazol-3-one shows anticancer and anti-mycobacterial activity. (3bR,6S,7aR)-2,7a-disubstituted-6-methoxy-octahydro-3H-pyrano[3',2':3,4]cyclopenta[1,2-c]pyrazol-3-one shows anticancer activity. (4Z)-4-{1-[(2E)-2-(2-hydroxybenzylidene)hydrazinyl]propylidene}-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one shows anticancer activity.

C. Anti-inflammatory and Analgesic Activity

Pyrazolones are pharmacophores displaying activities such as analgesic and antipyretic (propylphenazone, phenazone, metamizole), anti-ischemic (edaravone), and anti-anxiolytic. (4Z)-4-[4-(dimethylamino)benzylidene]-5-methyl-2,4-dihydro-3H-pyrazol-3-one (PYZI) shows analgesic, anti-inflammatory, antipyretic activities. 4-[(substituted amino)methyl]-5-methyl-2-[(2-oxo-2H-chromen-3-yl)carbonyl]-2,4-dihydro-3H-pyrazol-3-one possesses anti-inflammatory, analgesic, antibacterial properties.

D. Antifungal and Antimycobacterial Activity

1-(4-substituted benzyl)-2-(4-substitutedphenyl)-4-(4-chlorobenzoyl)-5-methyl-1,2-dihydro-3H-pyrazol-3-one shows activity against Mycobacterium tuberculosis. (4E)-4-[2-(4-substituted phenyl)hydrazinylidene]-2-(furan-2-ylcarbonoimidoyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one exhibits antibacterial and antifungal activities.

IV. CONCLUSION

On the basis of literature survey, pyrazolone derivatives exhibit antimicrobial, anti-inflammatory, analgesic, anticancer and antitubercular activities. This review gives an overview of various synthetic routes used to form a biologically rich pyrazolone moiety. The possible improvements in the activity can be further achieved by slight modifications in the substituents on the basic pyrazolone nucleus. This article proves to be helpful for further research work on the bioactive pyrazolone ring and as an important tool for the development of better medicinal agents.

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REFERENCES

[1] Mariappan G, Saha BP, Sutharson L, Garg S, Pandey L, Kumar D and Ankit S: The diverse pharmacological importance of pyrazolone derivatives. Journal of Pharmacy Research 2010; 3:2856-2859.

[2] Micha L: Hypersensitivity to pyrazolones. Thorax 2000; 55:S72-S74.

[3] Arnost M, Pierce A, Haar E, Lauffer D, Madden J, Tanner K and Green J: 3-Aryl-4-(arylhydrazono)-1H-pyrazol-5-ones: Highly ligand efficient and potent inhibitors of GSK3beta. Bioorganic and Medicinal Chemistry Letters 2010; 20:1661-1664.

[4] Gursoy A, Demirayak S, Capan G, Erol K and Vural K: Synthesis and preliminary evaluation of new 5-pyrazolinone derivatives as analgesic agents. European Journal of Medicinal Chemistry 2000; 35:359-364.

[5] Castagnolo D, Manetti F, Radi M, Bechi B, Pagano M, Logu AD, Meleddu R, Saddi M and Botta M: Synthesis, biological evaluation, and SAR study of novel pyrazole analogues as inhibitors of Mycobacterium tuberculosis. Bioorganic and Medicinal Chemistry 2009; 17:5716-5721.

[6] Sujatha K, Shanthi G, Selvam NP, Manoharan S, Perumal PT and Rajendran M: Synthesis and antiviral activity of 4,4'-(arylmethylene)bis(1H-pyrazol-5-ols) against peste des petits ruminant virus (PPRV). Bioorganic & Medicinal Chemistry Letters 2009; 19:4501-4503.

[7] Ghosh PP, Pal G, Paul S and Das AR: Design and synthesis of benzylpyrazolyl coumarin derivatives via a four component reaction in water. Green Chemistry 2012; 14:2691-2698.

[8] Sivakumar KK, Rajasekaran A, Senthilkumar P and Wattamwar PP: Conventional and microwave assisted synthesis of pyrazolone Mannich bases. Bioorganic & Medicinal Chemistry Letters 2014; 24:2940-2944.

