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Review: Pharmacological Applications of Pyrazole Derivatives

[1]**A. U. Nerkar**, [2]**V.R. Bagul** [3]**R.S. Shinde**

[1]Assistant Professor, [2]Assistant Professor, [3]Assistant Professor

[1]Department of Chemistry,

[1]Mahatma Gandhi Vidyamandir's MSG Arts, Science and Commerce College, Malegaon Camp, Malegaon, Nashik, India
(Affiliated to Savitribai Phule Pune University, Pune)

[2]Department of Chemistry, MGV's, Arts, Science, and Commerce College, Surgana, Dist.-Nashik.

[3]Department of Chemistry, MGV's, Arts, Science, and Commerce College, Manmad, Dist.-Nashik.

Abstract: Pyrazole is a five-membered heterocycle with two neighboring nitrogen atoms, are the central structure of a variety of compounds with pharmacological applications. The widespread use of pyrazole cores in biologically active compounds has prompted researchers to seek more elegant and efficient methods for producing these heterocyclic leads. Anti-tuberculosis, anti-cancer, anticonvulsant, antiparkinson, antioxidant, and anti-inflammatory are only a few of the fascinating pharmacological applications of this molecule. The purpose of this review is to present an overview of the pyrazole moiety's various pharmacological applications.

Index Terms – Pyrazole, anticonvulsant, antioxidant, anti-inflammatory.

I. INTRODUCTION

Pyrazole has the formula $C_3H_3N_2H$ and is an organic compound. It's a heterocycle with a five-membered ring made up of three carbon atoms and two nitrogen atoms.[1] Pyrazoles are a group of molecules containing the ring C_3N_2 with adjacent nitrogen atoms.[2] Although they are rare in nature, they are characterized as alkaloids due to their nature and pharmacological effects on humans. Drugs containing the pyrazole moiety have been shown to display a wide range of biological activities, including immunosuppressive, anti-inflammatory, and anti-cancer activity. [3-6] The pyrazole fraction's pharmacological potential has been demonstrated in several publications in which researchers produced and tested pyrazoles against a variety of biological agents. Our important aim in this study is to find the most effective molecules for diverse pharmacological actions with the fewest side effects. Pyrazole is a pharmacologically active heterocyclic molecule that has been thoroughly documented in the literature. Due to various wide range of biological applications, these compounds are the target of several research investigations. A review of the literature indicated that pyrazole compounds have a wide range of pharmacological activities

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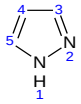
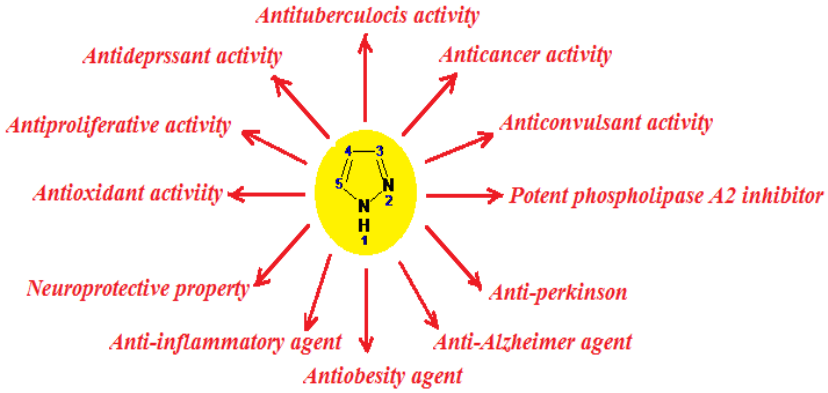


. Structure of Pyrazole

The pyrazole moiety represents a variety of Pharmacological applications



PHARMALOGICAL APPLICATIONS-

Antituberculosis activity-Nayak, Nagabhushana et al [7] developed a new series of isonicotinohydrazide based pyrazole derivatives. These derivatives showed antitubercular agents with MIC of < 64.9 µM which is much lower than the MIC of the first line antitubercular medication, ethambutol. The 3-chlorophenyl substituent at position-3 of the pyrazole ring (Fig.1) improved the antitubercular activity of the molecules.

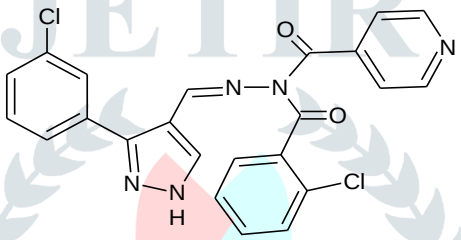


Figure 1.

Anticancer activity-

Fahmy, Hoda H. et al [8] synthesized a new series of polysubstituted pyrazole derivatives coupled to various nitrogenous heterocyclic ring systems at the C-4 position were produced. When compared to the conventional medicine sorafenib, the pyrimidine-2(1H)-thione derivative (Fig.2) demonstrated good anticancer action (GI_{50} MG-MID = 3.59 µM).

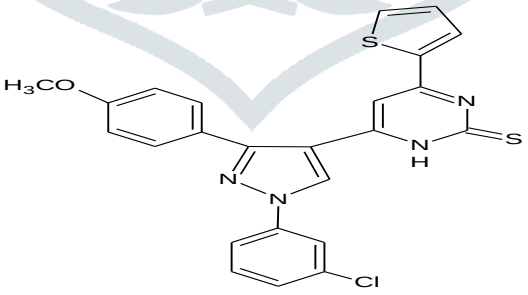


Figure 2.

Anticonvulsant activity-

Mohamed Abdel-Aziz et al [9] prepared a novel compound of pyrazole derivative (fig.3) shows the results of anticonvulsant activity are nearly close to phenobarbital sodium at a dose level of 30 mg kg^{-1}.

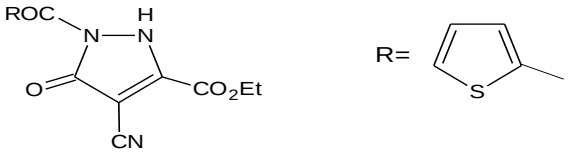


Figure 3.

Potent Phospholipase A2 Inhibitor-

Kumar et al. [10] observed the pyrazole with formamide at 1- position, methylthiophene at 2-position and Para methoxy phenyl at 5-position showed remarkable inhibition of phospholipase enzyme inhibition compound (Fig. 4.) which correlated with neuroprotective efficacy of the series.

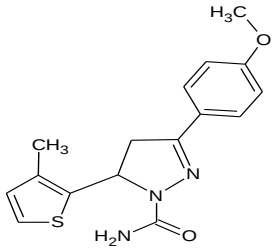


Figure 4.

Structure of 3-(4-methoxyphenyl)-5-(3-methylthiophene-2-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide

Anti-Parkinson Property-

Matsuo et al. [11] discovered that tricyclic pyrazole has antiparkinson properties. With phenyl/orthomethoxy phenyl at 1-position, para phenoxy butanoic acid at position- 3, and ortho chlorophenyl/phenyl group at position 5, two distinct pyrazoles were produced. Impaired motor coordination, alpha-synuclein accumulation, and dopamine level reduction produced by 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine were used to assess the structures (Fig.5).

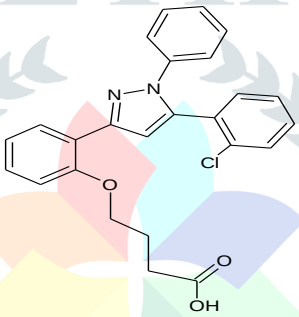


Figure 5.

Structure of Tricyclic pyrazole derivative

Anti-Alzheimer activity-

Guttiet al [12] produced a range of pyrazole and Spiro pyrazole derivative compounds. The compounds were tested against the enzyme's acetylcholinesterase and butyrylcholinesterase. The results showed that pyrazole with para chloro phenyl at 2-position and N-phenyl benzamide at 5-position, as well as 1,2 diaza spiro [4.5] dec-2-ene with N-(3-formyl phenyl) benzamide at 3-position and para chlorophenyl at 4-position, had greater inhibition against various forms of acetylcholine enzymes (Fig. 6), which was correlated with greater activity against Alzheimer's

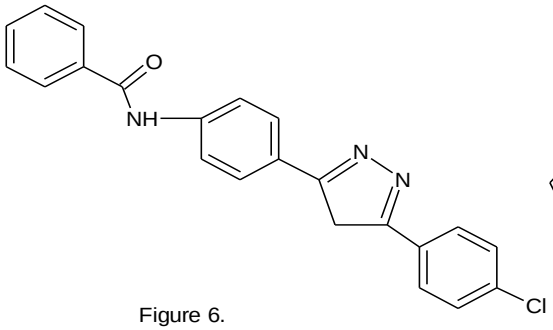


Figure 6.

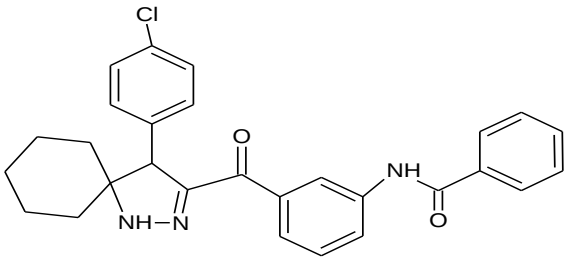


Figure 6a.

Structure of N-(3-(4-(-4chlorophenyl)-1,2-diazaspiro[4,5]dec-2-ene-3-carbonphenyl)bezamide

Antiobesity agents-

Alvarado et al [13] developed by the carboxamide series, hexadecyl pyrazole derivatives lacking chloro substituents, considerably reduced food consumption (7a and 7b). A variety of cannabinoid LH21 and Rimonabant-fatty acid amide analogues have been developed in the search for new antiobesity medicines.

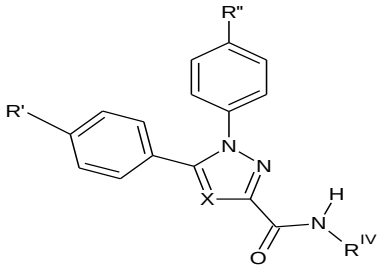


Figure 7.

7a, R',R"= H, X= C, R^{iv}= Hexadecyl
7b, R',R"= H, X= CMe, R^{iv}= Hexadecyl

Anti-inflammatory agent –

Masih, Anup, et al. [14] demonstrated the synthesis of new pyrazole derivatives as a strong anti-inflammatory drug in LPS-stimulated RAW 264.7 cells by suppressing NF-κB activation. Compound (Fig.8) was shown to be the most strong inhibitor of NF-κB transcription activity, a positive regulator of NF-κB activation (IκBα), and a considerable inhibitor of several proinflammatory cytokines. As a result, Compound (Fig.8) might be considered a possible lead for regulating the inflammatory response in SARS-CoV-2 infection.

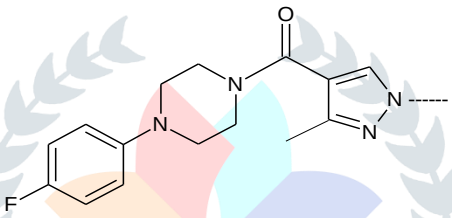


Figure 8.

Kumar, R. Surendra, et al [15] found that the compound (Fig.9) better activity against anti-inflammatory when compared with Diclofenac sodium.

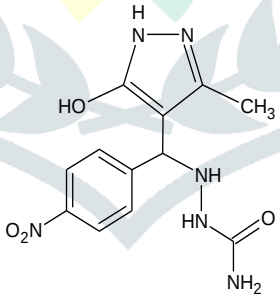


Figure 9.

Neuroprotective property-

McKenzie, Jordan A., et al. [16] reported by the novel pyrazolyl oxalamides in this study showed no cytotoxic effects and displayed moderate activity as inhibitors of neurotoxic secretions of microglia-like cells. Compound (Fig. 10) lay the groundwork for the development of more powerful neuroprotective medicines that act as inhibitors of microglia activation.

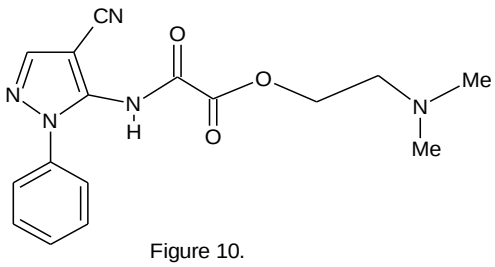


Figure 10.

Antioxidant activity-

Kaddouri, Yassine, et al [17] observed that the ligand (Fig.11) had the greatest antioxidant activity, with an of IC_{50} = 4.67 µg/mL, whereas the other compounds' IC_{50} values ranged from 20.56 to 45.32 µg/mL.

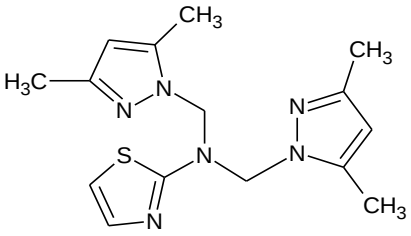


Figure 11.

Antiproliferative activity-

Ahmed Kamal et al. [18] have developed a new pyrazolo[1,5-a] series. The anticancer activity of pyrimidine-linked 2-aminobenzothizole conjugates was tested against five human cancer cell lines, including DU-145, using the MTT test. As a result, two compounds, (Fig.12 and Fig.13), with IC_{50} values of 3.16µM and 2.08µM, respectively, exhibit significant anticancer action.

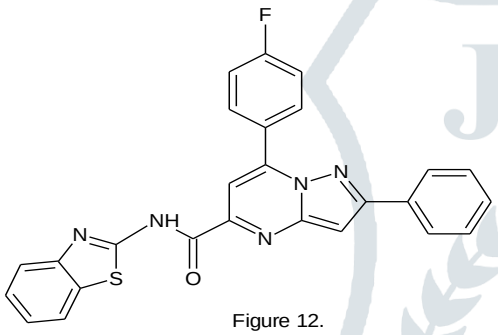


Figure 12.

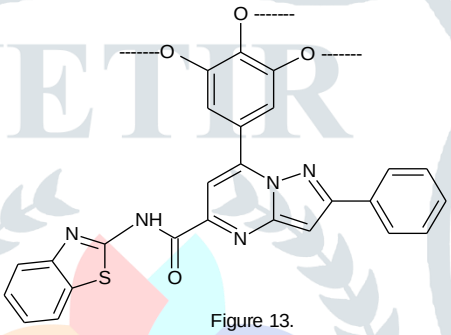


Figure 13.

Figure 12 and 13: Structures of pyrazolo[1,5-a] pyrimidine linked 2-aminobenzothizole conjugates showing antiproliferative activity.

Antidepressant activity-

Abdel-Aziz et al.,[19] described two synthetic pathways for the formation of diacylhydrazines, 5amino-1-substituted pyrazole-3,3,4-tricarbonitriles and oxadiazole, pyrazole derivatives, which showed antidepressant activity in the tail suspension behavioral despair test and anticonvulsant activity in mice when given pentylenetetrazol. At a dosage of 10 mg/kg, compounds 14a and 14b demonstrated good action when compared to imipramine [Figure14].

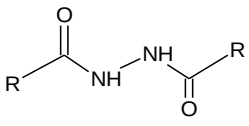
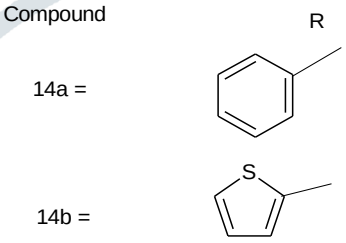


Figure 14.



RESULT AND DISCUSSION:

Pharmaceutical chemistry is devoted to the discovery and development of new agents for treating diseases.

Inorganic compound continues to be important in therapy, for example, as antacids, mineral supplements and radiopharmaceuticals, but organic molecules with increasingly specific pharmacological activities are clearly dominant. The objective of medicinal chemistry is design and production of compounds that can be use as medicine for the prevention, treatment and cure of humans or animal diseases. It is concerned with the invention,

discovery, design, identification of biologically active compounds, the study of their metabolism, interpretation of their mode of action at the molecular level, and the construction of the structure-activity relationship (SAR), the relationship between chemical structure and pharmacological activity for a series of compounds. An important aspect of medicinal chemistry has been to establish a relationship between chemical structure and

biological activity. The intellectual goal of researchers is to know the mode of action of drugs at the molecular level taken in the prospective sense. [20-23]

Previous research has demonstrated that altering the fundamental molecule's structural profile improves its pharmacological character, providing it with antibacterial, anticonvulsant, analgesic, anti-inflammatory, antiviral, antimalarial, and anti-cancer activities.

CONCLUSION:

Pyrazole is a heterocyclic system with five members that can inhibit a variety of diseases. It's a moiety that's been used to make a variety of biologically active chemicals that may be tested further for potential application against a variety of diseases The review included pyrazole analogs in particular, as well as powerful compounds reported for specific pharmacological activity. More research is needed to evaluate the actions of pyrazole in the treatment of various disorders that are difficult to treat in medical science. For the time being, scientists are focused on developing more powerful pyrazole derivatives with a wide range of biological activities.

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CONFLICT OF INTEREST

The author declares that he do not have any conflict of interest.

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