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Review Article

An Extensive Analysis of the Pharmacological Potential of Imidazole Derivatives

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ABSTRACT

Imidazole is a heterocyclic moiety with five members that include two nitrogen atoms, four hydrogen atoms, three carbon atoms, and two double bonds. Also referred to as 1, 3-diazole. It contains two nitrogen atoms, including pyrrole-type nitrogen, and one hydrogen atom.1, 3-diazole has both basic and acidic properties because it is amphoteric. This colorless or white substance is easily dissolved by water and other polar solvents. The positive charge of both nitrogen atoms allows for two equivalent tautomeric forms. Synthesis of compounds containing imidazoles involves the use of multiple techniques, and their diverse structural responses offer possibilities in the field of medicinal chemistry. Imidazole compounds exhibit multiple biological effects such as analgesic, antifungal, anti-tuberculosis, antibacterial, anticancer, and anti-HIV properties. Examining imidazole's pharmacological and synthetic profile in recent years is the aim of this study.

INTRODUCTION

Antimicrobial resistance (AMR) in medication therapy is currently causing an increase in public health issues. For the creation of a novel medication that combats AMR, thus, issues. Drugs with heterocyclic nuclei have historically had strong chemotherapeutic effects and served as a cure for the creation of new medications. Many heterocyclic substances are used in therapeutic settings to treat infectious illnesses. For this reason, heterocyclic ring-containing medications are quite important.[1,2,3]

Two annular nitrogen atoms make up the aromatic compound imidazole, which has five members.[4]

The chemical formula for this organic compound is $C_3N_2H_4$ (Fig.1). It is a colorless or soluble white material that makes water slightly alkaline. It is

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classified as a diazole in chemistry and is an aromatic heterocycle with nitrogen atoms that are meta-substituted but not next to one another. Imidazole and its derivatives have garnered more attention in recent years because of their practical chemistry and pharmacological properties. Numerous biological activity, including antibacterial[5,6], anticancer[7,8], anti tubercular[9,10], antifungal[11], analgesic[12] , ant diabetic[13] , and antiviral properties[14] are possessed by imidazole derivatives.

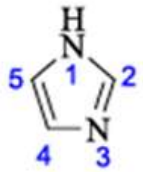

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Fig 1:

1,3-diazole can function as both an acid and a base due to its amphoteric behaviour. The dissociation constants of the two nitrogens in 1,3-diazole vary because the imidazole ring contains two distinct types of lone pairs: delocalised and non-delocalized (non-Huckle) lone pairs. Both delocalised and non-delocalized lone pairs have dissociation constants (pKa) of 7.4 and 14.9. Because of its amphoteric phenomena, the 1,3-diazole ring is vulnerable to both electrophilic and nucleophilic attacks.[15]

Alcohols are less acidic than imidazole, but imidazole is less acidic than carboxylic acid, phenol, and imides.Its dissociation constant is 14.5.The dissociation constant (pKa) of a basic imidazole is roughly 7, making it 60 times more basic than pyridine. The acidic proton is present in the first nitrogen atom of the imidazole ring.[16] The 1,3-diazole ring exhibits two equivalent tautomeric forms because each of the nitrogen atoms have a positive charge (Fig. 2).[17]

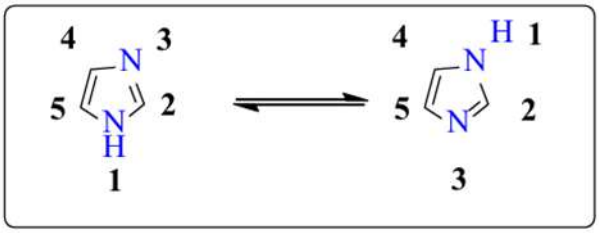


Fig 2:

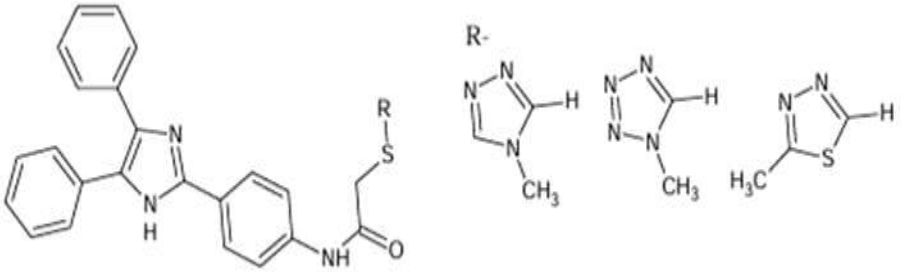
It is an aromatic compound due to the sextet of π-electrons on the ring. Because the second nitrogen atom, which is part of the aromatic sextet, has unshared pairs of electrons, the third-position nitrogen atom increases the imidazole ring's reactivity with the electrophilic molecule. The boiling point, melting point, and dipole moment of the imidazole ring in dioxane are all 4.8 D.[16]

The Relationship Between Imidazole Ring Structure and Activity

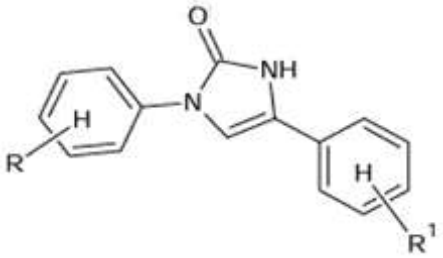
Imidazole's SAR revealed that the ring replaced only at position N-1 is crucial for the action. For activity, lipophilic substituents, typically one or more with a five- or six-membered ring structure, were added. The stronger antibacterial, antiviral, antidepressant, It has been reported that anticancer imidazoles may be annealed with imidazole rings that had halogen, hydroxy, or methyl substituents at positions 2, 4, and 6 or that had two or three aromatic substituents on the imidazole ring. The activity is usually reduced by adding additional alkyl substituents to the imidazole ring, but imidazoles with methyl groups on the N-1 or N-3 positions produce almost inert compounds. The imidazole ring's activity is reduced when aliphatic amines are substituted. Benzodiazepines and other pharmacologically active derivatives are produced when the imidazole ring is annealed with other heterocycles or aromatics. For instance, midazolam, an imidazobenzodiazepine, was frequently recommended as a strong anxiolytic. [18-24]

IMIDAZOLE'S PHARMACOLOGICAL ACTIVITIES:

The anti-cancer properties of imidazole:



Congiu et al. synthesised a number of 1, 4-diarylimidazole-2(3H)-one derivatives and assessed their anticancer potential in vitro. Compounds with a 3, 4, 5 trimethoxypheny ring joined to the imidazole ring at either the N-1 or C-4 position demonstrated action against leukemic cell lines that is anticancer. [25]

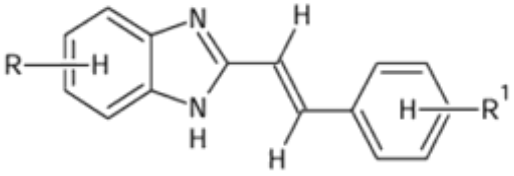


Imidazoles as anti-microbial agents:

Kallappa Hosamani et al. synthesised a novel family of 5-(nitro/bromo)-styryl-2-benzimidazoles by condensation of 5-nitro-o-phenylenediamine with trans cinnamic acids.

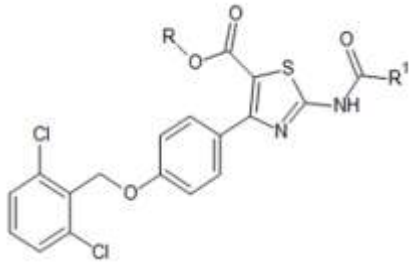
The synthetic compounds' anti-tubercular properties were assessed against the tests were conducted using antibacterial strains of Escherichia coli, Enterococcus faecalis, and Klebsiella pneumoniae, as well as antifungal strains of Candida albicans and Aspergillus fumigatus. Compounds shown strong effectiveness against the entire class of bacteria.[26]

Okay, et al. discovered eighteen new imidazole piperazine compounds. Using spectrum data from 1HNMR, IR, and EI-MS, the structures of the produced agents were described. Most of the chemicals synthesised exhibited significant anti-cancer cell line activity.



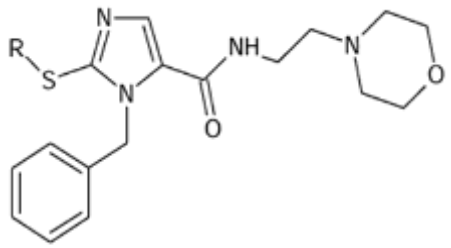
Imidazoles as anti-tubercular agents:

Derivatives of 4-(2, 6-dichlorobenzyloxy) phenyl thiazole imidazole were synthesised and published by Qidong You with colleagues. Using the Microplate Alamar Blue Assay (MABA), derivatives were assessed for their in vitro anti-tubercular properties against Mycobacterium tuberculosis H37Rv.Good anti-tubercular properties are demonstrated by compounds with MIC values ranging from 1µM to 61.2µM.[27]



Imidazoles as antidepressant agents:

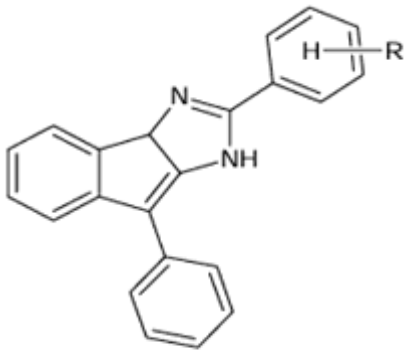
Using a forced swimming test, Kumarishalini assessed the antidepressant properties of imidazoles that had been replaced with a moclobemide phenyl ring. Compared to moclobemide, synthesised molecules exhibit more powerful action.[28]



R- CH_3, C_2H_5, $CH_2C_6H_5$

Imidazoles as anticonvulsant agents:

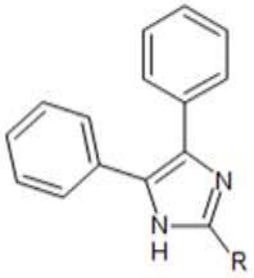
Imidazole compounds with nitro and chloro groups substituted at the second position in the ring were reported by Bhragual et al. to exhibit anticonvulsant efficacy without neurotoxicity.[29]



R- H, 2-Cl, 2-NO_2, 4-NO_2

Imidazoles as anti-inflammatory agents:

Using the carrageenan-induced rat paw oedema method, Mukeshdoble and A. Puratchikody reported 2-substituted-4, 5-diphenyl-1H-imidazole derivatives and assessed their anti-inflammatory properties. Maximum activity was demonstrated by derivatives with phenyl substitution at the Para position with -F, -Cl, $-NH_2$, -OH, OCH_3, and $-N(CH3)_2$.[30]



APPLICATIONS: [31]

1. Pharmaceutical Application

- Essential ingredients in antifungal medications such as clotrimazole, ketoconazole, and miconazole.
- Used in the creation of antiviral, antimicrobial, antiparasitic, and antihistamine compounds; they are also present in drugs used to treat cancer and reduce inflammation; and they block histamine receptors.

2. Biochemical Uses

- Used in scientific settings as a buffering agent to keep the pH at a neutral level (~7).
- Used in purification of proteins, especially Because it mimics the imidazole-containing side chain of histidine, it is useful in enzyme research and for eluting His-tagged proteins using affinity chromatography.

3. Role in Chemical Synthesis

- It serves as a ligand in coordination chemistry and as a base or catalyst in a variety of chemical processes.
- Acts as a bridge in the production of dyes, pesticides, and medicines.

4. Commercial Applications

- Acts as a curing agent for epoxy resins and plastics
- Prevents corrosion in metal surfaces and pipes.
- Acts as an accelerator to encourage rubber's vulcanisation.

CONCLUSION:

Imidazole compounds have advantageous pharmacological characteristics, including anti-tubercular, anti-cancer, ability to cure a wide range of human illnesses due to its antiviral, antifungal, antibacterial, antioxidant, and antiparasitic properties. We found that several imidazole derivatives have a promising bioavailability score and a manageable pharmacokinetic profile after analysing the results of multiple trials. In a nutshell, the existing evaluated study on imidazole scaffold recommends more research and improvement in order to identify novel and potent treatment candidates.

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