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Biological Activities of Imidazole Derivatives: A Review

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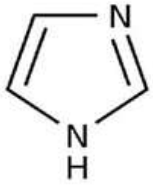
ABSTRACT:
Imidazole is a five-membered, planar heterocyclic ring with 3C, 2N, and N in the firstandthirdpositions.Purine,histamine,histidine,an dnucleicacidarejustafewexamplesof important natural compounds containing the imidazole ring. Because it is an aromaticchemicalthatispolarandionizable,itisusedas atreatmenttoimprovethesolubilityandbioavailability propertiesofproposedweaklysolublechemicalentities andthusimprovesbasicpharmacokineticparametersof leadmolecules.Imidazolederivativesholdaspecialpla ce in medicinal chemistry. The introduction of the imidazole nucleus is a significantsynthesis technique in the method used to find pharmaceutical medications. This articleaimstoreview previousyears'workonimidazolechemistryandbiolog icalactivities.
KEYWORDS: Imidazole,antibacterial,antifungal,h eterocyclic,biologicallyactive.

I. INTRODUCTION

Imidazole is a five-member heterocyclic aromatic compound with two Nitrogenatoms that are sp2 hybridized. Because the imidazole ring contains two types of lonepairs,delocalized andnon-delocalized(non-Huckle-lonepair),thepkaofeachNitrogendiffers.Nitrogenwit hadelocalizedlonepairhaspka=7,whilenitrogenwith a non-delocalized lone pair has pka=14.9. As a result, Imidazole is in amphotericnature,whichmeansitcanactasbothanacid andabaseandissusceptibletonucleophileandelectrop hilicattack[1]. Imidazole is a colorless or pale-yellow solid with an amine-like order. It is anaromatic heterocyclic categorized as a diazole and an alkaloid. It dissolves in water andother polar solvents. Because the hydrogen atom can be found on either of the twonitrogen atoms, it exists in twoequivalenttautomeric forms.The melting point ofimidazole is 88.9°C and the boiling point is 267.8°C. Imidazole is polar in nature and itsdipole moment is 4.8 Debye, the molecular formula is $C_3H_4N_2$, and the structuralformula[2,3].
Imidazolesareaheterocycleclasswithafive-memberringstructureandvariablesubstituents.Thisri ngsystemisfoundinimportantbiologicalskeletonsco mponentssuchashistidineandtheassociatedhormone histamine.Imidazolecanactasbothaweakacidandabas e.Nitroimidazoleandantifungaldrugsareexamples ofdrugswithanimidazolering.[4]
Heterocyclic compounds are useful in both pharmacology and agriculture. Anexaminationofresearchmanuscriptsfromthepast1 0decadesrevealedageneralpatternof research for novel pharmaceuticals involving modifications to current physiologicallyrobustmatrices and molecularapproachesofthecompounds'structures.



Indrugdiscovery,theimidazolenucleusisanimportant synthetictechnique.Imidazolederivativeshaveanti-inflammatory,anti-cancer,antimicrobial,analgesic, and antitubercular properties. [5,6] One of the most important properties ofimidazolederivativesistheiruseasamaterialforthetr eatmentofdenturestomatitis.Thehigh beneficial properties of imidazole-associateddrugs have encouraged medicinalchemists to prepare a large number of new chemotherapeutic materials. Imidazole drugshaveawidescopein thepharmaceuticalfield.[7]

PHARMACOLOGICALACTIVITIES:
Imidazoles are well-known heterocyclic compounds that are common andhaveanimportantfeatureinavarietyofmedicinalag ents.[8]Basedonvariousliteraturesurveys,imidazoled

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erivativesshow various pharmacologicalactivities:

1. Antifungalactivity
2. Anticanceractivity
3. Antibacterialactivity
4. Anti-tubercularactivity
5. Anti-HIVactivity
6. Anti-inflammatoryandanalgesicactivity
7. Antiviralactivity
8. Anthelminticactivity
9. Antidepressantactivity

1) ANTI-FUNGALACTIVITIES:

Inrecentyears,imidazoleandtriazolechemistryhavebeenthemainareasofattentioninthe hunt for novel antifungals. Unquestionably, the azole family of medications, a variety of 1-substituted imidazole and triazole chemicals, constitutes thecurrent method for treating fungal illness both topically and systemically. [9] Imidazolehas strong pharmacological and biochemical actions as an anti-fungal. Due to poorabsorption and substantial first-pass metabolism, the lipophilic Imidazoles, includingclotrimazole, econazole, and miconazole, showed poor systemic availability after oraladministration. As a result, their usage has been restricted to the topical treatment ofsuperficialfungalinfections.Ketoconazoleamorepolarimidazoleintroducedintotherapyinthelate1970s representedabreakthroughinthetreatmentofantifungaldisease.[10]

2) ANTI-CANCERACTIVITY:

To test their anticancer properties, several new imidazoles-(Benz) azoles andimidazolepiperazinederivativesweresynthesized .[11]Accordingtoanticanceractivityscreeningfindings,thesecompounds werethemostpotentinthegroup.

3) ANTIBACTERIALACTIVITY:

According to the literature study, the antibacterial action of imidazole derivatives is thesecondmostfrequentsignificantpharmacologicaleffect.Findingthisimpactissignificantbecause,withthediscoveryofnearlyallmajorantibioticgroups(tetracyclines,cephalosporins, aminoglycosides, and macrolides), these medications may become lesseffective due to the rise in microbial resistance. Currently, multidrug-resistant bacteria-relatedtreatmentfailures areamajorpublichealthconcernon aglobalscale.[12]

For instance, researchers looked into the bactericidal effects of imidazole compounds incombinationwithsilver.TheNationalUniversityofIreland'sJohnMcGinleyetal.(2013)synthesized 1-(3-amino propyl) imidazole and produced Schiff base ligands that weresimple to couple with Ag(I) centers. Studies were conducted on S. aureus, MRSA, E. coli, and P. aeruginosa strains. The majority of Ag (I) complexes exhibited modestantibacterialactivity asaconsequence.[13]

Theantibacterialresearchofbenzonitrilehexafluorophosphateandcoumarinsaltssubstituted with imidazolium, benzimidazolium, and silver complexes against Gram-positive (S. Aureus) and Gram-negative (E. coli) bacteria was carried out by (JawaharlalNehru Centre, India). While the antibacterial activity against S. aureus was only mild,both series of silver complexes demonstrated antibacterial action against E. coli. Thecomplicatedactionis connectedtothemetalcenter,itwas finallydetermined.[14]

4) ANTI-TUBERCULARACTIVITY:

Despite recent advancements in the treatment ofinfectious illnesses brought on byMycobacterium, these germs continue to pose a serious threat to global healthcare andarethemaincauseofinfectiousdisease-relatedfatalitiesworldwide.Despitetheexistenceofantituberculosismedications,TBremainsoneofthemostprevalentillnessesthatwarrantglobalattention.TheHIVepidemichasaggravatedthesituationbyincreasingthefrequencyofmultidrug-resistantTBandthedevelopmentofdrug resistantmicroorganisms.[15]Findingnoveltreatmentdrugstofight M.tuberculosisinfectionsisnecessaryfor lightof thesefindings.

ResearchersfromtheUniversityofPardubiceintheCzechRepublic,DanielCvejn,VeraKlimesova,andFilipBures16,examinedtheantimycobacterialpropertiesof2-phenyl imidazole derivatives made from -amino acids in 2012. Nitro group-containingmoleculesamong2-phenyl imidazolederivativesexhibitedtheabilitytoinhibitM.tuberculosis, however this ability was less potent than that of isoniazid. Isoniazid'seffectiveness was surpassed by M. avium and M. kansasii activity. The primary factorinfluencingtheantimycobacterialactionofthecompoundsinvestigatedwastheavailabilityof thenitro group.

5) ANTI-HIVACTIVITY:

AIDSortheAIDSRelatedComplex(ARC)iscausedbythepathogenicretrovirusknownasHIV-1(HumanImmunodeficiencyVirusType-

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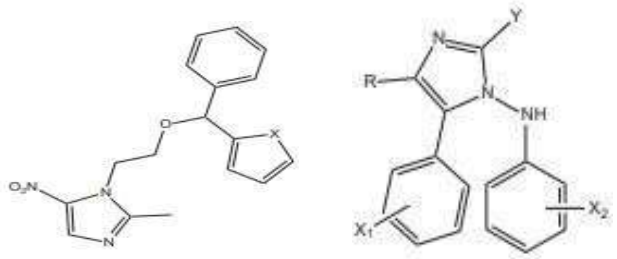
1).HIVinfectioncausesseveredeficiencies in cell-mediated immunity and targeting the monocytes that express surfaceCD4receptors.
Opportunistic infections (OIs), such as bacterial, fungal, viral, protozoal, and neoplasticdisorders,aswellaseventualmortality,areca usedbyopportunisticinfections(OIs)overtimeduetos ubstantialdepletionofCD4T-lymphocytes(T-cells)causedbyinfection17.An ideal anti-HIV drug would be able to fight off opportunistic illnesses includinghepatitis,TB,andotherbacterialinfectionsin additiontoinhibitingHIV reproduction.
Imidazoles have a history of being used as antiviral medications; capravirine18 is onesuchinstance.Several1-2-(diarylmethoxy)ethyl]weresynthesisedbySilvestriet al.(19)and De Martino et al. (20, 21).the racemic 1-2-[(thiophen-2-yl)phenylmethoxy]ethyl]-2-methyl-5nitroimidazole(EC50,0.03mol-1)beingthemostpotentamongalltheanalogues(Fig.1), exhibitinghigheractivitythanefavirenzagainstthevira lRTcarryingtheK103Nmutation.

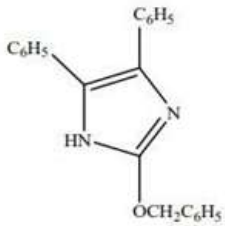


(**DAMNIsX:S,O NAIMs X, X:halogen,alkylR: alkyl,arylY: S, H,S)**

Similarly,N-aminoimidazoles(NAIMs)havealsobeenreportedtoi nhibitreplicationofthe WT virus as well as an HIV-1 strain that contained both the K103N and Y181Cmutations.

6) ANTI-INFLAMMATORYANDANALGESICACTIVITY:

Using the Carrageenan-induced paw edoema technique, a research on 2-substituted-4, 5-diphenyl-1H-imidazoles examined the anti-inflammatory effects. When compared toindomethacin,thischemicalhasthehighestlevelofaction.



2-(benzyloxy)-4,5-diphenyl-1H-imidazole

7) ANTIVIRALACTIVITY:

These are synthetic imidazole derivatives that have been tested for antiviral activity as 2-(substituted phenyl) imidazol-1-yl). Compounds A and B were shown to be the most effectiveantiviralmedicineswhen-methanonewasused againstvirusstrains.

8) ANTHELMINTICSACTIVITY:

Itwasshownthatextra-intestinalparasites,notablyintravascularandintestinal lyresidingparasites, are less vulnerable to imidazole than gastrointestinal parasites. In comparablesettings, the activity against developing phases is superior to that against arrested oradultstages.Atlevelsthatareineffectivein preventingtheformationofanadultinvivo,larvaldevel opmentandhatchingarehindered.Theymustbeeffecti veagainstnematodes at levels lower than those used to control cestodes and trematodes. [14]Agreater dosage of medication or numeroustreatments are required for cestode ortrematodemanagement.Ithasbeendiscoveredthatth eclassmember(2-alkylbenzimidazole) may eliminate several nematode and trematode species from diversehosts. Tetra chloro-2-trifluoromethylbenzimidazole (4, 5, 6, 7) exhibits strong actionagainst the nematodes Fasciola hepatica, Ancylostoma caninum, Haemonchuscontrtus,and ascaris. It has been discovered that many 2-5 disubstituted benzimidazoles, whichhave the ability to kill a number of different species of intestinal nematodes, also showactionagainstcestodiasisinhumansandanimals.

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Mebendazole100mg/kgisusedtotreatpatients with T. soliumand T. saginata.

9) ANTIDEPRESSANTACTIVITY:

Moclobemideanalogueswerecreatedbysubstitutingsubstitutedimidazoleforthemoclobemidephenylring,andtheirabilitytotreatdepressionwastestedusingtheforcedswimmingmethod.Itwasdiscoveredthatanalogue7a-cwasmoreeffectivethanmoclobemide.

II. CONCLUSION:

Thisreview onvariousimidazolederivatives,asignificantclassofheterocycliccompounds,hasfascinatingresultsforitsantibacterial,anticancer,antitubercular,antifungal, analgesic, and anti-HIV activities. It also showed promising results for mostpharmacological activities. Modifications to the imidazole nucleus have so far been seentohaveinterestingbiologicalactivity.Itwouldbefascinatingtoseehowmanyadditionalpharmacological profiles are added to it in the future because they are still unknown andmaybeusedasaguideforfutureresearchtoproduceseaferandmorepotentmolecules.

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