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Review Article

A MINI REVIEW: IMIDAZOLIUM COMPOUNDS AND THEIR POTENT BIOLOGICAL APPLICATIONS

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A B S T R A C T

Imidazole is a five-membered aromatic heterocyclic compound that occurs naturally in a variety of products. Its structure has a unique feature with electron-rich characteristics that are useful for imidazole and derivatives because they readily associate with enzymes and receptors in biological systems and have a wider range of bioactivities. Various imidazole derivatives are used in clinical practice to treat a variety of diseases with high therapeutic potency. This analysis covers the synthesis of imidazolebased derivatives and their applications as antibacterial, anticancer, antihypertensive, antimalarial, antifungal, antioxidant, antiviral, and analgesic agents, as well as their function in HIV-1 inhibitors, Alzheimer's disease treatment, and Chagas disease treatment.

INTRODUCTION

Medicinal chemistry is based on the classical field of chemistry, in particular organic chemistry, biology. Limited natural & synthetic products were directly used as therapeutic agents & lack speciality limits for their use in human & veterinary medicines, agriculture, etc. By destroying the chemical structure of these products, its therapeutically significant molecular section is removed, the portion of which is not used by the drug & considered as a result of biosynthetic effort on the parent organism to construct materials for its metabolic purpose. These drugs are formed by heterocyclic compounds. These compounds play a vital role in the metabolism of living cells, with more than five and six heterocyclic rings having one or more heteroatoms in them, such as nitrogen (N), oxygen (O), sulfur (S), etc.

Imidazole or imidazole is an azapyrole, the nitrogen atom is separated by a carbon atom. It was first prepared from Glyoxal & Ammonia, hence formerly known as Glyoxalin. It is a colourless solid with the formula $C_3H_4N_2$ and soluble in water, forming a mildly basic solution. It is a common component of a large number of natural products and pharmacologically active molecules. Since then, Imidazole has attracted the form of essential amino acid Histidine, DNA, etc. and the number of medicinal products of Imidazole structure, making it an important and attractive target for synthetic and medicinal chemist.

Many synthetic methodologies for the synthesis of Imidazole and its derivatives are given in this literature [1-8, 10, 12-16, 22-40]. Antibacterial [1,2], anticancer [3], antihypertensive [4], Chagas disease [5], antimalarial [8], antifungal [12-13,18], antioxidant [20], antiviral [21], analgesic [24], Alzheimer's disease [29], HIV-1 Inhibitor [32], antiparasitic properties.

Antibacterial

Two series of novel imidazole derivatives that replaced pyrazole moieties were synthesized [1] by the reaction of 3-aryl-1H-pyrazole-4-carbaldeydes with 1,2-diketones in the presence of ammonium acetate. Among them, one of the derivatives (A_1) showed excellent activity against P.aeruginosa relative to the standard drug Streptomycin (A_2), while showing similar activity to the standard against C.profigens. Synthesis of 2,4,5-Tribromoimidazole (TBI) &Co(II), Cu(II), Mn(II), Ni(II), & Zn(II) complexes [2] has been carried out. These complexes on evaluation shown positive activity against E.coli.

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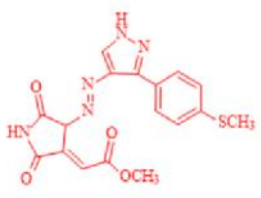
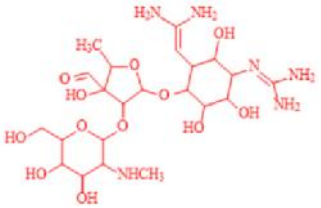


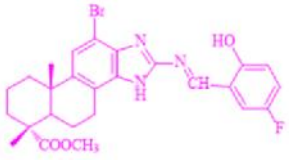
A1



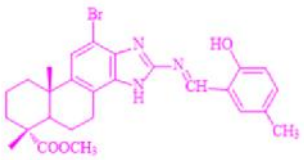
B2- Streptomycin

Anticancer

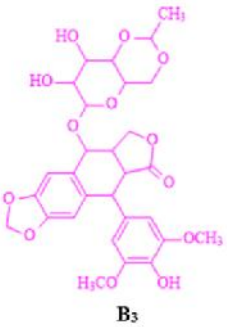
A sequence of new 1H-benzo[d]imidazole derivatives of dehydroabietic acid has been synthesized [3]. Several dehydroabietic acid derivatives have shown significant anticancer properties through DNA binding, apoptosis or oncosis-inducing mechanisms which indicate that dehydroabietic acid is a promising material for the study of new anticancer agents. Among the synthesized derivatives, the compound (B_1) showed the strongest activity against SMMC-7721 while the compound (B_2) showed the most potent activity against HepG-2. Activities were tested using Etoposide (B_3) as a standard compound.



B1



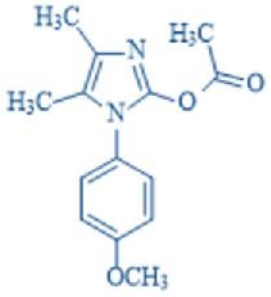
B2



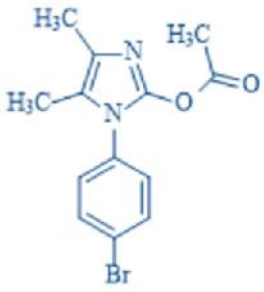
B3

Antihypertensive

Two new imidazole derivatives were prepared using solvent-free synthesis pathways[4], namely (1-(4-methoxyphenyl)-4,5-dimethyl-1H-imidazole-2-yl acetate (MPDIA) (C_1) & 1-(4-bromophenyl)-4,5-dimethyl-1H-imidazole-2-yl acetate (BPDIA) (C_2) and the molecular docking study showed potential interactions with antihypertensive protein hydrolase, docked ligands form stable complexes with hydrolase inhibition.



C1

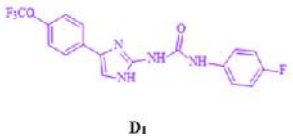


C2

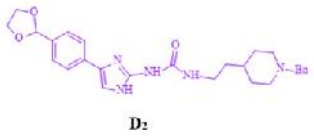
Chagas Disease

This disease is endemic in 21 Latin American countries, caused by the TrypanosomaCruzi protozoan parasite. 26 New Imidazole-related derivatives[5] bearing the urea pattern were synthesized and out of these ureaimidazoles (D_1, D_2, D_3, D_4, D_5) showed the most promising activity against the T.cruzi parasite.

C Disease



D1



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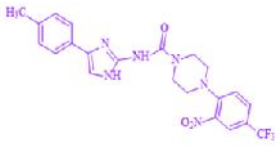
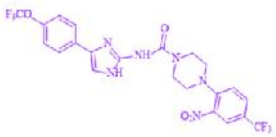
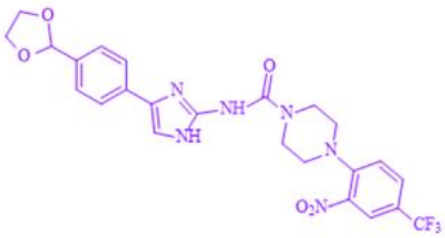


D4

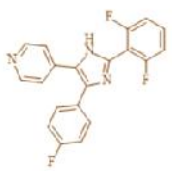


D5

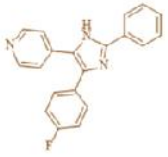


Antimalarial

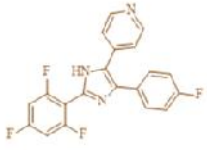
The novel derivatives of 2-substituted aryl-4-fluorophenyl-5-(2-chloropyridinyl)-1H-imidazole were synthesized in four steps [8] by the reaction of 2-(2-chloropyridin-4-yl)-1-(4-fluorophenyl) ethanone obtained by the reaction of ethyl-4-fluorobenzoate with 2-chloro-4-methylpyridine by the oxidation of selenium dioxide in Dioxane and by the cyclization of substituted aryl aldehydes in Acetic acid & Ammonium acetate. Both derivatives have been tested for antimalarial activity and the findings are compared with standard drugs Quinine (E_5), two of which (E_1, E_2) shows strong antimalarial activity against Plasmodium falciparum, while two (E_3, E_4) shows moderate activity against Plasmodium falciparum.



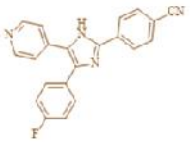
E1



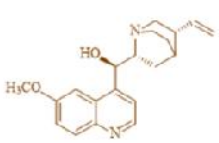
E2



E3



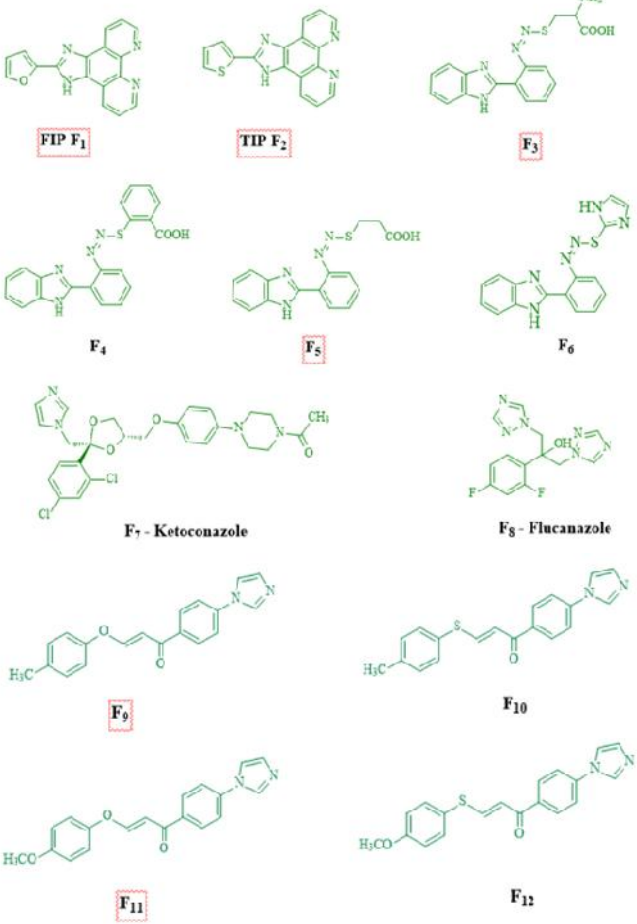
E4



E5- Quinine

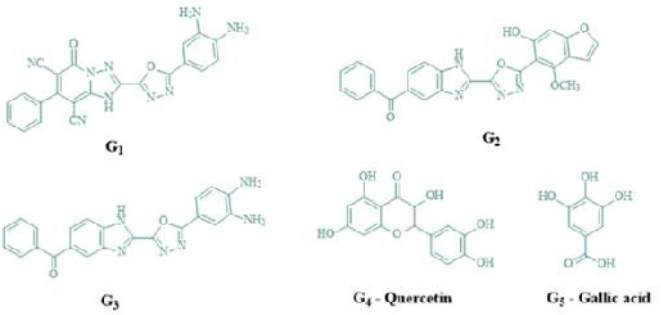
Antifungal

New Ni(II) and Cu(II) complexes comprising 2-(Furan-2-yl)-1H-imidazo[4,5-f] [1,10] [1,10] Phenathroline (FIP) (F1) and 2-(thiophene-2-yl)-1H-imidazo[4,5-f] [1,10] Phenanthroline (TIP) (F_2) has been synthesized [12]. Out of which the Cu complex has shown good behaviour against fungal organisms. The invention of imidazole & thiazole-sulfazane ligands for the first time [13] gives the sulfide-azo group in the same bond known as sulfazane. Many sulfazane ligands were synthesized and the antifungal activity tested and the results showed strong inhibition in sulfazane ligands (F_3, F_4, F_5, F_6). Fifteen new 1-(4-(1H-imidazole-1-yl)phenyl)-3-(4-substituted phenyl)prop-2-en-1-one derivatives [18] is synthesized and screened for antifungal activity against C.albicans, C.krusei, C.parapsilosis&C.glabrata compared to standard drugs Ketoconazole &Flucanozole (F_7,F_8) and four of the fifteen derivatives (F_9,F_{10},F_{11},F_{12}) were found to be more potent. F11 has shown comparable antifungal activity to Ketoconazole & Fluconazole against all Candida species and is the most active derivative in the sequence.



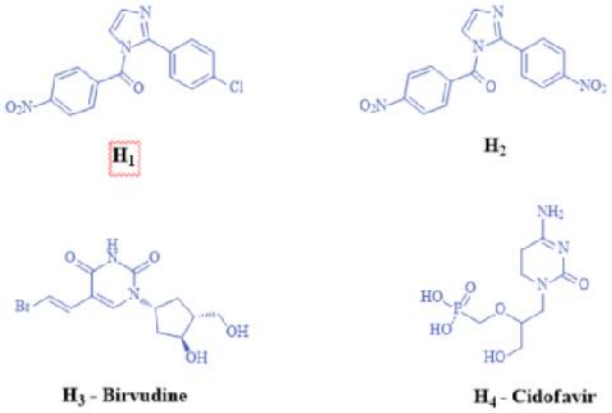
Antioxidant

A new sequence of (1,3,4-oxadiazol-2-yl)-1,5-dihydro-[1,2,4]triazolo[1,5-a]pyridine-8-carbonitrile derivatives[20] was synthesized and evaluated for antioxidant activity. These derivatives (G_1,G_2,G_3) have the highest antioxidant activity compared to the reference antioxidants Quercetin (G_4) & Gallic acid (G_5)



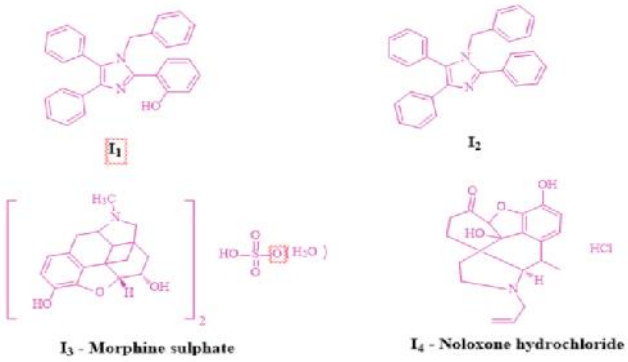
Antiviral

The herpes virus family contains eight known human viruses like Herpes Simplex Virus-1 (HSV-1) & Herpes Simplex Virus-2 (HSV-2) causes cold sores (HSV-1) & genital lesions (HSV-2) (HSV-2). In such cases, the imidazole-induced nucleus is effective. Synthesis of (substituted phenyl)-[2-(substituted phenyl)-imidazol-1-yl]-methanone analogues [21] for the antiviral study of these derivatives two of them (H_1, H_2) emerged as the most promising antiviral agents and their activity was found to be equivalent to the standard drugs Brivudin&Cidofovir (H_3, H_4) respectively. These two compounds (H_1, H_2) may be selected as lead compounds for the synthesis of newer antiviral agents.



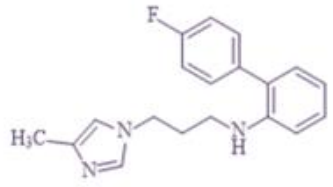
Analgesic

The derivatives of 1-Benzyl-2-substituted-4,5-diphenyl-1H-imidazole were synthesized[24] by treatment of distilled imidazole compounds with Benzyl chloride in the presence of sodium hydride, two of which (I_1, I_2) exhibited strong activity similar to the standard drug Morphine. They are non-toxic. The reference medications used were morphine sulfate and naloxone hydrochloride (I_3, I_4).



Alzheimer's Disease

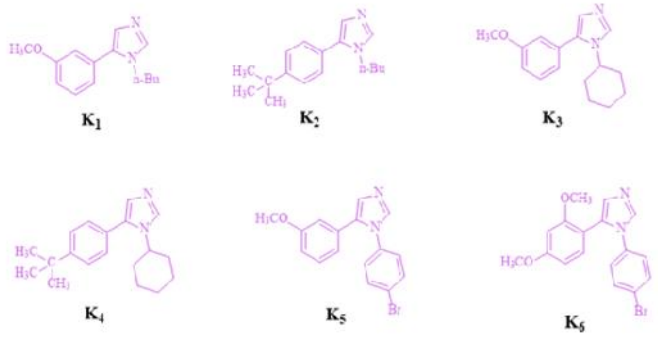
A derivative of 4'-Fluoro-N-(3-(4-methyl 1h-imidazole-1-yl)-propyl)[1,1'-biphenyl] is developed[28] for Alzheimer's disease. The effects of -2 -amine(J_1) are remarkably inhibitory &pE-Aβ3-42 in live cells have decreased and hQC activity has been inhibited.



J_1

HIV-1 Inhibitor

Synthesis of novel 1-substituted-5-aryl-1H-imidazole-5-aryl-4-tosyl-4,5-dihydro-1,3-oxazole and 5-aryl-1,3-oxazole derivatives by microwave-assisted cycloaddition of Para-toluenesulphonylmethylisocyne (TosMIC) to reduce &aldehyde[32]. The discovered derived derivatives found that they represent viable starting points for the design of inhibitors to specifically target HIV-1 IN & LEDGF/p70 and LEDGF/75 protein interaction. Out of these derivatives (K_1, K_2, K_3, K_4, K_5, K_6) shows potent activity.



CONCLUSION

Imidazole is a five-member heterocycle. There are many methods for the synthesis of Imidazole and its derivatives. It's basic because of the nitrogen atom. It rarely shows nucleophilic substitution, but it usually shows electrophilic substitution reactions. It is concluded from the above discussion that its therapeutic action has been used in recent years to synthesize various compounds with pharmacological activities. The literature survey explains its antibacterial, antifungal, anticancer, antimalarial, antituberculosis, antiprotozoal, antiviral, antioxidant activity, etc. Imidazole may be further used as a prospective against various diseases or disorders in the future

Acknowledgment

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