MINI REVIEW

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

A Review: Imidazole and its Biological Activities

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Received: 20. 06. 2024

Revised: 20. 07. 2024

Accepted: 23. 07. 2024

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Abstract

Imidazole is a planner heterocyclic five-member ring with 3C and 2N atom and in ring N is present in 1st and 3rd positions. The imidazole ring is a constituent of many important natural products, including purine, histidine, and nucleic acid. Being polar and ionizable aromatic compound, it improves pharmacokinetic characteristics of lead molecules and thus used as a drug to optimize solubility and bioavailability parameters of proposed poorly soluble lead molecules. Derivatives of Imidazole have occupied a critical place in the field of medicinal chemistry. imidazole nucleus is an important synthetic strategy in drug discovery. The high therapeutic properties of the imidazole related drugs have improved the medicinal chemists to synthesize enormous number of novel chemotherapeutic agents. Methods for the synthesis of imidazole and their various structure reactions offer enormous scope in the field of medicinal chemistry. This article seeks to review the work reported, their chemistry and biological activities of imidazole during past years.

Keywords: Imidazole, antibacterial, heterocyclic, biological activity

1. Introduction

Medicinal chemistry is the discipline concerned with determining the effect of chemical structure on biological activity and in the practice of medicinal chemistry developed from an empirical one involving organic compound synthesis based largely on the modification of structure and then identifies their biological activity (Foye, 2008). Medicinal chemistry concerns the discovery, development and the identification of mechanism of action of biologically active compounds(Singh & Kapoor, 2005). Various biologically active synthetic compounds have five-membered nitrogen-containing heterocyclic ring in their structures (Lednicer, 2007). Structural frameworks have been described as particular, N- containing polycyclic structures have been reported to be associated with a wide range of biological activity. The high therapeutic properties of the imidazole related drugs have encouraged the medicinal chemists to synthesize many novel chemotherapeutic agents. Imidazole drugs have broadened uses in remedying various dispositions in clinical medicines, antiaging agents, anticoagulants, anti-inflammatory, antibacterial, antifungal, antiviral, antitubercular, antidiabetic and antimalarial (Congiu, Cocco, & Onnis, 2008; Emami et al., 2008; Grimmett, 1997; Nakamura et al., 2004; Nantermet et al., 2004). This group presents in azoles antifungal which inhibit the accumulation of methylated sterols destroy the composition of the lipid bilayer of membranes. Some imidazole at high concentrations, could exert direct inhibitory action on membranes, without interference with sterols and sterol esters (Shingalapur, Hosamani, & Keri, 2009). Infectious microbial disease causes worldwide problem, because microbes have resisted therapy longer than any other form of life. In recent decades, problems of multidrug-resistant microorganisms have reached an urgent level in many countries around the world. Imidazole and its derivatives are reported to be physiologically and pharmacologically active and find applications in the treatment of several diseases (Sharma et al., 2009).

Imidazole's are heterocyclic compounds which are common and have important feature of a variety of medicinal agents. because of the hydrogen atom can be located on either of the two nitrogen atoms, it exists in two equivalent tautomeric forms. It is a highly polar compound evidenced by a calculated dipole of 3.61D and is completely soluble in water. The compound is aromatic due to the presence of a sextet of π-electrons. Imidazole is amphoteric, *i.e.* it can act as an acid and as a base.

Based on various literature surveys Imidazole derivatives shows various pharmacological activities

- Anti-fungal and Anti-bacterial activity
- Anti-inflammatory activity and analgesic activity
- Anti tubercular activity
- Anti-depressant activity
- Anti-cancer activity
- Anti-viral activity
- Antileishmanial activity

1.1. Antifungal and anti-bacterial activity

Ramya et al. synthesized a series of novel 5-(nitro/bromo)-styryl-2-benzimidazole derivatives and examined for the antibacterial activity against *Staphylococcus aureus, Escherichia coli,Enterococcus faecalis,* and *Klebsiella pneumoniae* and anti-fungal activity against *Candida albicans* and *Aspergillus fumigates*. This was comparable with ciprofloxacin (Sharma et al., 2009).

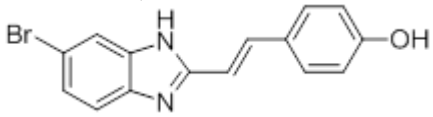


Fig. 1. 4-((E)-2-(6-bromo-1H-benzo[d]imidazol-2-yl)vinyl)phenol

Deepika Sharma et al. have synthesized 2-(substituted phenyl)-1H-imidazole and (substituted phenyl)- [2-(substituted phenyl)-imidazol-1-yl]-menthanone analogues and screened for antimicrobial activity against gram positive, Gram negative, and fungal species. Norfloxacin used as standard (Olender et al., 2009) and following compound is most potent.

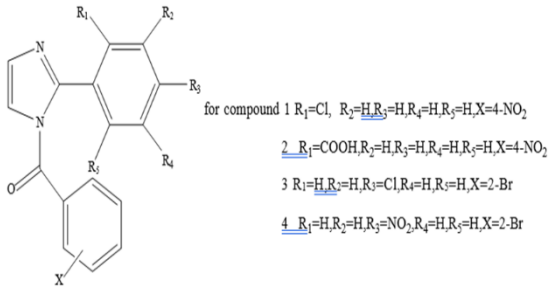


Fig. 2. 2-(substituted phenyl)-1H-imidazole and (substituted phenyl)- [2-(substituted phenyl)-imidazol-1-yl]-menthanone analogues.

Daniele Zampieri et al synthesized bis-imidazole derivatives and tested for antifungal and anti-mycobacterial activity. All compounds had moderate to good activity against Candidaalbicans and Candida glabrata. Miconazole used as reference drug (Puratchikody & Doble, 2007).

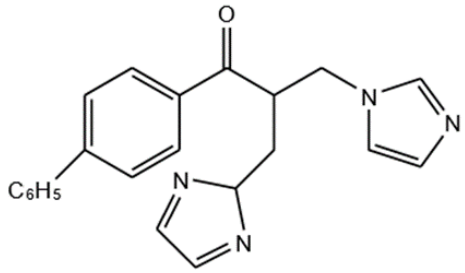


Fig. 3. Bis-imidazole derivatives as antifungal agent

Dorota Olender et al synthesized nitroimidazole derivatives and screened for their antifungal activity by the standard nutrient method against sclerophoma pityophila. This compound shows more potent fungistatic activity (Achar, Hosamani, & Seetharamareddy, 2010).

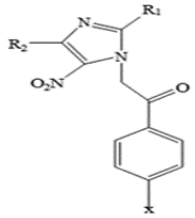
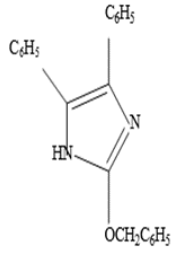


Fig. 4. Synthesized nitroimidazole derivatives

1.2. Anti-inflammatory and analgesic activity

Puratchikody A.et al studies on 2-substituted-4, 5-diphenyl-1H-imidazoles and checked the anti-inflammatory activity based on Carrageenan-induced paw edema method. This compound shows maximum activity and indomethacin used as reference drug (Shalini, Sharma, & Kumar, 2010).



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

Fig. 5. Substituted-4,5-diphenyl-1H-imidazoles.

Kavitha et al. synthesized a series of 2-methylaminibenzimidazole derivatives and synthesized compounds were screened for analgesic and anti-inflammatory activities. This compound shows analgesic activity and compares with standard nimesulide drug (Pandey et al., 2009).

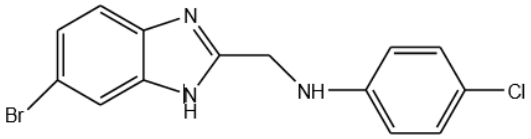


Fig. 6. N-((6-bromo-1H-benzo[d]imidazol-2-yl)methyl)-4-chlorobenzenamine

1.3. Antitubercular activity

Zampieri et al. synthesized series of novel 5-(nitro/bromo)-styryl-2-benzimidazoles derivatives and screened for in vitro anti-tubercular activity against *Mycobacterium tuberculosis*, and these compounds showed good antitubercular activities. Streptomycin was used as reference drug (Zampieri et al., 2007).

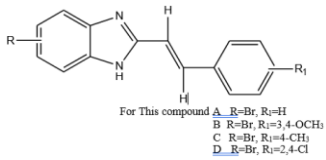


Fig. 7. substituted 1H-imidazole-4-carboxylic acid derivatives and 3-(2-alkyl-1H-imidazole-4-yl)-propionic acid derivatives

Preeti Gupta et al. describe anti-mycobacterium tuberculosis activities of ring substituted -1H-imidazole-4-carboxylic acid derivatives and 3-(2-alkyl-1H-imidazole-4-yl)-propionic acid derivatives against durg-sensetive and durg-resistent *M. tuberculosis* strains. 2f and 2h compounds were most potent compound (HADI, Hosseinzadeh, MOTAMED, SEYFI, & Kazemi, 2008).

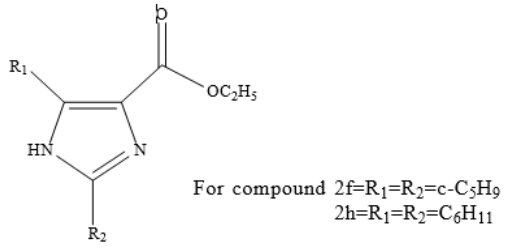


Fig. 8. 1H- imidazole-4-carboxylic acid derivatives and 3-(2-alkyl-1H-imidazole-4-yl)-propionic acid derivatives.

Jyoti Pandey et al. synthesized a series of imidazole derivatives and compounds were screened against M .tuberculosis where this compound showed good antitubercular activity (Refaat, 2010).

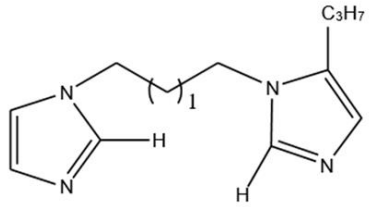


Fig. 9. 1-(3-H-imidazol-1-yl)propyl)-5-propyl-1H-imidazole

1.4.Antidepressant activity

Farzin Hadizadeh et al synthesized moclobemide analogues by reaction of moclobemide phenyl ring with substituted imidazole and tested for the antidepressant activity. Analogues 7a-c was found to be more potent than moclobemide (Tonelli et al., 2010).

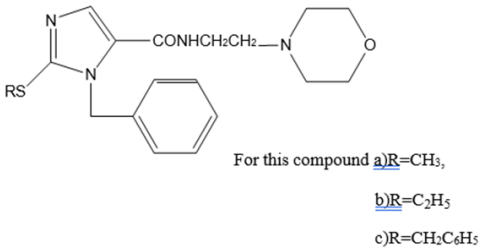


Fig. 10. Moclobemide analogues

1.5. Anticancer activity

Yusuf Ozkay et al. made many novel imidazole-(Benz) azole and imidazole epiperazine derivatives to examine the anticancer activity. Anticancer activity revealed that these were the most active compounds in the derivatives.Cisplatin was used as reference drug (Bhandari et al., 2010).

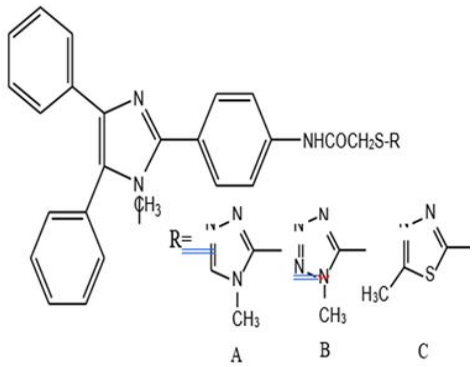


Fig. 11. Imidazole piperazine derivatives

Hanan M. Refaat synthesized 2-substituted benzimidazole. Several of these synthesized products were tested as anticancer screening which exhibited antitumor activity against human hepatocellular carcinoma, breast and human colon carcinoma. 3a and 4a showed the highest potency against human hepatocellular carcinoma (Storrie & Madden, 1990).

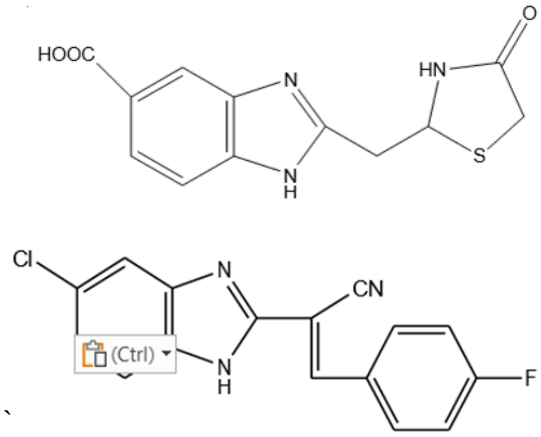
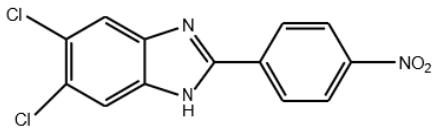


Fig. 12. 2-substituted benzimidazole

1.6. Antiviral activity

Michele Tonelli et al. synthesized 2-phenylbenzimidazole derivatives and evaluated for anti-viral activity against RNA and DNA viruses. Compound ([5,6-dichloro-2-(4-nitrophenyl) benzimidazole]) gave a high activity resulting more potent than reference drugs smycophenolic acid and 6-azauridine (Al-Azzawi, 2007).



5,6-dichloro-2-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole

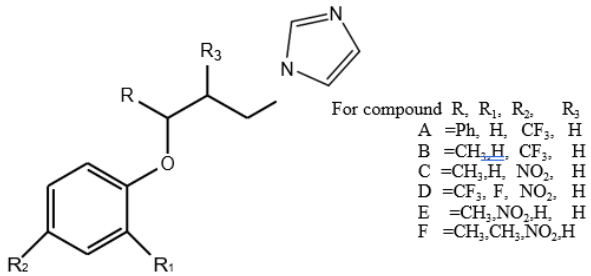


Fig. 13. 2-phenylbenzimidazole derivatives

1.7. Applications of imidazole

- Imidazole is in the purification of His tagged proteins in immobilized metal affinity chromatography (IMAC). An excess of imidazole is passed through the column, displaces the His-tagged from nickel co- ordination and free the His-tagged proteins.
- Imidazole can be used to prepare buffers in the pH range of 6.2-7.8 at room temperature. It is recommended that component of a buffer for assay of horseradish peroxides. (Storrie & Madden, 1990).
- The oral administration of imidazole showed good effects on psoriasis and seborrheic dermatitis. In psoriasis the improvement begins after a period of one and a half to three months. The benefits of this treatment occur without the need for applications of ointments or other topical applications.
- Imidazole's have been prepared as pharmacological agents Azomycine, Clotrimazole, Miconazole and Clonidine. One of the most important applications of imidazole derivatives is their used as material for treatment of denture stomatities(Al-Azzawi, 2007; Uçucu, Karaburun, & Işikdağ, 2001).
- Imidazole has become an important part of many pharmaceuticals. Imidazole's are present in many fungicides and antifungal and antihypertensive medications. Imidazole is part of the theophylline molecule, found in tea leaves and coffee beans, which stimulates the central nervous system.

2. Conclusion

Based on various literature survey imidazole derivatives show various activity against antimicrobial, anti-inflammatory, analgesic, antitubercular, anticancer etc. The possible improvements in the activity can be achieved by modifications in the substituents on the basic imidazole nucleus. structural similarity with histidine imidazole compound can bind with protein molecules with ease compared to some other heterocyclic moieties. Thus, imidazole gives better pharmacodynamic characteristics. Furthermore, some imidazole drugs, at high concentrations, exerted direct inhibitory effects on membranes, without interference with sterols and sterol esters. Various recent new drugs developments in imidazole derivatives show better effect and less toxicity.

Conflict of interest

The authors report no declaration of conflict of interest.

3. Reference

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