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Review Article

Quinoline containing benzimidazole and their biological activities

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ABSTRACT

Quinoline and derivatives of Benzimidazole are widely studied for their different activities. One of the essential classes of anti-malarial and anti-bacterial treatment is the quinoline derivatives. Quinoline and Benzimidazole are flexible lead molecules used to model the future molecules of drugs. The present review outlines the potential pharmacological activities of quinoline and Benzimidazole derivatives.

1. Introduction

Quinoline and benzimidazole derivatives are known for their excellent potential for various pharmacological activities. Many marketed drugs contain these two heterocycles in their structures.

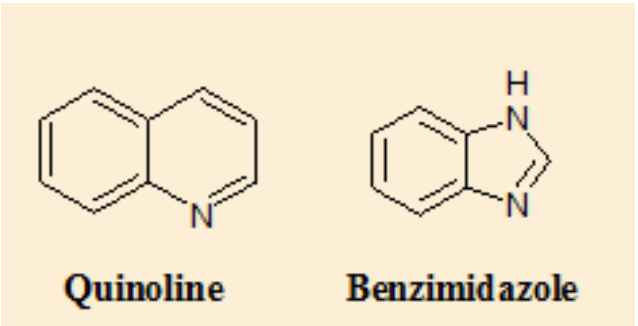

Fig. 1: Structure of quinoline and bezimidazole

Fluoroquinolone antibiotics, which have a fluorine atom in their molecular structure and are active against Gram-negative and Gram-positive bacteria, account for nearly all quinolone antibiotics currently in use.[1] Ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, and ofloxacin are fluoroquinolone antibiotics.[2] Thiabendazole, flubendazole, astemizole, lansoprazole, and omeprazole are some of the commercially available benzimidazole-containing medications.[3] There is an important place in drug discovery for quinolinyl and benzimidazole heterocycles. This review article focuses on quinolinyl and benzimidazole conjugates for their analgesic, anti-inflammatory, antibacterial, antifungal, antiviral, anti-parasitic, anti-Parkinson's disease, anticancer, antioxidants, antidiabetic, anticoagulant, and antimalarial activities. Most of the researchers have studied quinolinyl-based benzimidazole derivatives as models for the development of new antimicrobial agents.

The Quinoline ring system consists of heterocycles where a pyridine ring fuses the benzene ring. Quinoline derivatives have a range of biological activities such as antimicrobial[4], anti-tuberculosis[5], anti-inflammatory[6], and anti-cancer.[7] This review contains reported derivatives of quinoline and Benzimidazole and their biological activities.

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2. Quinoline Benzimidazole Conjugates

El-Feky, S. A.et al.synthesized Benzimidazole and fluorinated quinoline derivatives and tested for anti-inflammatory activity and ulcerative effect. As they were an ulcerogenic activity, the most active compounds (1a-f) were found to be superior to celecoxib. Compound 1a showed the highest anti-inflammatory activity as well as the best binding profiles at the COX-2 binding site. It is stated that the existence of the acetamide linker in compounds 1a–f could favor activity over the non-substituted benzimidazole derivative.(Figure 1).[6]

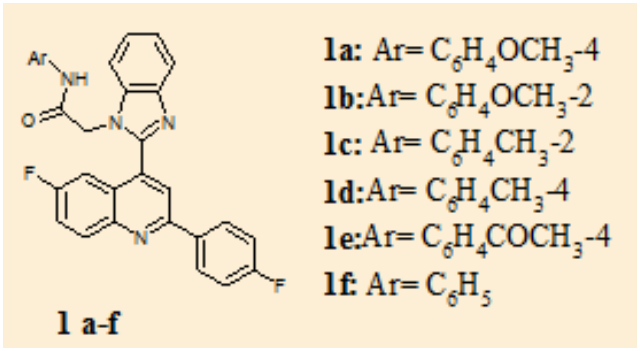

Fig. 2: Benzimidazole and fluorinated quinoline derivatives

Brajša, K. et al. synthesized amidino-replaced benzimidazole and benzimidazo[1,2a] quinoline derivatives and studied them in 2D and 3D cell culture systems for their cytotoxic activities. Synthesized compounds were tested as a small platform to compare antitumor activity in 2D and 3D cell culture systems and comparison with the relationship between structure and function. A human cancer breast (SK-BR-3, MDA-MB-231, T47D) and pancreatic cancer cells (MIAPaCa2, PANC1) have been tested with the 3D cell culture method. Compounds have shown moderate to potent activities as compared to standards (Figure 3).[7]

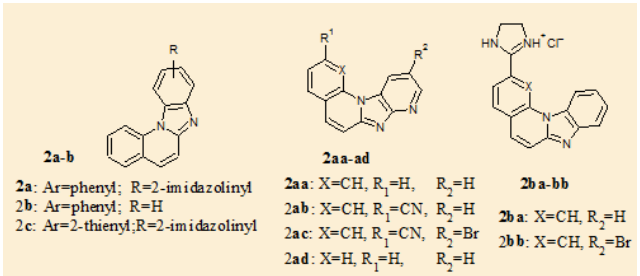

Fig. 3: Amidino-replaced benzimidazole and benzimidazo[1,2a] quinoline derivatives

Garudachari, B. et al. synthesized Benzimidazole-quinoline derivatives and tested them for antimicrobial activities. The compounds weres screened using a well plate method (inhibition zone) for their antibacterial and antifungal activity invitro. There result showed strong antibacterial activity in compounds *3c, 3d, 3ac,* and *3ad.* It was found that the compound *3ab* is a powerful antifungal agent. Compounds *3a, 3aa,* and *3af* showed Moderate to good antimicrobial activity.[8]

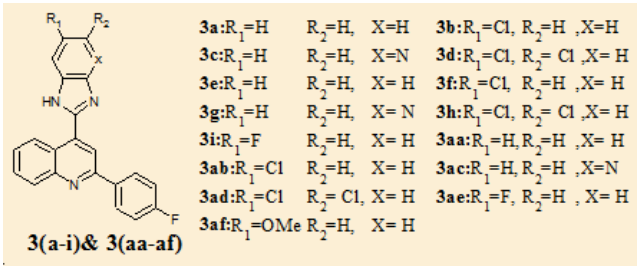

Fig. 4: Benzimidazole-quinoline derivatives

Mungra, D.C. et al synthesized benzimidazoles[1,5-a]quinoline-basedtetrazoloand tested for antimicrobial activity. Compound *4e* showed significant activity against Bacillus subtilis Gram-positive bacteria. Compounds *4a* and *4o* were found significantly active against Bacillus subtilis compared with ampicillin (Figure 5).[9]

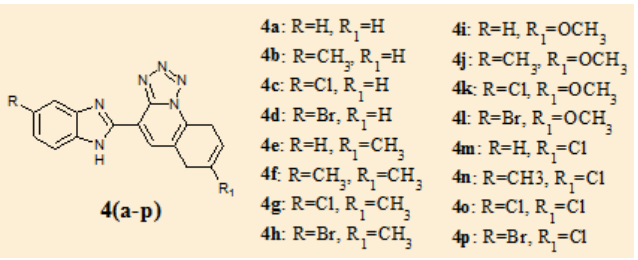

Fig. 5: benzimidazoles[1,5-a]quinoline- derivatives

Lamazzi, C. et al synthesized Cyanoindolo[3,2-c]quinolinesandBenzimidazo[1,2-c]quinazolinesand tested for cytotoxic activity. Compounds have shown excellent cytotoxic activity against murine L1210 leukemia cell line (Figure 6).[10]

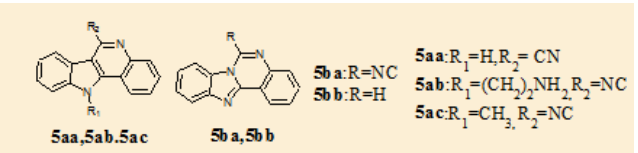

Fig. 6: Cyanoindolo[3,2-c]quinolinesandBenzimidazo[1,2-c]quinazolines

Perin, N. et al synthesized 2-substitutedbenzimidazo[1,2-a]quinolines and tested for their antitumor activity. Compounds have shown activities in the range of 0.2 ->10 μM against HCT116, 2.5- 39 μM against MCF-7, and 0.2 ->10 μM against H460 (Figure 7).[11]

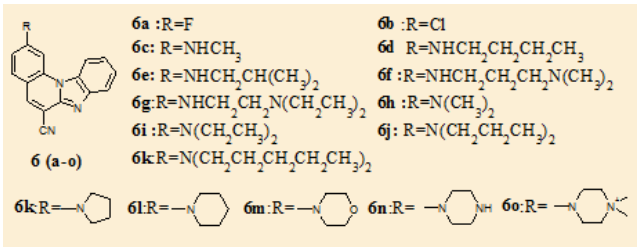

Fig. 7: 2-substitutedbenzimidazo[1,2-a]quinolines

Ukrainets, I.V. et al. synthesized Benzimidazol-2-ylamidesof1-r-4-hydroxy2-oxo-1,2-dihydroquinoline-3-carboxylic acids are synthesized and tested for their antithyroid and antituberculosis activities. Compounds have shown moderate to potent antithyroid and antituberculosis activities.(Figure 8)[12]

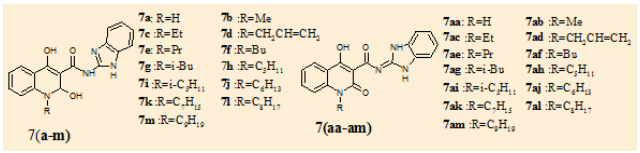

Fig. 8: Benzimidazol-2-ylamidesof1-r-4-hydroxy2-oxo-1,2-dihydroquinoline-3-carboxylic acids

Weinkauf. R. L. et al synthesized benzimidazo[1,2-b]-ouinoies,ndoo[2,3-]^{2}quinoines, and pyridocarbazoles and tested for antineoplastic activity against HCT-116, 9-KB, and Topoisomerase II. Compounds have shown cytotoxicity against HCT-116 in the range of 0.8- >150 μ/mL, 9-KB in the range of 2.2- >150 μ/mL and 0.1-10 μ/mL (Figure 9).[13]

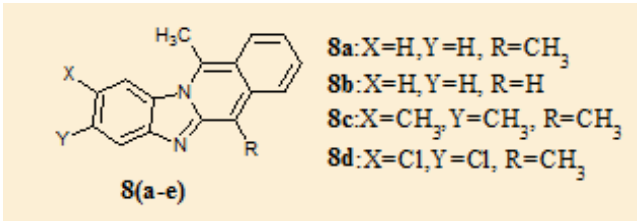

Fig. 9: Benzimidazo[1,2-b]-ouinoies,ndoo[2,3-]^{2}quinoines, and pyridocarbazoles

3. Conclusion:

For their anti-cancer and antibacterial activities, quinoline and Benzimidazole derivatives are mostly studied. Various derivatives identified have demonstrated excellent biological activity. Synthesis and study of such designed molecules can lead to potent drug candidates being discovered.

4. Source of Funding

None.

5. Conflict of Interest

None.

References

1. Heeb S, Fletcher MP, Chhabra SR, Diggle SP, Williams P, Cámara M. Quinolones: from antibiotics to autoinducers. *FEMS Microbiol Rev*. 2011;35(2):247–74. doi:10.1111/j.1574-6976.2010.00247.x.
2. Patton JH, Reeves DS. Microbiology, Pharmacokinetics and Clinical Use. *Fluoroquinolone Antibiotics*. 1988;36:193–228.
3. Yadav S, Narasimhan B, kaur H. Perspectives of Benzimidazole Derivatives as Anticancer Agents in the New Era. *Anti Cancer Agents Med Chem*. 2016;16(11):1403–25. doi:10.2174/1871520616666151103113412.
4. Sriram D, Bal TR, Yogeeswari P. Synthesis, Antiviral and Antibacterial Activities of Isatin Mannich Bases. *Med Chem Res*. 2005;14(4):211–28. doi:10.1007/s00044-005-0135-x.
5. Maddela S, Makula A. Design, Synthesis and Docking Study of Some Novel Isatin- Quinoline Hybrids as Potential Antitubercular Agents. *Anti Infective Agents*. 2016;14(1):53–62. doi:10.2174/2211352514011603021512 29.
6. El-Feky SA, Thabet HK, Ubeid MT. Synthesis, molecular modeling and anti-inflammatory screening of novel fluorinated quinoline incorporated benzimidazole derivatives using the Pfitzinger reaction. *J Fluorine Chem*. 2014;161:87–94. doi:10.1016/j.jfluchem.2014.02.012.
7. Brajša K, Vujasinović I, Jelić D, Trzun M, Zlatar I, Zamola GK, et al. Antitumor activity of amidino-substituted benzimidazole and benzimidazo[1,2-a]quinoline derivatives tested in 2D and 3D cell culture systems. *J Enzyme Inhib Med Chem*. 2016;31(6):1139–45. doi:10.3109/14756366.2015.1101093.
8. Garudachari B, Satyanarayana MN, Thippeswamy B, Shivakumar CK, Shivananda KN, Hegde G, et al. Synthesis, characterization and antimicrobial studies of some new quinoline incorporated benzimidazole derivatives. *Eur J Med Chem*. 2012;54:900–6. doi:10.1016/j.ejmech.2012.05.027.
9. Mungra DC, Patel MP, Patel RG. Microwave-assisted synthesis of some new tetrazolo[1,5-a]quinoline-based benzimidazoles catalyzed by p-TsOH and investigation of their antimicrobial activity. *Med Chem Res*. 2011;20(6):782–9. doi:10.1007/s00044-010-9388-0.
10. Lamazzi C, Léonce S, Pfeiffer B, Renard P, Guillaumet G, Rees CW, et al. Expeditious synthesis and cytotoxic activity of new cyanoindolo[3,2-c]quinolines and benzimidazo[1,2-c]quinazolines. *Bioorganic Med Chem Lett*. 2000;10(19):2183–5. doi:10.1016/s0960-894x(00)00427-3.
11. Perin N, Kleiner IM, Nhili R, Laine W, Cordonnier MHD, Vugrek O, et al. Biological activity and DNA binding studies of 2-substituted benzimidazo[1,2-a]quinolines bearing different amino side chains. *MedChemComm*. 2013;4(12):1537–50. doi:10.1039/c3md00193h.
12. Ukrainets IV, Grinevich LA, Tkach AA, Gorokhova OV, Kravchenko VN, Sim G. 4-hydroxy-2-quinolones. 191.* synthesis, tautomerism and biological activity of benzimidazol-2-ylamides of 1-r-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylic acids. *Chem Heterocyclic Compounds*. 2011;46(11):1364–70. doi:10.1007/s10593-011-0673-8.
13. Weinkauf RL, Chen AY, Yu C, Liu L, Barrows L, LaVoie EJ. Antineoplastic activity of benzimidazo[1,2-b]-isoquinolines, indolo[2,3-b]quinolines, and pyridocarbazoles. *Bioorganic Med Chem*. 1994;2(8):781–6. doi:10.1016/s0968-0896(00)82177-x.

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