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Design, Molecular Docking, Synthesis, and Antibacterial Activity of 1*H*-Benzimidazole-2-Carboxylic Acid (2-Oxo-1, 2-Dihydro-Indol-3-Ylidene)-Hydrazide Derivatives

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ABSTRACT This study reports the synthesis, design, and *in silico* and *in vitro* antibacterial evaluation of six benzimidazole and isatin hybrid derivatives. All six compounds were synthesized in three steps – (i) synthesis of esters of benzimidazole-2-carbxylic acids, (ii) formation of hydrazides hydrazinolysis of carboxylic esters with hydrazine hydrate, and (iii) the condensation of hydrazide with carbonyl group of the desired isatin derivative to obtain the target hydazide Schiff bases. The docking scores of compounds ranged between −6.6 and −8.4 kcal/mol. Compound 1e possessed the same docking scores as the standard drug, Norfloxacin (−8.4). The results revealed that -Cl and -NO_2 (electronegative groups) on benzimidazole as well as on isatin might be responsible for a good antibacterial activity.

KEYWORDS Benzimidazole, Isatin, Antibacterial, Hydrazides, Molecular docking.

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INTRODUCTION

Various Gram-positive and Gram-negative bacterial strains are among the most common and causative organisms for a variety of infectious diseases and these are found to be resistant to most of the existing antibiotics.[1,2] The recurrent and unfortunate use of antibiotics is responsible for the current status of antibiotic resistance which leads to decreased effectiveness of currently used antibiotics.[3,4] As per the current data (January 20, 2022), of global research on antimicrobial resistance (AMR), 1.27 million people died due to AMR worldwide including 4.95 million, in 2019.[5,6] Resulting, drug-challenging bacteria presented a severe risk to public health, and it is critical to developing novel and potent antibacterial drug candidates.[1]

Several benzimidazole derivatives have been synthesized and shown antimicrobial potential against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans*. Few benzimidazole derivatives are shown to have anthelmintic properties.[7] From the available literature, it can be deduced that the benzimidazole molecule has a variety of biological actions, including antihistaminic, anticancer, cytotoxic,[8] antitubercular,[9] antimicrobial,[10] antiviral,[11] and anti-inflammatory properties.[12] Benzimidazole nucleus has a diverse spectrum of biological functions such as antimicrobial, antiviral, anticonvulsant, anti-depressive, antihypertensive, analgesic, enzyme inhibition, antidiabetic effects, and other clinical uses.[13]

In 1841, Erdman and Laurent synthesized isatin by oxidizing indigo with nitric acid and chromic acids.[14,15] Many plants have isatin as their chemical constituent, including *Isatis tinctoria*, *Calanthe discolor*, and *Couroupita guianensis*, some plants also contain substituted isatins, such as *Melochia tomentosa's* melosatin alkaloids

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CONCLUSION

In this research, we have synthesized some new benzimidazole-isatin hybrids which might be an initiative for the synthesis of other hybrids of benzimidazole-isatin derivatives with improved antimicrobial and other pharmacological properties, than the drugs currently used in hospitals. The lack of antibacterial data and availability of reported antitumor data on isatin moiety suggested for the antitumor evaluation of the synthesized compounds.

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