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Synthesis and docking of new 4-(2-((1-phenyl-1H-1,2,3-triazol-4-yl) methoxy)phenyl)thiazol-2-amine derivatives as an antimicrobial agent

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ABSTRACT

The novel series of 4-(2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)phenyl)thiazol-2-amine **5a-h** have been synthesized by oxidation reaction of acetophenone tethered 1,4-disubstituted triazole derivatives with thiourea in the presence of iodine. All newly synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, HRMS, and elemental analysis techniques. The antibacterial activity of novel compounds were evaluated against *S. aureus*, *P. aeruginosa*, *E. coli* and *S. pyogenes* bacterial strains whereas antifungal activity were screened against *A. niger*, *C. albicans* and *A. clavatus* pathogen of fungi. The compounds **5a, 5b, 5f** and **5h** showed excellent antibacterial activity, whereas **5f** and **5g** showed excellent antifungal activity. This may be attributed due to the presence of 4-CH_3, 3-F, 4-F and 4-CF_3 functional groups in benzene ring. The all results were compared with standard Ampicillin and Griseofulvin antibacterial and antifungal drugs, respectively. The molecular docking studies of compounds were carried out to measure effective bindings and molecular interactions. The experimentally observed values of antifungal activity and binding affinities values of molecular docking showed good correlation.

1. Introduction

Antimicrobial resistance is now one of the most serious health problems in the world. Antimicrobial resistance endangers the effective prevention and treatment of an expanding number of infections caused by bacteria, fungi, parasites, and viruses [1]. Therefore it is important to develop new drugs with good activity against microbial infections. The synthesis of new pharmacophores to enhance biological activity is an important area of drug research [2]. Nitrogen and sulfur-containing heterocycles exhibit good antimicrobial activities [3,4]. Due to the many unique properties of the 1,2,3-triazole ring such as stability under physiological conditions, H-bonds, and π-π stacking interactions, etc., it is among the priority pharmacophore groups in drug research [5–8]. Compounds containing 1,2,3-triazole ring show a wide range of pharmacological activities such as antimicrobial, antifungal [9–11], antiviral [12,13], anti-inflammatory [14], antioxidant [15,16], anticancer [17, 18], DNA cleavage/binding [5,11] as well as 14α-sterol demethylase inhibitor [19] activities. Due to these activities of 1,2,3-triazole compounds, it is seen that this structure is included in the structures of many bioactive molecules designed in recent years [6]. Several antifungal medications, such as itraconazole, fluconazole, voriconazole, the antiviral drug ribavirin, and mubritinib, have the triazole ring as an essential component [20].

Moreover the thiazole ring is also an important heterocyclic compound found in many pharmacophores. The drugs such as Sulfathiazole, Abafungin, Dasatinib, and Dabrafenib contain a thiazole ring in their molecular structure [21,22]. In addition, thiazole derivatives exhibit various pharmacological activities such as antibacterial, antifungal [23, 24], antitubercular [25,26], antiviral [27], anticancer [28,29], DNA cleavage, and antioxidant [30] activities. Similarly, there are many studies related to the synthesis of the 1,2,3-triazole thiazole hybrids [31] showed enhanced activities and it has been reported that 1,2,3-triazole thiazole hybrids exhibit significant pharmacological activities such as anticancer [32,33], antimicrobial [34,35], antibiofilm [20], anti-anxiety, and anti-inflammatory [36]. Click chemistry allows for the easy production of 1,2,3-triazole using either copper or ruthenium-catalysed azide-alkyne cycloaddition. It is a bioisoster of amide, ester, carboxylic acid, and other heterocycles, and readily

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