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Antimicrobial Studies of Novel Furo fused BINOL based triazoles macromolecule

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Abstract: In the present research article, we have screened newly synthesized novel furo fused BINOL based triazole macromolecules **6** and **7,** for antimicrobial studies. The BINOL based triazole macromolecules were synthesized by click chemistry green reaction protocol. The Macromolecules **6** and **7** demonstrate potent antimicrobial activity at concentrations of 50 mg.

Keywords: Furo fused BINOL, 1,2,3 triazole, BINOL based Triazole, Antimicrobial agent.

Introduction: Among nitrogen-containing heterocyclic compounds 1,2,3-triazoles are privileged structure motifs and received a great deal of attention in pharmaceutical and medicinal chemistry.[1] Even though absent in nature, 1,2,3-triazoles have found broad applications in drug discovery.[2,3] Therefore, the development of a facile and straightforward methodology for the synthesis of 1,2,3-triazoles is of noteworthy interest. Triazole containing heterocyclic ring moieties are the core structure in various biologically active drug molecules such as Carboxyamidotriazole (CAI) (I), Cefatrizine (II), and Tazobactum (III) (Figure 1). The BINOL based macromolecules were found to have significant antimicrobial activity (IV), (V) and (VI).[4]

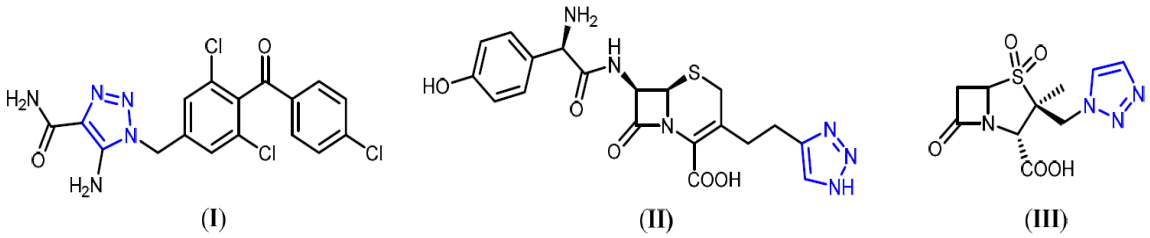

Figure 1. Chemical structures of pharmaceutical drugs containing 1,2,3-triazole rings.

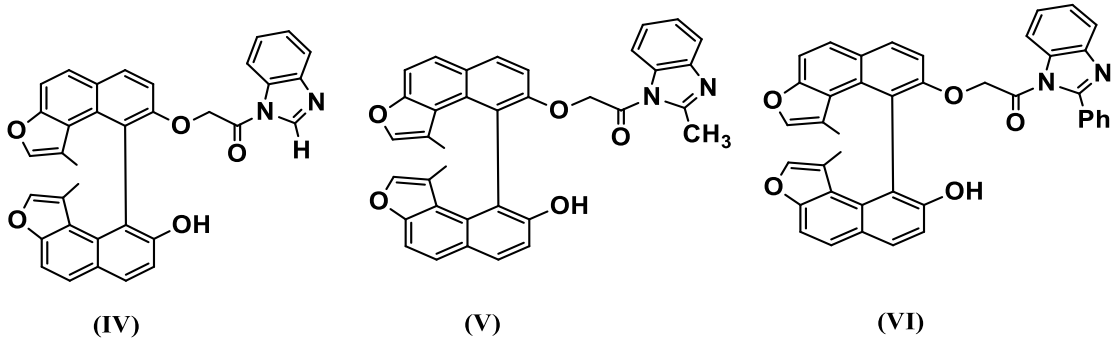

Figure 2. Chemical moieties of Furo fused BINOL based containing 1,2,3-triazole rings shows potent Antimicrobial activity.

Bacteria that cause food poisoning have been found to have extremely high rates of resistance. All WHO regions have common healthcare-associated and community-acquired infections (e.g., urinary tract infection, pneumonia).[5] Mutations alter the portions of the cell that are affected by medications, reducing their effectiveness. The development of antibiotic resistance in bacteria[6] and multiple drug resistance in fungi[7] are both risks to disease therapy. Multidrug-resistant organism (MDRO) infections can be more difficult to treat because there are fewer antibiotics that work against them. Resistance and tolerances of many bacteria and viruses have always prompted the search for new drugs.

Triazole compounds with three nitrogen atoms at 1,2,3 position in the five-membered aromatic azole ring are easily able to engage with a variety of enzymes and receptors in biological systems via non-covalent interactions, and so have a wide range of biological functions. The use of triazole-based derivatives as therapeutic medications has been a hot issue in recent years, with multiple great results. Specifically, a vast number of triazole compounds have been commonly used as clinical medications or candidates for the treatment of a variety of disorders, demonstrating their high development value and broad potential as medicinal agents.[8] On that account synthesis of triazole derivatives as a source of new antimicrobial agents got a lot of attention in recent years. The main focus of medicinal research continues to be the synthesis of novel triazole derivatives. Substituted triazole and heterocycles, which are structural isosteres of nucleotides with fused heterocyclic nuclei in their structures that allow them to interact easily with biopolymers, have potential activity with lower toxicities in the chemotherapeutic approach in man, according to the trends observed.[9-23]

In the current study, we have decided to screen newly synthesized novel furo fused BINOL based triazole macromolecules **6** and **7,** for antimicrobial studies as both compounds contain 2 triazole ring units with etheral linkage. Such an approach is a part of our ongoing research on the synthesis of biologically active compounds.

RESULTS AND DISCUSSION

The novel furo fused BINOL based triazole macromolecules **6** and **7** were synthesized and developed by click chemistry green protocols.[24]

Antimicrobial Activity

The antimicrobial activity of the synthesized compounds was tested by the *disc diffusion* method. They were sterilized by filtering through a 0.45m Millipore filter after being dissolved in DMSO. A 100L suspension containing 108 CFU/mL of each bacteria and fungus was utilized as the final inoculum. Nutrient agar (antibacterial activity) and Sabouraud's dextrose agar medium (antifungal activity) were prepared and sterilized in an autoclave (118°C and 14 Ibs for 22 minutes) before being transferred to pre-sterilized Petri dishes (9 cm in diameter). Petri plates were inoculated in aseptic condition with bacterial organisms in sterile nutritional agar medium at 45^{o}C and fungal organisms in sterile sabouraud's dextrose agar medium at 45^{o}C. The synthesized compounds were impregnated at a concentration of 50 mg/disc on sterile Whatmann filter paper discs (previously sterilized with a UV lamp) and placed in organism-impregnated Petri plates under sterile conditions. The plates were left at room temperature for 30 minutes to facilitate compound diffusion. Antibiotic discs of Gentamicin (100µg/disc) were used as a positive control, while DMSO was used as a negative control. The plates were then incubated at 371°C for 24 hours for antibacterial activity and 48 hours for antifungal activity. The zone of inhibition was determined by taking the smallest dimension of the no-microbial-growth zone around each disc. In vitro antibacterial activity of macromolecules **6** and **7** was tested against gram-negative bacteria Proteus vulgaris (NCTC 4635) and Klesibella pneumonia (ATCC 29655), as well as gram-positive bacteria Bacillus cereus (NL98) and Micrococcus luteus (ATCC 10240). These are the agents that commonly cause urinary tract infection, nosocomial infection, and biliary tract infection. Klesibella pneumonia is a gram-negative bacteria that cause pneumonia, bronco pneumonia, and bronchitis. Bacillus cereus and Micrococcus luteus are gram-positive bacteria that cause endocarditis, bacteremia, meningitis, and septicemia. From Table 1, it is evident that macromolecule **6** was shown to be more active against Klesibella pneumonia (ATCC 29655), Bacillus cereus (NL98), and Micrococcus luteus (ATCC 10240), whereas macromolecules **7** was found to be more active against Proteus vulgaris (NCTC 4635). Aspergillus niger and Aspergillus fumigatus were found to be more potent against macromolecules **6**. However, the synthesized compound's antibacterial activity against the tested organisms was found to be lower than that of the respective reference medicine at the dose level tested.

Organism	Diameter of zone of inhibition in mm		
	Macromolecule 6 (50mg)	Macromolecule 7 (50mg)	Gentamicin (100 µg)
Bacillus Cerus	17	13	34
Proteus Vulgaris	11	18	31
Klesibella Pneumonia	21	14	30
Micrococcus luteus	18	09	30
Aspergillus Niger	14	12	----
Aspergillus Fumigatus	16	10	----

Conclusion

In search of a novel potential bioactive drug, macromolecules **6** and **7** were synthesized and developed by click chemistry green protocols. Macromolecule **6** was found to be more capable than macromolecule **7** in respect of the antimicrobial activity, when screened and evaluated against both gram-positive and gram-negative bacteria but least capable than the standards used like Gentamicin.

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Conflicts of Interest

The authors declare no conflict of interest.

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