World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:12, No:09, 2018

Teicoplanin Derivatives with Antiviral Activity: Synthesis and Biological Evaluation

Authors : Zsolt Szucs, Viktor Kelemen, Son Le Thai, Magdolna Csavas, Erzsebet Roth, Gyula Batta, Annelies Stevaert, Evelien Vanderlinden, Aniko Borbas, Lieve Naesens, Pal Herczegh

Abstract : The approval of modern glycopeptide antibiotics such as dalbavancin and oritavancin which have excellent activity against Gram-positive bacteria, encouraged our research group to prepare semisynthetic compounds from several members of glycopeptides by various chemical methods. Derivatives from the aglycone of ristocetin, eremomycin, vancomycin and a pseudoaglycon of teicoplanin have been synthesized in a systematic manner. Interestingly, some of the aglycoristocetin derivatives displayed noteworthy anti-influenza activity. More recently our group has been focusing on the modifications of one of the pseudoaglycons of teicoplanin. The reaction of N-ethoxycarbonyl maleimide derivatives with the primary amino function, the copper-catalysed azide-alkyne click reaction and the sulfonylation of the N-terminus were utilized to obtain systematic series of compounds. All substituents provide a more lipophilic character to the new molecules compared to the parent antibiotics, which is known to be favourable for activity against resistant bacteria. Lipoglycopeptides are also known to have antiviral properties, which has been predominantly studied on HIV by others. The structure-activity relationship study of our compounds revealed the influence of a few structural elements on biological activity. In many cases, minimal changes in lipophilicity and structure produced great differences in efficacy and cytotoxicity. In vitro experiments showed that these compounds are not only active against glycopeptide resistant Gram-positive bacteria but in several cases they prevent the infection of cell cultures by different strains of influenza viruses. This is probably related to the inhibition of the viral entry into the host cell nucleus, of which the exact mechanism is unknown. In some instances, reasonably low concentrations were sufficient to observe this effect. Several derivatives were highly cytotoxic at the same time, but some of them displayed a good selectivity index. The antiviral properties of the compounds are not restricted to influenza viruses e.g., some of them showed good activity against Human Coronavirus 229E. This work could potentially lead to the development of antiviral drugs which possess the crucial structural motifs that are needed for antiviral activity, while missing those which contribute to the antibacterial effect.

Keywords : antiviral, glycopeptide, semisynthetic, teicoplanin
Conference Title : ICVVAD 2018 : International Conference on Viral Vaccines and Antiviral Drugs
Conference Location : Lisbon, Portugal
Conference Dates : September 24-25, 2018