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Chemical modifications of inhibitors of m2 ion channel of influenza virus

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Statement of the Problem: The Influenza Matrix 2 (M2) protein is the target of Amantadine and Rimantadine which block its H⁺ channel activity. However, the potential of these aminoadamantanes to serve as anti-flu agents is marred by the rapid resistance that the virus develops against them. This fact makes influenza a very dangerous pathogen able to cause pandemics with a high rate of mortality.

Currently, two classes of antiviral drugs have been approved for the prevention and treatment of influenza infection - the M2 channel inhibitors (aminoadamantanes- amantadine and rimantadine) and the neuraminidase inhibitors (NAIs- oseltamivir and zanamivir) Worldwide, virtually all 2009 H1N1 and seasonal H3N2 strains are resistant to the adamantanes (rimantadine and amantadine), and the majority of seasonal H1N1 strains are resistant to oseltamivir, the most widely prescribed neuraminidase inhibitor (NAI). To address the need for more effective therapy, we have synthesized and evaluated the in vitro activity of new analogues of amantadine and rimantadine with amino acids and peptides – methylglycine, dimethylglycine, glycyl-glycine, glycyl-glycyl-glycine investigated their antiviral activity against drug resistant seasonal and 2009 H1N1 influenza viruses. Conclusion & Significance: In summary, we have successfully constructed new adamantane analogues. The structures of new analogues were confirmed by NMR and MS spectra the in vitro cytotoxicity and antiviral activity of the new aminoadamantane derivatives were examined against influenza virus A strains H3N2. The highest antiviral activity of rimantadine analogs clearly demonstrate methylglycyl-rimantadine - its activity is about 3.5 times higher than that of amantadine, analogues of amino acids with amantadine do not show activity.

Biography

Ivanka Stankova conducts research in the field of medicinal chemistry - chemical modifications of drugs and more specifically antiviral drugs (drugs for the treatment of AIDS, anti-herpes and anti-influenza drugs) as well as those used in Alzheimer's disease.

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