International Conference on Natural Products and Physiologically Active Substances (ICNPAS-2004)
September 12-17, 2004, Novosibirsk, Russia
Poster Presentation

Influence of Cage Compounds Lipophilicity on Spectrum of Antiviral Activity

Yu. N. Klimochkin[1], E. I. Boreko[2], A. K. Shirayev[1], I. K. Moiseev[1], E. V. Golovin[1]

[1]*State Technical University, 244 Molodogvardeyskaya St., 443100 Samara, Russia, orgchem@samgtu.ru,*
[2]*Research Institute for Epidemiology & Microbiology, 23 Philimonova St., 220114 Minsk, Belarus, boreko@briem.ac.by*

Amines of the adamantane series (amantadine, rimantadine) are used for treatment and prophylaxis of influenza A for a long time. The mechanism of its activity is connected with blocking of transmembrane M2 protein realizing function of ion channel. At the same time some adamantane derivatives have activity against influenza B virus (adapromine) and herpes virus (tromantadine). This fact allows to propose both similar and another possible mechanisms of various viruses replicative cycle inhibition by cage compounds.

A series of adamantane derivatives including heterocycles have been synthesized, and their antiviral action against herpes simplex virus (HSV-I, C 1), vaccinia virus (VV, B-51), influenza virus (A/FPV/Rostock/34 (H7N1)), respiratory synthicial virus (RSV, Long), vesicular stomatitis virus (VSV, Indiana), venesuel equine encephalitis virus (VEEV-230), picornavirus ECHO-6 and rotavirus SA-11 have been investigated in cell culture experiments. More than 100 compounds have shown activity and some of them were active against several viruses. The most number of compounds are active against VV, FPV and HSV. The tested adamantane derivatives did not suppress ECHO-6 virus reproduction, and this suggests the adamantane derivatives inhibit the initial stages of entry characteristic for enveloped viruses. It is supposed the dependence of antiviral activity on lipophilic parameter (log P). The necessary requirement for inhibiting influenza virus is the presence of protonated amino group and relatively low lipophilicity of the molecule. The mean calculated log P value for 37 active compounds is 1.66. 11 of these compounds have shown strongly marked action (log P = 0.85 on the average). The activity was reduced when lipophilicity was increased in the certain limits in this series.

For DNA-containing VV and HSV the main factor for antiviral action is relatively high hydrophobic properties. The mean log P value for 44 compounds active against VV is 2.77, 7 highly active of them have the mean log P = 3.35. 41 compounds were active against HSV (log P = 2.99 on the average) including 4 most active (log P = 3.55 on the average). The antiviral action authentically grows according to increase of lipophilicity for this series. The established regularities allow concluding that the effective hydrophobic interaction is important condition for activity against DNA-containing viruses. The data on activity of compounds tested with rotavirus (10 compounds), RSV (20 compounds), VSV (17 compounds), and VEEV (15 compounds) do not permit to make statistically reliable conclusion on the dependence of antiviral action on log P.