Oral Session II

Antiviral Agents and Immodulators

8

Antiherpes Virus Activity of 5-Methoxymethyl-2'-deoxycytidine in Combination with Deaminase Inhibitors. P.J. Aduma, V.S. Gupta, A.L. Stuart and G. Tourigny. Departments of Veterinary Physiological Sciences and Chemistry, University of Saskatchewan, Saskatoon, SK, S7N OWO, Canada.

5-Methoxymethyl-2'-deoxycytidine (MMdCyd) is an antimetabolite with selective antiherpes activity and low cytotoxicity. MMdCyd is dependent upon initial activation by the viral-induced dThd/dCyd kinase for its activity against Herpes simplex virus (HSV). Antiviral activity of MMdCyd is cell-dependent and is influenced by the deaminase content of the cell line used for assays. The antiviral potency against HSV-1 was higher in RK-13 cells (ED_{50} 3 to 5 μM) than in VERO and HEP-2 cells (ED_{50} 14 to 26 μM). Potency of MMdCyd increased approximately 20-fold against HSV-1 and 2-fold against HSV-2 in the presence of tetrahydrodeoxyuridine (H_4dUrd, inhibits both dCyd deaminase and dCMP deaminase) in VERO cells. MMdCyd in combination with H_4dUrd was effective in preventing the cytopathogenic effect of HSV-1 and decreasing the production of infectious virus particles. The IC_{99} (concentration required to reduce the yield of infectious virus obtained 72 h after infection by 99% relative to control cultures) was 1.6 μM. In combination with tetrahydrouridine (H_4Urd, an inhibitor of Cyd/dCyd deaminase) the potency of MMdCyd was only slightly enhanced (ED_{50} 7 to 8 μM). Dihydrodeoxyuridine and deoxyuridine reversed the antiviral activity of MMdCYd. Minimum cytotoxic concentration for rapidly dividing cells (RK-13, HEP-2 and VERO) for MMdCyd was greater than 3 mM. H_4Urd and H_4dUrd were devoid of cytotoxicity and antiviral activity up to 2.12 mM.

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