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Potentiating Effect of Dextran Sulphate on the Antiviral Activity of Acyclovir and BVDU in the Treatment of Herpetic Keratitis in Rabbits. S.N. Pancheva. Institute of Microbiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

Dextran sulphate (DS, MW 5000) has been shown to be a potent and selective inhibitor of various enveloped viruses in vitro (Baba et al., 1988). Recently we have reported that DS is effective also in vivo against HSV-1 keratoconjunctivitis in rabbits (Pancheva, 1992, 1993). We have investigated now the effect of DS in the treatment of HSV-1 keratitis with acyclovir and BVDU. DS was administered before virus inoculation and continued for 10 days. Treatment with ACV and BVDU (parallel experiments) started 72 h after virus inoculation and applied for 7 consecutive days. DS potentiated the antiviral action of ACV and of BVDU manifested by decrease in both severity of corneal lesions and virus shedding in the tear film.
The antiherpes activity of DS and apparent lack of toxicity, demonstrated in rabbit eye after local administration of the drug, makes it a promising compound for the exploration of its antiherpes potentials in human as prophylactic and therapeutic agent alone or in combination with others antiherpes drugs.

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Peptidomimetic Ribonucleotide Reductase Inhibitors in the Treatment of Herpes Simplex Keratitis in Mice.
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Herpetic keratitis is the leading cause of blindness due to infectious disease in developed countries. Current antiviral therapy consists mainly of nucleoside analogs. We investigated the *in vivo* antiviral effects of two ribonucleotide reductase (RR) inhibitors, BILD 733 and BILD 1263. These inhibitors are peptidomimetic compounds that act by blocking the association of the two subunits of the virally encoded RR. BILD 1263 is approximately 10 times more potent than BILD 733 in inhibiting herpes simplex virus (HSV-1) growth in cell culture (EC_{50} of 3 and 32 μM respectively). Starting 3 hr post inoculation (PI), Balb/C mice inoculated with 10^6 plaque forming units of HSV-1 strain KOS were treated 6 times a day for 3 days and subsequently 4 times a day for 4 days with either ophthalmic cream or ophthalmic cream plus inhibitor. Animals were examined microscopically for signs of stromal keratitis and corneal vascularization, up to 21 days PI. Under the present experimental conditions, BILD 733 failed to show activity at a concentration of 5%. In contrast, BILD 1263 dose-dependently reduced the mean keratitis and mean neovascularization disease scores when administered topically at doses of 1% and 5%. Further development of peptidomimetic RR inhibitors could lead to a valuable alternative to nucleoside analogs in the treatment of herpes simplex infections.