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CTC 23 Efficacy in vitro and on HSV-1-induced Ocular Epithelial and Stromal Disease in the Rabbit. EC Dunkel, PA Geary, J Brooks and D Pavan-Langston, Eye Research Institute and Dept of Ophthalmology, Harvard Medical School, Boston, MA, 02114

Antiviral activity of a new class of organometallic compounds (Chai-Tech Corp., Greenvale, NY) was evaluated in vitro by plaque assay and in vivo during HSV-1 corneal epithelial and stromal infection in the rabbit. In vitro, the IC_{50} for HSV-1 by plaque reduction assay on HFF cell monolayers was 10 µg/ml. TFT resistant HSV-1 was sensitive to CTC 23 (IC_{50}=0.6-1µg/ml). Cytotoxicity was not demonstrated at concentrations up to and including 1 mg/ml. In vivo, CTC 23 efficacy was evaluated after topical inoculation of 10^5 PFU/ml HSV-1 McKrae strain (epithelial keratitis model) or after corneal intrastromal inoculation of 10^5 PFU/ml HSV-1 RE strain (stromal disease model). Therapy (5x/day) was initiated on day 3 PI with either: 1 mg/ml CTC 23 (n=30); 1% TFT (n=30); or placebo (sterile water, n=20). HSV-1 ocular disease was monitored daily by slit lamp exam and tear film virus recovery. 1 mg/ml CTC 23 therapy (epithelial keratitis model) demonstrated a significant reduction in disease severity compared to placebo ($p<0.02$), although there was no difference between CTC 23 and TFT therapies ($p>0.4$). CTC 23 at 1 mg/ml significantly reduced tear film HSV-1 recovery compared to TFT and placebo treatments ($p<0.02$). In eyes with mild stromal disease (0-0.5+; stromal disease model), 1 mg/ml CTC 23 therapy reduced stromal disease and HSV-1 recovery significantly compared to TFT and placebo therapy ($p<0.03$). In eyes with moderate stromal disease (>0.5+), neither CTC 23, TFT, nor placebo therapies were effective in reducing stromal disease development; however, CTC 23 therapy was more effective than TFT ($p=0.08$). These evaluations demonstrate that CTC 23 has antiviral activity in vitro and in in vivo models of epithelial and stromal HSV-1 infection in the rabbit. Although the in vivo efficacy of CTC 23 was comparable to that of TFT, CTC 23-treated animals exhibited a more favorable side effect profile in the therapeutically-effective dose range.

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Efficacy of a Recombinant Human Interferon Alpha B/D Hybrid (IFN-αB/D) Against Experimental Genital Herpes Infection in Male and Female Guinea Pigs.
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Genital herpes infections caused by HSV-2 continue to be a major cause of morbidity. IFN-αB/D is a cross-species active molecule and we have examined the activity of this compound in experimental genital herpes infection in male and female guinea pigs. The MS strain of HSV-2 was used throughout. Female guinea pigs were inoculated intravaginally; male guinea pigs were infected by inoculation onto a scarified area of the lower abdomen. One, prophylactic dose of IFN-αB/D ($1x10^7$ U/kg, s.c. 24 hours before infection) successfully protected both sexes from the full effects of infection; many animals were fully protected and showed no signs of infection. A lower dose ($3x10^6$ U/kg) of IFN-αB/D was less effective but still induced a significant level of protection. If treatment was commenced 3 hours after infection a similar but less marked protection was observed. When treatment was delayed until the appearance of genital lesions (3-4 days after infection) daily administration of $1x10^7$ U/kg caused a reduction in the severity and speed of development of the disease. We are at present investigating the influence of IFN-αB/D on latent infections in these models and the possible use of combination therapy with chemotherapeutic agents.