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Comparison of *n*-Docosanol Cream (LIDAKOL™) with Acyclovir Ointment (Zovirax™) in the Inhibition of Cutaneous Herpes Simplex Virus (HSV) Infections in Two Guinea Pig Model Systems. J.F. Marcelletti, R.R. McFadden, M.H. Khalil, L.E. Pope, R.C. Davis, L.R. Katz, and D.H. Katz. LIDAK Pharmaceuticals, 11077 N. Torrey Pines Road, La Jolla, CA 92037.

The antiviral activities of the topical formulations for *n*-docosanol (LIDAKOL™) and acyclovir (Zovirax™) were studied in a model of herpes simplex virus (HSV)-induced cutaneous disease in hairless and Hartley (haired) guinea pigs. Clearly identifiable HSV vesicles were observed in the hairless animals at approximately 30-48 hours after inoculation with HSV, which progressed to crusting by 72-78 hours post-infection (vesicle period ~48 hours). Vesicles typically arose later in the Hartley animal (72-96 hours), and were resolved by 144-168 hours post-infection (vesicle period ~96 hours). In hairless guinea pigs, significant and comparable antiviral activities for both acyclovir and *n*-docosanol were evident by ~56-60 hours post-infection with HSV. Substantially different results were obtained in Hartley guinea pigs. The antiviral activity of acyclovir was generally apparent as soon as vesicles appeared, at ~96 hours post-infection. The inhibitory activity of *n*-docosanol became evident another 24 hours later, *i.e.*, ~120 hours post-inoculation. The skin of the hairless guinea pig is substantially thinner than that of the Hartley animal, which may explain certain of these phenomena. It is possible that in the Hartley pig, the difference in the kinetics of antiviral activity exhibited by the hydrophilic acyclovir and the hydrophobic *n*-docosanol may relate to a difference in the respective skin penetration rates of the drugs; this may be less of a factor in the thinner-skinned hairless pig, yielding smaller differences in the antiviral kinetics of the two drugs.

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Effect of Polyanionic Compounds on Intracutaneous and Intravaginal Herpes Virus Infection in Mice: Impact on the Search for Vaginal Microbicides.

J. Neyts and E. De Clercq
Rega Institute for Medical Research, K.U.Leuven, B-3000 Leuven, Belgium

Several polyanionic substances, such as dextran sulfate (but not dextran), suramin and the co-polymer of acrylic acid with vinyl alcohol sulfate (PAVAS), were found to suppress intracutaneous infection of hairless mice with herpes simplex virus type 2 (HSV-2) when present at the time of inoculation. Since (i) sexual intercourse is a major route of infection with human immunodeficiency virus (HIV) in humans, (ii), due to the species-specificity of HIV, there is no small animal model to study intravaginal HIV infection, and (iii) HIV is equally or even more sensitive than HSV-2 to polyanionic substances, we used an experimental murine model of intravaginal HSV-2 infection to study the effect of polyanionic substances on virus transmission by the genital route. Under the conditions used, dextran sulfate conferred about 50% protection against mortality induced by intravaginal HSV-2 inoculation. The protective effect of PAVAS was more pronounced than that of dextran sulfate. These results should be helpful in planning further studies on the use of intravaginal formulations of polyanionic substances in the prevention of sexually transmitted HIV or HSV infections.