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A Modified Guinea Pig HSV-2 Infection Model Designed To Prevent Ingestion Of The Topically Applied Antiviral Drug R-837. Imbertson, L.M., Miller,R.L., Reiter,M.J., 3M Pharmaceuticals, 3M Co., St. Paul, MN. U.S.A.

R-837 [1-(2-methylpropyl)-1H-imidazo[4,5-c]quinolin-4-amine] is a low molecular weight interferon inducer that has demonstrat-ed antiviral and antitumor activity in animal models. The drug is effective when administered orally, parenterally, or topically. The vaginal HSV-2 infection model in Hartley guinea pigs was utilized to determine efficacy of several topical formulations of R-837. 100uL of a 5% R-837 formulation (25mg/kg) was applied to the backs of 2 groups (N=7). To eliminate the possibility of ingestion of the drug, the site of treatment was covered after drug application with a 2" strip of Medipore™ tape in one treatment group. All groups were treated bid for 4 days starting 24 hours after infection. Vaginal lesions were scored on days 8,9 and 10 after infection. The results showed efficacy was lost by covering the drug treatment site (100% protection in uncovered and 0% protection in covered group). Protection from HSV-2 infection correlated with serum interferon levels. We conclude the guinea pigs were likely ingesting the topically applied drug. A further study, housing the animals separately, indicated the guinea pigs were likely ingesting drug that was applied to their own backs. This modified drug testing model was utilized to select a new R-837 formulation that was efficacious even when the drug treatment site was covered.

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R837 treatment of recurrent genital HSV-2 disease in the guinea pig. C.J. Harrison[1], R.L. Miller[3], D.I. Bernstein[2]. Children's Hosp Res Fnd[1], J.N. Gamble Institute Med Res[2], Cincinnati, OH; and the 3M Pharmaceuticals, St. Paul, MN[3].

We have previously shown that R837 (Riker, 3M Pharmaceuticals), an immunomodulator, decreases acute primary genital HSV-2 disease when administered within 36h of intravaginal HSV inoculation of guinea pigs. We now report on topical R837 treatment of recurrent genital HSV-2 after recovery from primary infection. Compared to placebo (n=24), R837 (n=24) when applied as a 1% suspension at 5 mg/kg/d for 5d starting 15d after HSV-2 inoculation, decreased mean recurrent lesion days/animal from 0.25±0.30 to 0.10±0.12 ($p < 0.03$) during treatment but not thereafter. When R837 (n=29) or placebo (n=26) was applied at the same dose beginning 14d after HSV-2 inoculation but for 21d, R837 recipients had decreased mean recurrent lesion days/wk not only during the 3wk treatment (0.07±0.08 vs 0.24±0.11 days, $p < 0.0001$) but also for 5wk after R837 was stopped (0.03+0.04 vs 0.08±0.08, $p < 0.03$). The effects of treatment on humoral and cell mediated responses were mixed, with suppression of responses in the 5d R837 group but enhanced lymphocyte proliferation to HSV in the 21 day R837 group. NK activity and IL-2 were not enhanced by R837. Interferon levels were enhanced only during R837 treatment. Topical R837 therapy for 21d transiently increased interferon levels, appeared to upregulate some cell mediated but not humoral responses and reduced HSV recurrences.