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Efficacy of Topical Treatment with BV-araU Cream against Cutaneous Infection with Herpes Simplex Type 1 in Shaved Mice

H. Machida, K. Ijichi, N. Ashida, and S. Varia*

Biology Laboratory, Yamasa Shoyu Co., Ltd., Choshi, Japan and *Bristol-Myers Squibb Pharmaceutical Institute, New Bruswick, NJ

BV-araU cream was prepared by using polyethylene glycol and propylene glycol, and the effect of topical treatment with the BV-araU cream was tested against non-lethal cutaneous infection of shaved back skin of Balb/c mice with a low virulent strain of herpes simplex virus type 1. Mice were treated 4 times a day for 5 days. Progression of cutaneous symptoms caused by the virus infection was significantly inhibited by treatment with 5% BV-araU cream beginning one day postinfection (pi.). Most of the treated mice showed no symptom. The BV-araU cream was as effective as Zovirax cream (5%). In delayed therapy experiment, 5% BV-araU cream was effective for reduction of the mean maximum lesion score ($p<0.002$) but not for decrease in morbidity of mice (treatment began 2 days pi.). When treatment was started 5 days pi., further progression of symptom was suppressed during treatment period compared with the control group. Virus titer at the infected skin site markedly decreased and viral growth at symptom-appearing site was almost completely suppressed by treatment with BV-araU cream beginning one day pi. Virus growth was also inhibited when the treatment was started at 2 days pi. Although 1% cream was also effective against development of symptom, the efficacy reduced with decrease in the concentration of BV-araU.

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Phenotype of Ganciclovir-Resistant Mutants of Murine Cytomegalovirus

Y. Minamishima, K. Kumura and N. Shimada*

Department of Microbiology, Miyazaki Medical College, Miyazaki 889-16, *Research Laboratories, Nippon Kayaku Co., Ltd, Shimo 3-chome, Kita-ku, Tokyo 115, Japan.

Ganciclovir (DHPG), an effective anti-cytomegalovirus (CMV) drug, has been clinically used for diseases caused by human CMV (HCMV) in the immunocompromised hosts. The efficacy is, however, limited by the appearance of ganciclovir-resistant mutants of HCMV. In order to elucidate the mechanism of resistance and to search for effective agents against the resistant mutants, we isolated ganciclovir-resistant mutants of murine CMV (MCMV) as a model for HCMV. The ganciclovir-resistant MCMV showed 10 to 20 times more resistance to ganciclovir (median effective dose, ED_{50}: 120 to 240 μM) than the parental strain (the Smith strain, ED_{50}: 10.2 μM). Reduced pathogenicity, as evidenced by an increase in the median lethal dose (LD_{50}), was observed in one of the mutants. Since the mutant showed a prolonged eclipse period in the one step replication, this attenuation seems to be due to the delay of replication in cells. With higher dose, however, the mutants produced lethal infection and this system may be useful to assess the novel anti-CMV agents against the ganciclovir-resistant CMV. Oxetanocin G and carbocyclic oxetanocin G were effective against the mutants *in vitro* (ED_{50}: 5 μM) and are candidates for such agents.