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Toxicity Evaluation of 1-β-D-Ribofuranosyl-1,2,4-Triazole-3-Carboxamidine Hydrochloride (AVS 206) in Rhesus Monkeys: Comparison with Ribavirin. D.Y. Pifat[1], R.W. Sidwell[2], P.G. Canonico[1], [1]United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland, U.S.A., and [2]Utah State University, Logan, Utah, U.S.A.

1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamidine hydrochloride (AVS 206), a compound with known antiviral activity, was compared to ribavirin for its potential toxicity in non-human primates. Groups of rhesus monkeys were given 2 different regimens of either ribavirin or AVS 206. Hematologic parameters, serum chemistries, and body weights were monitored 3 times per week for 38 days. Animals receiving the highest drug dosage of either ribavirin or AVS 206 were treated with 60 mg/Kg on day 0, followed by 30 mg/Kg/day for 10 days. At this dose, animals receiving ribavirin exhibited significant decreases in red blood cell parameters (HCT, HGB, RBC). These animals also experienced significant increases in the number of platelets during the drug treatment and significant increases in reticulocyte counts immediately after termination of drug treatment. In contrast, the monkeys receiving similar doses of AVS 206 exhibited no significant changes in either red blood cell parameters, platelet or reticulocyte counts. Similar observations were made when animals received lower doses of the drugs, although the toxic effects of ribavirin were somewhat less severe. Although ribavirin and AVS 206 have similar antiviral properties, at the doses studied, AVS 206 appears to have none of the toxic effects associated with ribavirin, nor does it appear to cause any other observable side-effects in non-human primates.

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CELL-MEDIATED ANTIHERPETIC ACTIVITY OF A STREPTOCOCCAL PREPARATION (OK-432) IN IMMUNOCOMPROMIZED HOSTS. S. Ikeda, K. Sai, C. Nishimura, and A. Yamamoto*. School of Pharmaceutical Sciences, Kitasato University, Tokyo, and *Chugai Pharmaceutical Co. Ltd., Tokyo, Japan.

Problems of microbial infections and cancers in immunocompromized patients have been very important, especially in patients with either congenital and acquired immunodeficiency syndromes and in patients after transplantation. We have studied OK-432, a biological response modifier (BRM) originated from streptococcal preparation, to know the question whether it has a protective activity against herpes simplex virus (HSV). Administration of OK-432 to cyclophosphamide (CY)-treated mice prevented effectively HSV infection and inhibited viral growth in the peritoneal cavity in a dose-response manner. The numbers of peritoneal cells once decreased by CY-treatment had increased significantly by administration of OK-432 through intraperitoneal route. Macrophage and NK cell functions of CY-treated mice were also enhanced by administration of OK-432. These results suggest that OK-432 has a host-mediated antiviral activity against HSV by restoration of immunocompetent cells in compromized hosts.