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Efficacy of Topical Preparations Containing Lithium Against Herpes Simplex Virus Infections In The Mouse.

M D Winther and T J Hill., Scotia Pharmaceuticals Limited, Woodbridge Meadows, Guildford, GU1 1BA, UK and .Department of Pathology and Microbiology, University of Bristol, Bristol, BS8 1TD, UK.

Lithium ions inhibit the replication of herpes simplex virus although the precise mechanism of action is unknown (1). Virus DNA synthesis is inhibited but virus polypeptide synthesis continues at concentrations which are non-toxic to host cells. The threshold concentration for an effect was about 5mM and almost complete inhibition was achieved at concentrations over 30mM. Both HSV1 and HSV2 are inhibited by lithium. A topical preparation containing 8% lithium succinate was found to be effective against recurrent genital herpes in a placebo controlled study (2) and against labial herpes in an open study (3). We have used the mouse ear model to examine the mode of action of lithium in greater detail. Four week old female NIH mice were inoculated with 10^5 p.fu HSV1 by scarification of the shaved right neck (4). The inoculated animals were divided into groups of 14 or 15 animals. For the treatment groups the cream preparations were coded before use and applied to the dorsal surface of the right pinna starting on the third day after inoculation. Treatment was four times a day for four days. Mice were examined for erythema and for herpetic lesions (vesicles, pustules and scabs). Lithium containing preparations were found to reduce the number of herpetic lesions. Lithium was also shown to be a mild irritant to the mouse ear which contributed to a high erythema score in the treatment group.

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Efficacy of Single and Combination CTC 23 and Trifluorothymidine Topical Ocular Therapy on HSV-1-induced Stromal Disease in the Rabbit.

EC Dunkel, PA Geary, Q Zhu and D Pavan-Langston, Eye Research Institute and Department of Ophthalmology, Harvard Medical School, Boston, MA, USA.

CTC 23 is a new antiviral agent with demonstrated in vitro and in vivo activity against herpes simplex virus. CTC 23 has been demonstrated to have an anti-stromal disease effect similar to topical steroids on ocular stromal keratitis. In this study, CTC 23 was evaluated individually and in combination with Trifluorothymidine (TFT) during HSV-1-induced stromal disease in the rabbit. NZW rabbits were inoculated with 10^5 PFU RE strain HSV-1 by intrastromal injection. On day 3 PI, animals were divided into groups with matched ocular disease and treated topically with combination TFT + CTC 23 (4x/day for each drug; 8 therapies); or singly with TFT, CTC 23, or placebo (4x/day; 4 therapies). All eyes were monitored daily by slit lamp biomicroscopy and HSV was recovered from the tear film on days 3, 5 and 7 PI. Clinically, HSV stromal disease was significantly reduced in the combination drug-treated eyes compared to single-agent TFT and placebo therapies on days 5-7 PI. Development of stromal HSV-1 disease in the CTC 23 single-agent therapy eyes was significantly reduced when compared to TFT and placebo therapies (4 or 9 times/day), and was not statistically different from stromal disease development in combination drug-treated eyes. HSV recovery (titer) from combination TFT and CTC 23-treated eyes was lower than the HSV titer from single-agent treated eyes on days 5 and 7 PI. These results demonstrate that combination ocular therapy with TFT, a nucleoside analog, plus CTC 23, a virucidal/intracellular acting compound had an additive effect on reducing HSV replication in the eye and on reducing the severity of corneal stromal disease.