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Efficacy of Oral WIN 54954 for the Prophylaxis of Experimental Rhinovirus Infection. Ronald B. Turner and Frederick G. Hayden, Medical University of South Carolina, Charleston, and University of Virginia, Charlottesville.

The efficacy of oral WIN 54954 for prevention of rhinovirus (RV) infection and illness was tested in two randomized, double-blinded, placebo-controlled volunteer challenge studies. Volunteers were inoculated with RV 39 (MIC of WIN 54954=.17 μg/mL) at UVA and with RV 23 (MIC=.016 μg/mL) at MUSC. Volunteers received three doses of drug (600 mg/day) or placebo each day for six days and were challenged with virus after the third dose. No significant antiviral or clinical effect was detected in either study.

| Virus | Treatment Group (N) | No. (%) Infected | No. (%) Ill | Mean Total Symptom Score | Mean Nasal Mucus Wt. |
|---|---|---|---|---|---|
| RV 39 | Active (13) | 13 (100) | 10 (77) | 12 ± 10 | 13.6 ± 12.7 |
| | Plac. (12) | 12 (100) | 6 (50) | 7 ± 8 | 11.8 ± 13.4 |
| RV 23 | Active (22) | 18 (82) | 3 (14) | 4 ± 5 | 4.3 ± 7.4 |
| | Plac. (23) | 22 (96) | 7 (30) | 10 ± 13 | 9.7 ± 18.8 |

On the last day of drug administration, 38/39 (97%) had trough plasma levels of WIN 54954 greater than the MIC for the respective virus. Nasal wash specimens collected on the same day revealed a detectable level in only 6/24 (25%) at peak (range=6-24 ng/mL) and in only 2/14 (14%) at trough (6 and 7 ng/mL). No serious side effects of drug were seen; 3/40 drug recipients reported a drug-related macular skin rash. These results suggest that the lack of efficacy of WIN 54954 for RV may be related to an inability to deliver sufficient drug to the site of viral infection.

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Prophylactic Efficacy of WIN 54954 in Prevention of Experimental Human Coxsackievirus A21 Infection and Illness. G.M. Schiff, J.R. Sherwood, E.C. Young, L.J. Mason, James N. Gamble Inst Med Res, Cincinnati., OH USA

Enteroviruses cause serious morbidity and mortality. No specific treatment is currently available. Pre-clinical studies with WIN 54954 justified human efficacy studies using our Cox A21 challenge model. Fifty-one healthy male seronegative volunteers were placed in isolation and randomly assigned to receive either 600mg WIN 54954 or placebo TID x 17 oral doses. After 3 doses of study medication volunteers were inoculated intranasally with $10^2$ pfu Cox A21. Six additional seronegative placebo recipients were sham inoculated to serve as indicators of secondary transmission. One placebo recipient was eliminated from the analysis due to a dosing error. 25/27 drug recipients and 23/23 placebo recipients shed Cox A21 in nasal wash. Drug recipients shed significantly less virus than placebo recipients, mean AUC 22.0±9.2 vs. 28.1±7.8 (p=0.016). Drug recipients experienced significantly milder disease and significantly fewer met our illness criteria in the 5 days post inoculation:

| | Resp | Systemic | Illness | Moderate Illness |
|---|---|---|---|---|
| Drug | 2.6±4.3 | 2.3±4.3 | 3/27 | 0/27 |
| Placebo | 11.8±8.8 | 8.7±7.9 | 15/23 | 9/23 |
| p value | <0.0001 | 0.0007 | 0.0001 | 0.0003 |

There was no evidence of transmission to the sham inoculated controls and no serious adverse events were observed. WIN 54954 given prophylactically to volunteers inoculated with Cox A21 significantly reduced clinical illness attack rate and significantly reduced viral shedding.