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Lack of Inhibitory Effect of SCH-39304 (An Antifungal Agent) on the Antiviral Efficacy of AZT Against HIV-1 *In Vitro*. J. B. Kahlon[1], W. M. Shannon[1], A. D. Brazier[1], G. H. Miller[2], J. Schwartz[2] and R. J. Whitley[3]. Southern Research Institute, Birmingham, AL 35255 USA[1], Schering-Plough Corporation, Bloomfield, New Jersey 07003 USA[2], and University of Alabama in Birmingham, Birmingham, AL 35205 USA[3].

An anti-fungal agent for administration to AIDS patients and coded as SCH-39304 was tested for *in vitro* antiviral activity against the human immunodeficiency virus (HIV-1) in parallel with AZT using MT-2 cells (Harada *et al*, Science *229*:563-566). Cytopathology inhibition data demonstrated that the drug has no activity against HIV-1. *In vitro* data were also generated in order to demonstrate a lack of enhancement of HIV-1 replication. Target cells (MT-2) were infected with varying multiplicities of infection of HIV-1 obtained from a standard stock preparation of the virus. A standard non-cytotoxic concentration of each drug (SCH-39304 = 100 μg/ml and AZT = 0.32 μg/ml) was used to measure enhancement of HIV-1 cytopathology in the target cells infected at varying multiplicities of infection. End-points were measured as percent viable cells, read as optical density values with the use of a tetrazolium salt (MTT) used for measuring cell viabilities. A combination of SCH-39304 with AZT was studied *in vitro* to measure antagonism or synergism between the two compounds. Again a non-cytotoxic concentration (100 μg/ml) of SCH-39304 was tested in combination with six half $\log_{10}$ concentrations of AZT ranging from 0.032 μg/ml to 10 μg/ml in a viral cytopathology inhibition assay. Results demonstrated no antagonism between the two compounds at the tested concentrations. In an independent experiment, the effect of AZT and SCH-30394 combinations was studied for their potential ability to induce latent HIV-1 infections. U1 cells, a subclone of U937 cells, chronically infected with HIV-1 (Folks, T. M. *et al*, Science *238*:800-802, 1987) were plated in the log phase of replication and treated with various concentrations of the two compounds. At day 3 post-treatment the cells were processed for hybridization and probed for replicating mRNA using a probe specific for HIV-1 pol gene (Gene-Trak Systems). Hybridizations were performed according to manufacturers instructions. Results show no detectable induction of viral replication in the treated samples.

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Effect of Natural Products of Various Microbial Fermentations from Schering-Plough Corporation on the Replication of HIV-1 as Measured by CPE-Inhibition Assays in Infected Cells. P. Daniels[1], S. Watkins[1], J. Kahlon[1], R. Hart[2], A. C. Horan[2], V. Gullo[2], J. Schwartz[2], R. J. Whitley[3], and W. M. Shannon[1]. Southern Research Institute, Birmingham, AL 35255 USA[1], Schering-Plough Corporation, Bloomfield, New Jersey 07003 USA[2], and University of Alabama in Birmingham, Birmingham, AL 35205 USA[3].

A total of 2,000 samples, products of various microbial fermentations, were screened for antiviral activity against the human immunodeficiency virus (HIV-1). Samples were tested according to our standard operating procedure (SOP) designed and implemented by scientists at Southern Research Institute and Schering-Plough Corporation. According to this SOP, each sample was tested at a single concentration (1:20 dilution of the submitted broth), in duplicate on HIV-1 infected MT-2 cells to measure antiviral efficacy and at the same concentration on uninfected MT-2 cells to measure the cytotoxic effect of the product. Assays were set up in 96-well plates, 18 products were tested per plate and three replicates of virus control cultures (untreated, infected cells) and three replicates of cell control cultures (untreated, uninfected cells) were used. A panel of control cultures (AZT and ddC at various concentrations; alone and in combination with selected fermentation products) were set up with each test (196 samples per test). Assay end-points were read at Day 7 post-infection by MTT, a formazan-activating tetrazolium salt used to measure cell viabilities (Tada, *et al*, J. Immunol Methods, 93:157-165). Criteria for selection of active compounds included arbitrary limits of 49% or less viability of test sample = inactive; 50-74 percent viability = marginally active; and 75-100% viability = active. Active and marginally active compounds were re-tested to confirm activity. Compounds meeting criteria of active are undergoing further *in vitro* activity and cytotoxicity testing.