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Lack of Inhibition of HIV Replication in Chronically Infected Macrophages by Antiretroviral Compounds.

S. Crowe, H. Siregar and S. Sonza.
Macfarlane Burnet Centre for Medical Research, Fairfield Hospital, Melbourne, Australia.

Objective: HIV infects different cell types including $CD4^+$ lymphocytes and monocyte/macrophages (Mϕ). In our studies, we have examined the effect of several antiretrovirals in cultured human peripheral Mϕ. **Methods**: Mϕ were isolated from HIV seronegative donors by gradient centrifugation and plastic adherence. Cells were infected with HIV Ba-L for 3 hours (acute infection) or 14 days (chronic infection) prior to addition of drug (zidovudine, ddI, non nucleoside RT inhibitor U87201E and tat inhibitors Ro-5-3335 and Ro-24-7429). Inhibition of HIV replication by each drug was assessed by quantitation of HIV p24 in supernatant and HIV RNA analysis. Drug cytotoxicity was determined by trypan blue exclusion and MTT assay. **Results**: ZDV (0.001-10 μg/ml) and ddI (2-20 μM) resulted in 91-100% inhibition in acutely infected Mϕ and 19-52% inhibition in chronically infected cells. U87201E (1-10 μM) resulted in >99% inhibition in acutely infected cells. Ro-5-3335 (10 μM) and Ro-24-7429 (10 μM) resulted in 85% and 93% inhibition of acute infection respectively with a clear dose response curve; chronically infected Mϕ were less susceptible to Ro-3-3335 and Ro-24-7429 (10 μM) with inhibition ranging from 30-37% and 12-22% respectively. Viability of cells exposed to compounds at tested concentrations was >90%. RNA slot blot analysis is underway in an effort to confirm these data. **Conclusion**: ZDV, ddI and U87201E inhibited acute but not chronic HIV infection of Mϕ, similar to published lymphocyte studies. The tat inhibitors were also effective in inhibiting acute HIV infection in Mϕ but not in chronically infected cells, findings which differ from published studies using T cell lines. **References**: **1.** Crowe S, et al. J. Med Virol, 1989 29:176-180. **2.** Hsu M-C, et al. Science, 1991 254:1799-1802.

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Virucidal Activity of Available Chlorine Against the Human Immunodeficiency Virus Type 1 and the Effects of Protein Concentration on this Activity

Stein, Christian A., Race, E., *Cameron, J. M., Oxford, J. S.; The London Hospital Medical College, Academic Virology and Retroscreen Ltd., *Department of Forensic Medicine, London E1 2AD, UK.

Objectives: Relatively few studies have been performed on molecules to destroy virus on contact. We have initiated a search for detergent like molecules for use as vaginal virucide. The methodology involves the use of high titre virus stocks to allow removal of virucidal compounds by simple dilution. The present study uses this simple assay system to investigate the effect of chlorine on the destruction of HIV-1 and is directly related to the use of chlorine in swimming pool water as a disinfectant.

Methods: Toxicity assay: H9 and C8166 cells were grown at a density of $2x10^5$/ml in growth medium (10% FCS) and hypochlorite was added to give final concentrations ranging from 0.15 to 1000 ppm. Cell viability was assessed by trypan blue exclusion. Virucidal evaluation: Virus was incubated with hypochlorite ranging from concentrations of 1 to 1000 ppm in the presence from 0, 5, 10, 20 and 40% FCS at two different temperatures chosen to mimic swimming pool conditions. After 5/20 minutes incubation residual viral infectivity was determined by titration in C8166/H9 cells and monitoring of syncytium formation and p24 core protein levels after 3, 6 and 10 days.

Results: In swimming pool water (at 3 ppm) virus is still infective up to a dilution of 1 to 100. But virus is completely inactivated within five minutes at a concentration of 10 ppm. The presence of 10% FCS negates the virucidal efficiency of hypochlorite.

Conclusions and Discussion: There has been recent interest in virucidal agents against HIV both to destroy virus in dental water lines and also to act as a vaginal virucide to prevent person to person infection. Our study has addressed a very practical consideration of transmission of HIV via water in swimming pools. The hypochlorite concentrations found in swimming pools is not sufficient to inactivate the infectivity of HIV-1. The risk of infection by free HIV particles in swimming pools is still negligible because of the dilution factor and the low virus titres that would occur under *in vivo* conditions