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In Vitro Antiviral Activity Studies of Drug-Polyanionic Polymer Combinations

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Antiviral chemotherapy with most of the available antiviral drugs is hampered by the toxicity and the appearance of drug-resistant mutants. Combination antiviral chemotherapy provides an alternative therapeutic strategy since the dose of the individual agents may be lowered to reduce toxicity and limit the development of drug-resistant mutants. We have designed experiments to systematically examine the in vitro antiviral activities of polyanionic polymers combined with various low molecular weight (LMW) drugs. Antiviral data for the LMW drugs or polyanionic polymers alone and in combination is obtained through a primary anti-HIV drug screening assay using the MTT method for evaluating the ability of the drug and polymer to inhibit HIV-induced cell killing. A systematic approach to determine the optimal combination of polyanionic polymer with LMW drug, which will show the maximal synergism in antiviral activity and the minimal cytotoxicity, will be presented.

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IN VITRO ACTIVITY OF ALKALINE AUTOOXIDIZED CATECHINIC ACID (AOCA) AGAINST HIV1

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AOCA is a derived alkaline autoxidated compound from catechinic acid and catechin. Their activity against HIV1 is not known. We studied AOCA in vitro antiHIV 1 activity and citotoxicity. HIV 1, obtained from culture supernatant of H9/HTLVIIIB, was titrated 10^6 TCDI/ml. CEM-SS cells and PHA activated blasts from seronegative donors were infected with cell free, filtered infective supernatant obtained as previously described in presence or with subsequent addition (six hours) of AOCA at different concentration (from 500 mcg/ml to 0,5 mcg /ml) . Syncytia formation test and HIV-1 Ag p24 (Abbott ELISA system) quantitation on supernatant was evaluated respectevely at day 7 and at days 3,7,14. Infectivity of these supernatants was shown trough PHAblasts reinfection too. AOCA cytotoxicity was evaluated on CEM-SS lines and PHA activated blasts by [methyl-H3]thymidine incorporation test . The drug showed a 50% effective dose (E.D. 50) at 1,5 mcg/ml when it was added during infection in both assays; 3,5 mcg/ml and 9 mcg/ml, respectively for syncytia test and Ag p24 quantitation, when the drug was added six hours after infection. The PHA blasts reinfection with 3,7and 14 days supernatants showed a reduced ability to infect cells as Agp24 dosage shows . At 24 hours AOCA didn't show any toxic effects on the cells, while from 48 hours the 50% citotoxic dose (50 CD) on activated blasts was 250 mcg/ml. In conclusion AOCA revealed a good in vitro activity on HIV1 coupled with low toxicity. The drug probably acts in the first stages of infection inhibiting virus penetration into the cells.