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HSV1 MORPHOLOGIC FEATURES AFTER TREATMENT WITH ALKALINE AUTOOXIDIZED CATECHINIC ACID (AOCA): CONFIRMATION OF IN VITRO ACTIVITY

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AOCA is obtained from alkaline autoxidation of catechinic acid and catechin , which belong to natural polyphenols. Activity of these compounds against HSV1 has been already shown. We studied AOCA activity in vitro against HSV 1 and viral morphologic features after treatment. The activity of AOCA against HSV1 was performed in absence or presence of drug (added during infection or 1 hour after).The activity was evaluated by the inhibition of cytopathic effect of HSV1 on VERO monolayer cells with standard method. The citotoxicity was studied by using a[methyl-H3]tymidine incorporation test. To assess the effect of AOCA on the virus morphology , 2000000 PFU/ml HSV1 were treated with AOCA at dose of 125 mcg/ml at different time (0, 15', 45' and 60'). The samples were placed on a Formvar carbon-coated copper grid, stained and observed at EM(Philips EM201). Significative images were obtained at magnification of X45,000 and X70,000. The 50% effective dose (ED50) of AOCA was 2mcg/ ml when the drug was immediately added to the virus and 25 mcg/ml when the drug was added 1 hour later. The 50%cytotoxic concentration (CC50) of AOCA was 700mcg/ml. At EM the advanced time grid sections showed a core enlargement and a thin envelope. In conclusion AOCA revealed a good in vitro activity on HSV1 coupled with a low toxicity. The drug probably acts in the early stage of infection inhibiting virus penetration into the cells as supported also by EM observations.

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Toxicity of antivirals on cultured human corneal cells. M Berry*, DL Easty* and E DeClercq**.
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Minimal antiviral toxicity to normal and regenerating corneal epithelium and stroma is desirable in short-term use, and becomes critical in cases of long-term use, as in cases of recurrent stromal keratitis or after penetrating keratoplasty for corneal viral disease. We investigated the cytopathic effects of eleven antivirals on human corneal cells in culture, to compile a toxicity ranking and compare it with clinical experience of antiviral use. Low passage human corneal cell cultures rich in epithelial cells were plated in the presence of antivirals dissolved in tissue culture medium (RPMI 1640) and exposed for 2, 7, 14, and 21 days. The number of metabolically competent cells was assessed by measuring the activity of hexosaminidase, a phase I cytosolic enzyme. A high initial concentration of cells masked all cytopathic effects. Further reduction in initial cell numbers did not affect cytopathic effects when these occurred. There was significant interaction between toxicity and length of exposure (Kruskal-Wallis test, $p<.0001$); the shortest exposure was insufficient for toxic effects to be observed; the best discrimination was obtained after 14 days. In these conditions HPMPA caused cell death at 15.6µg/ml, with a 50% lethal concentration (LC50) between 31 and 62µg/ml. TFT was the second most toxic compound (LC50 around 250µg/ml), and HPMPC the third (LC50: 500µg/ml). ACV, BVDU, CEDU, EDU, DHPG, IDU, PFA and PMEA had an LC50 above 1000µg/ml, but with different effects on cell numbers. Overall they could be ranked as follows: PMEA ≤ DHPG ≤ ACV ≤ ≤CEDU < PFA ≤ IDU ≤ BVDU, though the exact order depended on the length of exposure.