

210

On Antiviral Properties of Some Drugs and Possible Role of Viruses in Formation of Cardiovascular Diseases

Amvrosieva T.V., Votyakov V.I., Vladyko G.V., Andreeva O.T.

Byelorussian Res. Inst. Epidem. & Microbiol. Minsk, USSR

Study of 11 known cardiovascular (CV) drugs, such as nicotinamidum, strophantinum, corglyconum, curantyl, cavinton, papaverini hydrochloridum, acidum nicotinicum, xantinylo nicotinas, isoptin, parmidinum, halidor by virologic screening detected antiviral activity in 9 of them. Investigations were conducted on cell cultures of epithelioid and fibroblast origin, using laboratory strains of 7 viruses: herpes simplex (HSV), viriolovaccine, influenza, vesicular stomatitis, respiratory-syncytial, Venezuela equine encephalitis, ECHO and rotaviruses. Characteristic peculiarity of the studied drugs was their great activity against DNA-containing viruses and rotavirus. More than half of them proved to be highly effective inhibitors of virus activity with high chemiotherapeutic index. The greater prospects in terms of further virological investigations had 3 drugs: papaverini hydrochloridum, strophantinum and corglyconum. Their antiviral properties were proved on the model of herpetic meningoencephalitis of mice. The obtained data suggest that not only HSV, but a number of other viruses can participate in the formation of CV diseases. We can suppose that antiviral action is an integral part of CV drugs therapeutic effect.

211

Are Eukaryotic Topoisomerases Potential Targets For Antiviral Therapy?

B. Maschera, M. Rassu, E. Ferrazzi, M. Toni, G. Palu'

Institute of Microbiology, University of Padova, Padova, Italy

Camptothecin and Etoposide, eukaryotic topoisomerases inhibitors, were evaluated for their activity against simian virus 40 (SV40), a virus that should depend on topoisomerases I and II for some of its replicative steps. Nalidixic acid was also assayed for a comparison, since the compound has been previously reported to affect papovavirus growth. Our results indicate that anti-eukaryotic topoisomerase drugs significantly inhibit viral DNA replication but at concentrations at which cytotoxicity and DNA-strand scission are produced in uninfected cells. Following Etoposide treatment, a relatively higher number of DNA-protein cross-links was found in virus-infected cells, as compared to uninfected control cells, and a clear alteration of SV40 DNA topology was also observed. These effects, however, were not therapeutic. Nalidixic acid displayed some degree of selectivity for inhibiting SV40 DNA synthesis more effectively than the synthesis of cellular DNA, with no sign of genotoxicity and without appreciable reduction of cell growth. This activity does not originate from interference with topoisomerase II and deserves further evaluation. Time course experiments, measuring inhibition of viral DNA production and formation of DNA-protein cross-links, produce evidence that topoisomerase II is preferentially associated with replicating SV40 chromatin, in the late stage of the infection.