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Inhibition Of Herpes simplex type 1 By Meliacine, A Peptide Of Plant Origin.
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Meliacine, a cyclic glycopeptide isolated from green leaves of Melia azedarach L. (*) exert a broad range of antiviral effect on DNA and RNA enveloped viruses. Since this active compound exhibited a potent antiviral activity against HSV-1(F) (Selectivity Index > 250), attempts were made in order to identify the step in viral replication being the target for meliacine. When Vero cells were treated with meliacine and infected with HSV-1(F), the inhibitory dose varied with the time of addition: 50% effective concentration (EC50) were 0.32 and 0.12 ug/ml when the antiviral compound was present for 2 hours before infection and during 24 hours after virus adsorption, respectively. Analysis of early events following HSV-1(F) infection showed that meliacine did not interfere with viral adsorption. Likewise, the kinetics of HSV-1(F) penetration in meliacine-treated cells followed a similar pattern as observed in untreated cells. Meliacine was also found to have no effect on protein synthesis in uninfected cells; nevertheless, it strongly inhibited selective 35S-labelled infected cell polypeptides (ICP). The fact that antiviral action of meliacine may be attributed to the inhibition of the synthesis of polypeptides expressed late in infection correlates with low EC50 values obtained by post-treatment.

(*) Andrei G.M. et al. (1993) Antiviral Chemistry and Chemotherapy, in press.

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Comparative antivirial activity of compounds against thymidine-kinase deficient acyclovir resistant mutants of herpes simplex virus type 1
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To understand drug mode of action by studying cross resistance and to investigate the possibility mapping viruses according to their antiviral spectrum, we have evaluated antiviral activity of more than 20 various compounds, most of them nucleoside analogues, against 10 acyclovir(ACV)-resistant mutants of herpes simplex virus type 1 (HSV-1) strain F in Vero cell culture system by using CPE-inibition assay. Eight of them were recently obtained by 3 times plaque-purification after a challenge virus-infected Vero cells with high doses of ACV. None showed thymidine kinase activity and all of them except one were about 100 times more resistant to ACV than the wild type. The one showed 3-fold increased resistance to both of phosphonoformic acid and phosphonoacetic acid and over 200-fold to ACV. Alteration of drug sensitivity was dependent on virus strains and 4 mutant viruses showed high resistance to several compounds and similar drug sensitivity to all other tested compounds. Although detailed genetical changes of the mutants should be confirmed, we can assume there is a vulnerable site(s) to drug resistance.