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Effect of HPMPC on the Replication of Herpes Simplex Virus Type 1 in Monkey Kidney and Human Fibroblast Cells. S. Chatterjee, P. Burns, R. Whitley, and E. Kern, University of Alabama at Birmingham, Birmingham, Alabama, U.S.A.

Treatment of African green monkey kidney cells with 1 μg/ml of 1-[(3-hydroxy-2-phosphonyl methoxy) propyl] cytosine (HPMPC) inhibited the release of infectious herpes simplex virus type 1 (HSV-1) from the treated cells by greater than 90%. Analysis of virus-specific proteins by the immunoblot technique showed HPMPC significantly blocked the expression of HSV-1-specific proteins in HPMPC-treated monkey kidney cells. Electron microscopic observations of HPMPC-treated monkey kidney cells demonstrated few extracellular virus particles and they were without dense cores. Virus particles (although very reduced in number) released from HPMPC-treated cells displayed reduced quantities of glycoproteins B and D. Similar type of results were obtained when human fibroblast cells were used instead of African green monkey kidney cells. The possibility of an HPMPC-induced block at an early stage in virus replication will be discussed.

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Macrophage membrane lectins: their potential for antiviral drug targeting.

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To increase the therapeutic efficiency of drugs, macromolecular carriers can be used to target cells selectively. Taking into account the presence of sugar binding receptors, named membrane lectins, on various cells we have developped glycosylated carriers usable to target immunomodulators or antiviral drugs.

Macrophages from various origins express membrane lectins that mediate the binding and uptake of mannose and mannose-6-phosphate bearing conjugates. Using fluoresceinylated neoglycoproteins prepared by substituting serum albumin with glycosylphernylisothiocyanate or poly-L-lysine modified with glycosides, the residual cationic charge of which being neutralized by N-acylation,(1) we have shown by flow cytometry that macrophages efficiently endocytosed these mannosylated (or 6-phosphomannosylated) conjugates in acidic compartments. After internalization proteolytic digestion occured rapidly, allowing the release of drugs bound to the polymer either directly or through a glycyl-glycyl spacer.

The antiviral drug, 9-(2-phosphonylmethoxyethyl)adenine (PMEA) linked to the mannosylated polymer allowing its internalization in human macrophages infected by herpes virus is more efficient *in vitro* than the free drug in preventing lysis of macrophages (2).

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1-Derrien, D. *et al* (1989) Glycoconjugate J. 6:241-255.
2-Midoux, M. *et al* (1990) Biochem. Biophys. Res. Commun. in press.