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Differential inhibitory effects of sulfated polysaccharides on the replication of various myxo- and retroviruses

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Sulfated polysaccharides (i.e. dextran sulfate), and sulfated polymers [i.e. sulfated polyvinylalcohol (PVAS) and sulfated copolymers of acrylic acid with vinylalcohol (PAVAS)] were found to be potent and selective inhibitors of the replication of respiratory syncytial virus (RSV) and influenza A virus, but not of other myxoviruses (parainfluenza-3, measles and influenza B). The compounds were also inhibitory to human immunodeficiency virus type 1 (HIV-1), type 2 (HIV-2) and simian immunodeficiency virus (SIV), but not simian AIDS-related virus (SRV). The mode of antiviral action of the sulfated polysaccharides (polymers) can be attributed to an inhibition of virus binding to the cells (HIV-1), inhibition of virus-cell fusion (influenza A virus) or inhibition of both virus-cell binding and fusion (RSV). The fact that the sulfated polysaccharides (polymers) are inhibitory to some myxo- and retroviruses, but not to others, seems to depend on the composition of the amino acid sequences of the viral envelope glycoproteins that are involved in virus-cell binding and fusion. All myxo- and retroviruses that are sensitive to the sulfated polysaccharides (polymers) share a common tripeptide segment (Phe-Leu-Gly) in their envelope glycoproteins.

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The Anti-HIV-1 Activity Of CD4 Synthetic Oligopeptides Is Not Related To Gp120 Binding.

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We have recently synthesized two peptides corresponding to the residues (37-53)(A) and (37-55)(B) of the V1 domain of CD4, which are believed to represent the gp120 binding site. Both peptides were capable to inhibit the infectivity of HIV-1 strains IIIB, RF and GB8 in three different cell lines, as measured by the production of p24, RT and infectious virions in the culture supernatants. The antiviral effect was dose-dependant, showed an ED_{50} of 10 ug/ml (ED_{50} of sCD4 = 0.4 ug/ml) and was clearly not related to cytotoxicity. A synthetic peptide of similar complexity to that of A and B but totally unrelated in aa sequence was completely devoid of anti-HIV-1 activity.
In contrast with their apparently specific antiretroviral effect, A and B failed to inhibit syncytia formation by chronically infected H9 cells. To try to understand these conflicting results, the binding between radioiodinated gp120 and $CD4^+$ Jurkat cells was studied using A and B in competition experiments. Neither peptide was capable to displace the gp120/CD4 interaction to any significant extent at variance with an IgG conjugated form of the V1-V2 regions of CD4 (Kd 10^{-10} M). Thus, a more complex structural configuration than the one presented by our oligopeptides and/or a different region of CD4 are requested for gp120 binding. The anti-HIV-1 efficacy of the above substances has therefore to be ascribed to an interference with a target different from the viral receptor. Such an observation should be taken into account when planning the synthesis of peptide molecules with anti-HIV therapeutic potential.