In Vitro evaluation of the antiviral activity of heparan sulfate mimetic compounds against enterovirus 71

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Currently there is no vaccine or approved antiviral drug for the prophylaxis or treatment of Enterovirus 71 (EV71) infection. Despite many reports that suggest Heparan sulfate-like compounds are effective antiviral agents against a number of different viruses, no research has been undertaken to examine the possible antiviral activity of HS compounds against EV71 infection. Therefore, this study investigated the in vitro antiviral effect of three of Heparan sulfate (HS) mimetics and explored the mode of action of these compounds against EV71 infection. The inhibition assay revealed that HS, heparin sodium (Hep) and pentosan polysulfate (PPS) all exhibited antiviral action with IC₅₀'s of 358, 133, and 165 µg/ml, respectively. Cytotoxicity testing of the compounds revealed that there were minimal effects on cell viability at the concentrations of the compounds shown to have antiviral activity. Among the compounds tested, Hep exhibited the most effective and safe antiviral activity at 7.81 µg/ml (p < 0.05) resulting in 92% viral inhibition. The ability of the compounds to block viral binding and entry was tested in both viral attachment and viral penetration assays. The results demonstrated that all of the compounds tested were capable of exerting some antiviral activity through attachment either to the virus or the host cells thus interfering with virus-host cell interactions. However, this does not appear to be the sole mode of their antiviral activity. The results from the time of addition assays showed that the antiviral activity of the compounds was affected by the time in which they were added to infected cells. In conclusion, this research revealed that HS mimetic polysulfated compounds inhibit EV71 infection in vitro and may have potential as therapeutic compounds for the treatment of EV71 infection.

Keywords: antiviral, heparan sulfate, mode of action, enterovirus 71