

POSTER 38**LOW MOLECULAR WEIGHT LIGNINS AS POTENT INHIBITORS OF VIRAL ENTRY INTO MAMMALIAN CELLS**

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Cell surface glycosaminoglycans (GAGs), especially heparan sulfate (HS), enable the entry of herpes simplex virus (HSV) into cells. HS is a highly complex, negatively charged polysaccharide that plays critical roles in number physiological processes. To develop inhibitors of HSV infection, we designed a library of organic molecules as functional mimetics of HS. The library consisted of 50 molecules including flavonoid and isoquinoliny sulfates, and sulfated and unsulfated 4-hydroxy cinnamic acid-based oligomers. Of these, the oligomers of 4-hydroxy cinnamic acid were found to potently inhibit viral entry into cells. The oligomers were synthesized using horseradish peroxidase oligomerization of monomers ferulic and caffeic acid followed by sulfation using sulfur trioxide - alkyl or aryl amine complexes. A mutant HSV-1(KOS)gL86 strain containing the *lacZ* gene was used for entry into HeLa cells and the quantitation of β -galactosidase activity measured to assess the level of target cell penetration by the virus. The unsulfated oligomers of caffeic acid showed a size-dependent decrease in the IC₅₀ of viral entry beyond 0.8kDa chain length. The sulfated derivatives of oligomers of both caffeic and ferulic acids displayed inhibition potency comparable to the unsulfated one suggesting minimal requirement for sulfated anchor. Synthetic small molecules were found to not inhibit viral entry. Cellular toxicity studies show that our molecules are non toxic at concentration as high as 50 mg/L. Overall, these results indicate that the unsulfated oligomers possessing an aromatic backbone are novel molecules potently inhibiting HSV-1 entry into cells and could be developed for use in a topical form.