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Anti-Herpesvirus activity of a xylomannan isolated from the red seaweed Nothogenia fastigiata. E.Damonte*, H.Kim*, H.Haines**, M.C.Matulewicz**, A.Cerezo** and C.E.Coto*. *Laboratorio de Virología and **Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina.

Purified sulfated polysaccharides fractions obtained from the red seaweed Nothogenia fastigiata were tested against Herpes simplex virus type 1 (HSV-1) grown in Vero cells. Five out of seven fractions tested inhibited significantly HSV-1 replication without toxicity for the host cell. The most active polysaccharide fraction named F6 was a xylomannan consisting of α-(1$\rightarrow$3)-linked mannan backbone, 2- and 6-sulfated, having simple stubs of β-(1$\rightarrow$2)-linked D-xylose. It was found to be a highly selective antiviral substance causing no impairment of Vero cell growth at concentrations that were at least 10 fold in excess over the ED50 which was 4.3 ug/ml. Furthermore, F6 had no direct inactivating effect on virions by in-vitro incubation in a virucidal assay. F6 afforded a greater than 90% inhibition in HSV-1 yield if added to the cell cultures simultaneously with virus inoculum, but had no effect when it was added 3 h after infection. By a plaque reduction assay it was demonstrated that F6 was highly effective against HSV-1 replication even when present only during the virus adsorption. Further studies confirmed that the anti HSV-1 effect of F6 was due to inhibition of virus adsorption whereas virus internalization was not impaired. The mode of action of this xylomannan is similar to that reported for other polyanionic substances.

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Benzimidazole Ribonucleosides: Design, Synthesis, and Evaluation of 2-Chloro-5,6-diiodo-1-(ß-D-ribofuranosyl)benzimidazole, an Analog of TCRB.

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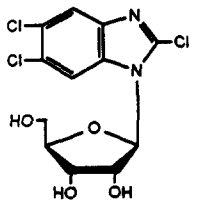

TCRB

As part of our comprehensive structure activity relationships study related to TCRB, we have prepared a number of 2-chloro-5,6-disubstituted-1-(ß-D-ribofuranosyl)benzimidazoles. The desired substitutions at the 5 and 6 position of the benzimidazole ring system can be achieved by functional group transformations either on the benzene ring prior to ring annulation of the imidazole moiety, on the heterocycle prior to the ribosylation procedure, or on the nucleoside, per se. However, the reaction conditions, in most cases, will dictate which option is available. In this case, a number of selective chemical transformations were performed on the heterocyclic moiety. The appropriate benzimidazole derivative was ribosylated and then deprotected to afford the title compound. The title compound has been evaluated for its ability to inhibit the replication of human cytomegalovirus and for its cytotoxicity toward uninfected human diploid cells (HFF cells). The synthesis and a comparison of antiviral activity and cytotoxicity between the title compound and TCRB will be presented. This research was supported by federal funds from the Department of Health and Human Services research contracts NO1-A1-72641, NO1-A1-42554 and research grant UO1-AI31718 from the National Institute of Allergy and Infectious Diseases.