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Inhibitors of Glycoprotein-Trimming Enzymes Block HIV and CMV Growth. D.L. Taylor and A.S. Tyms. Division of Sexually Transmitted Diseases, Clinical Research Centre, Middlesex, UK and Division of Virology, St Mary's Hospital Medical School, London, UK.

Plant alkaloids, with a structural resemblance to monosaccharides belong to one of three structural types, namely polyhydroxy derivatives of octahydroindolizine, piperidine or pyrrolidine. Castanospermine (octahydroindolizine) and DMDP (pyrrolidine) inhibit α-glucosidase I and DNJ (piperidine), α-glucosidase I and II of the glycoprotein trimming enzymes. These are responsible for the removal of the outermost glucose residues of the pre-formed glycan which is transferred intact to the nascent polypeptide chain during glycoprotein synthesis. In cell culture these substances are non-toxic. The larger envelope gene product of HIV 1, gp120, is heavily glycosylated and is the surface component of the virus responsible for attachment to the CD4(T4) receptor on target cells. Its expression on the surface of infected cells causes cell depletion by fusion. Treatment of C8166, JM or H9 cells infected with HIV 1 using CAST, DNJ, DMDP has a marked effect on the formation of syncytial cells and prevents the production of infectious virus. The growth of four human CMV strains but not herpes simplex virus type 2 was also affected by the three glucosidase inhibitors. Results will be presented for HIV and CMV showing that virions are produced which are defective in glycoprotein structure and incapable of inducing a productive infection. The importance of these inhibitors in identifying key viral antigens will be discussed.

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Anti-Influenza Virus Activity of Rimantadine: Sensitivity of Recent Epidemic Strains Tested by Three Methods and Comparison with Amantadine and the New Antiviral Compound ICI 130,685. R. L. Cerruti, I. S. Sim, Hoffmann-La Roche Inc., Nutley, N.J., USA and R.B. Belshe, Marshall University School Of Medicine, Huntingdon, W.V. USA.

The antiviral activity of rimantadine, ICI 130,685 and amantadine (Symmetrel, Du Pont) was assessed in cell culture antiviral assays. In a plaque reduction assay rimantadine was very inhibitory to the replication of several isolates of influenza A virus. Recent virus isolates, e.g., A/Taiwan/1/86 (H1N1) and A/Leningrad/360/86 (H3N2) were similar to isolates of a decade ago in their sensitivity to the drug. In contrast to previous reports, in our hands rimantadine was approximately 10-fold more active than amantadine. Similar results were obtained using a cytopathic effect inhibition (cpe) assay and a single cycle virus replication assay (inhibition of virus HA expression detected by ELISA). In both the plaque reduction and cpe inhibition assays, rimantadine was more effective than ICI 130,685, which was only as inhibitory as amantadine.