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Effect of Polyene Macrolide Antibiotics and their Derivatives on Human Immunodeficiency Virus (HIV)

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The polyene macrolide antibiotics amphotericin B and its methylated derivatives bind to the sterols in the membranes of eucaryotic cells and exhibit potent anti-HIV activity by this mechanism. Several heptaene macrolides were compared to assess their anti-HIV activity in assays of H9 cells infected with HIV. The results of these experiments show amphotericin B and its mono-methylated derivatives, AME and N-ornithyl AME, were active in the range of 1-10ug/ml in inhibiting the effects of HIV in the cultures as measured by cell viability, reverse transcriptase activity and viral protein expression, in the range of 1-10ug/ml. The toxic level of these drugs occurs at levels of 50-100ug/ml. In contrast to this, candicidin was cytotoxic and had no anti-HIV activity whereas its methylated derivative, CME, was active at 10ug/ml and not cytotoxic at this level. These drugs offer a viable alternative to currently used chemotherapy that may prove useful for the clinical management of AIDS patients.

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Inhibition Mechanisms of Antiretroviral Compounds. K. Ono, M.D., Ph.D., Laboratory of Viral Oncology, Aichi Cancer Center Research Institute, Chikusa-ku, Nagoya 464, Japan.

Most of the antiretroviral compounds have been found for reverse transcriptase as a target molecule. These compounds exhibit inhibitory effects on reverse transcriptase activity with either of the following two underlying inhibition mechanisms - competition with template primers or with deoxynucleoside triphosphates for binding to reverse transcriptase. Typical examples were shown with suramin and HPA23 for the first group of the compounds and with azidothymidine for the other. On the other hand, most of these compounds have been shown to have some degrees of cytotoxic effects and these undesirable effects seem to be reflections of their inhibitory effects on cellular DNA and/or RNA polymerases responsible for cellular DNA replication and repair. Thus, parallel tests of the compounds in inhibition of reverse transcriptase as well as those of cellular DNA and RNA polymerases is useful to provide some informations as to not only the efficacy but also the selectivity of antiretroviral compounds.