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Quinobene, a New Synthetic Sulfonated Dye with Potent Anti-HIV Activity. D.J. Clanton, R. Haugwitz, and J.P. Bader; National Cancer Institute, Bethesda, Maryland 20852, USA

Sixty sulfonated dyes and related compounds with anti-HIV activity were compared for potency and toxicity in the cell based assay of the National Cancer Institute (NCI) AIDS antiviral screen. The location of sulfonic acids and linkage groups in highly active, minimally toxic compounds were considered in a lead development program, synthesizing and testing a variety of sulfonated compounds. The most potent of this series was Quinobene, a stilbene-linked compound, with an EC_{50} of 1 μM in the anti-HIV assay. Studies with Chicago Sky Blue, another potent sulfonated dye, showed that inhibition of HIV is due to interference with the interaction of viral envelope and cellular membrane which occurs after virion binding. These studies are being repeated with Quinobene. Quinobene inhibits both HIV-1 and HIV-2, as well as the murine leukemia viruses, Rauscher and LP-BM5. The compound is water soluble, may be orally bioavailable, and anticipated metabolic products are unlikely to be carcinogenic, as is the case with some diazo-sulfonated dyes. Quinobene currently is under consideration by the NCI for clinical development.

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Non-nucleoside Inhibitors of an Early Stage of HIV Reproduction. John P. Bader; National Cancer Institute, Bethesda, Maryland 20852, USA

Three non-nucleoside compounds in different structural classes have been shown to inhibit HIV-1 at an early stage of reproduction. Oxathiin carboxanilide (OC), diaryl sulfone, and thiazolobenzimidazole all apparently act at a stage in virus reproduction intermediate between HIV-1 binding and reverse transcription; virus binding to cells occurs in the presence of effective concentrations of the compounds, and neither OC nor diaryl sulfone affect the enzymatic activities of HIV-1 or HIV-2 reverse transcriptase. Thiazolobenzimidizole at high concentrations inhibits the reverse transcriptase of HIV-1, but not HIV-2. None of the compounds affect virus production from established infected cells, and the inhibitory activity of all three is reversible if the compound is removed within 24 hours after infection. The stage of reverse transcription, as measured by the inhibitory activity of dideoxycytidine, occurs within the first few hours after infection in this system. However, OC, diaryl sulfone, and thiazolobenzimidizole all can delay the requirement for reverse transcription. Detailed mechanism of action studies on these and some non-nucleoside reverse transcriptase inhibitors will be presented.