ABSTRACTS

Oral Session I

Retrovirus Infections I

1

Synthesis, Mode of Interaction with the Enzyme and Biological Activities of a Series of Novel Inhibitors of HIV-Proteinase Derived from Penicillins

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A series of novel selective C_2-symmetric inhibitors of HIV-1 proteinase with nanomolar activity have been synthesised from readily available penicillins. Structure-activity data and protein nmr studies supported a symmetric mode of interaction with the enzyme which was confirmed by the crystallisation of key members of the series with recombinant HIV-1 proteinase. Many of the compounds show sub-micromolar antiviral activity in cellular assays without exhibiting appreciable cytotoxicity. These studies together with the pharmacokinetic profile of representative members of the series will be described and an assessment will be made of their potential as chemotherapeutic agents for the treatment of AIDS.