P03 High-performance liquid chromatographic assay and oral pharmacokinetics of new anti-HIV uracil derivatives, KR-V analogues, in rats

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A number of uracil derivatives have been developed as anti-AIDS drugs having a mechanism of inhibiting cellular reverse transcriptase. A simple and rapid assay technique for recently synthesized KR-V analogues was developed using a high-performance liquid chromatography, and oral pharmacokinetics was examined for assessing their oral bioavailabilites. Plasma samples were analyzed by reversed-phase HPLC using an ODS column with an ultraviolet detection system. All the analogues were eluted within 12 min and the LOQ was 15-30 ng/ml. The extraction recoveries were higher than 85%, except KR-V1039, 1068 and 1720 having ester group. This chromatic method was well applied to the kinetic studies for KR-V analogues. Among 16 analogues tested in the present work, the 6 compounds including KR-V1123, 1122, 1784, 1783, 1736 and 1700 were found to be bioavailable for oral administration to rats.