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Pharmacokinetics and tissue distribution of Kendine 91, a novel histone deacetylase inhibitor, in mice

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Abstract

Purpose The present investigation was undertaken to characterize the pharmacokinetics and oral bioavailability

of Kendine 91 in mice and to compare it with other HDAC (histone deacetylases) inhibitors. **Methods** After administration of a single intravenous dose (10 mg/kg) or a single oral dose (50 mg/kg) blood and tissues samples were collected and analysed by HPLC/MS/MS.

Results Elimination half-life was higher than that of SAHA (5.87 vs. 0.38 h after intravenous (IV) administration and 10.29 versus 0.75 h after oral administration). Absolute oral bioavailability was found to be 18%. Total body clearance (7.72 l/h/kg) was greater than the hepatic blood flow of 5.4 l/h/kg in mice and larger than glomerular filtration rate in mice (0.84 l/h/kg). Tissue levels and distribution volume indicate a high capacity of Kendine 91 to distribute into tissues. **Conclusions** This preliminary pharmacokinetic evaluation prompts us to believe that it is worth pursuing further development of Kendine 91 as an anticancer drug.