



Comparison of Cultured Hepatocytes Results with Human Liver Microsomes (HLMs) for the Glucuronidation Elimination of Zidovudine (AZT)

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SUMMARY. *In vitro* species study of pharmacokinetics will be helpful for selection of animal models for pharmacokinetic study of drugs in human. Hepatocytes and liver microsomes incubation systems are the most common methods. The aim of the present study was to evaluate the species difference of AZT's metabolism using liver microsomes, and compare the data with those using hepatocytes. The results showed that Hill equation can be used to fit the kinetic data obtained from human liver microsomes (HLMs), monkey liver microsomes (MkLM), dog liver microsomes (DLMs), and rat liver microsomes (RLMs). The K_m values for HLMs, DLMs, RLMs, and MkLMs were calculated to be 544.7 ± 88.3 , 550.6 ± 49.3 , 1074.3 ± 187.0 , and $611.5 \pm 43.8 \mu\text{M}$, respectively. The V_{\max} values were determined to be 19.9 ± 2.0 , 3.6 ± 0.2 , 4.3 ± 0.6 , and $32.1 \pm 1.2 \text{ pmol/min.mg protein}$. Similar with the hepatocytes data, the orders of intrinsic clearance rate were listed as follows: MkLM>HLM>DLM>RLM. All the above data showed that monkey is more suitable than other animals for predicting the pharmacokinetics of AZT in humans.

KEY WORDS: Zidovudine (AZT), Species differences, Hepatocytes, Liver microsomes.

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