

7th International Conference and Exhibition on

Analytical & Bioanalytical Techniques

September 28-30, 2016 Orlando, USA

Utility of capillary microsampling for rat pharmacokinetic studies: Comparison of tail-vein bleeds to jugular vein cannula sampling

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Serial sampling methods have been routinely used for rat pharmacokinetic (PK) studies. It is still common to take 100-250 μ L of blood at each point of time when performing a PK study in rats using serial sampling. Recently, microsampling (<50 μ L) techniques have been reported as an alternative process for collecting blood samples from rats. In this report, three proprietary compounds and two marketed drugs, fluoxetine and glipizide, were dosed orally into rats. Whole blood (and plasma) and capillary microsampling (CMS) samples were collected from jugular vein cannula (JVC) and tail-vein from the same rats. For the three proprietary compounds, the blood AUC as well as the blood concentration-time profile obtained from the tail vein was different from that obtained via JVC sampling. For fluoxetine, the blood AUC was not statistically different when comparing tail-vein sampling to JVC sampling, while the blood concentration-time profile that was obtained from the tail vein was different than the one obtained from JVC sampling. For both fluoxetine and glipizide, the blood concentration profiles obtained from CMS were equivalent to the blood concentration profiles obtained from the standard whole blood sampling, regardless of the sampling site. Thus, it is recommended that a consistent blood sampling method should be used for serial micro-sampling in discovery rat PK when testing new chemical entities. If the rat tail-vein sampling method is selected for PK screening, a bridging study on the lead compound is recommended to confirm that PK from JVC sampling is comparable to the tail vein sampling.

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