Pharmacology Discovery Services

A Eurofins Discovery Partner Lab

Microsampling in *In Vivo* Pharmacokinetic Studies

Serial sampling of mice to reduce animal usage for pharmacokinetic analysis

Pharmacokinetics (PK)

Pharmacokinetics (PK) is a study of the time course of drug absorption, distribution, metabolism, and excretion (ADME). Preclinical PK studies are usually performed in mice and rats to understand how living organisms deal with the drug. With an appropriate dose and sampling intervals, a concentration-time curve of a drug can be constructed, from circulating blood. Typical parameters, including area under the concentration-time curve (AUC), half-life ($T_{1/2}$), clearance, volume of distribution, maximal concentration (C_{max}), and time at which maximal concentration occurs, can be identified or computed from the study. The PK profiles of drugs after intravenous administration and other dosing routes, such as oral gavage or subcutaneous, assess the bioavailability of a drug.

Microsampling PK Studies in Mice

Considering individual variations between different animals, serial blood sampling from the same animals is usually performed in rats. In mice, serial bleeds can be performed but with far lower volume per collection due to much less amount of blood in mice compared to rats. It is generally recommended that ≤ 20% of circulatory blood volume is drawn from a mouse within 24 hours.

Three common bleeding paradigms for a standard mouse PK study: serial, semi-serial, and terminal bleeds, are compared in Table 1. Serial bleeds provide the least amount of plasma per collection. Typically, singlet bioanalysis can be performed; only 3 mice are needed for a standard study, and the cost is the lowest. The semi-bleeds paradigm provides a slightly larger plasma volume per collection, which is only enough to run bioanalysis in singlet; however, 6 mice are needed, and the cost of in-life proportion is higher. For terminal bleeds, each mouse yields one data point, and a total of 24 mice will be used for a study; the sampled volume is usually sufficient to run duplicate or even triplicate analysis. Since each animal is only sampled once, the overall in-life cost is the highest. PDS offers all 3 bleeds paradigms for mouse PK studies according to the study design and the sensitivity of the test articles and routinely performs serial bleeds in rats.

Type of Blood Sampling	Minimal Plasma Volume per Collection	Collection Time Points (Total Sample #) *	Bioanalysis Replicates	# of Mice	Time Points/Mouse
Serial Bleeds	20 µL	8 (24)	Singlet	3	8
Semi-serial Bleeds	50 µL	8 (24)	Singlet	6	4
Terminal Bleed	150 µL	8 (24)	Duplicate or Triplet	24	1

Table 1. Standard mouse PK (IV or PO) sampling schemes comparison
*8 time points are collected within 24 hours, 3 mice per time point, totally 24 samples

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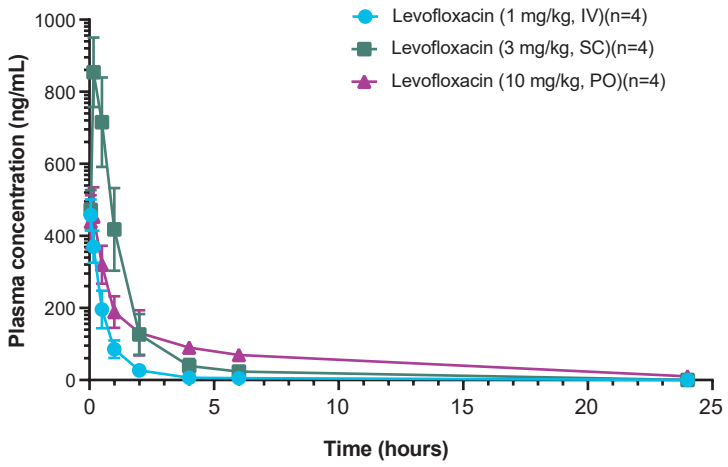

	$T_{1/2}$ (h)	AUCInf (h*ng/mL)	AUC/D (h*kg*ng/mL/mg)	F (%)
1 mg/kg, IV	0.88	344	344	-
3 mg/kg, SC	2.35	1368	456	133
10 mg/kg, PO	4.56	2038	204	59

Figure 1. Levofloxacin was administered to 4 mice per group. The exposure levels (ng/mL) of Levofloxacin in mouse plasma samples after levofloxacin (1 mg/kg, IV, 3 mg/kg, SC, and 10 mg/kg, PO) administration were analyzed through the LC-MS/MS. The mean ± SD values vs. time were plotted in line chart (semi-log).

At PDS, we can obtain blood and/or tissue (e.g., brain) samples following dose administration (ICV, ID, IM, IP, IT, IV, PO, SC, also short- or long-term continuous IV infusions) and both serial or parallel sampling for PK. Blood-brain barrier (BBB) study is also available. Please contact PDS if you are interested in learning more about our PK capabilities.

Available Pharmacokinetics Studies

Study	Type	Species	Sampling Option	Item #
PK-Plasma	In-life	Mouse	Semi-serial sampling	515550
		Rat	Serial sampling	515500
	In-life and Bioanalysis	Mouse	Semi-serial sampling	515555
		Mouse	Serial sampling	515560
		Rat	Serial sampling	515510
PK-BBB	In-life	Mouse	Terminal collection	515570
		Rat	Terminal collection	515520
	In-life and Bioanalysis	Mouse	Terminal collection	515580
		Rat	Terminal collection	515530

References

1. Max Sauter *et al.*, Bioanalysis of selinexor in mouse plasma micro-samples utilizing UPLC-MS/MS. *J Chromatogr B Analyt Technol Biomed Life Sci.* 1176:122781, 2021 https://doi.org/10.1016/j.jchromb.2021.122781
2. Ove Jonsson *et al.*, Capillary microsampling and analysis of 4-µl blood, plasma and serum samples to determine human α-synuclein elimination rate in mice. *Bioanalysis.* 5:449-462, 2013 https://doi.org/10.4155/bio.12.337
3. Walter Korfmacher *et al.*, Capillary microsampling of whole blood for mouse PK studies: an easy route to serial blood sampling. *Bioanalysis.* 7:449-461, 2015 https://doi.org/10.4155/bio.14.275

For more information on PK Capabilities, please visit: pharmacologydiscoveryservices.com