Pharmacelsus®
CONTRACT RESEARCH ORGANISATION

In Vivo Early Stage PK

Purpose

In addition to the *in vitro* potency, the ADME properties of a compound are further crucial parameters for determining its *in vivo* potency. The pharmacokinetic profile of compound is provided following dosing by the intended route and by the determination of relevant pharmacokinetic parameters such as clearance, volume of distribution and bioavailability.

Our test model

Discrete compound testing is applied for rodent in life pharmacokinetic studies. Various routes of administration can be utilized for full PK studies, including po, iv, sc, or ip.

The compound is administered and serial or non-serial bleeding is applied. Typically, 8-10 samples are taken during 24h post-dosing. Collection of blood samples can be prolonged if required.

After sample preparation by protein precipitation the plasma concentrations of the drug are measured by LC-MS/MS.

Pharmacokinetic parameters

Since repeated blood sampling is performed on each single rat, the pharmacokinetic parameters can be determined both on individual and on group mean profiles.

The following parameters calculated using a non-compartmental model can be determined:

- C_z; t_z
- $C_{max\ obs}$; $t_{max\ obs}$
- $t_{1/2z}$
- AUC_{0-tz}; $AUC_{0-\infty}$
- CL; V_c; f/F

Model validation

Figure 1 shows the concentration of a model compound in plasma following intravenous (i.v.) and per oral (p.o.) administration to (n = 5). PK parameters for i.v. and p.o. dosing are calculated by using the computer-generated regression.

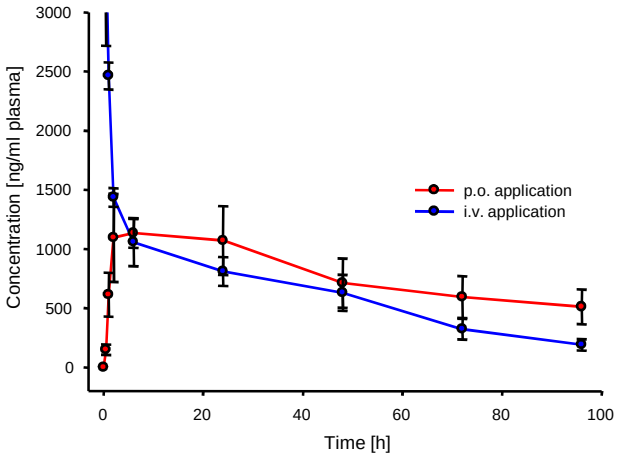

Figure 1: Plasma concentration of test item after iv and po application

Benefits of the model

The advantages of our method are

- Low variability of results since each individual is used as its own control
- Application of serial bleeding allows a reduction of stressful handling during blood sampling
- Numerous blood samples per 24h possible

Please don't hesitate to contact us for a customized quotation

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