Study of Mouse Pharmacokinetics Using Serial Blood Sampling Technique

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**INTRODUCTION**

1. Mice are one of the most common animal models for preclinical efficacy and PK assessment in early drug discovery stage.

2. Because of the small body size, parallel blood sampling is generally used, i.e. each mouse is subject to only one blood draw through cardiac puncture. However, the number of animals required can be large, depending on the numbers of time points and replicates.

3. Consequently, much more amount of test compound would be needed for administration.

4. Furthermore, much more amount of test compound would be needed for administration.

**MATERIALS & METHODS**

1. ANIMALS, CHEMICALS AND MATERIALS

   a. Male CD-1 (ICR) mice weighing 20-30 g, were purchased from Charles River Laboratories (MA), 10 per group.

   b. The test compounds were purchased from Sigma (St. Louis, MO).

   c. Male CD-1 mice [Crl:CD1(ICR)] weighing 20-30 g were used for each independent serial sampling experiment. Blood samples were collected at 5, 15, 30, 60, 120, 360, and 1440 min from each animal via saphenous vein, with 20-30 µL withdrawn at each time point. Fifteen microliters of blood sample were then submitted for quantitative bioanalysis by HPLC-mS/mS.

   d. Using less amount of test compound is needed for administration.

   e. Using fewer animals is needed for administration.

   f. Large sample size, which is only excessive blood loss.

2. RESULTS

   a. The results obtained from serial sampling were compared to those from parallel sampling (based on 3 independent compounds mentioned in Abstract, 3 more compounds were added).

   b. Blood concentration time profiles and PK parameters are presented.

   c. Overall the parameters generated from these two sampling methods are very close to those for caffeine and suflodizide, which showed low Cl.

3. DISCUSSION

   a. We have established a technique for serial blood sampling using mice.

   b. The average circulating blood volume for mice is 72 µL/kg (Dempsey, 2001). Therefore, the blood volume that could be withdrawn would be 1.8 mL. The total blood volume we sampled from one mouse was approximately 175 µL, representing about 1.1% of the total blood volume.

   c. The results obtained from serial sampling were compared to those from parallel sampling (based on 3 independent compounds mentioned in Abstract, 3 more compounds were added).

   d. Overall the parameters generated from these two sampling methods are very close to those for caffeine and suflodizide, which showed low Cl.

**REFERENCE**