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Editorial

A Simple Method for Animal Dose Calculation in Preclinical Research

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In preclinical research, the experimental animals are dosed according to their body weight. The selection of doses is usually decided based on acute oral toxicity studies. In most cases, at least three doses of a test compound will be used to demonstrate the dose-dependent effect. If the preclinical research is based on clinical findings, the human dose is converted into corresponding animal dose using this formula:

Animal dose (mg/kg) = Human dose (mg/kg) × Human (Km)/Animal (Km)

The correction factor (Km) = Body weight (kg)/Body surface area (m^2)

Km for Human = 60/1.6 →37; Rat= 0.15/0.025 → 6; Mouse= 0.02/0.007 → 3

For example, Human dose of telmisartan = 0.67 mg/kg

The rat dose of telmisartan is calculated as 0.67 × 37/6 = 4.13 mg/kg

The mouse dose of telmisartan is calculated as 0.67 × 37/3 = 8.26 mg/kg

Next, it is important to determine the volume of injection according to the body weight of animals. Calculating the volume of injection for each animal is time consuming and there is a chance of error. To overcome this issue, the following tips can be useful.

For rats

In case of drug stock solution for a test compound which is sparingly soluble in water that intended to be administered at a dose of 100 mg/kg, i.p., the concentration of drug solution could be used as follows.

For example, if the dose of rats is 100 mg/kg, a stock solution of 100 mg/ml has to be prepared.

If the dose is 200 mg/kg, prepare a stock solution of 200 mg/ml and so on.

1. This compound is sparingly soluble in water. Therefore, the test compound should be prepared as suspension using suspending agents like sodium carboxymethylcellulose (CMC), acacia and tragacanth. Use of organic solvents that commonly used in *in vitro* studies is not recommended in *in vivo* animal studies.

2. This drug solution should be prepared sterile due to its parenteral route of administration. A suspension of 0.5% w/v of CMC in sterile water for injection or in normal saline could be used for drug stock solution preparation.

From the drug stock solution of 100 mg/ml, an appropriate volume of the drug solution could be administered according to the body weight of animals. For example, if the body weights of rats are 300, 350, 400, 250, 320 and 380 g, it is suggested to inject 0.30, 0.35, 0.40, 0.25, 0.32 and 0.38 ml respectively from the stock solution (100 mg/ml). Now the volume of injection is maintained constant at (1 ml/kg body weight of the rats).

If the stock solution is prepared in the concentration of 20 mg/ml, we can achieve the constant volume of 5 ml/kg body weight of the rats. In that case, the injection volume should be multiplied to 5 times (i.e. 5 × (0.30, 0.35, 0.40, 0.25, 0.32 and 0.38 ml) = 1.5, 1.75, 2, 1.25, 1.6 and 1.9 ml).

For mice

All procedures mentioned for rats are same with mice except the concentration of stock solution.

If the dose for mice is 100 mg/kg, a stock solution of 1/10th of dose/volume (i.e. 10 mg/ml) has to be prepared and if the dose is 200 mg/kg, a stock solution of 20 mg/ml has to be prepared.

According to the body weight of the animal, an appropriate volume of drug solution should be administered. For example, if the body weights of the mice are 30, 35, 40, 25, 32 and 38g, it is suggested to inject 0.3, 0.35, 0.4, 0.25, 0.32 and 0.38 ml respectively from the stock solution (10 mg/ml). Thus, the constant volume of injection is maintained at 10 ml/kg body weight. The maximum volume of injection allowed in rats and mice is shown in table 1.

Table 1*: The maximum volume of injection in rats and mice.*

Route of drug administration	Mouse (ml/kg) [max]	Rat (ml/kg) [max]
p.o.	10 [50]	10 [40]
s.c.	10 [40]	5 [10]
i.p.	20 [80]	10 [20]
i.m.	0.05 per site [0.1]	0.1 per site [0.2]
i.v. (bolus)	5	5
i.v. (slow inj.)	25	20

In conclusion, it is suggested to use a simple method for animal dose calculation to avoid dosing error that leads to erratic results in preclinical research.

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