GOOD PRACTICE GUIDELINES

Administration of Substances (Rat, Mouse, Guinea Pig, Rabbit)

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ADMINISTRATION OF SUBSTANCES (RAT, MOUSE, GUINEA PIG, RABBIT)

Introduction

Many research programmes require the administration of substances to laboratory species. The effect of this on the animals concerned may be minimal or profound, depending on the substance itself, the formulation, the volume, the frequency of dosing and the skill of the operator. Practical expertise in a particular method should be gained by guidance from an experienced person and carried out under supervision until competence is attained. A good skill level then needs to be maintained by regular use of the method.

Substance and formulation

Every effort should be made to find out as much as possible about likely toxicity and to choose a dose which will avoid unnecessary toxic effects.
Solubility problems are not uncommon. Therefore information and advice should be sought in order to ensure that formulations are effective, of minimal toxicity and compatible with the route of administration required.

Dosing technique

Recommended sites and methods in rats, guinea pigs and rabbits are outlined in the table below. General recommendations include:

1. Firm but sympathetic restraint is essential for all methods.
2. Always use the smallest needle diameter which will allow reasonably swift injection of the substance. Make certain the needle is only long enough to reach the intended site of injection.
3. Always use the smallest possible volume compatible with the solubility of the substance.
4. Use aseptic technique for injections wherever possible.
5. Always observe the animals carefully after dosing for any adverse effects.

Common sites for dosing

	Mouse	Rat	Guinea-pig	Rabbit
Oral	Gavage, or in food or water	Gavage, or in food or water	Gavage, or in food or water	Drench (small volumes) or gavage
Subcutaneous	Scruff or flank	Scruff or flank	Scruff or flank	Scruff or flank
Intramuscular	Anterior thigh	Anterior thigh	Anterior thigh	Anterior thigh
Intravenous	Tail vein	Tail vein	Ear vein or saphenous vein	Ear vein

A) Oral dosing

Key points include:

1. Gavage using a flexible catheter attached to a syringe is a practical method in the species listed. Inflexible cannulae can be used, but great care is required to avoid trauma The gavage catheter is passed via the mouth, which induces swallowing movements so that the catheter passes down the oesophagus into the stomach. Proper restraint of the animal is critical.
2. It is essential that the catheter does not pass into the trachea, as "lung dosing" is likely to be fatal. Pre-measure the length of catheter required to reach the stomach, on the outside of the animal. There should be no resistance to passing the catheter and any encountered may indicate that it is in the trachea - withdraw it and reintroduce the catheter no more than once or twice only.
3. Administration via the food or water is less stressful than by gavage, but many substances are not palatable and there is also less certainty about the amount of substance which is received by the individual animal.

B) Subcutaneous dosing

Key points include:

1. Use sites where the skin is loose and mobile.
2. Keep the angle of the injection needle shallow to avoid damage to underlying tissues.

C) Intramuscular dosing

Intramuscular injection in small laboratory species can be difficult because of the lack of big muscles. It is a route which is not recommended unless there are good scientific reasons for using it.

Key points include:

1. Use very small volumes in small laboratory species (see table).
2. Make certain the substance is not irritant.
3. Be certain about the local anatomy: avoid veins, arteries and nerves.

D) Intravenous dosing

Key points include:

1. Aseptic technique is essential.
2. Dilate the vein to aid visualisation and needle entry. Avoid the use of xylene for this purpose.
3. Penetrate the vessel with a hypodermic needle and check for evidence of blood at the hub of the needle before injecting.
4. Apply haemostasis after removing the needle and ensure bleeding has stopped before returning the animal to its housing.

E) Intraperitoneal dosing

Key points include:

1. Use short needles to avoid damaging abdominal organs.
2. Aim to make the injection into one of the posterior quadrants of the abdomen.
3. Aspirate on the syringe to ensure that the gut has not been penetrated

Recommended maximum volumes for dosing

	Mouse	Rat	Guinea-pig	Rabbit
Oral	20 ml/kg	20 ml/kg	20 ml/kg	10 ml/kg *
Subcutaneous	20 ml/kg	5 ml/kg	5 ml/kg	1 ml/kg
Intramuscular	0.05 ml total	0.1 ml total	0.1 ml total	0.25 ml/kg/site
Intravenous **	10 ml/kg	5 ml/kg	5 ml/kg	2 ml/kg
Intraperitoneal	20 ml/kg	10 ml/kg	10 ml/kg	4 ml/kg

* for doses by gavage.
** limits quoted are for bolus injection carried out over a relatively short period of time (less than 1 minute).
The limits described are for once daily dosing on a routine basis. Exceptions are certainly possible, but may need special care and supervision.

References

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