

Unit I

Experimental Animal Studies

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1 Laboratory Animals

Animals used in laboratory for testing purposes are largely supplied by vendors who specialized in selling them to universities, medical and veterinary schools and companies that provide contract animal- testing services.

Selection of an animal model is one of the most important steps in any of the experimental pharmacological study.

This version of the *Guide for the Care and Use of Laboratory Animals* (the *Guide*) strongly affirms the principle that all who care for, use, or produce animals for research, testing, or teaching must assume responsibility for their well-being. The *Guide* is created by scientists and veterinarians for scientists and veterinarians to uphold the scientific rigor and integrity of biomedical research with laboratory animals as expected by their colleagues and society at large.

The *Guide* plays an important role in decision making regarding the use of vertebrate laboratory animals because it establishes the minimum ethical, practice, and care standards for researchers and their institutions. The use of laboratory animals in research, teaching, testing, and production is also governed or affected by various federal and local laws, regulations, and standards; for example, in the United States the Animal Welfare Act ([AWA 1990](#)) and Regulations (PL 89-544; [USDA 1985](#)) and/or Public Health Service (PHS) Policy ([PHS 2002](#)) may apply.

Animal model preferred for the study must be producing similar disease profile as in the human. Hence, suitable animal model should be selected which follows three main:

Objectives

1. Use of an animal phylogenetically closer to man or
2. Use of an animal in which the process under investigation is as close as possible to that in man,
3. The Anatomy, Physiology and Biochemistry are considered to be similar

Goal

In the *Guide*, *laboratory animals* (also referred to as *animals*) are generally defined as any vertebrate animal (i.e., traditional laboratory animals, agricultural animals, wildlife, and aquatic species) produced for or used in

research, testing, or teaching. *Animal use* is defined as the proper care, use, and humane treatment of laboratory animals produced for or used in research, testing, or teaching.

Laboratory animals or animals: Any vertebrate animal (e.g., traditional laboratory animals, agricultural animals, wildlife, and aquatic species) produced for or used in research, testing, or teaching.

- 1. Albino mouse:** White mice (Swiss strain) are the smallest laboratory animals used. Mice are likewise simple, easy to breed and maintain. They are small in size (25-30) and therefore, easy to handle. They are delicate to most of the drugs used in experimental pharmacology. Mice are used extensively in toxic study, bioassay of drugs (insulin), testing of analgesics, CNS active drugs and chemotherapeutic agents. More recently mouse brain tissue as well as primary cell culture of mouse spinal cord neurons are used in neuropharmacology for studying neurotransmitter receptor functions. The other strains of mice used are Laca and Bulb/C.



Figure 1.1 Albino Mouse

Experimental uses

1. Toxicological studies, specifically acute and subacute toxicity. They are also used in teratogenicity (foetal abnormalities).
 2. Bioassay of insulin.
 3. Screening of analgesic and anticonvulsants.
 4. Screening of chemotherapeutic agents.
 5. Studies related to genetics and cancer research.
 6. Study of drugs acting on Central Nervous System.
- 2. Albino rat:** (200-250g) Rat is the most commonly used animal in the biomedical research. The randomly bred strains are used almost exclusively and are derived from the Norway rat (*Rattus norvegicus*) which is thought to have originated in the area between the Caspian Sea and Tobolsk. Among these, “Wistar rat” and the “Sprague Dawley rat” are preferred because of easy handling, sensitivity and low cost.

Nude rats resemble nude mice in their lack of a normal thymus and functionally mature T cells and are phenotypically hairless with possible fine-sparse hair growth and most preferred model in immunological research.

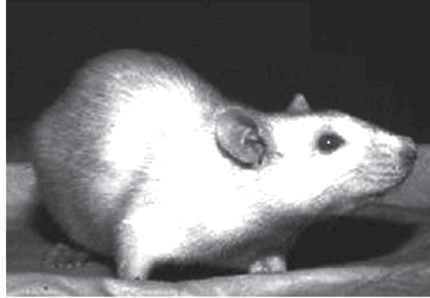


Figure 1.2 Albino Rat

Advantages and characteristics

- It is small in size compared to other animals so drugs are required in small quantity.
- Vomiting centre is absent and so drug can be administered orally.
- Gall bladder and tonsil are absent. Because of the absence of gall bladder in rat there is continuous flow of bile into intestine.
- This facilitates the study of drugs acting on bile, cholesterol reabsorption etc.
- Pancreas is diffused, therefore, difficult to produce panereactomy.
- In stomach, fundus and pyloric parts have clear lining between them.

Experimental use

1. Psychopharmacological studies.
2. Study of analgesics and anticonvulsants.
3. Bioassay of various hormones such as insulin, oxytocin, vasopressin etc.
4. Study of estrus cycle, mating behavior and lactation.
5. Studies on isolated tissue preparation like uterus, stomach, vasdeferens, anococcygeus muscles, fundus strip, aortic strip, heart etc.
6. Chronic study on blood pressure.
7. Gastric acid secretion studies.
8. Study of hepatotoxic and antihepatotoxic compound.
9. Acute and chronic toxicity studies.

10. Study on mast cells using peritoneal fluid and mesenteric attachments.

3. Guinea Pig: (*Cavia porcellus*)- 400-600g

There are 3 major varieties of strains used in the experimental studies and is the member of rodents suborder “Hystricomorpha”. Guinea pig is herbivorous and eats green foods, seeds and roots, but now in many laboratories feed is provided with a readymade chow diet which fulfills its daily dietary requirement. But, it is essential to add vitamin C (Ascorbic acid) in the chow, while it is important to note that GP are not able to synthesize the required vitamin C daily. It is recommended that when GP is provided with the greens, then ascorbic acid should be given at the rate of 1gm/L of drinking water on a weekly basis.



Figure 1.3 Guinea pig

Experimental use

1. Evaluation of bronchodilators.
 2. Anaphylactic and immunological studies.
 3. Study of histamine and antihistamines.
 4. Bioassay of digitalis
 5. Evaluation of local Anaesthetics.
 6. Hearing experiments because of sensitive cochlea.
 7. Studies on isolated tissues specially, ileum, tracheal chain vas-deferens teania coli, heart etc.
 8. Study of tuberculosis and ascorbic acid metabolism.
- 4. Hamster:** Among small rodents, hamster a brown to gold color animal has become the third most commonly used laboratory experimental animal in the biomedical research. They have different strains namely Syrian hamsters (Golden), Chinese hamster (striped back), European hamster and Armenian hamster (gray).

Syrian hamster is the most commonly used in biomedical research because of availability and ease of reproduction. They are relatively free from spontaneous disease and susceptible to many introduced pathogenic agents.

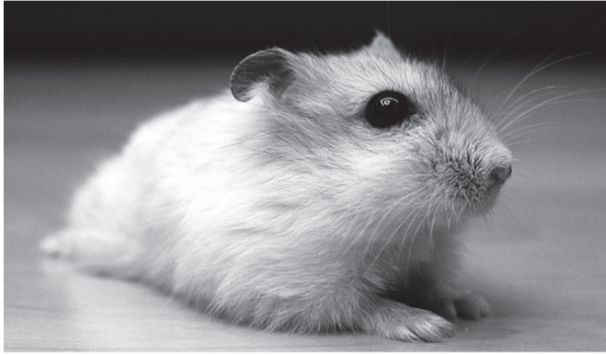


Figure 1.4 Hamster

Experimental Uses

1. Chinese hamsters have less chromosome number making it useful for cytological investigations, genetics, tissue culture and radiation research.
2. Research on Diabetes mellitus
3. Research related to virology, immunology and implantation studies.
4. Bioassay of prostaglandins.
5. **Rabbit:** Domestic rabbits (2-3kg) are generally used for pyrogen testing. Some of the tissue or organs from rabbits used in heart, aorta, duodenum and ileum. One peculiar thing about rabbits is that they are resistant to the actions of atropine as they contain atropinesterase enzyme, the presence of which is generally determined.



Figure 1.5 Rabbit

Experimental uses

1. Pyrogen testing
2. Bioassay of anti- diabetics, curareform drugs and sex hormones.
3. Screening of agents affecting capillary permeability.
4. Irritancy test.
5. Study of Drugs used in Glaucoma
6. Pharmacokinetic studies.
7. Screening of embryotoxic agents and teratogens
8. Studies related to reproduction (antiferility agents)
9. Study of local anaesthetics
10. Study of miotics and mydriatics

6. Frog: (*Rana tigrina*):

Frogs (150-200g) are also extensively used in experimental pharmacology. Isolated frog heart, rectus abdominis muscle preparation, study of muscle nerve preparation and ciliary movements are some of the organs of frog used. Frog is also used for the study of nerve block type of Local anaesthesia. Frogs are inexpensive and easily available

This is one of the most commonly used experimental animals used in physiology, pharmacology and toxicology. It has been used in the experiments for more than 200 years. It is easily available during rainy season. It is an amphibian animal and safe to handle. It cannot be bred in laboratory. Adrenaline is neurotransmitter in the sympathetic system.

Experimental uses

1. Study of isolated tissues such as rectus abdominis muscle and heart preparation.
2. Study of drugs acting on Central nervous system
3. Study of retinal toxicity of drugs, light bleaches rhodopsin in eye within one hour and is regenerated within one hour in dark.
4. Study of drugs acting on neuromuscular junction (using gastrocnemius sciatic muscle nerve preparation).
5. **Cat:** It is a carnivores, relatively easy to obtain and to use for experimental reason. The physiology of circulatory and neuromuscular system is very much similar to that of man. It has a highly developed nictitating membrane (which is contracted by sympathetic nerves). Morphine produces excitation of central nervous system in cat.

Experimental uses

1. Acute experiments for drugs affecting blood pressure.
2. Bioassay of noradrenaline.
3. Studies on ganglion blockers (using nictitating membrane in vivo)
4. Studies on neuromuscular system (using gastrocnemius-sciatic muscle nerve preparation).
5. Toxicity studies of compounds like acetanilide.

Dog

Commonly Mongrel or Beagle dogs are used. It is easily available and large sized animal. Dogs can be easily tamed as well as trained. It has a small stomach and short intestinal tract resembling those of human beings. It can be conditioned to carry a stomach cannula. The cervical sympathetic and vagus nerves run together inseparately in the same trunk (vagosympathetic nerve)

Experimental uses

- Gastric acid secretion studies (Pavlov's pouch)
- Acute experiment for drugs affecting blood pressure, intestinal movements etc.
- Studies on anti-diabetic agents
- Pharmacokinetic study

Cats, dogs and monkey are used for pharmacological examination of drugs. Cats and dogs are commonly used to study the blood pressure experiments. Chronically prepared fistula and pouches of dogs are used to study the gastric secretory function.