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Dr. Sonu P
Associate Professor, Department of Pharmacy, Govt. Homoeopathic Medical College, Calicut, Kerala, India

Corresponding Author:
Dr. Sonu P
Associate Professor, Department of Pharmacy, Govt. Homoeopathic Medical College, Calicut, Kerala, India

Experimental pharmacology (animal testing): A homoeopathic glimpse

Dr. Sonu P

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Abstract
The usage of drugs was well established in prehistoric times, and many plants and animals were known to have either useful or poisonous effects. The foundation required for a fundamental understanding of how a drug acts at the organ and tissue levels was supplied by breakthroughs in chemistry and the burgeoning of physiology in the 18th, 19th, and early 20th centuries. It is a subfield of pharmacology that examines how medications interact with living things in controlled settings, including people and animals, and uses that information to generate novel therapeutic agents. Experimental pharmacology, often known as drug proving or Homoeopathic pathogenetic testing, is the foundation of Homoeopathic medicine. In the traditional method of pharmacological screening, novel chemical entities or biological extracts are first tested in isolated organs before being tested on whole animals or people. Acceptance of the Homoeopathic claims necessitates supporting proof of feasible mechanisms as well as excellent research examining its efficacy in experimental settings.

Keywords: Experimental pharmacology, homoeopathy, animal models, anaesthesia, euthanasia

Introduction
Over 11.5 crore animals are utilized annually in the biomedical industry for exploration or for research purposes [1]. Biomedical exploration has constantly used animals throughout its history. Two Greek physicians and researchers, Aristotle (384- 322 BCE) and Erasistratus (304-258 BCE), conducted experiments on living animals. Galen a mammoth in the past era and a Greek croaker who rehearsed in Rome (129 -199/217) also undertook beast trials to enhance knowledge of reconstruction in pathology, physiology, and pharmacology. In the 12th century Moorish Spain, an Arab croaker named Ibn Zuhr Avenzoar invented beast testing as an experimental approach before applying surgical techniques to lethal situations. In the discipline of Homoeopathy, beast models are used to test the idea of dilution or potentization as well as to investigate medications in a veterinary terrain.

Why animal study?
1. To enhance the scientific knowledge of the functioning of living beings. The analysis of animals is considered a crucial component of this process, as many typical biological processes are identical in all animals and categories of organisms, regardless of their classification [2].
2. As experimental specimens for researching the cause of disease phenomena. Numerous diseases that affect both humans and animals are similar. For instance, dogs are more likely to develop cancer, diabetes, cataracts, ulcers, and bleeding disorders like haemophilia, and rabbits are more likely to develop atherosclerosis, arthritis, and obesity.
3. In the advancement and research of probable forms of treatment, particularly medications from the pharmaceutical industry. Data from animal research are considered pivotal before new therapeutic medications and techniques are used on human patients because drugs are always researched on animals in preclinical settings.
4. In determining safety. In order to identify any possible negative effects, new medications are evaluated on suitable animals [3].

Animal studies -Homoeopathy-Goals
1. Preclinical trials involve trailing medications on animals before using them on men.
2. Innovating non-harmful animal therapies for research in the veterinary field.

3. Examining specific factors and techniques of the homoeopathic attitude in controlled and repeatable settings, which has two major themes.
- The high dilution effects. Whether and how substances diluted and potentised could have medicinal effects.
- A similar instrument of action is how substances known to have disease-producing power in healthy beings can be therapeutic agents in diseased organisms.

The value of using animal testing to avert or stop human catastrophe

Animal drug trials gained importance during the 20th century. In 1937, a pharmaceutical company in the USA created a sulfanilamide a pharmaceutical formulation and were ignorant of DEG's toxicity to people. They sold the combination of sulfa medication dissolved in DEG after merely adding the raspberry flavour. Thousands of people were fatally poisoned and killed as a result of the preparation. Animal testing wasn't done. The violent public wrath caused by these incidents and other similar tragedies led to the passage of the Federal Food, Drug, and Cosmetic Act of 1938, which required that drugs should be tested on animals for safety.

Thalidomide-associated calamities with pharmaceutics befell in the 1950 and 1960s. After it was found to be a powerful neuroleptic and sedative, it was proclaimed as a "wonder drug" for insomnia, coughs, colds, and headaches. When it was discovered that the medication had a restraint effect, many expectant mothers used it as a solution to their morning sickness. Approximately 10,000 babies from 46 different countries were consequently born with birth defects such as phocomelia and amelia. The medicine was withdrawn after a prolonged crusade in 1961 and 1968. The cases mentioned above demonstrate how using medications that haven't been examined on animals can be dangerous for people.

Ethical mulling and advances in the acknowledgement of beast trial

Concerning the value of animal study in research studies, there is a wide range of ethical perspectives. It is widely acknowledged that laboratory beasts may be needful in some situations to enhance our knowledge of men, animals, or the surroundings. There is broad agreement that beasts have moral status and that our attitude towards them should be morally justified. The positions that follow reflect these opinions [4].

1. Protect and respect the animals' innate and inherent values
2. Since animals are conscious of pain their interest should be mattered considerably.
3. Even though they are used for trials and studies, our treatment towards them mirrors our outlooks and influences our moral behaviour.

The "3 Rs" of reducing, improving, and replacing animal use received significant attention in William Russell and Rex Burch's seminal 1959 book 'The Principles of Humane Experimental Technique'. Beasts should only be employed in research trials and studies in the smallest amount considered compulsory, with the least amount of agony and hurt and as far as possible, non-animal substitutes should be added in their place. Despite Russell and Burch's and upcoming attention to this matter, the importance of beast experiments and testing increased, raising important ethical, moral and technical questions [5].

Choice of the trial beast

The selection of the species to be examined should be a crucial aspect. Victory and disappointment in animal experiments is related to the trial subject. The consideration of this aspect is crucial to avoid wasteful animal lives; also it can result in loss of time and inconvenience for the researcher. It has been evaluated that more than 1,200,000 species of creatures have been portrayed, but 97% of the creatures utilized for biomedical reasons have a place to as it were 10 of them. They are rodents, mouse, rabbits, chickens, canines, guinea pigs, pigs, hamsters, monkeys, and cats.

Specific neurotic, physiological, anatomical and/or mental particulars must be taken into account when choosing the right creature.

Species-associated elements

a. Accessibility

b. Attributes

1. Body configurations and anatomic features.
2. Age and longevity.
3. Dietary habits.
4. Hereditary features.
5. Alternative phenotypes.
6. Replication.
7. Well-being.
8. Primordial factors.

c. Needs

1. Nourishment.
2. Habitat.
3. Spacing and confining.

Elements of study project

a. The agent is under investigation.

b. The drug dosage and administration schedule.

Elements of investigator

a. Familiarity with the subject under study and current knowledge

b. Curiosity

In practice, animal size and shape can be important parameters. Small animals have several advantages. In general, they are less costly, easier to manage, have a faster reproductive rate, and have a higher rate of metabolism. Larger animals, instead, are easier to perform surgery and intravenous injections and can supply large quantities of tissue and fluids. Additionally, the age, gender, and reproductive stature of the animal also should be taken into account. The life span and the growth rate of the animal model may have a significant role in the study duration. Animal conformation is important for studies that require long-term fixation. The cardiovascular systems of pigs and non-human primates mimic that of humans. However, for studies that require long-term observation and monitoring, primates are the ideal choice. A researcher's past experience is often the most important factor in species selection, but the knowledge regarding the specific species, genus and strain of test animals is also an important factor [6].

Biomaterial research involves the use of pathogen-free

(SPF) laboratory animals for evaluation. These animals are surgically delivered and kept in a well-managed atmosphere called a barrier enclosure to avoid pathogen contact. Animals designated as SPF have undefined microbiota unless specific pathogens are known to be absent.

Characteristics and advantages of different animals

The Rat (Rattus norvegicus)

The majority of animals used in biomedical research are rats. Randomly propagated strains, descended from the Norwegian rat (Rattus Norvegicus), are believed to have come from the area between the Caspian Sea and Tobolsk, and are almost exclusively used. The "Wistar rat" and "Sprague-Dawley rat" are best among these due to their simplicity in handling, sensitivity, affordability, and other factors. The first mutation likely found and purposefully bred was the albino rat, also known as the Pink-Eyed White or PEW rat. In the 1800s, albino rats were introduced to England by travelling performers.

Due to a missing vomiting centre, rats do not vomit. Rats lack a gall bladder and tonsils. Due to their severely diffused pancreas, creating a diabetic rat through pancreatectomy is challenging. The rat being omnivorous resembles man nutritionally. Oestrus Cycle makes its appearance at puberty at the age of two to three months, and the whole cycle lasts for about four to five days being divided into four stages according to the cell types found in the vaginal smear. Rats are particularly suitable for.

- Testing of psycho-pharmacological agents.
- They are also utilized for the assay of different hormones and for the study of the oestrus cycle, mating behaviour and lactation.
- These animals are also employed for the study of the effect of drugs on the blood pressure, in acute as well as in chronic or surviving experiments.
- The status of the rat as an experimental animal in the study of gastric secretion is unique, since a continuous secretion though of a low order appears in the fasting animals in contradistinction to large animals like cats, dogs, etc.
- Analgesic drugs are studied by applying radiant heat to the tail of rats.
- They have been employed routinely in the toxicity studies, both acute and chronic, especially the latter because the drug can be administered and effects observed throughout their short life span of about three years.
- The 24-hour-old rat is said to be physiologically similar to a 6-1nonth-old. Infant and is used for evaluation of compounds supposed to be administered in infants of this age group.
- Since the liver regenerates almost entirely over the course of a week following partial hepatectomy (even after removing more than 60% of the liver tissue), 1t is especially well suited for the study of the functional physiology of the organ.
- It is possible to test drugs for their teratogenicity and ca rcinogenicity using rats.
- Different tissues, including the uterus, stomach and col on are commonly utilized for the investigation of drug effects.
- A new bioassay method uses adrenaline to inhibit the ut erus contraction in rats.

Guinea Pig (Cavia porccllus)

The most useful laboratory experimental beast is a guinea or cavy. They are easily housed in captivity, much like other laboratory rodents. They are docile in nature unlike other laboratory rodents and highly vulnerable to tuberculosis and anaphylaxis. They exhibit a high level of histamine sensitivity.

Experimental uses

1. The assessment of bronchodilator compounds for experi mental asthma (acetylcholine aerosols or histamine) is carried out using Guinea pigs.
2. They are used for the biological standardisation of digitalis and for the investigation of local anaesthetics.
3. Since Guinea pigs have hyperactive cochlea, they are appropriate for auditory test analysis.
4. They are acceptable for oxygen usage tests because of their pliant nature and are more defiant to hypoxia than rats and mice.
5. It is the only common experimental animal in resemblance with man, in requirement of extrinsic vitamin C, so highly employed in the research of ascorbic acid metabolism.
6. Being a relevant host for mycobacterial infection, it is targeted for the study of tuberculosis.
7. For the study of isoniazid toxicity guinea pig is more reminiscent of human than rats.
8. Many isolated organs and tissues such as the ileum, tracheal chain, vas deferens, etc. are applied for pharmacological research of various compounds. The terminal ileum is highly sensitive and is commonly used for preparatory studies of spasmodic or antispasmodic compounds, and is especially intuitive and worthy for the identification and analysis of histamine and related compounds.

Mouse (Mus musculus)

The smallest laboratory trial animals that can be easily procreated uniformly are Albino rats which are inexpensive and simple to handle, and because they are so small, they are sensitive to very low doses of a drug substance. The most popular strain of mice used in laboratories is the Swiss albino mouse.

Rabbit (Oryctolagus cuniculus)

Rabbits are very docile animals, having atropine esterase in the liver and plasma. So it can tolerate large doses of Belladonna (atropine). Usually employed for the pyrogen testing of intravenous fluids. It is especially suitable for research on reproduction as ovulation is nonspontaneous.

Hamster

Two species of hamsters are commonly used as laboratory animals, the Syrianor Golden hamster (Mesocricetus auras) and the Chinese hamster (Cricctulus griseus). Chinese hamsters are most commonly used in research on diabetes, because of the high incidence of spontaneous diabetes mellitus in this species, presumably due to the deficiency of B-cells, or the presence of defective B-cells in the pancreas. This species is also used as a host in certain parasitological investigations. Chinese hamsters have a chromosome number (22) which is low as regards other laboratory animals and this makes them excellent tools for cytological investigations, genetics, tissue culture and radiation study

trials.

Cat

Cats are common beings among carnivores that are relatively easy to obtain and to apply for the research study purpose. They are employed in studies on the physiology of the circulatory and neuromuscular systems because the behaviour of these systems corresponds more closely to that of man. Cats are used for the studies where stable blood pressure is required.

Dog

Among the large laboratory trial animals dogs (such as Mongrel and Beagles,) are beneficial as they are easily domesticated and trained. It functions as the model animal for studies on gastric secretion and digestion because dogs can be trained to carry a stomach cannula and because their small stomach and short intestinal tracts resemble those of humans.

Monkey

Monkeys and humans belong to the category of primates, the highest order of mammals. Anatomically and physiologically apes and monkeys share many traits with humans. Primates are harnessed in the fields of virology, parasitology, immunology and immunosuppression, nutrition, and reproduction,

Frog

Since all amphibians absorb moisture through their skin, they must be provided with water. It is almost impossible to breed frogs in the laboratory without inducement by some hormone. They are commonly used in the study of the action of drugs on the cerebrospinal system, on the heart, and on the neuromuscular junction [7].

Animal model research in Homoeopathy

Animal research is important for creating new, better ways to detect and cure illnesses that impact both humans and animals. Animals make excellent research subjects since they share many biological traits with humans. A mouse and a chimpanzee both have more than 98% of their DNA in common with humans. Animals can thus be used as disease study models to research disease processes because they have many of the same health issues as people. The fact that the animals turn over so quickly is another significant benefit. The overall life process occurs in a fairly little period of time frame in comparison to humans, making it possible to study a lifetime or several generations. Additionally, scientists are able to quickly manipulate an animal's domain, including its feed, lighting and temperature, which is difficult for human beings to do.

There are many animal models in which the effects of homoeopathic dilution and the fundamental concepts of homoeopathic medicine have been tested. Small dosages of the homoeopathic medication causticum administered to rats' hind paws cause an inflammatory reaction and the development of oedema in the first hour itself, proving that causticum has oedema-inducing properties. The duration of the birth-to-death cycle is incredibly brief [8].

Studies on the action of thyroxine in diluted form on the transfiguration of frogs were carried out in the nineties. Over the following two decentres, this project offered exceptionally contentious illustrations of the biological impacts of extreme dilution. The application of animal trials in homoeopathy and high-dilution study projects was the subject of another significant conceptual review that came out in 2010. These trials' primary reflection is the clarification of the biotic signature and principle of much dilution's actions on biological organisations, which represents a significant advancement in our knowledge regarding the principle of Homeopathic drug action [9].

Procedures for anaesthesia and euthanasia in laboratory beasts

In research studies using beast models, a convenient, efficient, and problem-free anaesthetic strategy is crucial because it could skew the results of a study. There is currently no widely acknowledged procedure for onset, conservation, and anaesthesia reclamation. Because it is a safe and simple control method, endotracheal intubation with the help of inhalation anaesthesia is employed very frequently for big-size trial beasts. But, due to the much high level of mechanical effort required, it is uncommon for small trial beasts [10].

Uncontrolled or untreated pain can make an animal stressed, which leads to the release of uncontrollable compounds. Finally, it may cause a number of unfavourable alterations to the body. This will ultimately affect how the experiment turns out.

Because of these factors, it is both ethically and scientifically necessary to use anaesthetic and analgesia rationally.

When an animal must be sacrificed, when an experiment must be stopped, or for other moral reasons, euthanasia is used. The process should be completed promptly, painlessly, and in an environment free from worry or dread. A euthanasia method must have an initial depressed effect on the central nervous system to provide immediate insensitivity to pain in order to be accepted as compassionate. The type of study and the species of animal to be killed will determine the procedure to be used (Annexure - 6, CPCSEA Standard Operating Procedures (SOP) for IAEC). The procedure must always adhere to the following specifications:

a. The death occurs with the least amount of pain, anguish, or delay phase [11].
b. The death occurs with the least amount of pain, anguish, or delay.
c. Minimal alterations in physiology and psychology.
d. Compatibility with the intended study and little operator emotional impact.
e. The location needs to be free of environmental toxins and isolated from animal rooms.
f. Before performing a euthanasia operation on larger species like dogs, cats, and monkeys, tranquillizers must be given.

Conclusions

Future developments call for a discussion of core homoeopathic research programmes, and methods as well as the organised replication or validation of certain experimental setups that can advance our comprehension of the Homoeopathic Similia Similibus principle. When biological research is effectively replicated and the outcomes are consistent, they are more revelatory. According to a systematic study analysis, independent replication of homoeopathic preclinical studies is lacking,

most homoeopathic research is concerned with examining interactions between animals, disease processes, and efficacious drugs in expectation of attaining more information regarding the modus operandi of homoeopathic drugs.

Conflict of Interest
Not available

Financial Support
Not available

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