Laboratory Animals and Experimental Research in a Sustainable Scientific Development

Metehan UZUN
University of Onsekiz Mart, School of Health Science, ÇANAKKALE, TURKEY,
e-mail: metehanuzun@hotmail.com

Birkan TOPÇU
University of Kafkas, Atatürk Vocational School of Health Services, Kars, TURKEY
e-mail: birkantopcu_23@hotmail.com

Abstract: Laboratory animals are used and the experimental research is run in various scientific fields such as human and animal health, disease control, sustainable environmental health, health industry and product innovation, and biosafety planning. The experimental research includes those studies that are not yet proven to be completely safe or those not possible to be run on humans. Rats, mice and rabbits are commonly used in these studies. Based on the kind of the study, cats, dogs, guinea pigs, hamsters, sheep, cattle, chicken, sparrows, goats, horses, nonhuman primates, invertebrates, fish and fly species can be used. Though labaratory animals provide significant contributions to the humans and development in science, they require protection by humans and require to be protected from unfair use. Ethical boards and rules are formed to accomplish those goals prohibited the use of the laboratory animals in experimental research under unethical conditions and ruled that any research shall use methods that require the least amount of pain and suffering. The boards ruled not only on research methods but also on feeding and management practices to uphold the main principles of animal welfare. It is obvious that these rulings are the already late responsibility of human kind.

Introduction

Millions of animals have been used in the identification and treatment of disease, biomedicine and health industry and product innovation. Laboratory animals used as models in biomedicine research should have biological, anatomical and physiological similarities to humans. Various laboratory animals have been used in biomedical research and toxicity tests aimed that developing new methods for human diseases. Laboratory animal usage has been increasing in worldwide. When an experimental model is chosen, the genetic definition has to be taken into account. Mice and rats are the best-studied mammalian species in terms of their biology, physiology and genetics after humans. Taylor et al (2008) estimated that 58.2 million animals in 179 countries were used in experiments or for educational purposes in 2005. In England, 3.7 million scientific experimental procedures were started in 2008. Mice, rats and all other rodents together accounted for the seventy-seven percent (77%) of the total (Figure 1). The number of animals used in experimental studies has been increasing exponentially and the species used in these experiments are changing. There were increases in usage of some species (Figure 2). On the other hand, a decrease in some species was recorded in 2008 (Figure 3). For example, rat (8%), domestic fowl (4%), guinea pig (8%), rabbit (13%) and beagle (17%) usage decreased (Figure 3; Home Office, 2008).

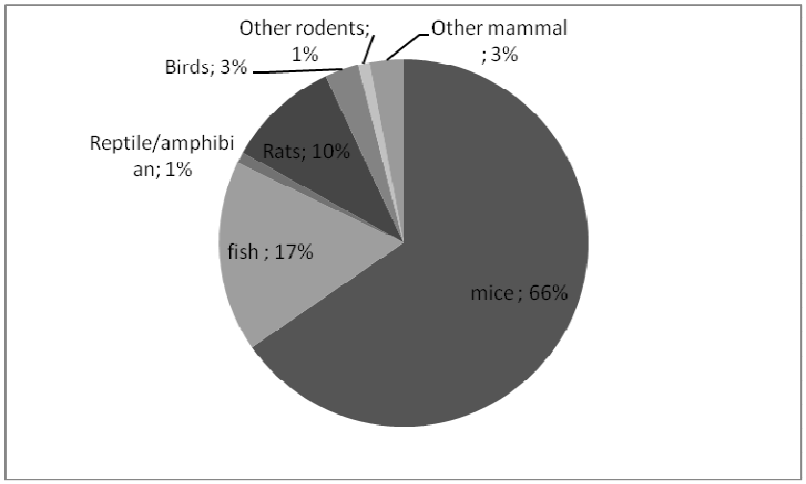

Figure 1. Usage of the species of animals in 2008.

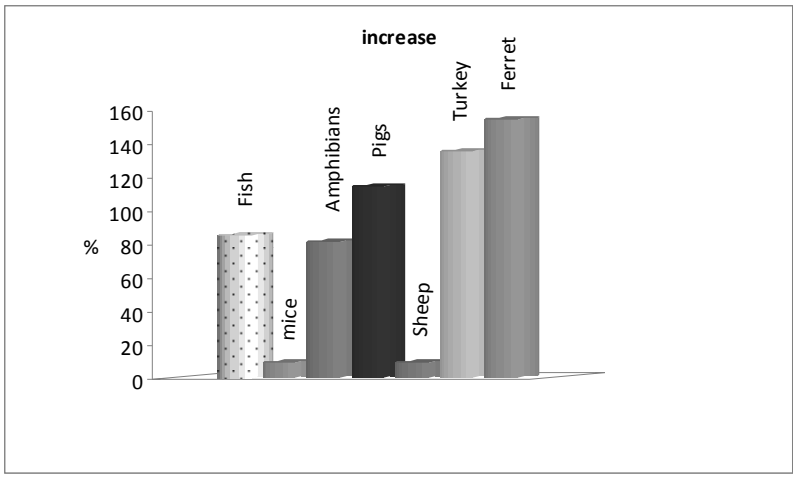

Figure 2. The increasing rate in usage of some species in 2008.

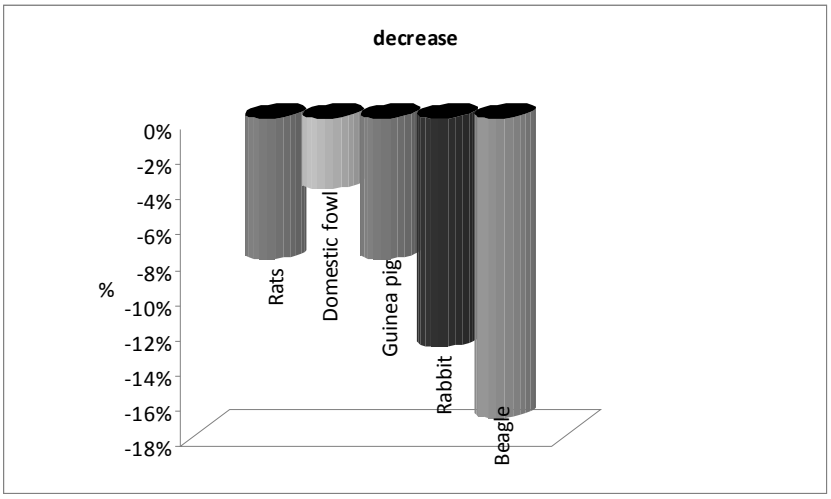

Figure 3. The decreasing rate in usage of some species in 2008.

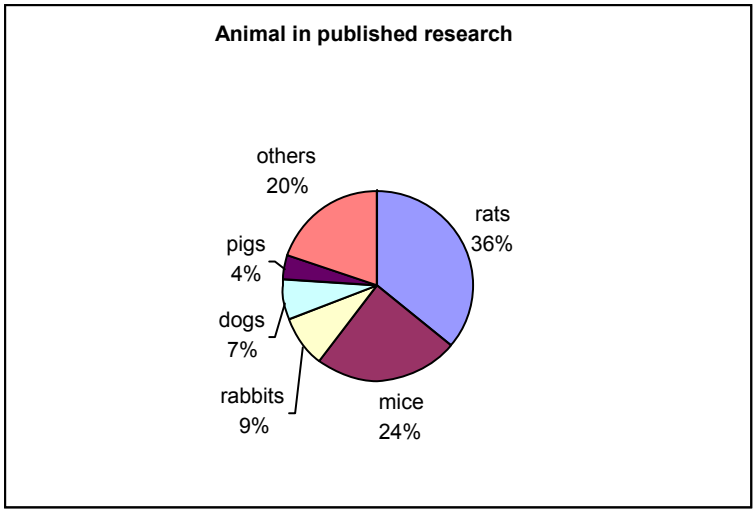

Figure 4. The percentage of laboratory animals in published research in 1995-2005 (Zhao et al, 2007).

Zhao et al (2007) retrieved the Pub Med biomedicine database and searched for publications related to laboratory animals and reported that rat and mice have majority of species used in biomedical research. The research was done in 1995-2005 Pub Med records and was carried out on mice (24 %), rat (36 %) and rabbit (9 %) adding up to a total of 69 per cent. The research carried out on pig, dog and other animals have only % 31 rate (Figure 4; Zhao et al., 2007).

In the year 2010, marine species have been started to be used in experimental studies in significant numbers. Additionally, animals such as the C. elegans and Drosophila melanogaster have been increasingly used as a screening tool. These organisms have advantages of having genetic amenability, low cost and culture conditions that are compatible with large-scale screens in addition to allowing high-throughput screening in a whole-animal context (Giacomotto and Segelati, 2010).

Mice biology and genetics allow these animals to be the best-studied mammalian species. Mice and rats have been used extensively in experimental research and are valuable model organisms thanks to their small size, short lifespan and fast reproduction.

3Rs Principles

Though laboratory animals provide significant contributions to the humans and development in science, they require protection by humans and require to be protected from unfair use. To accomplish this, 3Rs were developed.

The principle of the 3Rs was developed and was considered essential to good laboratory animal practice in scientific experiments and product testing. The 3Rs includes;

1. Replacement: Replacement of animal use with non-animal alternatives. The use of non-sentient organisms rather than higher animals for experiments is recommended. Microorganisms, metazoan parasites, and higher plants can be suggested as possible alternatives to laboratory animals.

2. Reduction: Reduction of the number of animals used should be kept at minimum. Reduction can be considered as obtaining the best quality and most precise information with the smallest possible number of animals.

3. Refinement: Refinement of animal use, in order to avoid or minimize animal pain, distress, or other adverse effects. Refinement referred to all changes in protocols that reduced the severity of stress experienced by animals used in experiments (Russell and Burch, 1959).

Replacement alternatives

Knight (2008) reviewed that non-animal methodologies is available within biomedical research and toxicity testing. For example, physicochemical evaluation and computerized modeling, including the use of structure-activity relationships and expert systems, minimally-sentient animals from lower phylogenetic orders or early developmental vertebral stages may be used, in addition to a variety of tissue cultures, including immortalized cell lines, embryonic and adult stem cells, microorganisms and higher plants, and organotypic cultures, in vitro assays utilizing protozoal, bacterial, yeast, mammalian or human cell cultures exist for a wide range of toxic endpoints.

Reduction Alternatives

De Boo and Hendriksen (2005) reviewed intra and extra experimental reduction strategies for animal use in experimental research. Intra-experimental reduction may be achieved by the design and statistical analysis of individual experiments. Purpose of the supra-experimental reduction is to reduce the number of animals by a change in the setting in which a series of experiments take place. These include reduction of breeding surpluses, improved education and training, critical analysis of test specifications, and re-use of animals.

Refinement Alternatives

Some of the refinements techniques include the use of analgesic and anesthetic techniques to avoid unnecessary pain and suffering (De Boo and Knight, 2008).

In addition, Guide for the Care and Use of Laboratory Animals states that laboratory animals used in research, teaching, or testing must assume responsibility for their health and general well-being. Laboratory animals include any vertebrate animal that are involved in the guide and some principles are provided below:

- Using the suitable animal species, quality, and the number of animals
- Avoiding or minimizing discomfort, stress, and pain.
- Using suitable sedation, analgesia, or anesthesia.
- Establishing experimental end points.
- Provision of appropriate animal husbandry directed and performed by qualified people
- Conducting the experiments on living animals only under the close supervision of qualified and experienced people.

Today, these suggestions have become very important and have been accepted in many countries around the World. Many scientists have tried to decrease usage of the animals in their experiments. However, humans still require animals in their experimental procedures. Many significant knowledge is based on animal experiments. Using animals in experiments can only be fair, ethical and successful if they make use of the 3Rs.

Year	Researcher	Experimental animal	Research subject
2004	Axel R and Buck LB	mouse	odorant receptors and the organization of the olfactory system
2002	Brenner S, Horwitz HR, and Sulston J	worm	genetic regulation of organ development and programmed cell death
2001	Hartwell LH, Hunt RT and Nurse PM	Different animal species	key regulators of the cell cycle
2000	Carlsson A, Greengard P and Kandel ER	Mouse and guinea pig	concerning signal transduction in the nervous system
1999	Blobel G	Different animals and their cells	proteins have intrinsic signals that govern their transport and localization in the cell
1998	Furchgott RF, Ignarro LJ and Murad F	rabbit	concerning nitric oxide as a signaling molecule in the cardiovascular system
1997	Prusiner SB	Hamster & mouse	Prions - a new biological principle of infection

1996	DohertyPC and Zinkernagel RM	mouse	specificity of the cell mediated immune defense
1995	Lewis EB, Wieschaus EF and Nusslein-Volhard C	Drosophila Melanogaster	genetic control of early embryonic development"
1992	Fischer EH and Krebs EG.	Rabbit	reversible protein phosphorylation as a biological regulatory mechanism
1991	Neher E and Sakmann B	Frog	the function of single ion channels in cells
1990	Murray JE and Thomas ED	Dog	organ and cell transplantation in the treatment of human disease
1989	Varmus JM and Bishop HE	Chicken	the cellular origin of retroviral oncogenes
1987	Tonegawa S	mouse	genetic principle for generation of antibody diversity
1984	Milstein C, Köhler KJF and Jerne NK	mouse	specificity in development and control of the immune system and the discovery of the principle for production of monoclonal antibodies"
1982	Bergström SK, Samuelsson BI and Vane JR	Sheep, rabbit, guinea pig	prostaglandins and related biologically active substances
1981	Sperry RW, Hubel TH and Wiesel TN	Cat and monkey	functional specialization of the cerebral hemispheres, information processing in the visual system
1980	Benacerraf B, Dausset J and Snell GD	Mouse and guinea pig	genetically determined structures on the cell surface that regulate immunological reactions

Table 1. Animal experiments which resulted in Nobel Prizes between the years 1980-2004 (http://nobelprize.org).

Animal	Model	Reference
Rabbit	Osteoarthritis	Kim et al, 2010
Rat	Renal impairment	Salman et al, 2010
Rabbit	Epstein-Barr virus infection	Okuno et al, 2010
Mouse	endometriosis	Altan et al, 2010
Zebra Fish	Polycystic kidney disease	Bouvrette et al, 2010
Zebra Fish	Fetal alcohol exposure and cardiovascular abnormalities	Dlugos and Rabin, 2010
Rat	Hypertension and associated metabolic disturbances	Pravenec and Kurtz, 2010
Rabbit	Venous thrombosis	Konishi et al, 2010
Rat	Acute asthma	Sun et al, 2010
Cynomolgus macaques	Chikungunya virus infection	Labadie et al, 2010
Rabbit	Atherosclerosis	
Mice and rat	Rheumatoid arthritis	Chen et al, 2010
Rat	Double-hemorrhage	Güresir et al, 2010
Rat	Choroidal neovascularization	Baba et al, 2010
Zebra Fish	Cancer	Mione and Trede, 2010
Rabbit	Vaccinia keratitis	Altman et al, 2010

Mouse	Neurodegeneration	Dawson et al, 2010
Rat	Acute pancreatitis	Qian et al, 2010.
Rat	Spinal cord compression injury	Schültke et al, 2010
Rat	Nerve injuries	Ma et al, 2010
Rat	Chronic mild stres and depression	Wu and Wang, 2010
Rat	Aging, stress and stroke	Merrett et al, 2010
Rat	Gastric carcinogenesis	Manikandan et al, 2010
mice	Ulcerative colitis associated Carcinogenesis	Chromik et al, 2010
Mouse	T Lymphotropic Virus Type-1-Associated Adult T-Cell Leukemia/Lymphoma	Zimmerman et al, 2010
Mouse	Down Syndrome	Yu et al, 2010
Mouse	Human cancer	Walrath et al, 2010
Mouse	Central nervous system embryonal Tumors	Momota and Holland, 2010
Mouse	Chronic lymphocytic leukemia	Hamblin, 2010
Drosophila melanogaster	Neurodegenerative disease	Berg et al, 2010
Drosophila melanogaster	Neuroscience.	Bellen et al, 2010
Drosophila melanogaster	Epilepsy	Kliman et al, 2010
Guinea pig	Acute nerve injury and peripheral nerve regeneration	Cho et al, 2010
Guinea pig	Dermatophytosis	Ghannoum et al, 2010
Guinea pig	Asthma	Kloek et al, 2010
Guinea pig	Osteoarthritis	Gurkan et al, 2010
cynomolgus macaques	Shigella dysenteriae type 1 infection	Shipley et al, 2010
cynomolgus monkey	Peripheral nervous system injury	Wakao et al, 2010
cynomolgus monkey	Hepatitis A virus	Amado et al, 2010

Table 2. Examples of studies in which animals were used as a model .

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