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REVIEW

Alternatives to animal testing: A review

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Abstract   The number of animals used in research has increased with the advancement of research and development in medical technology. Every year, millions of experimental animals are used all over the world. The pain, distress and death experienced by the animals during scientific experiments have been a debating issue for a long time. Besides the major concern of ethics, there are few more disadvantages of animal experimentation like requirement of skilled manpower, time consuming protocols and high cost. Various alternatives to animal testing were proposed to overcome the drawbacks associated with animal experiments and avoid the unethical procedures. A strategy of 3 Rs (i.e. reduction, refinement and replacement) is being applied for laboratory use of animals. Different methods and alternative organisms are applied to implement this strategy. These methods provide an alternative means for the drug and chemical testing, up to some levels. A brief account of these alternatives and advantages associated is discussed in this review with examples. An integrated application of these approaches would give an insight into minimum use of animals in scientific experiments.
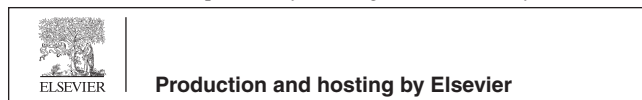
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1. Introduction

Use of animals for various purposes like food, transportation, pets, sports, recreation and companionship is as old as the human beings itself. Using animals for the purpose of research is one of the extended uses. Various animals like mice, rats, hamsters, rabbits, fishes (examples – zebra fish, trout), birds (mainly chicken), guinea pigs, amphibians (xenopus frogs), primates, dogs, cats etc. are being used in research for a long time (CULABBR, 1988). Drug testing and toxicological screenings which are useful in the development of new treatments for infectious and non-infectious diseases is the main purpose of such studies. Animals also serve as a tool to understand effects of medical procedures and surgical experiments. Moreover, they are used to obtain products like vaccines, antibiotics etc. which are used in diagnostics as well as treatments (Giacomotto and Segalat, 2010; Hendriksen, 2009, 2007). The number of animals used in research has gone up with the advancement in medical technology. Every year, millions of experimental animals are used all over the world. For example, in UK, 3.71 million animals were used for research in the year 2011 (www.rspca.org.uk). The total number of animals used in the USA in the year 2009 was estimated to be 1,131,076, while that in Germany reached up to 2.13 million in 2001 (Rusche, 2003). This huge population of experimental animals usually comes from the breeding centers located in various universities and national breeding centers. All of these are known as class-A dealers, while the brokers who acquire the animals from miscellaneous sources (like auctions and animal shelters) are identified as class-B dealers. At few instances use of the wild animals such as monkeys and birds is also followed (Baumans, 2005). In clinical testing laboratories, animals are isolated from their groups and used as a tool irrespective of their natural instincts. For the experimental procedures, either a whole animal or its organs and tissues are used. For this purpose animals are euthanized (killed) by established methods. Many times, the animals surviving the clinical testing are euthanized at the end of an experiment to avoid the later pain and distress (Rusche, 2003). In some cases (for example in LD 50 analysis) animals die as a result of the experiment.

The pain, distress and death experienced by the animals during scientific experiments have been a debating issue for a long time. Argument is that being alive, animals have the rights against pain and distress and hence, their use for experimentation is unethical and must be stopped (Rollin, 2003). Various acts and laws have been passed to bring the control over unethical use of animals and minimize the pain to animals during experimentation. For example, in 1824, the organiza-

tion for animal rights was formed by the Royal Society for the Prevention of Cruelty to Animals. In 1876, an act for prevention of cruelty to animal was formed in the UK (Balls, 1994). It came into existence in India, France and USA in the year 1960, 1963 and 1966, respectively. At present, many rules and acts are followed at the international level, to protect the animals against the cruelty and misuse. The organizations like ICH (International Conference on Harmonization of technical requirements for registration of pharmaceuticals for human use), CPCSEA (Committee for Purpose of Control and Supervision on Experiments on Animal), NIH (National Institute of Health), and OECD (Organization for Economic Cooperation and Development) provide the guidelines for animal house keeping, breeding, feeding, transportation, and mainly for their use in scientific experiments (Rollin, 2003). Besides the major concern of ethics, few more disadvantages of animal experimentation are requirement of skilled/trained manpower and time consuming protocols. Moreover, very high cost involved in breeding, housing and lengthy protocols of animal experiments is another drawback (Balls, 1994).

2. Three Rs: reduction, refinement and replacement

Alternatives to animal testing were proposed to overcome some of the drawbacks associated with animal experiments and avoid the unethical procedures. A strategy of 3 Rs is being applied which stands for reduction, refinement and replacement of laboratory use of animals (Ranganatha and Kuppast, 2012). Different methods and alternative organisms are applied to implement this strategy. The concept of replacement of animals was first discussed in 1957 by Charles Hume and William Russell at the Universities Federation for animal welfares (UFAW) (Balls, 1994). Russell and Burch (1959) suggested some ways to make the animal experiments more humanly, which was later called as 3 Rs. This approach motivates the use of minimum number of animals i.e. 'reduction' in the total number of animals used in an experiment. The use of animals must be planned and 'refined' carefully in such a way that pain and distress caused during the experiment should be minimized. Moreover, if possible higher animals should be 'replaced' with alternative methodologies and lower organisms (Ranganatha and Kuppast, 2012; Zurlo et al., 1996). Animal replacement is defined as, 'any scientific method employing non-sentient material which may replace use of conscious living vertebrates in animal experimentation'. Two types of replacements were distinguished as 'relative' and 'absolute' replacement. In relative replacement the animals are used but not exposed to any distress during experiment. No use of