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ARTICLE

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REINVENTING PRECLINICAL SCIENCE: ETHICAL AND TRANSLATIONAL POWER OF EMERGING ANIMAL MODELS

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Animal models remain central to drug discovery by enabling the study of disease mechanisms, drug responses, and toxicity in biologically relevant systems. This review evaluates the scientific and translational value of traditional and non-primate models, analyses ethical-legal considerations and species-specific limitations, and highlights emerging innovations such as genetically engineered organisms and advanced in-vivo imaging. Emphasis is placed on Drosophila, zebrafish, Xenopus, planarians, and sea urchins, whose unique strengths advance mechanistic insight and support 3Rs-aligned, next-generation drug research.

Introduction

Animal models have long been a major component of biomedical research, particularly in the field of drug discovery. Before a medicinal chemical is considered safe and effective for human use, it must pass a series of rigors preclinical tests to determine its pharmacological properties, toxicity profile, and potential therapeutic benefits. Using animal models, researchers can study diseases in controlled biological systems that are physiologically, anatomically, and genetically similar to humans. These similarities make them crucial for understanding complex biological interactions, predicting human reactions, and weighing the benefits and drawbacks of new therapeutic options[1].

Despite technological advancements like organ-on-a-chip systems, computational modelling, and high-throughput screening increasing the tools available for drug discovery, animal research remains an essential step in bridging the gap between laboratory science and clinical application[1].

The use of animals in drug development is based on the concept of translational research, which seeks to convert laboratory findings into practical medical solutions. Using animal models, researchers can replicate human diseases, monitor the natural progression of pathological processes, and evaluate how potential drugs interact with biological systems over time[1].

For conditions like cancer, diabetes, neurodegenerative diseases, and infectious diseases, animal research offers insights that are often not possible with in-vitro or purely computational methods[2].

Ethical concerns about animal suffering have also led to stricter legal frameworks and the development of the "3Rs" principle—Replacement, Reduction, and Refinement—to guide the moral use of animals in research. The European Medicines Agency (EMA), the Food and Drug Administration (FDA) in the United States, and national committees in a number of countries are among the regulatory bodies that now demand comprehensive justifications for the choice of animal models as well as humane treatment during the research process[3].

The review study also looks at new innovations and technological advancements that will impact animal-based drug research in the future, like the use of big data and computational modelling, genetically modified animals, and humanised animal models[3].

Animals were initially employed in experiments to discover the effects of various chemicals, according to

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historical records. However, our understanding of diseases and the development of animal models advanced significantly during the Renaissance and the succeeding eras[4].

In the 16th and 17th centuries, scientists like Paracelsus and Galen conducted experiments on animals to investigate the effects of different chemicals and medicinal herbs. These early studies laid the foundation for understanding pharmacological principles and the potential therapeutic benefits of particular compounds[4].

The 19th century saw significant advancements in the creation of animal models for pharmacological research. One of the pioneers in this field is the French biologist Claude Bernard[4]. His studies on dogs and rabbits, particularly in the examination of how drugs affect physiological systems, provided valuable insights into the functioning of pharmaceuticals and paved the way for additional research. One of the most important developments in early animal models was the development of the frog heart model by physiologist Otto Loewi in the early 20th century[3,4].

All things considered, animal models remain essential in the hunt for and development of new drugs, serving as a critical step in ensuring that novel treatments are both safe and effective for use in humans, Although the field is still in its infancy, combining traditional animal research with state-of-the-art technologies offers a promising path towards more reliable, compassionate, and successful drug discovery processes[5].

Objectives

The study's goals are to evaluate the scientific and translational value of animal models in understanding diseases, predicting drug responses, and assessing toxicity; analyse the ethical and legal frameworks and the advantages and disadvantages of commonly used laboratory species; and identify new innovations and alternatives that promote the 3Rs in drug research, such as genetically modified models and in-vivo imaging.

Scientific Relevance and Translational Potential of Non-primate Models

The scientific value of non-primate animal models has increased significantly due to developments in molecular biology, genomics, and regenerative science. In addition to mammalian systems used in late-stage validation, simpler organisms now offer remarkable insights into developmental signalling, toxicity mechanisms, and high-throughput genetic screening[6].

Key benefits shared by models like Drosophila melanogaster, *Danio rerio* (zebrafish), *Xenopus laevis*, *Schmidtea mediterranea* (planarians), and *Strongylocentrotus purpuratus* (sea urchins) include rapid reproduction, external development, genetic manipulability, and conservation of human disease genes, making them effective tools for understanding disease pathways and speeding up drug discovery (Fig. 1)[6].

Drosophila Melanogaster allows for accurate modelling of neurodegeneration, metabolic disorders, cardiomyopathies, and developmental syndromes and offers approximately 75% conservation of human disease genes[6]. It is perfect for high-throughput screening and functional genomics due to its short life cycle, low maintenance costs, and sophisticated genetic tools (RNAi, CRISPR, GAL4-UAS), which enable discoveries in Parkinson's, Alzheimer's, muscular dystrophy, and paediatric rare diseases[6].

In a similar vein, *Danio rerio (zebrafish)* conserves more than 80% of genes linked to disease and shares about 70% of its genes with humans. Its usefulness in cancer biology, cardiotoxicity, metabolic disorders, and neurodevelopmental studies is increased by the direct visualisation of organogenesis, vascular development, and neural patterning made possible by transparent embryos[6].

With approximately 79% gene homology to humans and easily manipulable embryos, *Xenopus laevis* makes a substantial contribution to our understanding of developmental toxicity, morphogenesis, and embryogenesis (Fig. 1). Ion channel and receptor pharmacology studies are uniquely supported by its large oocytes[6].

Ethical–legal Considerations, Strengths, and Limitations of Commonly used Species

Each model has drawbacks that affect translational relevance despite its scientific benefits.

Despite strong genetic power, *Drosophila*'s invertebrate physiology limits organ-specific toxicology and mammalian metabolic modelling, Although the vertebrate context supports early toxicity evaluation, differences in drug absorption, metabolic rate, and dose scaling in *zebrafish* make direct extrapolation to humans difficult[6].

Due to slower reproductive cycles, greater space requirements, and genome complexity brought on by allotetraploidy, which affects genetic precision, *Xenopus laevis* is limited[6].

Despite being incredibly effective for researching stem cells, regeneration, and neuroactive compound screening,

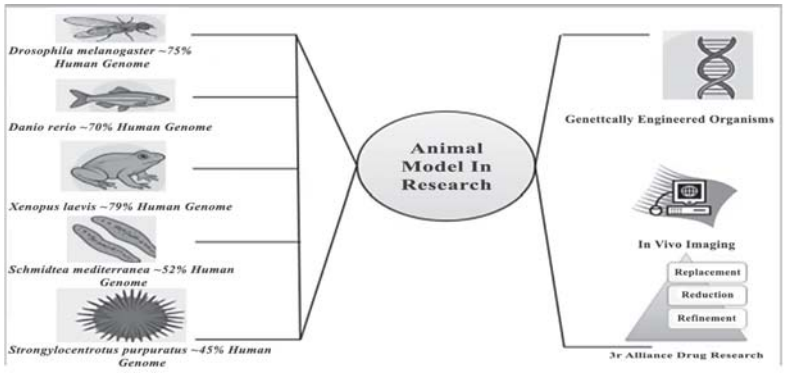

Fig. 1: Role of Different animal models in Research.

Schmidtea mediterranea (planarians) lack important mammalian organs (heart, kidney, and lungs), which limits predictions of systemic toxicity[6].

Although they are not very useful for organ-specific disease modelling, *Strongylocentrotus purpuratus* (sea urchins) have historically made advances in cell cycle, chromosomal segregation, and mitotic regulation possible (Fig. 1)[7].

Emerging Alternatives and Innovations Supporting the 3Rs

Additionally, a number of these models are state-of-the-art substitutes that promote drug research refinement, reduction, and replacement. In line with the 3Rs, planarians are prime examples of natural regenerative models that enable repeated, non-lethal evaluations of stem cell dynamics, apoptosis, and behavioural toxicity. Real-time monitoring of wound healing, neural repair, and anti-proliferative drug responses in affordable, scalable systems is made possible by their ability to regenerate the entire body[7].

Zebrafish embryos facilitate high-throughput chemical screening with minimal animal use and non-invasive imaging technologies like fluorescent reporters because of their transparency and high fecundity[7].

Similarly, *Xenopus* and *Drosophila* offer platforms that are highly compatible with live-imaging tools and genetic engineering (CRISPR, transgenics), allowing mechanistic clarity while lowering dependence on higher vertebrates[8].

Lastly, *sea urchins* continue to be useful low-complexity models that enable mechanistic investigation of cell division with little ethical burden due to their historical contributions to mitotic biology (Fig. 1)[9].

When taken as a whole, these non-primate species show how creative, genetically manageable, and morally acceptable systems can speed up drug development while meeting the growing need for humane and scientifically sound research methodologies[10].

Conclusion

Each of these organisms—*Strongylocentrotus purpuratus, Danio rerio, Xenopus laevis, Schmidtea mediterranea,* and *Drosophila melanogaster*—brings unique benefits to the study of drug development. Their biological transparency, regenerative potential, ease of manipulation, and genetic conservation make them indispensable tools in early scientific research. Together, they provide a comprehensive framework for identifying therapeutic targets, understanding disease mechanisms, and assessing potential drug options. Their combined efforts validate the continued importance of non-primate models in shaping human health and pharmaceutical research.

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References

1. P. Mukherjee, S. Roy, D. Ghosh, and S. K. Nandi, *Lab. Anim. Res.*, **38**(1), 18 (2022).
2. IntechOpen, *IntechOpen*, (n.d.).
3. C.A. MacRae and R.T. Peterson, *Syst. Pharmacol. Toxicol.*, 43–64 (2015).
4. E.M. Verheyen, *Dis. Model. Mech.*, **5**(3), 231–236 (2012).
5. S. Cassar et al., *HHS Public Access*, **33**(1), 95–118 (2020).
6. U.S. Dep. Health Hum. Serv., *Product Development Under the Animal Rule*, (2015).
7. R. Greek and A. Menache, *Int. J. Med. Sci.*, **10**, 206–221 (2013).
8. S.K. Aminabee et al., *J. Pharm. Sci. Res.*, **13**(2), 198–209 (2023).
9. S.S. Sakat, O. Bagade, G. Mhaske, P. Taru, M. Sagar, and M. Rastogi, *J. Pharm. Res. Int.*, **12**(10), 11–19 (2022).
10. M. Ivankovic et al., *Int. J. Dev. Biol.*, **63**, 0–1 (2019).