

New Drug Screening Platforms Instead of Animal Testing

**Dr. Prasad Vasantrao Patrekar, Mr. Mahesh Hanmant Mohite, Mr. Pradeep Chavagonda Patil
Mr. Dipak Vijay Patil, Mrs. Savita Amar Baravkar**
Eklavya College of Pharmacy, Tasgaon, India

Abstract: *The trend of drug screening wants novel and time saving techniques to test the drug and bring it as early as possible to the market without compromising the safety studies and efficacy studies, hence the scientists are looking for novel methods for drug screening which can give promising results along with saving time. This article focused on the novel trends which can be an alternative option for a safe, fast and effective drug screening method.*

Keywords: Alternatives to Animal Testing, Models in Clinical and Biomedical Research, animal testing, Alternatives To Animal Testing, Human Cell- And Tissue-Based Testing, Organs On A Chip, replace animals in drug and cosmetics testing, skin grown in lab, drug and cosmetics testing, Non-animal methods, Human 3D Tissue-Engineered Models, Alternative to Animal Testing, artificial tissue, organs on chip, ex vivo technique

I. INTRODUCTION

Animal models have been employed in scientific studies since at least the Ancient Greek period. In the sixth century B.C., for example, Alcmaeonid of Croton investigated the brain with dogs. Since then, many different models have been used for various applications, including the nematode *Caenorhabditis elegans*, the fly *Drosophila melanogaster*, the zebrafish, the frog *Xenopus*, the mouse, the rat, rabbit, dog, and the primate rhesus macaque. (1, 2, 3, 4)

The mouse and rat are by far the most commonly utilized animals. In recent years, animal models have improved, and these modified animals now provide more realistic models for medical study. Scientists, for example, can manipulate animal genomes by adding or removing genes to imitate sickness or explore the function of these genes. These animals are referred to as transgenic animals. The transgenic mouse is the most frequent transgenic animal, however this technology also applies to rats, cats, and rabbits. (1, 5, 6, 7, 8)

Background of drug screening & Animal Testing:

Animals play crucial and distinctive roles in biological and behavioral research. Much medical advancement that benefits people is the result of animal research investigations.

Scientists pick and justify certain animal models used in study based on their likeness to humans in anatomy, physiology, genetics, or even ordinary living situations. Animals are used as "models" to investigate certain elements of biological phenomena. There are other occasions when animal models, such as fish and frogs, are utilized, whose anatomy and physiology are substantially different from humans but can nevertheless assist researchers address fundamental biological processes that are common across species in order to acquire information to enhance human health.

Animals make excellent study subjects for a number of reasons. They are physiologically identical to humans and are prone to many of the same health issues. They also have short life cycles, allowing them to be studied over their whole life span or throughout several generations. Furthermore, scientists may manipulate the environment around the animal (food, temperature, lighting, etc.), which is harder to accomplish with humans. However, the most significant argument for using animals is that it would be immoral to purposely expose humans to health hazards in order to study the progression of a disease. (11)

Reality of cruel animal testing

Think about living inside a locked closet with no control over your life. You have no control over when and what you eat, how you spend your time, whether or not you have a spouse and children, or who that partner is. You don't even know when the lights turn on and off.

Consider living your entire life as a prisoner, even if you have committed no crime. This is how an animal in a laboratory lives. It is poverty, solitude, and suffering.

There are the experiments on top of the deprivation. Animals can be burnt, shocked, poisoned, secluded, starved, drowned, drugged, and brain-damaged under US law. No experiment, no matter how painful or insignificant, is permitted - and no painkillers are necessary. Even when alternatives to animal usage are available, the law does not force them to be used—and they are frequently not.

Animals are infected with illnesses they would never usually catch, small mice develop tumors the size of their bodies, kittens are purposefully blinded, rats are forced to have convulsions, and primates' heads are sliced open and electrodes inserted. Experimenters force-feed drugs to animals, perform many surgeries on them, implant wires in their brains, break their spines, and do a variety of other things.

Animals are generally placed back into a cage without any medications after suffering these horrific, excruciating surgeries. Video from inside laboratories shows animals cowering in fright whenever someone goes past their cages. They are unsure if they will be taken from their cells for an injection, blood withdrawal, a painful operation, surgery, or death. They frequently see the slaughter of other animals directly in front of them.

Cats, dogs, fish, mice, pigs, monkeys, rabbits, and rats are just a few of the animals regularly employed in these tests. (9, 11)

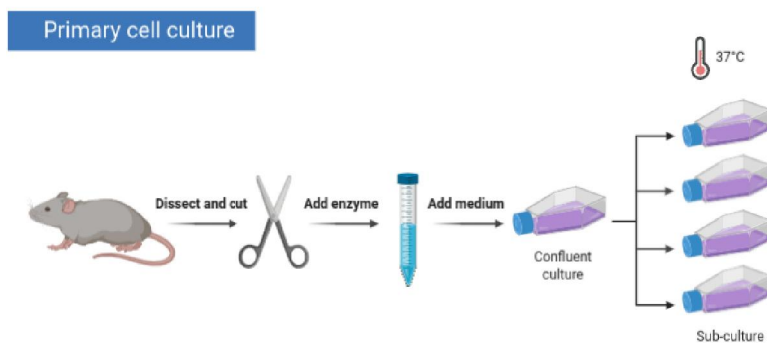
Alternatives for Animal Testing:

Non-animal approaches are frequently less expensive, faster, and more effective. Replacing animal tests does not imply endangering human patients. It also does not imply putting a halt to medical advancement. Rather, substituting animals used in research will increase both the quality and compassion of our work.

Fortunately, the development of non-animal technologies is accelerating. Animal experiments are being phased out in fields such as toxicity testing, neurology, and medication development due to scientific advances. However, much more has to be done. (10)

Types of non-animal methods

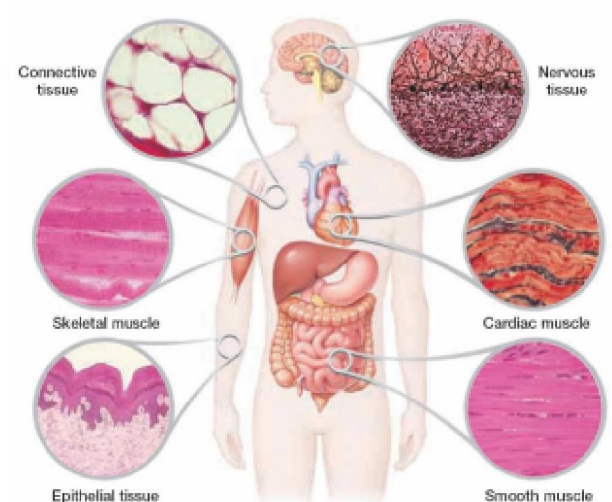
A. Cell cultures:



In the laboratory, nearly any variety of human and animal cell may be generated. Scientists have even coaxed cells to develop into 3D structures like tiny human organs, which can give a more realistic approach to test novel medicines.(9,10) Human cells have been employed to develop novel "organs-on-chips" gadgets. Animals can be replaced with these to research biological and disease processes, as well as medication metabolism. Devices that accurately imitate the lung, heart, kidney, and stomach have already been developed. The ultimate objective is to develop a "human-on-a-chip" using these chips.

Cell cultures have been instrumental in major breakthroughs in fields such as cancer, sepsis, renal disease, and AIDS, and are now frequently employed in chemical safety testing, vaccine manufacturing, and medication research.

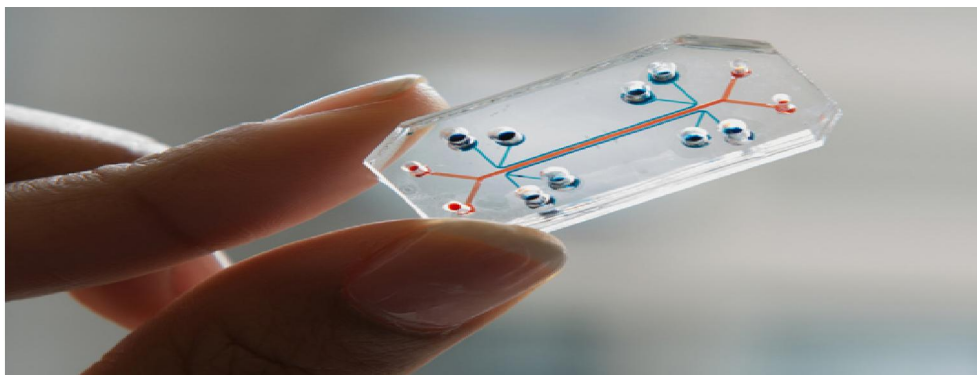
Human tissues:



Human volunteers' healthy and sick tissues can give a more meaningful approach of researching human biology and illness than animal studies. Human tissue can be given as a result of surgery (for example, biopsies, cosmetic surgery, and transplants). Skin and eye models built from reconstituted human skin and other tissues, for example, have been produced to replace the brutal rabbit irritation tests.

Human tissue can also be utilized after a person has died (for example, in post-mortem examinations). Post-mortem brain tissue has yielded vital insights on brain regeneration as well as the impacts of Multiple Sclerosis and Parkinson's disease.

Computer models:



The ability to "model" or re-create the features of human anatomy is becoming increasingly achievable as computer technology advances. Computerized representations of the heart, lungs, kidneys, skin, digestive, and musculoskeletal systems already exist. They may be used to do virtual experiments based on existing knowledge and mathematical facts. There are also data mining methods that can assist create predictions about the possible hazard of one chemical based on existing data from other, comparable compounds.

Volunteer studies:

Technological advancements have enabled the creation of advanced scanning devices and recording techniques that can be utilized to safely research human participants.

Brain imaging equipment that can 'see' within the brain can be used to track and treat the course of brain illness. By comparing them to healthy participants, they can help researchers understand the causes. Micro dosing, a novel approach, can also be employed in volunteers to assess how extremely small dosages of possible new medications react in the human body. These micro doses are radiolabeled, injected into human volunteers, and quantified (typically in blood samples) with an accelerator mass spectrometer, a highly sensitive measurement equipment.

Drug Screening Platforms by Using Tissue Engineering

When a medicine leaves the lab and is tested in animals, the reaction does not necessarily correspond to what is found in people. Cancer and diabetes can be extremely similar in animals, but there are variances. Human tissue research can aid by examining the effects of medications in donated tissue samples (e.g., skin, cancer biopsies, blood) to rule out potential adverse effects before testing in humans. (12) Hundreds of researchers across the world are utilizing human tissue research to better medication testing and development. (11, 12, 18)

Ex Vivo Technique

Most ex vivo research developed with cancer, with tumor samples used to describe the distinctions between cancer types, laying the groundwork for many tissue networks that remain a significant focus for drug development. Human tissue research now encompasses a wide range of therapeutics, from cardiovascular illness to respiratory disorders such as asthma and COPD. (19)

Artificial Lab Grown Tissue

The lab grown tissue can be a milestone in the field of drug testing. Scientists now developing a technique where they culture the human tissue in the lab for drug testing this technique can allow the new way to test the drug on actual tissue this technique can give an actual and real time effect of drug meant to effect on intended tissue. Hence the animal testing phase and the time both factors can be significantly minimized. (15,16,17,18,19)

In this technique the human tissue is isolated and grown in lab the latest example of this technique is artificial lab grown meat (13, 14, 15, 16, 17, 18, 19) By introducing Organs-on-chips (OoCs) which are microfluidic chips that contain artificial or natural tiny tissues. These chips are meant to manage cell microenvironments and retain tissue-specific functionalities in order to better resemble human physiology. These chips have received interest as a next-generation experimental platform to research human pathophysiology and the effect of medicines in the body, combining breakthroughs in tissue engineering and microfabrication. Because there are as many instances of OoCs as there are applications, it can be difficult for novice researchers to comprehend what makes one OoC better suited to a certain application than another. This Primer is designed to provide an overview of the features of OoC that must be addressed while designing an application-specific OoC. The Primer discusses the guiding concepts and concerns for designing, fabricating, and operating an OoC, as well as the following assaying methodologies for extracting biological information from OoC devices. Along with this, there will be a discussion of present and prospective uses of OoC technology to help influence design and operational decisions throughout OoC system installation. (17, 18, 19)

II. CONCLUSION

Novel drug screening methods are rapidly evolving in order to meet rising customer demands for health, environmental sustainability, and animal welfare. Small-scale cultured cell production might be doable soon, but large-scale deployment is difficult and, even if successful, will take time. These procedures should be pushed in the direction of cruelty-free, ecologically friendly drug screening systems. Animal testing is currently the only option for drug screening. However, innovative drug screening approaches will not totally replace traditional drug screening procedures. Still Extensive research, support, and investment from government and industry are required to translate new approaches and replace traditional drug screening procedures.

REFERENCES

- [1]. Bédard, P., Gauvin, S., Ferland, K., Caneparo, C., Pellerin, È., Chabaud, S., & Bolduc, S. (2020). Innovative Human Three-Dimensional Tissue-Engineered Models as an Alternative to Animal Testing. *Bioengineering*, 7(3). <https://doi.org/10.3390/bioengineering7030115>
- [2]. Ericsson A.C., Crim M.J., Franklin C.L. A brief history of animal modeling. *Mo. Med.* 2013;110:201–205. [PMC free article] [PubMed] [Google Scholar]
- [3]. Gore A.V., Pillay L.M., Venero Galanternik M., Weinstein B.M. The zebrafish: A fantastic model for hematopoietic development and disease. *Wiley Interdiscip. Rev. Dev. Biol.* 2018;7:e312. doi: 10.1002/wdev.312. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [4]. Pérez-Guijarro E., Day C.-P., Merlino G., Zaidi M.R. Genetically engineered mouse models of melanoma. *Cancer.* 2017;123:2089–2103. doi: 10.1002/cncr.30684. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [5]. Lang C.N., Koren G., Odening K.E. Transgenic rabbit models to investigate the cardiac ion channel disease long QT syndrome. *Prog. Biophys. Mol. Biol.* 2016;121:142–156. doi: 10.1016/j.pbiomolbio.2016.05.004. [PubMed] [CrossRef] [Google Scholar]
- [6]. Cho S.J., Bang J.I., Yu X.F., Lee Y.S., Kim J.H., Jeon J.T., Yee S.T., Kong I.K. Generation of a recloned transgenic cat expressing red fluorescence protein. *Theriogenology.* 2010;73:848–855. doi: 10.1016/j.theriogenology.2009.09.008. [PubMed] [CrossRef] [Google Scholar]
- [7]. Filipiak W.E., Saunders T.L. Advances in transgenic rat production. *Transgenic Res.* 2006;15:673–686. doi: 10.1007/s11248-006-9002-x. [PubMed] [CrossRef] [Google Scholar]
- [8]. Demetrius L. Aging in mouse and human systems: A comparative study. *Ann. N. Y. Acad. Sci.* 2006;1067:66–82. doi: 10.1196/annals.1354.010. [PubMed] [CrossRef] [Google Scholar]
- [9]. <https://www.peta.org/issues/animals-used-for-experimentation/animals-laboratories/#:~:text=Animals%20are%20infected%20with%20diseases,electrodes%20are%20implanted%20in%20them>
- [10]. Sonali K. Doke, Shashikant C. Dhawale, Alternatives to animal testing: A review, Saudi Pharmaceutical Journal, <https://doi.org/10.1016/j.jsps.2013.11.002>.
- [11]. Akhtar A. The flaws and human harms of animal experimentation. *Camb Q Healthc Ethics.* 2015 Oct;24(4):407-19. doi: 10.1017/S0963180115000079. PMID: 26364776; PMCID: PMC4594046.
- [12]. What is Human Tissue Testing? By Roland Linder 14 March 2022, <https://www.reprocell.com/blog/biopta/what-is-human-tissue-testing>
- [13]. Datar, I (January 2010). "Possibilities for an in vitro meat production system". *Innovative Food Science & Emerging Technologies.* 11 (1): 13–22. Doi:10.1016/j.ifset.2009.10.007.
- [14]. https://en.wikipedia.org/wiki/Cultured_meat
- [15]. "Lab-Grown Chicken Could Soon Be On Your Plate". *Sky News.* 12 July 2016. Retrieved 5 August 2016.
- [16]. Chang, Lulu (11 July 2016). "Would you eat lab grown chicken? SuperMeat sure hopes so". *Yahoo News.* Archived from the original on 9 August 2016. Retrieved 5 August 2016.
- [17]. ^ Tobin, Andrew (13 July 2016). "The Israeli Startup That Lets You Eat Meat - Without Eating the Animal". *Haaretz.* Retrieved 5 August 2016.
- [18]. Daniel Sergelidis, Laboratory of Food Hygiene of Animal Origin-Veterinary Public Health, School of Veterinary Medicine, Thessaloniki 54124, Greece DOI: 10.26717/BJSTR.2019.17.002930
- [19]. Leung, C. M., De Haan, P., Kim, G., Ko, J., Rho, H. S., Chen, Z., Habibovic, P., Jeon, N. L., Takayama, S., Shuler, M. L., Frey, O., Verpoorte, E., & Toh, Y. (2022). A guide to the organ-on-a-chip. *Nature Reviews Methods Primers*, 2(1), 1-29. <https://doi.org/10.1038/s43586-022-00118-6>
- [20]. Wang, Y., Gao, Y., Pan, Y., Zhou, D., Liu, Y., Yin, Y., Yang, J., Wang, Y., & Song, Y. (2023). Emerging trends in organ-on-a-chip systems for drug screening. *Acta Pharmaceutica Sinica B*, 13(6), 2483-2509. <https://doi.org/10.1016/j.apsb.2023.02.006>
- [21]. Owens, R.M. Advanced tissue engineering for in vitro drug safety testing. *MRS Communications* 13, 685–694 (2023). <https://doi.org/10.1557/s43579-023-00421-7>

[22]. doi: 10.1126/science.aal0907

[23]. Marei, I., Samaan, T. A., Al-Quradaghi, M. A., Farah, A. A., Mahmud, S. H., Ding, H., & Triggle, C. R. (2022). 3D Tissue-Engineered Vascular Drug Screening Platforms: Promise and Considerations. *Frontiers in Cardiovascular Medicine*, 9. <https://doi.org/10.3389/fcvm.2022.847554>