

# Review on Bioprinting of Tissues for Drug Testing a Promising Strategy to Reduce Animal Experimentation

Kadagoni Pravalika<sup>1</sup>, Nannapaneni Akshitha<sup>2</sup>, Sai Chandan Kanchari<sup>3</sup>, Vudumu Rama<sup>4</sup>,  
Yesupogu Bhargavi<sup>5</sup>, Talari Kavya<sup>6</sup>

<sup>1,2,3,4,5,6</sup>*Department of Pharmaceutical Analysis, Marri Laxman Reddy Institute of Pharmacy, Dundigal, Hyderabad, Telangana, India-500043*

**Abstract**—Animal experimentation has long played a central role in preclinical drug development. However, growing ethical concerns, high costs, and limited ability to accurately predict human responses have highlighted significant shortcomings of animal-based models. In recent years, three-dimensional (3D) bioprinting has emerged as a promising and transformative technology in pharmaceutical research. This approach enables the fabrication of human-relevant tissue models using living cells combined with biocompatible biomaterials. Bio-printed tissues closely replicate the structural and functional features of native human organs, providing more reliable platforms for drug screening, toxicity assessment, and disease modelling. The application of tissue bioprinting in drug testing offers a practical and ethical alternative to conventional animal models while improving the predictability of human drug responses. This article discusses the fundamentals of tissue bioprinting, its role in pharmaceutical drug testing, advantages over traditional animal experimentation, current limitations, and future perspectives. The increasing adoption of bio-printed tissue models in preclinical research has the potential to redefine ethical, efficient, and human-centered drug development practices.

**Index Terms**—Bioprinting, Drug testing, Alternatives to animal models, 3D tissue models, pharmaceutical research

## I. INTRODUCTION

Preclinical drug evaluation is a vital step in the pharmaceutical development process, traditionally relying heavily on animal models to assess drug safety, efficacy, and toxicity. While animal studies have contributed significantly to medical progress, they often fail to accurately predict human responses due to fundamental physiological and genetic differences

between species. As a result, many drug candidates that appear promising in animal studies ultimately fail during clinical trials, leading to substantial financial losses and delayed therapeutic advancements. Moreover, ethical concerns surrounding animal experimentation and increasingly stringent regulatory guidelines have intensified the search for reliable alternative testing approaches.

Recent progress in tissue engineering and additive manufacturing has led to the emergence of three-dimensional (3D) bioprinting as an advanced and innovative technology capable of fabricating functional biological tissues using living cells. Unlike traditional two-dimensional (2D) cell culture systems, bio-printed tissues provide a complex three-dimensional microenvironment that supports natural cell-cell and cell-matrix interactions, closely resembling native human tissue architecture. This enhanced biological relevance makes bio-printed tissue models particularly valuable for pharmaceutical research [1].

In the context of drug development, tissue bioprinting offers a human-specific platform for drug screening, toxicity evaluation, and disease modelling. By enabling the use of human-derived and patient-specific cells, bio-printed tissues support more accurate prediction of drug responses while aligning with the global commitment to the 3Rs principle—Replacement, Reduction, and Refinement of animal use in research. As this technology continues to evolve, bioprinting is poised to play a critical role in reshaping preclinical testing strategies within the pharmaceutical industry.

## II. PRINCIPLES OF 3D BIOPRINTING

3D bioprinting is a cutting-edge technique that builds tissues layer by layer using bio-inks, which are composed of living cells combined with biocompatible materials such as hydrogels. The entire process is digitally controlled, allowing precise construction of tissues with complex and well-defined architecture.

The key components of bioprinting include:

- **Bio-inks:** These are mixtures of living cells—such as stem cells or primary human cells—suspended in supportive biomaterials like alginate, gelatin, or collagen.
- **Bioprinting techniques:** Various methods exist to deposit bio-inks, including inkjet-based, extrusion-based, and laser-assisted printing, each offering different advantages depending on the tissue type and application.
- **Scaffolds:** These structures provide physical support for the cells, promoting attachment, growth, and proper differentiation to form functional tissue [2].

Together, these components work in harmony to create tissues that closely replicate the structure, function, and physiological behaviour of native human tissues, making them highly valuable for applications such as drug testing, disease modelling, and regenerative medicine.

## III. GENERAL WORKFLOW OF TISSUE BIOPRINTING FOR DRUG TESTING APPLICATIONS

The process of tissue bioprinting begins with cell sourcing, where suitable human cells such as primary cells, stem cells, or patient-derived cells are carefully selected based on the intended application. These cells are then expanded under controlled laboratory conditions to ensure that enough cells are available for printing.

Next, the cells are mixed with biocompatible biomaterials, which can include natural or synthetic hydrogels, to create bio-inks. These bio-inks not only support cell survival but also mimic the natural extracellular matrix, providing a favourable environment for tissue formation. Once prepared, the bio-inks are loaded into a 3D bioprinter, and tissues

are constructed layer by layer according to a precise digital design [3].

After printing, the tissue constructs undergo maturation and conditioning in bioreactors. This step encourages the cells to differentiate, organize, and integrate functionally, forming a tissue that closely resembles its natural counterpart. Once fully matured, the bio-printed tissues are exposed to pharmaceutical compounds to evaluate drug efficacy, toxicity, metabolism, and dose-dependent responses.

By providing human-relevant data, bio-printed tissues offer a highly effective platform for drug testing while significantly reducing the need for animal experiments. This makes them an ethical, reliable, and practical tool in modern pharmaceutical research [4].

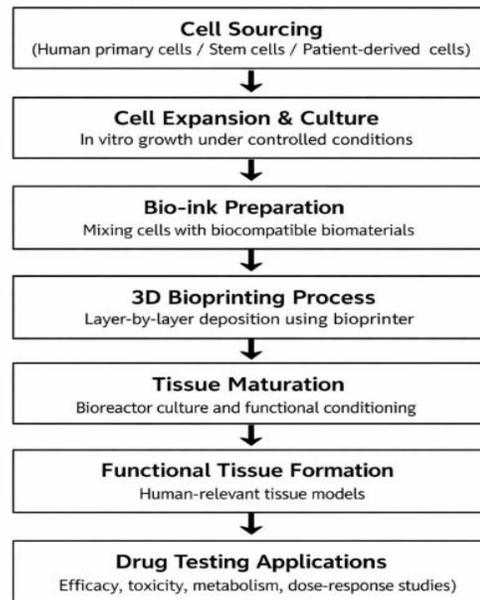


Figure 1: General workflow of tissue bio-printing for drug testing

### 1.1. APPLICATIONS OF BIO-PRINTED TISSUES IN DRUG TESTING

Bio-printed tissue models are being increasingly adopted across various stages of drug development due to their ability to closely mimic human biology.

Key applications include:

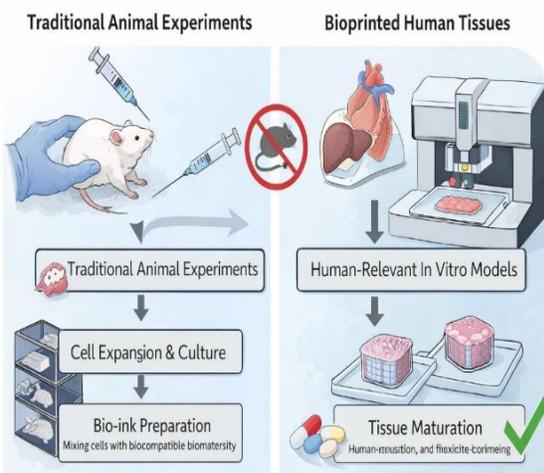
- **Drug efficacy screening:** Using human-specific tissues allows researchers to evaluate how a drug performs in a more clinically relevant environment.
- **Toxicity testing:** Bio-printed tissues, particularly liver and cardiac models, are highly valuable for assessing hepatotoxicity and cardiotoxicity.

- Disease modelling: Complex tissues can be engineered to study conditions such as cancer, fibrosis, or other organ-specific diseases.
- Dose optimization and metabolism studies: Bio-printed tissues provide insights into how drugs are processed and how effective doses can be determined.

Commonly used bio-printed tissue models for drug testing include liver, heart, skin, and tumour constructs, each offering detailed information on organ-specific responses to pharmaceutical compounds. These models help improve the accuracy of preclinical testing while reducing reliance on animal studies [5].

#### IV. ROLE OF BIOPRINTING IN REDUCING ANIMAL EXPERIMENTS

Bio-printed tissues provide a practical and reliable alternative to traditional animal models by offering human-relevant biological responses. Because these tissues are derived from human cells, they avoid the variability seen between species, resulting in more accurate and predictive drug testing outcomes. This technology also supports ethical research practices, aligning with regulatory efforts to reduce animal use in scientific experiments. Additionally, the ability to perform repeated tests on the same tissue construct helps minimize experimental redundancy, making the drug development process more efficient and sustainable [5].



Role of bioprinting in reducing animal experiments

Figure 2: Role of bio-printing in reducing animal experiments

#### V. RECENT ADVANCEMENTS IN 3D BIOPRINTING

##### a. More Human-Relevant Tissue Models

Researchers are now creating complex, multicellular bio-printed tissues that mimic human architecture far better than traditional 2D cultures and animal models. For example, advanced liver models with vascular features and high cell density improve the predictability of toxicity and metabolism studies, which is critical in early drug screening.

##### b. Improved Bioinks and Biomaterials

There has been significant progress in developing stimuli-responsive and composite bioinks that enhance cell survival, material stability, and functional performance of printed tissues. Innovations include modified hydrogels and decellularized extracellular matrices that better replicate native tissue environments, enabling more realistic drug responses.

##### c. Advanced Printing Technologies

Bioprinting systems are becoming faster, more precise, and more scalable. Novel approaches such as adaptive volumetric printing and AI-enabled print monitoring improve structural fidelity and viability of bio-printed constructs — allowing more complex tissue geometries essential for reliable drug testing.

##### d. Tissue-in-a-Well Screening Platforms

Institutions like NCATS are developing microplate bioprinting models that integrate directly with automated drug screening workflows. These “tissue-in-a-well” systems provide customizable human-like tissues for high-throughput pharmacological testing, addressing the limitations of standard 2D assays and animal models.

##### e. Moves Toward 4D Bioprinting

Next-generation technology 4D bioprinting incorporates time-responsive biomaterials that change shape or function after printing. This has exciting implications for controlled drug delivery, dynamic tissue responses, and adaptive in vitro systems that better model disease progression.

##### f. Market and Industry Growth Driving Innovation

The bioprinting industry is rapidly expanding, with increasing investment and commercial partnerships accelerating new technology development. Growth in demand from pharmaceutical research and regenerative medicine is driving improvements in printer hardware, bioinks, and tissue models [6].

VI. ADVANTAGES OF BIOPRINTED TISSUE MODELS

- 3D Microenvironment Simulation
- Unlike 2D cultures, bio-printed tissues provide a realistic three-dimensional cellular microenvironment that supports cell-cell and cell-matrix interactions.
- Long-Term Functional Stability  
Advanced bio-printed constructs maintain tissue viability and function for extended periods, enabling chronic drug exposure and toxicity studies.
- High Human Relevance  
Bio-printed tissues closely mimic the structural and functional characteristics of native human tissues, providing more accurate prediction of human drug responses compared to animal models.
- Reduction in Animal Experimentation  
These models support ethical research by significantly reducing or replacing the use of animals in preclinical drug testing, aligning with the 3Rs principle (Replacement, Reduction, Refinement).
- Improved Predictive Accuracy  
Human-derived cells eliminate species-specific variations, leading to better assessment of drug efficacy, toxicity, and metabolism.

- Cost- and Time-Effective Drug Screening  
Bio-printed tissues enable faster screening of drug candidates and reduce the overall cost of preclinical testing and late-stage drug failures.
- Reproducibility and Standardization  
Controlled printing parameters ensure consistent tissue architecture and experimental reproducibility across multiple batches.
- Organ-Specific Toxicity Assessment  
Bio-printed liver, cardiac, skin, and kidney tissues allow targeted evaluation of organ-specific toxicity, improving drug safety assessment.
- Compatibility with High-Throughput Screening  
Bio-printed tissues can be integrated into microplate-based assays and automated systems, supporting large-scale drug screening.
- Personalized Medicine Applications  
Use of patient-derived cells allows personalized drug testing and selection of optimal therapies based on individual responses [7].  
Comparative evaluation of animal models and bio-printed tissue models in drug testing and pharmaceutical research is illustrated in table 1 [3].

Table 1: Comparative evaluation between animal models and bio-printed tissue models

PARAMETER	ANIMAL MODELS	BIO-PRINTED TISSUE MODELS
Biological Relevance	Limited human relevance due to species-specific differences	High human relevance using human-derived cells
Predictive Accuracy	Often poor correlation with human drug responses	Improved prediction of efficacy, toxicity, and metabolism
Ethical Concerns	Significant ethical issues related to animal use	Ethically favorable; supports reduction of animal testing
Cost	High costs for animal maintenance and experimentation	Lower long-term costs after initial setup
Time Efficiency	Time-consuming due to breeding and handling	Faster drug screening and testing
Reproducibility	Biological variability among animals	High reproducibility with controlled printing parameters
Throughput	Low to moderate throughput	Compatible with high-throughput screening platforms
Organ-Specific Testing	Limited precision in organ-specific toxicity assessment	Enables targeted testing using organ-specific tissues
Personalized Medicine	Not suitable for personalized drug testing	Supports patient-specific drug response studies

Regulatory Trend	Increasing regulatory restrictions	Growing regulatory acceptance as alternative models
3D Microenvironment	Native but non-human tissue environment	Human-relevant 3D cellular microenvironment
Long-Term Studies	Suitable but ethically challenging	Suitable for chronic exposure studies with stable constructs

## VII. FUTURE PROSPECTS

The future of bio-printed tissue models is extremely promising, with the potential to revolutionize preclinical drug development and significantly reduce dependence on animal testing. Ongoing improvements in bio-ink formulations, including stimuli-responsive and tissue-specific materials, are expected to enhance cell survival, mechanical stability, and long-term tissue functionality. Incorporating strategies for vascularization and innervation will further improve nutrient delivery and the physiological realism of complex tissue constructs. Cutting-edge technologies such as 4D bioprinting, where tissues can dynamically respond to environmental cues over time, may provide more accurate models for studying disease progression and drug responses. Additionally, combining artificial intelligence and machine learning with bioprinting is anticipated to optimize printing precision, tissue maturation, and the analysis of drug screening results [8].

From a pharmaceutical standpoint, bio-printed tissues are likely to become key tools in high-throughput screening systems, organ-on-chip platforms, and personalized medicine applications using patient-derived cells. With growing regulatory support and validation, these tissue models may soon be recognized as standard alternatives in safety pharmacology and toxicology testing, accelerating drug discovery while addressing ethical concerns.

## VIII. CONCLUSION

Bioprinting of tissues marks a revolutionary step forward in pharmaceutical research, providing a human-relevant, ethical, and efficient alternative to traditional animal models. By closely replicating the structure and function of native human tissues, bio-printed models offer more accurate assessments of drug efficacy, toxicity, and metabolism. Their ability to support reproducible experiments, high-throughput

screening, and personalized drug testing makes them invaluable tools in modern drug development.

While challenges such as standardization, scalability, and regulatory approval still exist, ongoing technological advances are steadily addressing these hurdles. Overall, tissue bioprinting represents a transformative approach with the potential to greatly reduce reliance on animal experimentation and reshape the landscape of preclinical drug testing and translational medicine.

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