ISSN: 2767-8245

Available online on http://www.ijdcs.com/

International Journal of Dental and Clinical Studies 2026; 7(2) 1-7

Organ-On-A-Chip Technology in Drug Development

Neha Kumari[1], Bhupendra Singh Rathor[2], Indu[3], Pawan Kumar Basniwal[4]

[1]Scholar, Sri Balaji College of Pharmacy, Jaipur, Rajasthan, India
[2]Scholar, Sri Balaji College of Pharmacy, Jaipur, Rajasthan, India
[3]Assistant Professor, Sri Balaji College of Pharmacy, Jaipur, Rajasthan, India
[4]Professor & Principal, Sri Balaji College of Pharmacy, Jaipur, Rajasthan, India

Corresponding author: Neha Kumari
Conflict of interest: No conflict of interest

Abstract:
Organ-on-a-Chip (OoC) technology is an emerging microengineering approach that combines microfluidics, living human cells, tissue engineering and biomaterials to reproduce selected structural and functional characteristics of human organs in vitro. The technology has gained attention as a human-relevant complement to conventional two-dimensional cell culture and animal models in pharmaceutical research. OoC systems can support drug discovery, disease modelling, drug screening, pharmacokinetic and pharmacodynamic studies, ADME evaluation, toxicity assessment and personalized medicine. By providing controlled fluid flow, tissue interfaces, mechanical cues and real-time monitoring, these systems can generate information that is difficult to obtain from simplified models. Patient-derived cells and induced pluripotent stem-cell-based models further create opportunities for investigating inter-individual differences in drug response. However, variability in cell sources, device design, standardization, reproducibility, scalability, cost, validation and regulatory acceptance remain important limitations. Overall, OoC technology represents a promising evidence-generating platform that may improve the human relevance, predictability and efficiency of drug development when appropriately integrated with existing pharmaceutical approaches.
Keywords: organ-on-a-chip; microfluidics; human-relevant models; drug development; ADME; toxicity; personalized medicine; pharmacology.

Introduction

Changing Landscape of Drug Development

Drug development increasingly requires evidence that can explain how a candidate behaves within complex human biological environments. A promising compound must demonstrate an appropriate relationship between exposure, biological activity, therapeutic effect and potential adverse response before it can progress through development. Traditional experimental systems remain valuable, but simplified cell cultures may not reproduce tissue organization, dynamic exposure, cell–cell communication or organ-level function.

Organ-on-a-Chip technology has emerged from the convergence of cell biology, tissue engineering, microfluidics and bioengineering. Rather than simply making a miniature organ, an OoC platform provides a controlled microenvironment in which selected aspects of human biology can be investigated under measurable conditions. Its value therefore depends on the biological question being asked and the quality of the evidence generated.

Human-Relevant Evidence

The objective of preclinical research is not only to produce a measurable response but to obtain information that can help anticipate human outcomes.

Human biology involves interconnected cell populations, tissue architecture, biochemical communication, physical forces and time-dependent changes. OoC systems can incorporate some of these features and therefore provide a bridge between simplified cellular experiments and more complex physiological responses.

Rationale and Significance of OoC in Drug Development

The rationale for incorporating OoC into drug development arises from the need to connect experimental observations more closely with human biological behaviour. A drug does not act only on an isolated molecular target; its effects can depend on exposure conditions, tissue environment, cellular

interactions, metabolism and the timing of biological responses.

OoC technology allows these relationships to be investigated within controlled human-relevant experimental environments. It can provide information at cellular, tissue and functional levels.

The technology is particularly useful when the biological question requires dynamic conditions, tissue interfaces or interactions that are difficult to reproduce in conventional static culture.

Aim and Scope of the Review

This review examines Organ-on-a-Chip technology from a drug-development and evidence-generation perspective. It focuses on how OoC systems can contribute human-relevant information during candidate evaluation, efficacy and safety assessment, exposure-related studies, pharmacological investigation, personalization and preclinical progression. The review also considers reliability, integration with existing pharmaceutical workflows and emerging opportunities.

Evolution of Experimental Strategies

From Molecular Targets to Functional Drug TestingEarly pharmaceutical research often concentrated on molecular interactions such as receptor binding, enzyme inhibition and pathway activation. These approaches are useful for screening large numbers of compounds, but molecular activity does not always predict the response of living tissue. Cellular context, transport, compensatory pathways and interactions between cell populations may alter the final outcome.

Increasing Biological Complexity

Experimental models have therefore progressed toward cellular, tissue-level and integrated human systems. Increasing complexity should not be viewed as an objective by itself.

The important principle is relevant complexity: each component should be included because it contributes information needed to answer the study question. OoC technology fits this progression because its microenvironment can be designed around a defined biological purpose.

Importance of Tissue-Level Response

Drug effects may emerge from interactions within organized tissues rather than from isolated molecular events. Tissue architecture influences communication, transport, differentiation and drug access. OoC models can maintain cells in organized microenvironments and measure endpoints such as permeability, barrier integrity, secretion, metabolic activity and tissue-specific biomarkers.

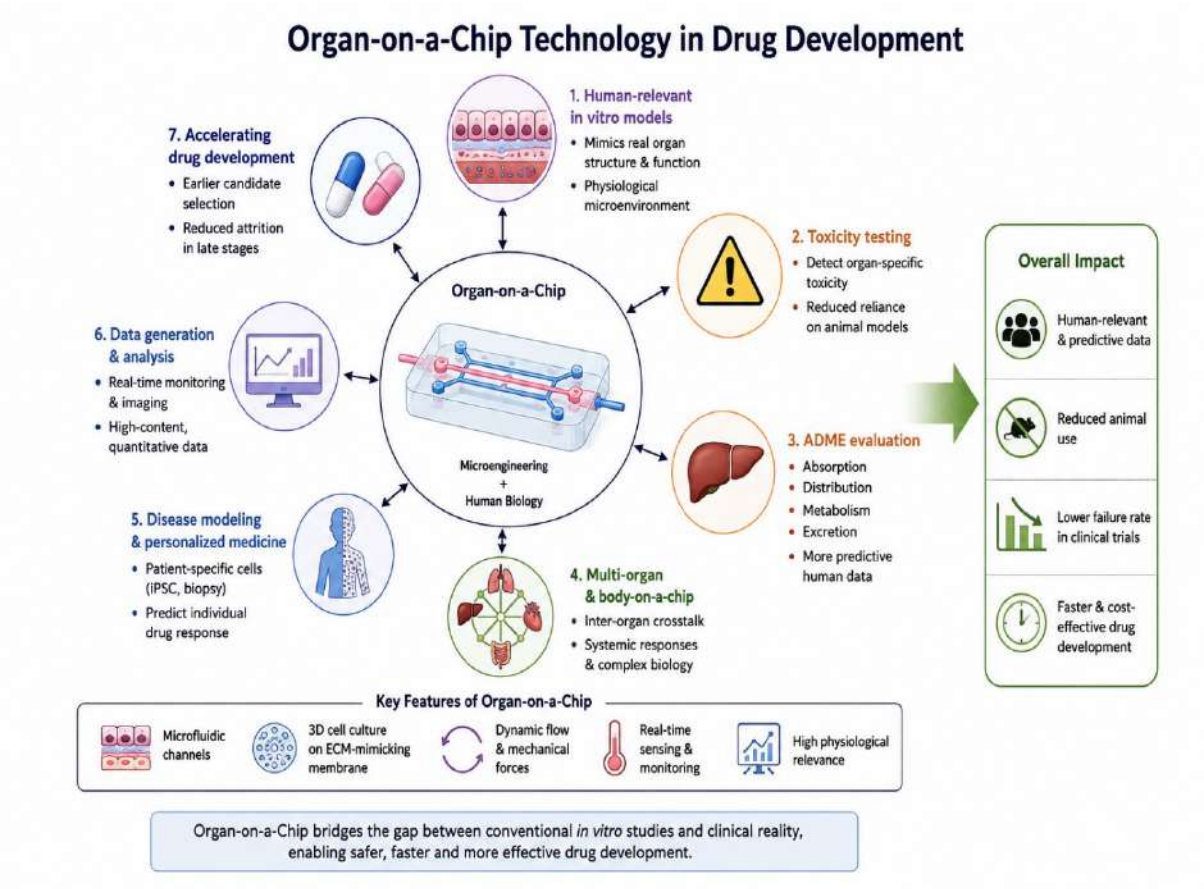

Figure 1. Organ-on-a-Chip technology and its applications across drug development.

Constructing a Drug-Responsive Human Micro-environment

The response of human tissue to a drug depends not only on the compound but also on the biological environment in which exposure occurs. Cells receive signals from neighbouring cells, extracellular materials, surrounding fluids and physical forces. Therefore, an OoC model should contain the essential biological elements required for a meaningful drug-response study rather than attempting to reproduce every feature of a complete organ.

Selection of Relevant Human Cells The cellular composition of an OoC model is a major determinant of the information it can generate. Depending on the application, models may use primary human cells, established cell lines, stem-cell-derived cells or combinations of cell populations. Cell maturity, stability and functional responsiveness are important because cell survival alone does not guarantee physiological relevance.

Tissue Organization and Cellular Communication: Human cells normally function within organized tissues. Cell position, orientation and communication with neighbouring cells can influence differentiation, inflammatory responses, metabolism and tissue function. Co-culture or spatial organization may therefore be useful when the response of one cell population depends on signals generated by another.

Extracellular Environment and Matrix

The extracellular environment provides structural and biochemical signals that influence cell attachment, morphology, differentiation and function. Matrix selection should therefore be treated as part of biological model design rather than simply as a material used to hold cells in place.

Vascular and Barrier Components

Blood vessels, epithelial layers and other barriers regulate movement of nutrients, drugs, metabolites and signalling molecules. Reproducing a relevant interface can be important for studies involving permeability, transport and tissue exposure.

These components should be incorporated when they contribute directly to the biological question.

Biochemical and Mechanical Conditions

Nutrients, oxygen, pH, biochemical signals, fluid movement and mechanical forces can influence cellular function.

OoC platforms provide opportunities to control these conditions more precisely than static systems. The final design should follow the principle of physiological relevance with experimental control.

Dynamic Exposure and Functional Maintenance

Drug exposure in the body changes with time. OoC systems can control the movement of culture medium and compounds, allowing investigation of concentration, duration and exposure patterns.

The quality of a model should ultimately be judged by whether it maintains the functional tissue behaviour required for the intended study.

The Journey of a Drug through an OoC Platform

A drug can be followed through a sequence of exposure, transport, cellular uptake, distribution, biotransformation and pharmacological response.

The concentration initially introduced into a chip may differ from the concentration that reaches relevant cells because of flow, dilution, adsorption, binding, transport and metabolism. Understanding this journey improves interpretation of OoC data.

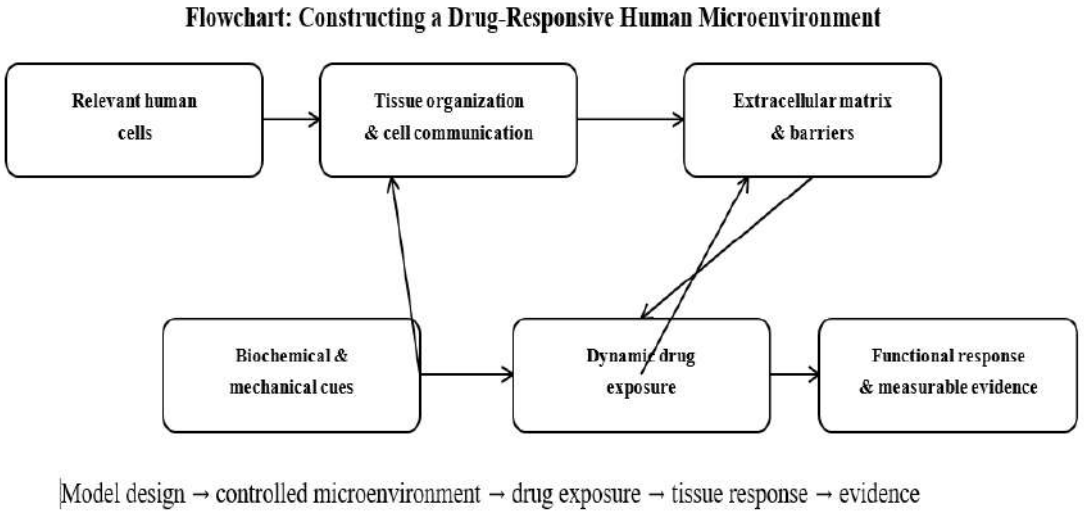

Figure 3. Key steps in constructing a drug-responsive human microenvironment for OoC studies.

Drug Entry, Transport and Cellular Uptake

Drug Entry and Exposure

The first stage is introduction of the drug into the experimental system.

The route and manner of exposure should reflect the purpose of the study. Exposure conditions should clearly define dose or concentration, duration and sampling conditions.

Transport through Biological Interfaces

A drug may need to cross biological barriers before reaching its site of action. Permeability, transporter activity and barrier integrity can influence the amount of drug that becomes available to target cells. OoC systems can investigate transport as an important determinant of pharmacological response.

Cellular Uptake and Tissue Distribution

Intracellular drug availability may differ from concentration in the surrounding medium. Within a tissue model, distribution can also be influenced by tissue architecture, cell density and extracellular materials. These factors can help explain differences in local pharmacological or toxicological responses.

Biotransformation and Metabolite Generation

Metabolically competent cells can transform parent compounds and generate metabolites with different biological properties. This is important because efficacy or toxicity may result from the parent drug, its metabolites or both.

Pharmacological Response and Clearance

The final objective is to relate actual exposure to changes in cellular activity, tissue function, biomarkers, barrier properties or other measurable endpoints. Drug removal may occur through metabolism, uptake, movement between compartments or removal with circulating medium. In-chip clearance should be interpreted as a model-specific process rather than as direct whole-body human clearance.

Evidence Generated by OoC for Pharmaceutical Research

OoC systems can generate structural, functional, pharmacological, molecular, biomarker and time-dependent evidence. Their value depends not on the number of measurements but on whether the measurements provide meaningful information about tissue structure, function and drug behaviour.

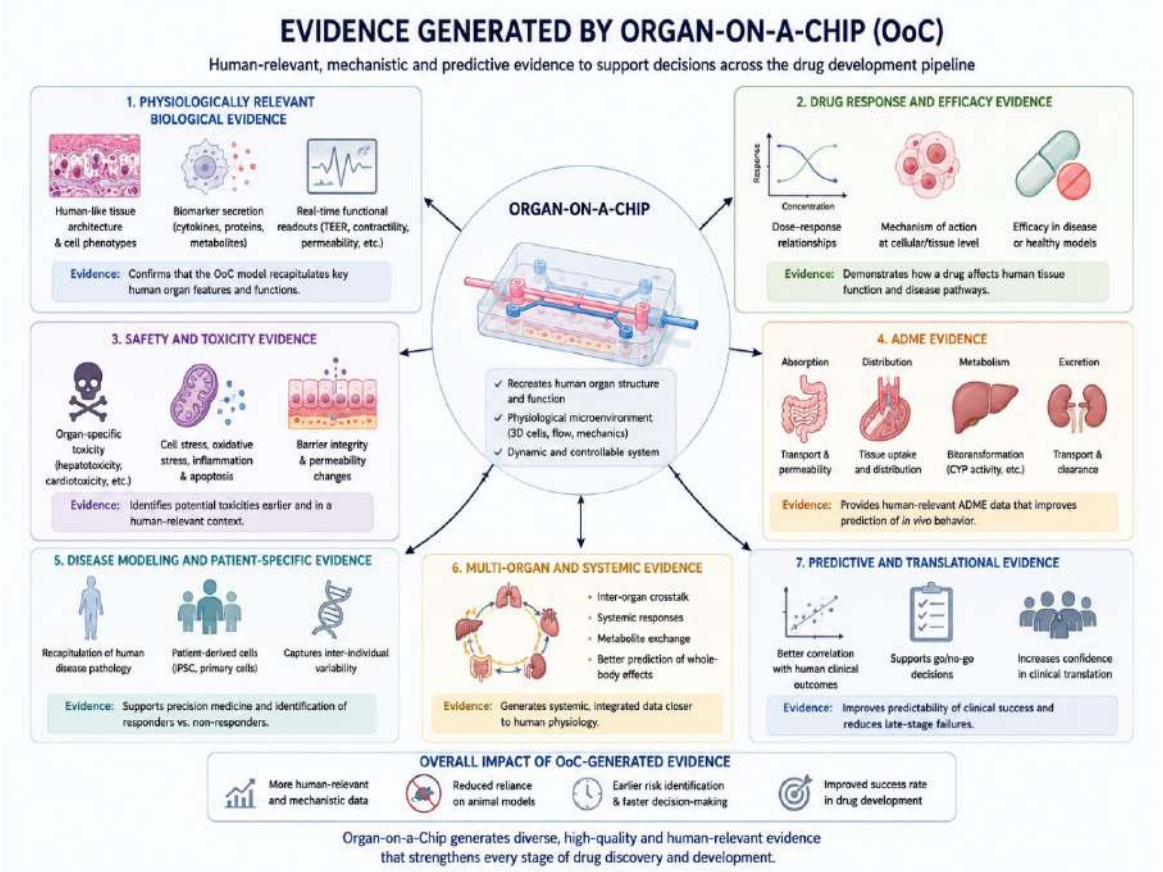

Figure 2. Evidence generated by Organ-on-a-Chip systems for pharmaceutical research and drug development.

Types of Evidence Generated by OoC

Structural and Functional Evidence

Structural evidence may include changes in cellular arrangement, tissue morphology and barrier organization. Functional evidence can include transport, secretion, barrier performance, metabolic activity and tissue-specific functions. Combining structural and functional information provides a stronger description of biological state than either alone.

Pharmacological and Molecular Evidence

Pharmacological evidence describes the biological response produced under defined exposure conditions. Molecular measurements such as changes in gene expression, proteins or signalling molecules can help explain mechanisms, especially when they are connected with measurable functional outcomes.

Biomarker-Based and Time-Dependent Evidence

Biomarkers can indicate pharmacological activity, tissue injury, inflammation and metabolic changes. Measuring responses at multiple time points can reveal onset, progression and persistence of effects, including early changes that may occur before major structural alterations become visible.

Quantitative Interpretation: Quantitative analysis can relate response magnitude to drug concentration, exposure duration and other experimental variables. Exposure–response and time–response relationships can strengthen comparison between compounds and support later pharmacological or computational analyses.

OoC Across the Pharmaceutical Development Journey

Early Drug Discovery and Target Evaluation

OoC systems can investigate whether a candidate produces a relevant biological effect in a human-derived tissue environment and whether target modulation produces an expected tissue-level response.

Lead Selection and Candidate Prioritization

OoC-based testing can compare candidates under similar conditions using functional response, tissue-specific activity and early adverse effects. This can add human-relevant evidence to candidate prioritization.

Efficacy Assessment: Disease-relevant OoC models can examine whether expected therapeutic effects occur in an appropriate biological environment and can provide information about response magnitude and duration.

Safety and Early Toxicity Assessment

OoC models can monitor tissue function after exposure and identify early undesirable biological effects. However, OoC findings should remain part of an overall safety evidence package rather than being treated as a standalone replacement for complete preclinical assessment.

Dose and Exposure Evaluation

Concentration–response and time–response relationships can help identify exposure ranges associated with desirable or undesirable effects and support pharmacological interpretation.

Combination Therapy and Drug Repurposing

OoC platforms may be used to investigate interactions between therapeutic compounds and to examine known drugs against new disease-related biological processes in a human-relevant tissue setting.

Personalization of Drug Development

Personalized drug development focuses on differences between individuals.

Patient-derived cells and induced pluripotent stem-cell-based models can be used to create disease-relevant OoC systems and investigate variability in efficacy, toxicity and biological response. Data from different patient models may support patient stratification and precision-oriented treatment strategies.

Patient-Specific OoC Strategy

A patient-specific approach can be represented as: patient sample → patient-derived cells or iPSCs → personalized OoC model → disease-specific drug testing → response analysis → patient stratification → precision treatment. The purpose is not to predict every clinical outcome from a chip, but to investigate biological differences that may be relevant to treatment response.

Reliability and Confidence in OoC-Derived Evidence

Biological Relevance

A reliable model should represent the important structure and function of the intended human tissue. Appropriate cell types, tissue interactions, dynamic conditions and organ-specific responses contribute to biological relevance.

Experimental Reproducibility

Reproducibility means obtaining similar results when an experiment is repeated under comparable conditions.

Cell source, culture conditions, chip design, concentration and exposure time should be controlled and documented.

Inter-Laboratory Comparability

Results should be comparable across laboratories. Differences in devices, materials, cells and protocols can create variation, making harmonized procedures and common reporting standards important.

Controls and Reference Compounds

Positive and negative controls help distinguish drug-related effects from changes caused by the experimental system. Reference compounds with known biological effects can also be used to evaluate model performance.

Benchmarking and Human Evidence

OoC findings can be strengthened by comparison with established laboratory models and, where suitable, human clinical evidence.

Agreement with independent evidence can increase confidence in model performance and translational relevance.

Fit-for-Purpose Evidence

Not every OoC model needs to reproduce the complete human body. Validation should depend on the intended application. A toxicity model may require different performance criteria from a disease model or an efficacy platform.

Integrating OoC with the Drug-Development Ecosystem

OoC and Conventional In-vitro Studies

OoC models can complement conventional cell culture by providing controlled human-cell-based environments for efficacy, toxicity and tissue-specific studies.

OoC and Animal-Based Evidence

OoC systems can provide human tissue-level information alongside animal studies. Combining different evidence sources may provide a broader basis for preclinical decisions.

OoC and Clinical Pharmacology

Human-specific OoC models can contribute information about efficacy, toxicity and individual variability and may support interpretation of pharmacological behaviour.

Computational and Quantitative Integration

OoC data can be integrated with pharmacokinetic/pharmacodynamic modelling, computational analysis and other evidence streams. This can help transform experimental measurements into interpretable information for development decisions.

Emerging Opportunities for Next-Generation Drug Development

Future OoC systems are expected to become more physiologically relevant through improved cell models, tissue interactions and dynamic conditions. Patient-specific models may support investigation of inter-individual response. Integrated sensors can provide real-time information, while artificial intelligence may assist in analysing complex datasets. Combining OoC with quantitative pharmacology may improve understanding of concentration, exposure and biological effects. Multi-organ systems may also provide broader information about systemic drug behaviour.

Challenges and Limitations

Important challenges include variation in cell sources, lack of standardized protocols, reproducibility issues, sensor limitations, manufacturing complexity, cost, scaling and high-throughput screening, long-term stability, incomplete validation and limited regulatory acceptance. Increased complexity does not automatically guarantee increased predictive value. Each platform therefore requires validation according to its intended context of use.

Conclusion

Organ-on-a-Chip technology has emerged as a promising human-relevant platform for modern drug development. By combining living human cells with microengineered environments, OoC systems can reproduce selected structural and functional features of human tissues and provide controlled conditions for investigating drug-induced responses. Their applications in disease modelling, efficacy, pharmacokinetics, toxicity and patient-specific studies can complement conventional preclinical approaches.

The future impact of OoC will depend on reproducibility, standardization, scalability, quantitative validation and responsible integration with existing pharmaceutical and regulatory workflows. OoC should therefore be viewed not simply as a replacement for established methods, but as an additional source of human-relevant evidence that can help reduce uncertainty and improve decision-making.

References

1. Moon HR, Surianarayanan N, Singh T, Han B. Microphysiological systems as reliable drug discovery and evaluation tools: Evolution from innovation to maturity. Biomicrofluidics. 2023;17(6):061504. doi:10.1063/5.0179444.
2. Baker TK, Van Vleet TR, Mahalingaiah PK, Grandhi TSP, Evers R, Ekert J, et al. The current status and use of microphysiological systems by the pharmaceutical industry. Drug

Metab Dispos. 2024;52(3):198-209. doi:10.1124/dmd.123.001510.
3. Mansouri M, Lam J, Sung KE. Progress in developing microphysiological systems for biological product assessment. Lab Chip. 2024;24:1293-1306. doi:10.1039/D3LC00876B.
4. Kimura H, Nishikawa M, Kutsuzawa N, et al. Advancements in microphysiological systems: Exploring organoids and organ-on-a-chip technologies in drug development. Drug Metab Pharmacokinet. 2025;60:101046. doi:10.1016/j.dmpk.2024.101046.
5. Ko J, Song J, Choi N, Kim HN. Patient-derived microphysiological systems for precision medicine. Adv Healthc Mater. 2024;13. doi:10.1002/adhm.202303161.
6. Zhou C, Li Z, Lu K, et al. Advances in human organs-on-chips and applications for drug screening and personalized medicine. Fundam Res. 2025;5:1258. doi:10.1016/j.fmre.2023.12.019.
7. Levner D, Ewart L. Integrating liver-chip data into pharmaceutical decision-making processes. Expert Opin Drug Discov. 2023;18:1313-1320. doi:10.1080/17460441.2023.2255127.
8. Yamazaki D, Ishida S. Global expansion of microphysiological systems and path to regulatory acceptance. Drug Metab Pharmacokinet. 2025;60:101047.
9. Araújo-Gomes N, Middelkamp HHT, Loessberg-Zahl J, et al. From concept to context-of-use: A framework for organ-on-chip development. NAM J. 2026;2:100097. doi:10.1016/j.namjnl.2026.100097.
10. Low LA, Mummery C, Berridge BR, Austin CP, Tagle DA. Organs-on-chips: into the next decade. NatRevDrug Discov. 2021;20:345-361.
11. Ingber DE. Human organs-on-chips for disease modelling, drug development and personalized medicine. Nat Rev Genet. 2022;23:467-491. doi:10.1038/s41576-022-00466-9.
12. Corral-Nájera K, Chauhan G, Serna-Saldívar SO, Martínez-Chapa SO. [Reference details as present in the document.]
13. Shin YC, Than N, Min S, Shin W, Kim HJ. Modelling host–microbiome interactions in organ-on-a-chip platforms. Nat Rev Bioeng. 2024;2:175-191. doi:10.1038/s44222-023-00130-9.
14. Zhou L, Huang J, Li C, et al. Organoids and organs-on-chips: Recent advances, applications in drug development, and regulatory challenges. Med J. 2025;6(4):100667. doi:10.1016/j.medj.2025.100667.
15. Rahman SM, Krishna A, Sullenberger C, et al. Opportunities and challenges for human microphysiological systems in drug development. ALTEX. 2025;42(2):224-256. doi:10.14573/altex.2409221.
16. Mendes M, Morais AS, Carlos A, Sousa JJ, Pais AC, Mihil SM, Vitorino C. Organ-on-a-chip: Quo vademus? Applications and regulatory status. Colloids Surf B Biointerfaces. 2025;249:114507. doi:10.1016/j.colsurfb.2025.114507.
17. Ning B, et al. Microphysiological systems as an emerging in vitro approach for the evaluation of drug absorption, distribution, metabolism, and excretion and toxicity. Drug Metab Dispos. 2025;100187. doi:10.1016/j.dmd.2025.100187.
18. Sone N, Gotoh S. Micro-physiological system of human lung: The current status and application to drug discovery. Drug Metab Pharmacokinet. 2025;60:101050. doi:10.1016/j.dmpk.2024.101050.
19. Vulto P, Joore J. Adoption of organ-on-chip platforms by the pharmaceutical industry. Nat Rev Drug Discov. 2021;20:961-962.
20. 20. Loewa A, Feng JJ, Hedtrich S. Human disease models in drug development. Nat Rev Bioeng. 2023;1:545-559. doi:10.1038/s44222-023-00063-3.