



MICROPHYSIOLOGICAL SYSTEM (ORGAN-ON-CHIP) IN DRUG DISCOVERY

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ABSTRACT

Microphysiology Systems (MPS), or Organ-on-a-Chip (OoC), are advanced in vitro models that mimic key functions of human organs using microfluidics, biomaterials, tissue engineering, and human cells. They are increasingly used in drug development to evaluate drug absorption, metabolism, efficacy, toxicity, and the performance of delivery systems such as nanoparticles and liposomes. Patient-derived cells can support personalized medicine by enabling assessment of individual drug responses, while multi-organ systems help study interactions between organs and complex drug effects. MPS can provide real-time insights into cellular and tissue responses under controlled physiological conditions. They may also help reduce the time and cost associated with conventional drug screening and animal experimentation. With continued technological development and standardization, MPS are expected to become increasingly valuable in pharmaceutical and biomedical research. Despite challenges including cost, technical complexity, and standardization, MPS offer a promising human-relevant approach for safer drug development, toxicity testing, precision medicine, and innovative drug delivery research.

Keyword: Microphysiology Systems (MPS); Organ-on-a-Chip (OoC); Drug Development; Toxicity Testing; Personalized Medicine; Drug Delivery Systems.

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INTRODUCTION

Microphysiology Systems (MPS), also known as Organ-on-a-Chip (OoC) technology, are advanced in vitro models that replicate the structural and functional characteristics of human organs using microfluidics, biomaterials, tissue engineering, and human cells. By simulating physiological conditions such as fluid flow, nutrient transport, and mechanical stimulation, MPS provides a realistic environment for studying human biology and evaluating drugs [1]. Conventional cell cultures and animal studies often fail to accurately predict human drug responses due to differences in tissue complexity and species-specific physiology. MPS offers a promising alternative by improving the relevance of preclinical drug testing and supporting safer, more effective drug development [2-3].

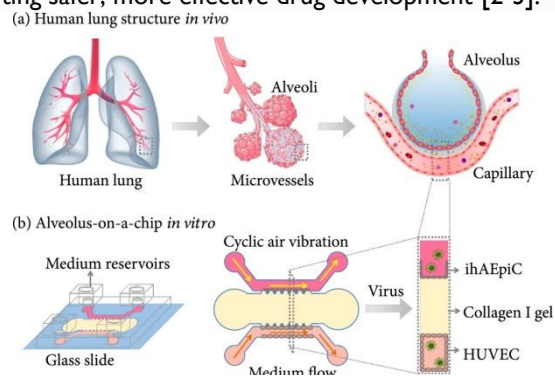


Figure 01: The 3D alveolus-on-chip representation. (a) schematics of the alveolar-capillary barrier in vivo. (b) Design and structure of the microfluidic chip containing ihAEpiC and HUVEC channels.

For a clear and impactful article on drug delivery and preclinical research, the three best subjects to compare are Conventional 2D Cell Culture, Animal Models, and Microphysiology Systems (Organ-on-a-Chip). Comparing these three highlights the technological evolution, biological relevance, and practical trade-offs in drug testing [4].

Table 01: Comparison of Conventional 2D Cell Culture, Animal Models, and Microphysiology Systems (Organ-on-a-Chip) [5-7].

Feature / Parameter	Conventional 2D Cell Culture	Animal Models	Microphysiology Systems (Organ-on-a-Chip)
Microenvironment & Dynamics	Static culture conditions without fluid flow or mechanical stimulation.	Dynamic whole-body physiological environment, but non-human.	Recreates dynamic physiological flow, nutrient transport, and mechanical stress.
Human Clinical Relevance	Low; often fails to reflect human organ function and tissue complexity.	Moderate to low; species-specific physiological differences lead to trial failures.	High; closely mimics human organ architecture, cellular responses, and toxicity.
Ethical Impact	No animal welfare issues.	High ethical concerns due to animal experimentation.	Reduces or replaces the dependence on animal testing.
Personalized Medicine Potential	Low; limited capability to model individual patient profiles.	Poor; cannot replicate patient-specific human genetics.	High; uses patient-derived cells to predict individual drug responses.
Cost & Technical Complexity	Low cost and simple, widely standardized operating procedures.	High maintenance, animal housing costs, and variable protocols.	High development cost, complex fabrication, and specialized expertise required.

An Organ-on-a-Chip is fabricated using biocompatible materials containing tiny interconnected channels through which culture medium flows continuously, mimicking the circulation of blood. Human cells are cultured within these channels in a three-dimensional arrangement that resembles natural tissue architecture. The controlled microenvironment allows researchers to maintain cell viability and function while exposing the tissues to drugs under conditions similar to those found in the human body. This approach enables real-time observation of cellular responses and physiological changes [8].

Present Scenario of Organ-on-a-Chip in Drug discovery

The present scenario of microphysiological systems (MPS), commonly known as organ-on-a-chip technology, shows rapid development in pharmaceutical and biomedical research. These systems are designed to reproduce important structural and functional characteristics of human [9].

organs using human cells, microfluidic channels, biomaterials and controlled physiological conditions.

1. Increasing use in drug development

MPS platforms are currently being investigated for drug screening, absorption, distribution, metabolism, toxicity and efficacy studies. They provide a more human-relevant environment than conventional two-dimensional cell cultures.

2. Application in drug-delivery research

Organ-on-chip models are increasingly used to evaluate advanced drug-delivery systems such as:

- Nanoparticles
- Liposomes
- Polymeric drug carriers
- Micelles
- Targeted delivery systems
- Controlled-release formulations

They help study drug transport, cellular uptake, permeability and tissue interactions.

3. Development of organ-specific chips

Several organ models are currently being developed, including:

- Gut-on-chip – oral drug absorption and intestinal permeability
- Liver-on-chip – drug metabolism and hepatotoxicity
- Kidney-on-chip – renal transport and nephrotoxicity
- Lung-on-chip – inhalation drug delivery and pulmonary toxicity
- Brain-on-chip – blood–brain barrier and neurological drug delivery

- Heart-on-chip – cardiovascular drug responses

4. Multi-organ systems

Current research is moving beyond individual organ models toward interconnected multi-organ systems. These systems allow researchers to examine how a drug or its metabolites affect different organs sequentially [10].

5. Use of human-derived cells

The use of primary human cells, stem-cell-derived cells and patient-derived cells is increasing. This improves the biological relevance of MPS and provides opportunities for studying differences in individual drug responses.

6. Integration with modern technologies

MPS is increasingly combined with:

- Artificial intelligence and machine learning
- 3D bioprinting
- Organoid technology
- Real-time biosensors

These combinations improve monitoring, data analysis and prediction of drug responses.

7. Personalized medicine

Patient-specific organ chips are being explored to predict how a particular individual may respond to a drug. This could eventually support personalized drug selection and dose optimization.

8. Reduction of animal experiments

MPS is being investigated as a complementary approach to traditional animal studies. Because the systems can use human cells and reproduce specific human tissue functions, they may improve the prediction of human drug responses.

9. Current limitations

Despite significant progress, widespread pharmaceutical and clinical use is still limited by:

- Lack of standardized protocols
- Variability between laboratories
- Difficulty reproducing complete human physiology
- Complex manufacturing requirements
- Limited long-term stability
- Need for stronger validation with clinical data

10. Current direction [11-12].

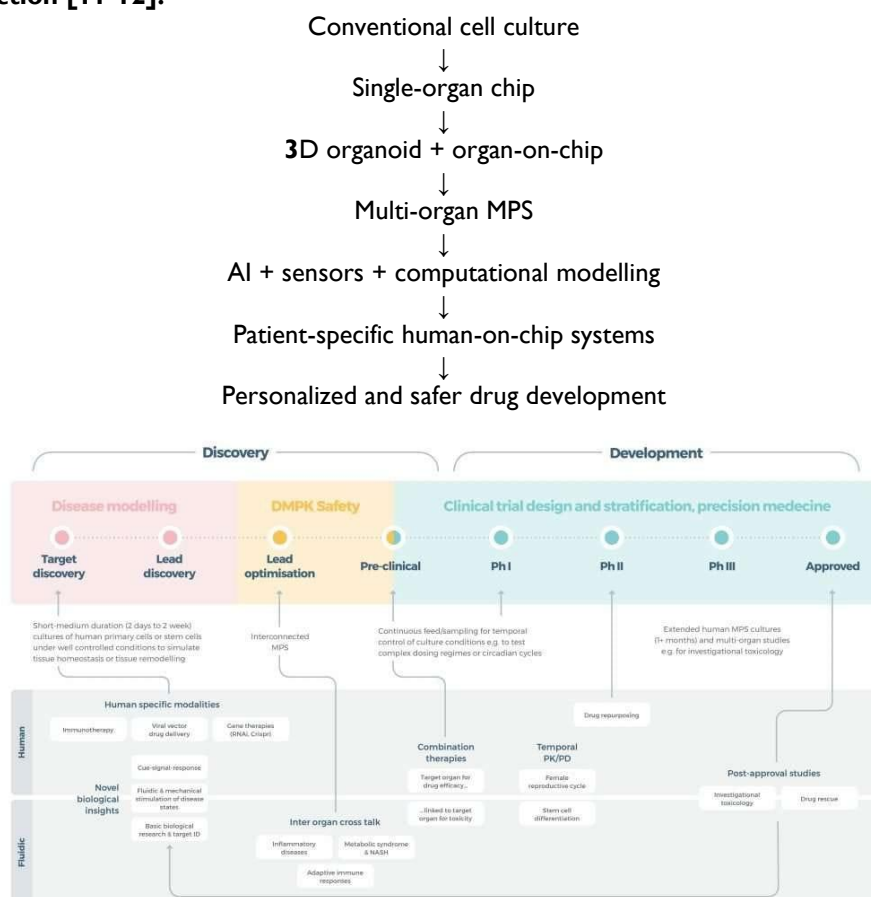


Figure 02: Schematic representation of Microphysiological systems discovery and development

RECENT TRENDS IN MICROPHYSIOLOGICAL SYSTEMS (MPS) IN DRUG DISCOVERY [4,6,9,13-16].

1. Development of multi-organ platforms

Modern MPS technology is progressing from individual organ models toward interconnected systems such as gut–liver, liver–kidney and lung–liver chips. These platforms help researchers study the movement, metabolism and elimination of drugs in a more integrated physiological environment.

2. Patient-specific organ-on-chip models

Human cells obtained from individual patients and stem-cell-derived cells are increasingly incorporated into organ chips. Such models can help predict differences in drug responses among individuals and support personalized therapeutic approaches.

3. Combination of organoids with microfluidic chips

Three-dimensional organoids are being incorporated into microfluidic devices to produce more physiologically representative tissues. This approach provides improved opportunities for investigating drug activity, toxicity and disease mechanisms.

4. Integration of artificial intelligence

Artificial intelligence and machine-learning techniques are increasingly being applied to data generated from MPS platforms. These technologies can assist in identifying drug-response patterns, analyzing cellular changes and predicting possible toxicity.

5. Real-time monitoring using biosensors

Advanced organ chips are being equipped with optical, electrical and biochemical sensors. These sensors enable continuous observation of cellular and tissue responses during drug exposure, reducing the need for repeated sampling.

6. Improved prediction of drug absorption

Gut-on-chip models are increasingly used to investigate intestinal permeability, drug transport and absorption. Because these systems can reproduce fluid movement and other physiological conditions, they may provide more relevant information than conventional static cell cultures.

7. Evaluation of advanced drug-delivery systems

Organ-on-chip platforms are being applied to investigate the behavior of nanoparticles, liposomes, micelles, polymeric carriers and other advanced delivery systems. They can help evaluate drug release, tissue interaction and cellular uptake under physiologically relevant conditions.

8. Disease-specific organ chips

Specialized MPS models are being developed to reproduce diseases such as cancer, liver disorders, kidney disease, cardiovascular conditions and neurological disorders. These models allow potential medicines to be evaluated in disease-relevant environments.

9. Application of 3D bioprinting

The combination of 3D bioprinting with organ-on-chip technology is an emerging area. It enables researchers to construct complex tissue structures and reproduce important characteristics of the natural cellular environment.

10. Human-on-a-chip technology

Researchers are working toward connecting several organ models through microfluidic circulation. Such systems can simulate interactions between organs and provide information about the overall fate of a drug after administration.

11. Reduction in dependence on animal experiments

MPS technology is being investigated as a human-relevant alternative or complementary method to conventional animal studies. It can provide valuable information about drug toxicity and efficacy before progression to clinical studies.

12. Standardization and regulatory development

Current research is increasingly focused on making organ-on-chip systems reproducible, reliable and suitable for regulatory evaluation. Standard operating procedures, quality-control methods and validation against human data are important areas of development.

13. High-throughput drug screening

Miniaturized microfluidic platforms can allow several compounds or drug concentrations to be examined simultaneously. This can increase the efficiency of early-stage drug screening while reducing the amount of biological material and drug required.

14. Integration with PK/PD modelling

Experimental information obtained from MPS platforms can be combined with pharmacokinetic and pharmacodynamic models. This combination can improve predictions of drug concentration, tissue exposure, therapeutic effects and toxicity.

15. Movement toward clinical application

One of the most important emerging directions is the validation of organ-on-chip results against human clinical observations. Improved sensors, standardized sampling methods and advanced analytical techniques are helping move MPS technology closer to practical pharmaceutical and clinical applications.

Table 02: Comparing Gut-on-a-Chip, Liver-on-a-Chip, and Kidney-on-a-Chip effectively demonstrates how different platforms evaluate drug fate and safety.

Organ-on-a-Chip Model	Primary Physiological Function Replicated	Dynamic & Structural Features Replicated	Primary Drug Testing Application	Key Monitored Endpoints
Gut-on-a-Chip	Oral drug absorption and tissue interaction.	Recreates microfluidic flow, nutrient transport, and mechanical movement.	Evaluating oral drug bioavailability, intestinal permeability, and barrier disruption.	Intestinal barrier integrity, drug absorption rates, and epithelial transport.
Liver-on-a-Chip	Drug metabolism and biotransformation.	Mimics vascular circulation, biomaterial interaction, and 3D tissue architecture.	Assessing drug clearance, formation of active metabolites, and drug-induced hepatotoxicity.	Hepatotoxicity, cell damage, metabolic pathways, and cell viability.
Kidney-on-a-Chip	Renal filtration, tubular transport, and drug excretion.	Simulates fluid flow, nutrient delivery, and biological membrane structures.	Investigating renal excretion mechanisms, transport rates, and nephrotoxicity.	Renal clearance, nephrotoxicity, cell viability, and barrier integrity.

Biomedical Applications of Microphysiology System (Organ-on-a-Chip)

Microphysiology Systems (MPS), also known as Organ-on-a-Chip (OoC) technology, have emerged as powerful tools in biomedical research by providing physiologically relevant models of human organs. These systems bridge the gap between conventional cell culture methods and clinical studies, enabling researchers to investigate human biology with greater accuracy [11,14,15,17].

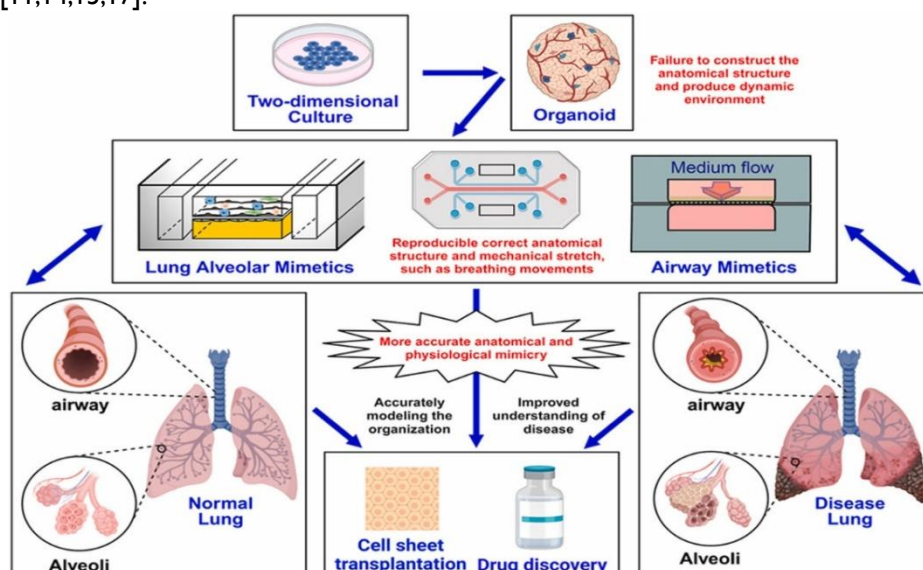


Figure 03: Micro-physiologicalsystem of human lung: Lung organoids and 3D-visualisation of organ-on-chip

1. Drug Discovery and Development

Organ-on-a-Chip platforms are widely used to evaluate the safety, efficacy, and pharmacological activity of new drug candidates. They provide early information on drug performance, helping to reduce the time and cost involved in drug development.

2. Drug Delivery Studies

MPS enables the assessment of drug absorption, distribution, metabolism, excretion (ADME), and controlled drug release. These systems are particularly useful for evaluating targeted drug delivery systems such as nanoparticles, liposomes, hydrogels, and polymeric drug carriers.

3. Disease Modeling

Organ-on-a-Chip technology is used to create models of human diseases, including cancer, diabetes, liver disorders, cardiovascular diseases, kidney diseases, neurodegenerative disorders, and infectious diseases. These models help researchers understand disease mechanisms and evaluate new treatment strategies.

4. Toxicity Testing

Microphysiology Systems provide a reliable platform for studying drug-induced toxicity in organs such as the liver, kidney, heart, and lungs. Early detection of toxic effects improves drug safety and reduces the likelihood of clinical trial failures.

5. Personalized Medicine

By using patient-derived cells, Organ-on-a-Chip devices can predict an individual's response to specific medications. This approach supports personalized treatment plans and improves therapeutic outcomes while minimizing adverse drug reactions.

6. Cancer Research

Tumor-on-a-Chip models reproduce the tumor microenvironment, allowing researchers to investigate cancer progression, metastasis, and the effectiveness of anticancer drugs and immunotherapies under realistic conditions.

7. Regenerative Medicine

MPS supports research on tissue repair and regeneration by evaluating stem cell differentiation, biomaterials, and tissue-engineered constructs for potential therapeutic applications.

8. Infectious Disease Research

Organ-on-a-Chip platforms are used to study interactions between pathogens and human tissues. They assist in understanding disease progression and evaluating antiviral, antibacterial, and antifungal therapies.

9. Vaccine Development

These systems enable researchers to study immune responses, vaccine safety, and vaccine efficacy using human-relevant tissue models, thereby accelerating vaccine research.

10. Reduction of Animal Testing

One of the major biomedical applications of MPS is reducing the dependence on animal experiments. Human cell-based models provide more clinically relevant data while supporting ethical research practices [5,7,9,11,18].

RESULTS MONITORED

Microphysiology Systems (MPS) enable continuous and real-time monitoring of biological responses during drug testing. The data generated help researchers evaluate the effectiveness, safety, and mechanism of action of drug candidates under conditions that closely resemble human physiology.

1. Drug Absorption

- Measures the rate and extent of drug absorption across biological barriers.
- Evaluates membrane permeability and bioavailability.

2. Drug Distribution

- Monitors the movement of drugs between tissues and different organ models.
- Assesses tissue-specific drug accumulation.

3. Drug Metabolism

- Determines how drugs are metabolized by organs such as the liver.
- Identifies active metabolites and metabolic pathways.

4. Drug Excretion

- Evaluates the elimination of drugs and metabolites through kidney-on-a-Chip and liver-on-a-Chip models.
- Studies renal clearance and excretory mechanisms.

5. Drug Efficacy

- Assesses the therapeutic effectiveness of a drug.
- Measures improvement in cellular function and reduction of disease-related markers.

6. Toxicity Assessment

- Detects organ-specific toxicity, including hepatotoxicity, nephrotoxicity, cardiotoxicity, and neurotoxicity.
- Evaluates cell damage and adverse effects at different drug concentrations.

7. Cell Viability and Proliferation

- Monitors cell survival, growth, and proliferation after drug exposure.
- Determines whether the drug supports or inhibits normal cellular activity.

8. Biomarker Expression

- Measures changes in biochemical and molecular biomarkers associated with disease progression or therapeutic response.
- Evaluates protein and gene expression levels.

9. Inflammatory Response

- Monitors the release of inflammatory cytokines and other immune mediators.
- Assesses immune activation and inflammatory reactions.

10. Barrier Integrity

- Evaluates the integrity and permeability of biological barriers such as the blood–brain barrier, intestinal barrier, and lung epithelium.
- Detects disruption caused by drugs or disease conditions.

11. Mechanical and Physiological Responses

- Measures tissue contraction, electrical activity, fluid flow, oxygen consumption, and mechanical stress.
- Provides information on the functional performance of organs such as the heart and lungs.

12. Real-Time Imaging and Sensor Data

- Uses integrated biosensors and microscopic imaging to continuously monitor cellular behaviour, morphology, pH, oxygen levels, and metabolic activity during experiments [4,9,16,19].

DRAWBACKS OF MICROPHYSIOLOGY SYSTEM (ORGAN-ON-A-CHIP)

Although Microphysiology Systems (MPS) or Organ-on-a-Chip (OoC) technology offers significant advantages in drug delivery and biomedical research, several limitations still restrict its widespread use.

1. High Development Cost

- Fabrication of microfluidic chips and specialized equipment is expensive.
- Maintenance and operation require significant financial investment.

2. Technical Complexity

- Designing, manufacturing, and operating Organ-on-a-Chip devices require expertise in microfluidics, tissue engineering, and cell biology.
- Skilled personnel are essential for successful experimentation.

3. Limited Whole-Body Representation

- Most Organ-on-a-Chip models replicate only one or a few organs.
- They cannot yet fully reproduce the complex interactions of the entire human body.

4. Standardization Issues

- There is no universally accepted protocol for chip design, cell culture, or experimental procedures.
- Variations between laboratories can affect the reproducibility of results.

5. Limited Long-Term Cell Viability

- Maintaining healthy and functional human cells on the chip for extended periods remains challenging.
- Cell function may gradually decline during prolonged experiments.

6. Difficulty in Mass Production

- Manufacturing identical, high-quality chips on a large scale is technically demanding.
- This limits commercial availability and widespread adoption.

7. Incomplete Immune System Simulation

- Many current models do not fully replicate the complexity of the human immune system.
- Immune-mediated drug responses may therefore be underestimated.

8. Limited Availability of Human Cells

- Obtaining high-quality primary human cells or patient-derived cells can be difficult and costly.
- Cell availability may limit experimental studies.

9. Regulatory Challenges

- Regulatory acceptance of Organ-on-a-Chip technology is still evolving.
- Additional validation is required before it can replace conventional preclinical testing in many settings.

10. Data Interpretation Challenges

- Large volumes of data generated from sensors and imaging systems require advanced analytical tools.
- Data analysis can be time-consuming and computationally intensive [1,4,6,20].

CONCLUSION

The results monitored in Microphysiology Systems provide comprehensive information on drug absorption, distribution, metabolism, excretion, efficacy, toxicity, and tissue function. These measurements improve the prediction of human drug responses, support the development of safer medicines, and reduce dependence on animal testing. Despite these limitations, continuous advances in microfluidics, biomaterials, tissue engineering, and artificial intelligence are helping to overcome many of these challenges. As the technology matures, Microphysiology Systems are expected to become more standardized, cost-effective, and widely used in drug discovery, drug delivery, and personalized medicine.

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DECLARATION COMPETING INTEREST

Not Declared

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INFORM CONSENT AND ETHICAL CONSIDERATION

Not Applicable

REFERENCES

1. Huh D, Hamilton GA, Ingber DE. From 3D Cell Culture to Organs-on-Chips. *Trends in Cell Biology*. 2011;21(12):745–754.
2. Bhatia SN, Ingber DE. Microfluidic Organs-on-Chips. *Nature Biotechnology*. 2014;32(8):760–772.
3. Esch EW, Bahinski A, Huh D. Organs-on-Chips at the Frontiers of Drug Discovery. *Nature Reviews Drug Discovery*. 2015;14(4):248–260.
4. Low LA, Mummery C, Berridge BR, Austin CP, Tagle DA. Organs-on-Chips: Into the Next Decade. *Nature Reviews Drug Discovery*. 2021;20(5):345–361.
5. Ronaldson-Bouchard K, Vunjak-Novakovic G. Organs-on-a-Chip: A Fast Track for Engineered Human Tissues in Drug Development. *Cell Stem Cell*. 2018;22(3):310–324.
6. Zhang B, Korolj A, Lai BFL, Radisic M. Advances in Organ-on-a-Chip Engineering. *Nature Reviews Materials*. 2018;3:257–278.
7. Shuler ML. Organ-, Body-, and Human-on-a-Chip Systems for Drug Testing and Precision Medicine. *Trends in Pharmacological Sciences*. 2017;38(6):497–509.
8. Ingber DE. Human Organs-on-Chips for Disease Modelling, Drug Development and Personalized Medicine. *Nature Reviews Genetics*. 2022.
9. Zhang YS, Aleman J, Shin SR, et al. Multisensor-Integrated Organs-on-Chips Platform for Biomedical Applications. *Proceedings of the National Academy of Sciences (PNAS)*. 2017.
10. Marx U, Akabane T, Andersson TB, et al. Biology-Inspired Microphysiological Systems to Advance Patient Benefit and Animal Welfare in Drug Development. *ALTEX*. 2020.
11. Rang HP, Ritter JM, Flower RJ, Henderson G. Rang & Dale's Pharmacology. 10th Edition. Elsevier; 2023.
12. Brunton LL, Hilal-Dandan R, Knollmann BC, editors. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 14th Edition. McGraw-Hill Education; 2023.
13. Aulton ME, Taylor KMG. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 6th Edition. Elsevier; 2022.
14. Remington JP. Remington: The Science and Practice of Pharmacy. 23rd Edition. Pharmaceutical Press; 2020.
15. Allen LV, Popovich NG, Ansel HC. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. 12th Edition. Wolters Kluwer; 2021.
16. Karp G. Cell and Molecular Biology: Concepts and Experiments. 9th Edition. Wiley; 2021.
17. Lodish H, Berk A, Kaiser CA, et al. Molecular Cell Biology. 9th Edition. W.H. Freeman; 2021.
18. Alberts B, Johnson A, Lewis J, et al. Molecular Biology of the Cell. 7th Edition. Garland Science; 2022.
19. Jain NK. Controlled and Novel Drug Delivery. CBS Publishers & Distributors; 2019.
20. Yadav AV, Murthy MSN. Pharmaceutical Technology and Drug Delivery Systems. Career Publications; 2021.