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Review Article

## A Review Article on Organ-on-a-Chip Platforms: A Novel Approach for Disease Modeling and Drug Discovery

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### ABSTRACT

An innovative method that addresses the drawbacks of conventional two-dimensional (2D) cell cultures and animal models in biomedical research is organ-on-a-chip (OoC) technology. The intricate microenvironment of human tissues cannot be replicated by conventional methods, and using animals for research is expensive, time-consuming, and unethical. OoC devices, sometimes referred to as microphysiological systems, mimic physiological circumstances such as fluid flow, mechanical stresses, and biochemical gradients by combining microfluidics with three-dimensional (3D) tissue engineering. The biocompatibility, transparency, and affordability of polydimethylsiloxane (PDMS) make it a common manufacturing material. High-throughput drug testing, quick analysis, and improved tissue microenvironment representation are some benefits of OoC systems. Their promise in drug screening and illness modeling is demonstrated by applications such as kidney-on-a-chip and heart-on-a-chip. Notwithstanding obstacles such as surface effects and fluid mixing restrictions, OoC technology offers a viable, moral, and effective substitute for developing individualized medication and enhancing the results of scientific research.

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### INTRODUCTION

The microenvironment of cells, which are the basic building blocks of life, is essential for controlling their migration, proliferation, and differentiation. The intricacy of human tissues is difficult to duplicate using conventional in vitro models, such as animal models and 2D cell cultures. Dynamic physiological circumstances are absent in two-dimensional cultures.[1]

Animals have been widely employed in research for physiological and disease investigations as well as medication testing because traditional 2D cell culture is unable to replicate complicated in vivo circumstances. But using animals for study may be costly, time-consuming, and ethically problematic. Furthermore, the outcomes of animal experiments are frequently not immediately relevant to comprehending human physiology or forecasting how humans will react to illnesses, medications, or other stimuli. The goal of the 3Rs (Replacement, Reduction, Refinement) approach is to either utilize fewer animals in research or substitute them with other methods. Organ-on-a-chip

(OOAC) technologies are regarded as a useful substitute instrument [2].

Microphysiological systems (MPS) or organs-on-a-chip (OoC) are small-scale biomimetic cell culture technologies. They combine microfluidic technology with three-dimensional tissue engineering [1]. The engineered manipulation of fluids at the submillimeter scale is what defines microfluidics. Lab-on-a-chip technologies or miniaturized complete analysis systems are frequent terms used to describe the microscale devices in microfluidics. Microfluidics concentrated on downsizing previously large-scale tests during the 1990s and 2000s. Several innovative technologies outperformed the conventional approaches within a few years. Organ-on-a-chip technologies, surface tension-assisted immunoassays, and paper-based analytical devices for diagnostics are a few examples [5].

Cellular microenvironments are accurately replicated by these systems. They include metabolic gradients, mechanical stresses, and fluid flow at physiologically relevant scales. Microfluidic OoC models greatly improve drug screening,

customized medicine, and disease modeling despite their technological complexity. Perfusion and mechanical stress are two important aspects of organ physiology that this technology replicates. The structure and function of human organs are successfully replicated by means of a continuously perfused micron-scale microfluidic network [1].

#### ADVANTAGES:

- It can produce results quickly [4].
- Manufacturing costs are low [4].
- In-house accessories can be used for fabrication without the need for specialist equipment [3].
- It is possible to test many medications and dosages at once.[4]
- It closely resembles the tissue microenvironment it replicates. The OoC outperforms basic Petri recipient microsystems because of its three-dimensional structure, which is crucial to the test's dependability [4].
- Microfluidic chips can evaluate several physiological problems and are portable and easy to utilize [4].
- Because of its compact size, several microfluidic systems may be combined on a single chip, saving both money and space.[4]

#### DISADVANTAGES:

- Because the fluids' dimensions are so tiny, the surface effects outweigh the volume impact. This might result in subpar analysis and partial adsorption of the desired product [4].
- The relevant fluids may not mix effectively because laminar flow exists at the junction of numerous fluids [4].
- Materials used in the production of OoC:

The substance that is utilized is called polydimethylsiloxane (PDMS). This substance is a synthetic, polymetric elastomer made of silicon and carbon. The actual production process involves combining liquid PDMS with a substance that aids in PDMS solidification. After that, the slurry is put into a mold to give the chip its shape. The body can be adhered to another chip or to the lass once the paste has solidified the chips. [4]

The PDMS gained popularity because of several of its features, including its transparency, which benefits the user by allowing them to observe how the OoC operates. The material is inexpensive and straightforward to utilize in this application because of its recognized decreased cytotoxicity.[4]

#### DIFFERENT SUPPORTING MATERIALS:

Collagen is employed extensively due to its benefits for many organs, however it needs some mechanical support in order to stay intact for a little period of time. To get the best results, extra equipment may be necessary in some situations. [4]

First, the external flow of the micro and nanofluids must be managed. Pressure generators are often straightforward devices that include a pressure source, such as a compressor, a pressure regulator, and a manometer to gauge the present pressure. The pressure may be altered considerably more quickly with a pressure multiplexer.

Flux sensors, which convert the control signal from pressure to flow, can be added to pressure generators as an additional improvement. Pressure syringes offer the benefit of controlling flow without being impacted by disturbances brought on by fluid resistance.[4]

#### ORGAN ON CHIP

##### Kidney on chip:

A published kidney-on-a-chip features two chambers in its original concept. While the bottom chamber is filled with media and resembles interstitial space, the upper channel has fluid flow and resembles the urinary lumen. Compared to lung or endothelial cells, kidney cells experience far less shear stress. Rat distal tubular cells, or MDCK cells, were utilized in this apparatus, and its shear stress was around 1 dyn/cm<sup>2</sup>. The identical concept was applied in a second publication, although human proximal tubular cells were employed. The authors attempted to replicate cisplatin nephrotoxicity in this model. Shear stress is significantly lower in proximal tubular cells (~0.2 dyn/cm<sup>2</sup>). Podocytes are glomerular visceral epithelial cells whose foot processes provide a size- and charge-selective barrier to plasma protein. When this barrier is disrupted, podocyte damage and proteinuria result. Podocyte-on-a-chip has been tested by certain scientists, although it remains difficult. It could be due to the fact that podocytes need complex culture conditions and are subjected to extremely low shear stress in vivo [5].

##### Heart on chip:

A heart-on-a-chip (HoC) is a microengineered device that combines concepts from tissue engineering, microfluidics, and biomaterials research to mimic the form and function of human cardiac tissue in vitro. Careful material selection is the first step in building HoC; biocompatibility, optical transparency, and simplicity of production are crucial. Common materials include poly(methyl methacrylate) (PMMA), which is appropriate for large-scale manufacturing despite its reduced oxygen permeability, and polydimethylsiloxane (PDMS), which is prized for its flexibility, gas permeability, and transparency. These materials' surfaces are altered with extracellular matrix (ECM) proteins like collagen and fibronectin to encourage cardiomyocyte adherence because they do not inherently facilitate cell attachment.

However, three-dimensional (3D) scaffolds and hydrogels are used since conventional 2D growth conditions are insufficient to replicate the natural cardiac milieu. While hydrogels like gelatin methacrylate (GelMA) better mimic the extracellular matrix (ECM), they may need to be reinforced with conductive materials like carbon nanotubes or gold nanoparticles to increase mechanical strength and electrical conductivity. Materials like polycaprolactone (PCL) and polylactic acid (PLA) are used to create porous scaffolds via methods like 3D printing and electrospinning.[6]

Another crucial factor is the selection of the cell source. A variety of cells are used by researchers, such as native cardiomyocytes, immortalized cell lines (such H9C2 and HL-1), and cardiomyocytes produced from stem cells, such as those from induced pluripotent stem cells (hiPSCs).

Although they are more complicated and expensive to employ, stem cells are especially useful since they can accurately mimic human heart function and even enable patient-specific disease models. Soft lithography, 3D printing, and laser cutting are some of the methods used in the chip's actual fabrication. The most popular technique for precisely replicating microchannel architectures is soft lithography, particularly for PDMS-based devices. While laser cutting provides a more straightforward and affordable option for channel design creation, 3D printing allows for quick prototyping and even bioprinting of heart tissues.[6]

Stimulation is necessary to produce functioning heart tissue. Compression, pneumatic systems, or fluid-induced shear stress are examples of mechanical stimulation that aids in cell alignment, maturation, and the development of appropriate contractile activity. In order to improve synchronization and the electrophysiological characteristics of the tissue, electrical stimulation is also frequently employed. Electrodes composed of materials like carbon or platinum are utilized to simulate the electrical signals that control heartbeats. Lastly, on-chip sensing technologies that enable real-time heart function monitoring are integrated into HoC devices. These devices use microelectrode arrays to monitor electrophysiological signals and evaluate contractility using

techniques such as tracking fluorescent particles, cantilever displacement, and deformation of elastic substrates. Heart-on-a-chip platforms are powerful tools for drug testing, disease modeling, and personalized medicine because they closely resemble the human heart thanks to the integration of advanced materials, precise fabrication techniques, appropriate cell sources, controlled stimulation, and real-time sensing.[6]

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