International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

Nano-Navigators- Pioneering precious medicines as well as organ functioning with Organ-on-a-Chip

Rutuja Vijay Bhasme
Student, P. R. Pote Patil College of Pharmacy, Amravati

Submitted: 10-04-2024 Accepted: 20-04-2024

ABSTRACT:
Organ-on-a-Chip" technology involves creating small devices that replicate the functions of human organs on a microscale. These tiny systems, or "chips," contain living cells and are designed to simulate the behaviour of actual organs. The innovation lies in how these chips provide a more accurate representation of human physiology compared to traditional methods. Researchers can use them to study how organs function, how diseases develop, and how different drugs might affect the body. It's like having miniature versions of organs in a lab, allowing scientists to gain insights into complex biological process. This technology has the potential to revolutionize areas such as drug testing, disease research, and personalized medicine by providing a more realistic and efficient way to understand how our bodies work and how they respond to various treatments. Current review article gives information on Recent approaches in the field of Organ On a chip, application, uses and it's Future Approaches.

Keywords: Organ-on-a-Chip, Miniature organ in a lab, Drug Testing, Personalized Medicines, Micro physiological Chip, Drug Toxicity

I. INTRODUCTION:

In recent years, interest in organ on a chip (OoC) (also known as micro-physiological systems or "tissue on a chip") has increased significantly due to their use in many fields, especially precision medicine and medicine. construction and analysis [2]. An organ-on-a-chip, also known as organ-on-a-chip, tissue-on-a-chip, or micro-physiological system (MPS), is a small cellular device designed for the product of many tissues or functions of the Body. [3] Body-on-chip technology can monitor important human physiological processes and provide in-depth studies of body function and disease pathophysiology [2]. Over the past decade, advances in this research have led to a new way of creating new models in vitro, called organs-on-a-chip [3]. This method takes advantage of the accuracy and control provided by micro-engineering technology. Organ-on-a-chip offers a promising platform for animal testing by providing a platform to model the structure and function of complex human tissues and organs, which cannot be done in cell culture models [3].

The unique advantage of body-on-chip technology is that it combines drug metabolism and toxicity processes in a single device, making it easier to evaluate the toxicity of drug metabolites [4]. By using three-dimensional (3D) culture scaffolds and new in vitro techniques for the integration of different cell types, attempts have been made to improve the ability of culture cultures to replicate the complex process of community to maintain the animal's boundaries. producing. model [3].

Animal models are frequently used in toxicity tests and preclinical testing [4]. However, results from animal models often differ from humans, which has led to many drugs being withdrawn from the market due to side effects [4]. Conventional in vitro two-dimensional culture can transform animal models but cannot simulate the in vivo cell body [4]. Additionally, the lack of cell-cell and cell-matrix contact in 2D culture often leads to loss of cell function [4]. Therefore, the creation of stable and biomimetic in vitro research models is rapidly gaining popularity [4].

By studying multiple organ systems and disease models, multi-organ-on-a-chip (multi-OoC) devices facilitate inter-organ communication. The use of an OoC model may influence new findings [6]. Endocrine circuits that regulate peripheral tissues are essential for the ability to regulate many tissues of the foetus [6]. Pancreatic islets also secrete insulin to promote glucose absorption from the liver. Understanding and modelling the physiological processes involved in bodily functions depends on organ communication and communication.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

Strength and Limitation of Organ-on-a-Chip:

Strength:

- Organ-on-a-Chip are relatively inexpensive to make; It can be done using inexpensive gadgets, does not require special equipment, and can analyse many drugs and medications simultaneously.
- The similarity of the OoC concept to the organizational context it replicates makes it different.
- In this comparison, OoC outperforms the simple Petri receptor microsystem because its 3D structure is important for validity testing.
- Due to its small size, many microfluidic systems can be used on a single plate, saving time and money.

Limitation of Organ-on-a-chip:

- The first drawback to include is the presence of surface effects. Because the size of the liquid is very small, surface effects cause volume effects. This may affect analytical quality and some of the material of interest will be adsorbed.
- Another limitation of these platforms is that special precautions must be taken to get good results in some tests.

Classification on Organ on a Chip:

1) Single Organ on a Chip
2) Multiple Organ on a Chip

1] Single Organ on a Chip:

Organ-on-a-chip (OOAC) is a novel in vitro micro-bionic platform that helps reconstruct the physical environment of the human body. Single organs often allow for a high degree of biomedical realism, allowing the evaluation of the responses of organs to compounds or combinations of substances [5]. These technologies include cell biology, engineering, and materials science to simulate in vivo tissue [1]. Animal and human in vivo experiments are frequently used to study the function of the body, but many other methods have been investigated over the past two decades, including 2D and 3D in vitro models and computational models [7].

There are different types of single organ on a chip:

A. Liver on a chip
B. Kidney on a chip
C. Breast Tissue and Tumour on a chip
D. Heart on a chip
E. Pancreas on a chip
F. Gut on a chip
G. Lung on a chip

A] Liver on a chip:

The heart is one of the most important organs of the human body and its many functions are to control the body's activities. It has the ability to regenerate itself to prevent damage that may be caused by chemical or physical use [2]. Recently, due to the drug metabolism, excretory capacity and fragility of the liver, many research groups and biotechnology companies have worked hard to develop a "one-inch heart" ex vivo liver culture system. one]. In some cases, the injury can be serious and is often caused by an allergic reaction to a different drug or disease. Before the advent of OoC technology, very good in vitro models were not available. Drugs are often tested in vivo on animals. Subjects sometimes suffer from drugs that can be fatal [2].

OoC technology can detect whether different drugs cause mental damage. The process involves placing liver cells on a plate and using drugs in different ways. The chip is analysed and if the cells are dead, the use of the drug in the body is considered dangerous. Therefore, it can be concluded that this system can be used in hepatotoxicity studies. Advanced technologies such as spheroid culture, co-culture, perfusion and 3D bioprinting have been used in liver cancer research, making liver cancer simulations increasingly realistic. The combination of organoids and liver tissue shows great potential and is a future research project. In the evaluation of liver toxicity, liver chips have the advantage of high accuracy, high sensitivity and strong detection ability, and there is hope [4].

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

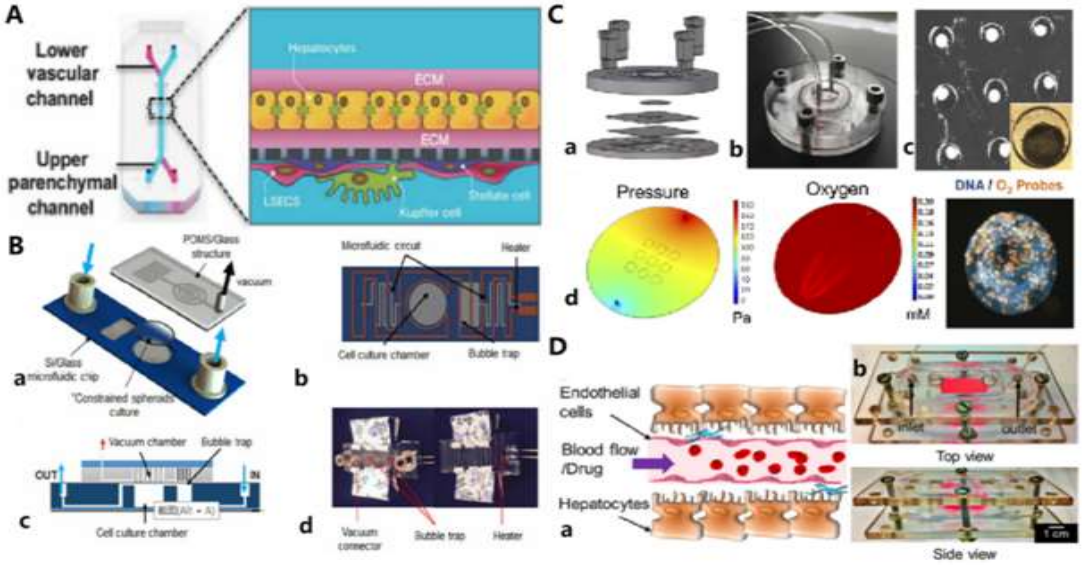

Figure 1. A liver chip system for drug toxicity testing.[4].

Liver-on-a-chip models have also been used to study the hepatotoxicity of nonsteroidal anti-inflammatory drugs (NSAIDS). The first mouse hepatocytes were used for toxicity testing of diclofenac and acetaminophen in perfusion incubator liver chips [7]. For the initial study of apigenin metabolism using a microfluidic chip, Caco2 (for colon) and HepG2 (for liver) cell layers were used [7]. A spheroid-based microfluidic chip containing rat primary hepatocytes and hepatic stellate cells (HSCs) was developed as a model of liver injury. The role of HSCs in liver recovery from chronic alcoholism has been studied. There is currently no specific treatment for non-alcoholic steatohepatitis (NASH); This is mainly due to the lack of models that can reproduce the hepatocyte microenvironment and the complexity of NASH. Frege et al. NASH-on-a-chip was developed to study disease pathogenesis and the development of anti-NASH drugs [7].

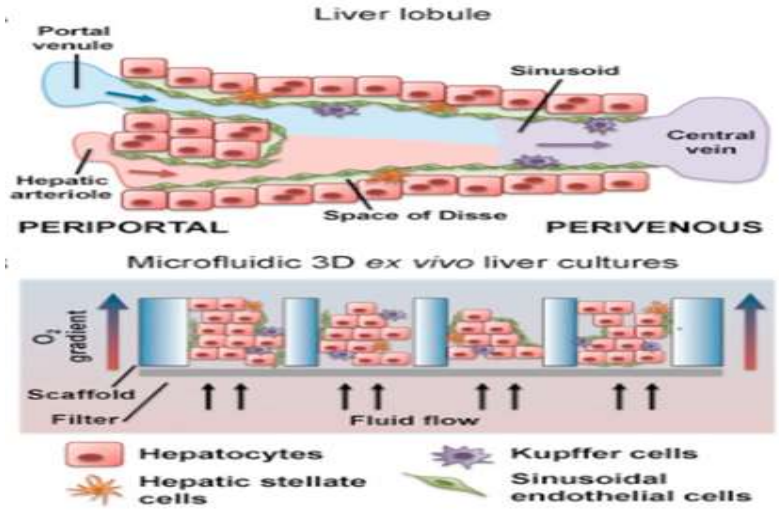

Fig. 2. Liver on a chip [1]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

B] Kidney on a chip:

The original design of the kidney chip consists of two parts; the first represents the urinary tract and fluid flow, and the other simulates the midsection. This device uses tubular cells of rat kidney. In 2013, Jang et al. reported the development of a kidney-on-a-chip microfluidic model [7].

Completion of drug nephrotoxicity studies using microchips. Membrane permeability and drug-related toxicity of cisplatin, gentamicin and cyclosporin A were investigated. One of the studies investigated glomerular function using human adult podocytes derived from human induced pluripotent stem (hiPS) cells that mimic doxorubicin-induced proteins. Many body-on-chip models [7]. Animal and cell models are currently the tools used to test DIN. Due to differences between animals and humans, accurate predictions of nephrotoxicity using animal models are poor. Recently, the kidney model has been used for nephrotoxicity testing, which can realize the integration of various cells, simulation of the in vivo microenvironment, and in vitro biomarker analysis. Such models have the potential to become future models for DIN analysis [4].

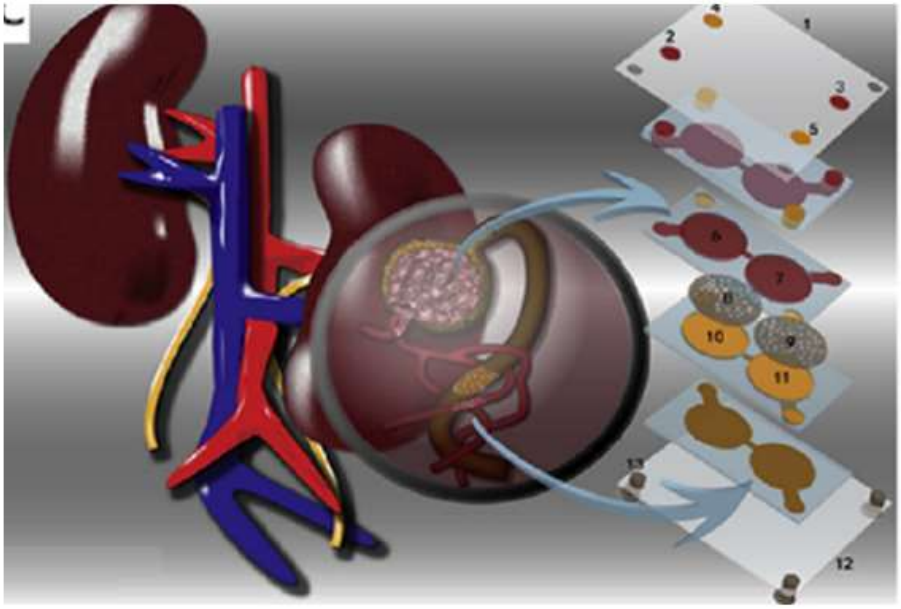

Figure 3. Kidney on a chip[4]

C] Tissue and Breast Tumour on a chip:

Understanding the anatomy of breast cancer can help better diagnose breast cancer, one of the most common cancers in women. Its danger arises from its nature and its treatment is difficult[2]. This ToC tool for breast cancer can be used for drug screening by examining different chemotherapy drugs and their effects on the model, or for personalized medicine when using the first bed. Understanding the factors that may cause resistance in tumours may help find new therapeutic strategies in the treatment of this disease [2].

With this knowledge, treatment risk can be reduced and personalized medicine may be the next step in treating malignant tumours. For example, this model can be used to study the interaction of malignant clones with adipocytes, as this cell type often induces tumorigenesis and can promote drug response [2].

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

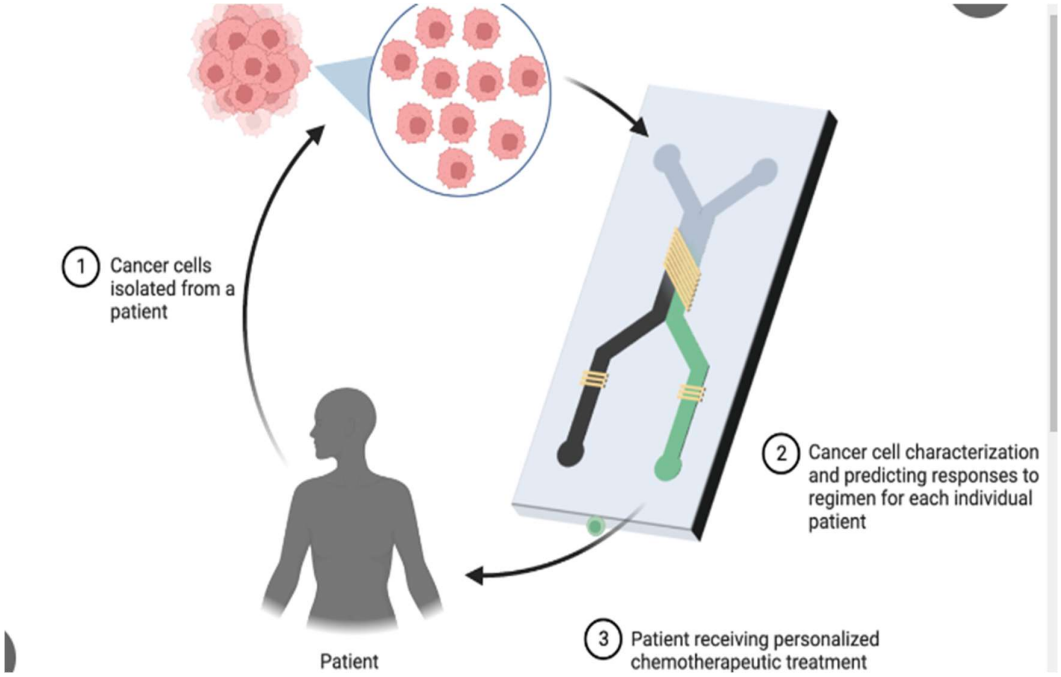

Figure 4. Tissue on a chip[9]

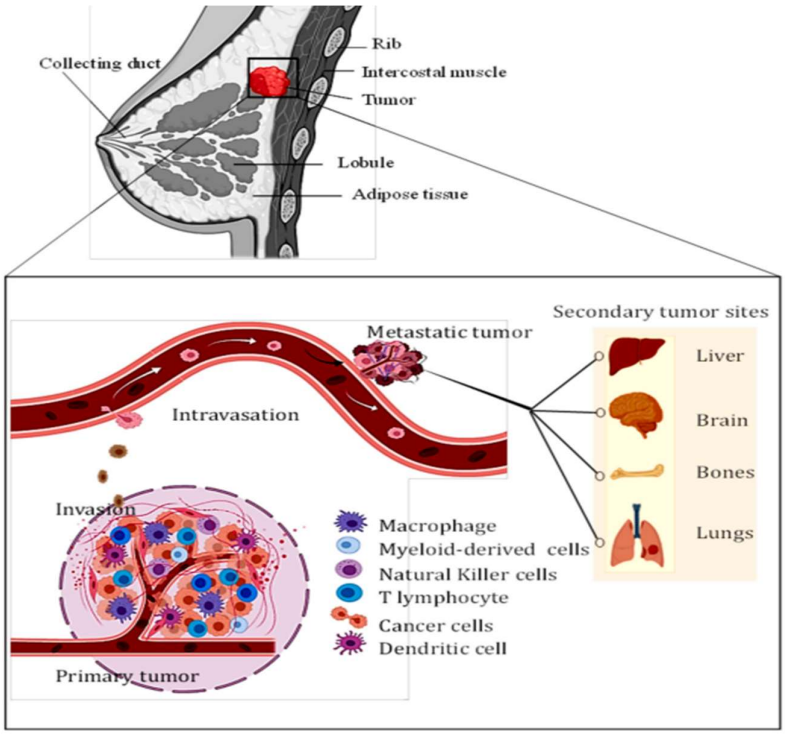

Figure 5. Breast Tumour on a chip[10]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

D] Heart on a chip:

Cardiovascular disease (CVD) is the leading cause of death in some countries. The major problems in the development of cardiovascular drugs are animal models of CVD do not predict human response well; A study of AstraZeneca's pipeline between 2005 and 2010 found that 82% of programs were shut down in the pre-clinical phase due to safety concerns. The rate of heart failure is approximately 17%, the highest rate of any other organ identified [7]. The heart-on-a-chip can be used to simulate hypoxia, arrhythmias, tachycardia patterns, and any stimulation from heart cells [7].

The calcium channel drugs, isoproterenol and verapamil produce a dose response, suggesting potential tools for drug screening and cardiotoxicity testing [4].

Regarding the myocardium, studies on heart structures and systems, as well as on the heart and other tissues in the body, have been published in recent years. Ellis et al. A microfluidic device was developed to simulate the human myocardium and surrounding microvasculature by controlling the integration of CM and endothelial cells. Kamei et al. reported a lithography-based microfluidic device that used pneumatic valves and pumps to produce sufficient fluid to simulate the side effects of cancer drugs [4].

The system contains a series of cell cultures with a microfluidic system that simulates blood circulation and connects multiple cells. Human healthy heart cells (hCM) and hepatoma cells (HepG2) were co-cultured in separate chambers. The device measures the side effects of doxorubicin on heart cells, which are caused by HepG2 cells sending toxic metabolites to heart cells through the circulation. Designed for heart tissue, this device can be used to estimate changes in cardiomyocytes. The device can create cardiovascular microtissues and improve mechanical and electrical connections between adjacent cells. This model demonstrates the positive chronotropic effect of isoproterenol and thus demonstrates its potential use in drug discovery and toxicity [7].

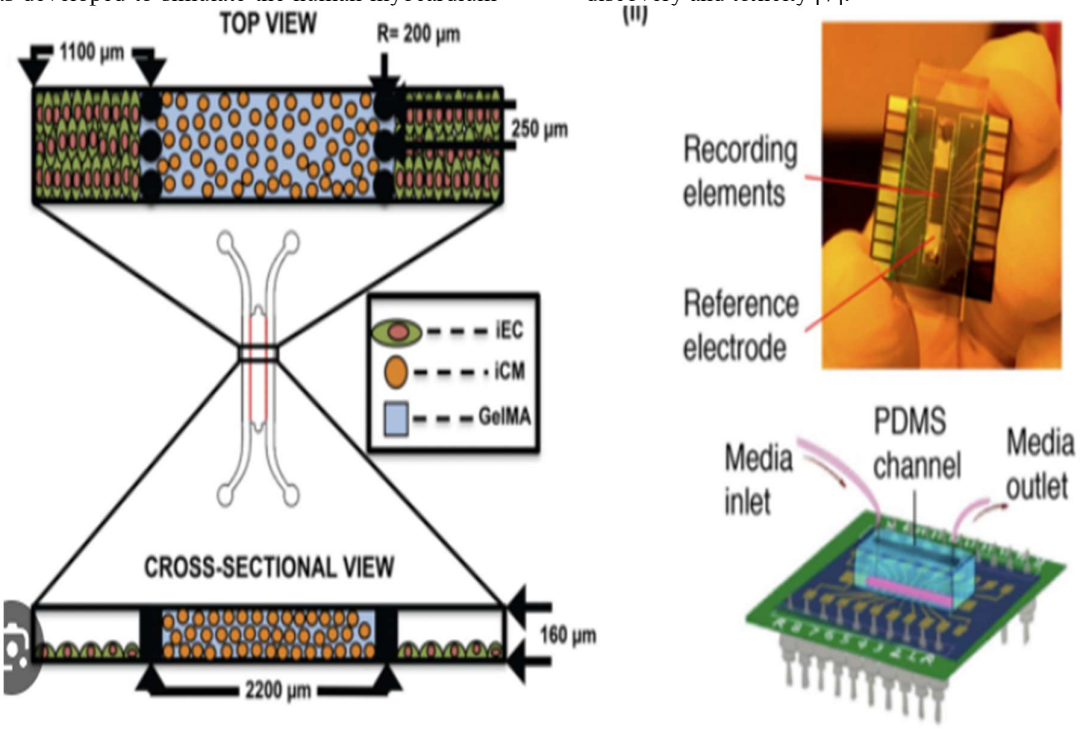

Figure 6. Heart on a chip[11]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

E] Pancreas on a chip:

Pancreas-on-a-chip (PoC) essentially refers to the study of the endocrine part of the pancreas on a microfluidic chip, which can be used as a real-time measurement model to evaluate the efficiency and quality of islets [12]. First, it is resistant to medications and tumours are difficult to remove surgically. It is thought that the poor prognosis of this disease is due to the cancer reaching an advanced stage in a short time as a result of the breakdown of cancer cells (2).

Researchers adopted an OoC approach using transparent, flexible plastic sheets containing microfluidic channels. To replicate the behaviour of the virus, they used pancreatic cancer cells collected from mice in one channel and seeded human endothelial cells into the adjacent channel. The wafers are then examined to examine the behaviour of these cells. After the experiment, the same method was applied, but human cells were used instead of mouse pancreatic cancer cells. Consistent behaviour indicates that sickness behaviour does not vary across species [2]. OoC is also used to find treatments by adding experimental drugs to cells on a chip and then observing their behaviour [2].

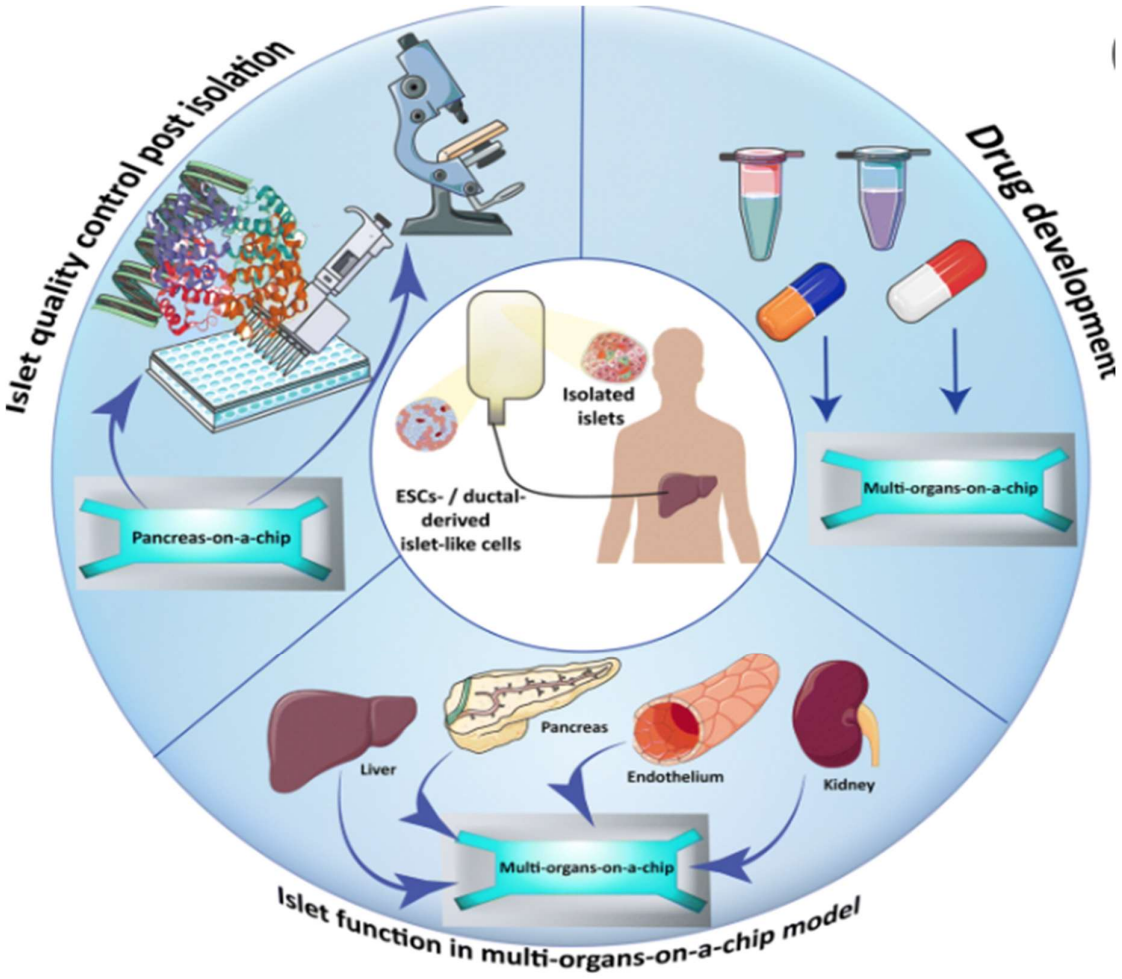

Figure7. Pancreas on a chip technology[12]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

F] Gut on a chip:

The gut is an important site for drug metabolism and is where most drugs undergo all metabolism in the first place. It is important to develop a reliable in vitro model to study the gastrointestinal effects of drugs involving many pathogens [4]. Different cells used in this model include Caco2, human umbilical vein endothelial cells, intestinal organoids, human intestinal microvascular endothelial cells, human lymphatic microvascular endothelial cells, and peripheral blood mononuclear cells. Intestinal microarrays have been used to study drug pharmacokinetics, host gut microbiota interactions, and nutrient metabolism [7].

Li's team created a gut microbiome in which intestinal epithelial cells formed a layer of cells that showed elevated levels of alkaline phosphatase (ALP) and stress-insensitive (SI) genes compared to handcrafted samples. They used this tool to measure the metabolic potential of verapamil and isofluramide, and the results showed that intestinal bacteria had high levels of CYP450 enzyme expression, thus improving the metabolism of oral drugs [4].

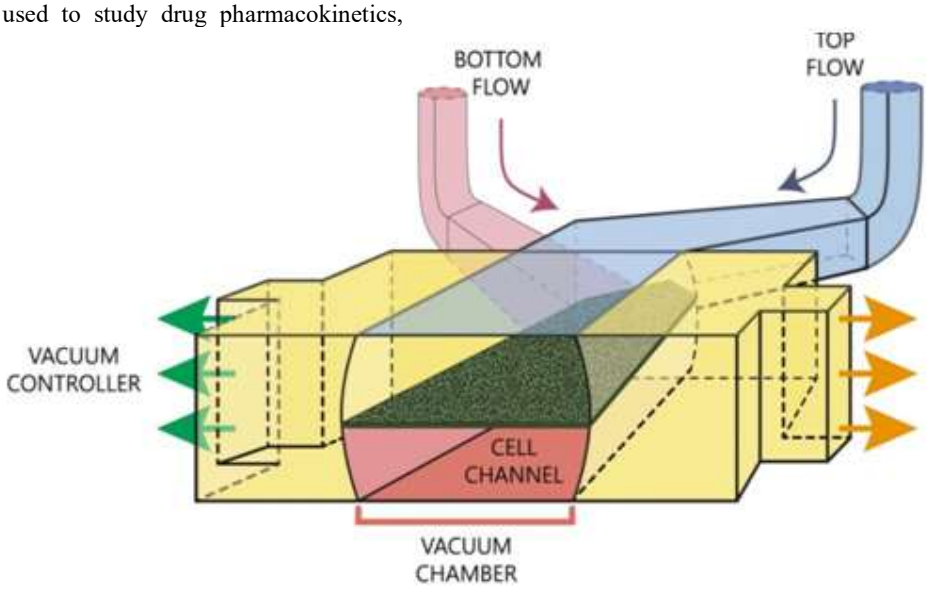

Figure 8. Gut on a chip [13]

G**] Lung on a chip:**

During inhalation, intrapleural pressure decreases and air drawn into the lungs causes the alveoli to expand, causing endothelial cells to expand the alveolar epithelium and adjacent micro-vessels [4]. Smoking is an important factor in the treatment of exacerbations in patients with asthma and chronic obstructive pulmonary disease (COPD). Benam et al. An inhalable and exhalable chip was developed to study the effects of smoking on the lungs [7].

They confirmed that the results obtained using the lung model were close to those obtained in animal experiments. The team studied the up- and down-regulation of genes by smoking and used the model to discover new biomarkers [7]. Animal models such as rats and mice are widely used to study the pathophysiology of respiratory diseases, identify new biomarkers, drug targets, and toxicity studies [14]. New drug compounds can first be evaluated using animal models, which is important for new drug discovery [14].

Animal models are important for studying lung diseases such as chronic obstructive pulmonary disease, asthma, obstructive pulmonary disease, lung cancer, pulmonary fibrosis, cystic fibrosis, and respiratory diseases. However, animal models cannot truly represent the physiology, disease, and genetics of humans and therefore cannot predict response to drugs in humans [14] .

Many drugs, especially some chemotherapy drugs, can cause lung toxicity. Lung toxicity can be divided into two groups according to the cause of lung toxicity [4]. Drugs that affect

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

the balance of respiratory diseases are important factors in lung disease (4). At the same time, artificial nanoparticles (NPs) that humans are exposed to through inhalation can be toxic [4].

These models were developed using human bronchial epithelium and lung endothelium for infection, cytokine production, and circulating cells. Drugs such as nafamostat, oseltamivir, amodiaquine, and hydroxychloroquine have been studied for protection against pseudo-typed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza A [7].

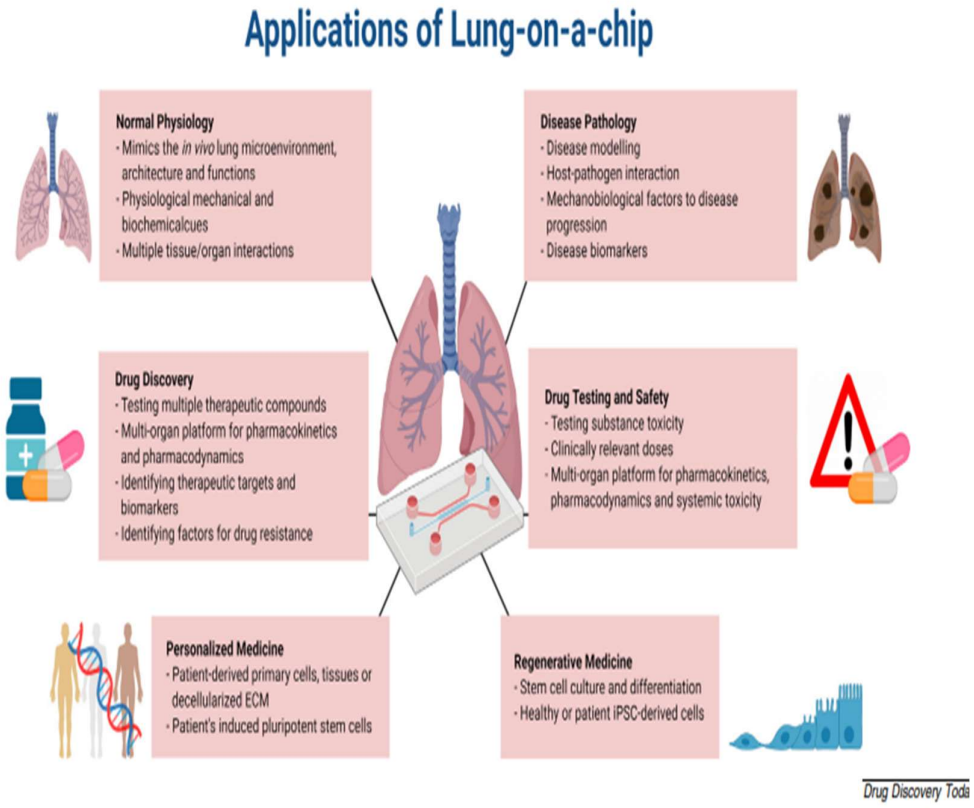

Figure 9. Application of Lung-on-a-Chip[14]

With further development, these models may simultaneously reduce the dependence on animal models for drug testing and toxicology research [14].

Organ on a Chip	Applications/ Model
Lung on a Chip	Model for viral infection, in-vivo setting for human airways, and model for pulmonary oedema
Heart on a Chip	cardiac electrophysiology, electrical stimulation, and various heart conditions
Liver on a Chip	Liver specific Protein Synthesis,
Kidney on a chip	Drug induced nephrotoxicity, Glomerular filtration
Pancreas on a chip	For cancer detection and toxicity detection
Gut on a chip	used to study drug metabolism and related diseases[4].
Breast tissue and Tumour on a cell	Used to study about the breast cancer and other cancer related to different organs

Table No. 1. Summary Of the application of Organ On a Chip[7]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

Organs	Cells
Lungs	Human induced pluripotent stem cells
Liver	HepG2 cells
Kidney	Mature human podocytes derived from human induced pluripotent stem
Gut	Caco 2 cells
Skin	Induced pluripotent stem cells (iPSC) or commercially available reconstructed skin tissues (Epiderm-FT, Epi-derm, Epi-Skin, Strati-CELL)
Heart	Human induced pluripotent stem cells (iPSCs) – derived 3D cardiac cells
Pancreas	Culturing of Human Islets

Table No. 2. Common Sources of cell used in Organ on a Chip[12]

2] Multiple organ on a chip :

Single-body models cannot necessarily predict the full pharmacokinetics and safety profile of drugs, and multi-body models may reduce or replace the use of animals [15]. Organ communication in cancer can lead to metastasis, which is the cause of cancer. Metastasis is driven by the intravasation of CTC and their colonization in other organs, which is known to occur in preferred niches. To understand the mechanisms involved in this metastatic disease and develop new therapeutic strategies, multi-organ models combining tumour and metastatic disease are greatly needed [6].

Jong et al. developed a microfluidic device connected to the liver, tumour, and bone marrow, in which cells are guided through hydrogels and microchannels and act as vessels to test the cytotoxicity of antibody pain [4]. Entero-renal imaging has been successfully performed and used to study the absorption and nephrotoxicity of digoxin in combination with cholestyramine and verapamil [7]. One of the first heart-on-a-chip designs, developed by MIT's Linda Griffith, was used to create 4-, 7-, and 10-way organ models that demonstrate long-term organ function for approximately 4 weeks [15]. An enterohepatic microchip was created that divided into three parts: enterocytes, liver cells, and breast cancer cells [7]. Caco2 cells (for colon) and HepG2 cells (for liver) were used to study the absorption and hepatic metabolism of cyclophosphamide, Epirubicin, 17-beta Estradiol, and liquid isoflavones [7]. The anti-inflammatory effects of the drugs/drugs after passing through HepG2 cells were further evaluated using MCF-7 cells (which cause human breast cancer) [7].

A similar method using a 4-organ plate coupled to intestine, liver, kidney and bone marrow was used to estimate the pharmacokinetics of cisplatin [15]. Maschmeier et al. Create 2-organ and 4-organ plates and use the 4-organ plates to interconnect iPSC-derived human intestine, liver, brain, and kidney models that should be maintained for 2 weeks using the universal culture averaging rule [15].

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

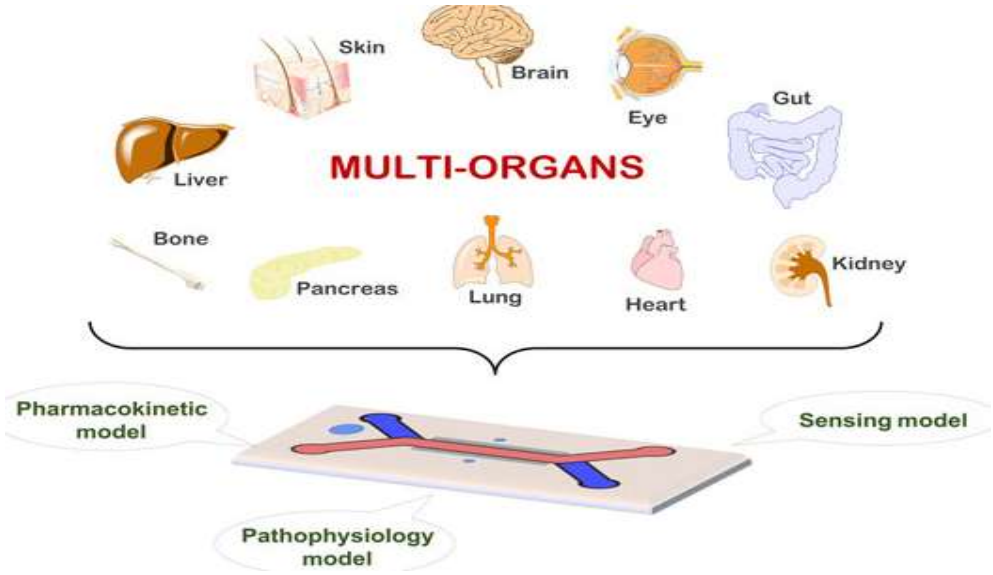

Figure 10. Multiorgan on a chip[16]

Preparation of organ junctions via microporous membranes and microchannels. Caco-2, HepG2 and A549 cells represent the small intestine, liver and lung, respectively [7]. This model was used to study the pharmacokinetics of three antibiotics (epirubicin, irinotecan, and cyclophosphamide), and the results showed that the device was able to reproduce the chemical properties of the drug that blocked infection of cells[6].

It has been shown that the lung tumour spreads to different cells in distant organs (brain, bone and liver) equipped with micro-vessels, is observed on the wafer plate of many organs and undergoes EMT (epithelial-mesenchymal transition). Cells migrate to all three target organs [6] In cancer, organ communication can lead to metastasis, which is the cause of cancer. Metastasis is known to be driven by CTC intravasation and their colonization in other organs occurring in preferred niches [6]. To understand the mechanisms involved in this metastatic disease and develop new therapeutic strategies, multi-organ models combining tumour and metastatic disease are greatly needed [6].

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

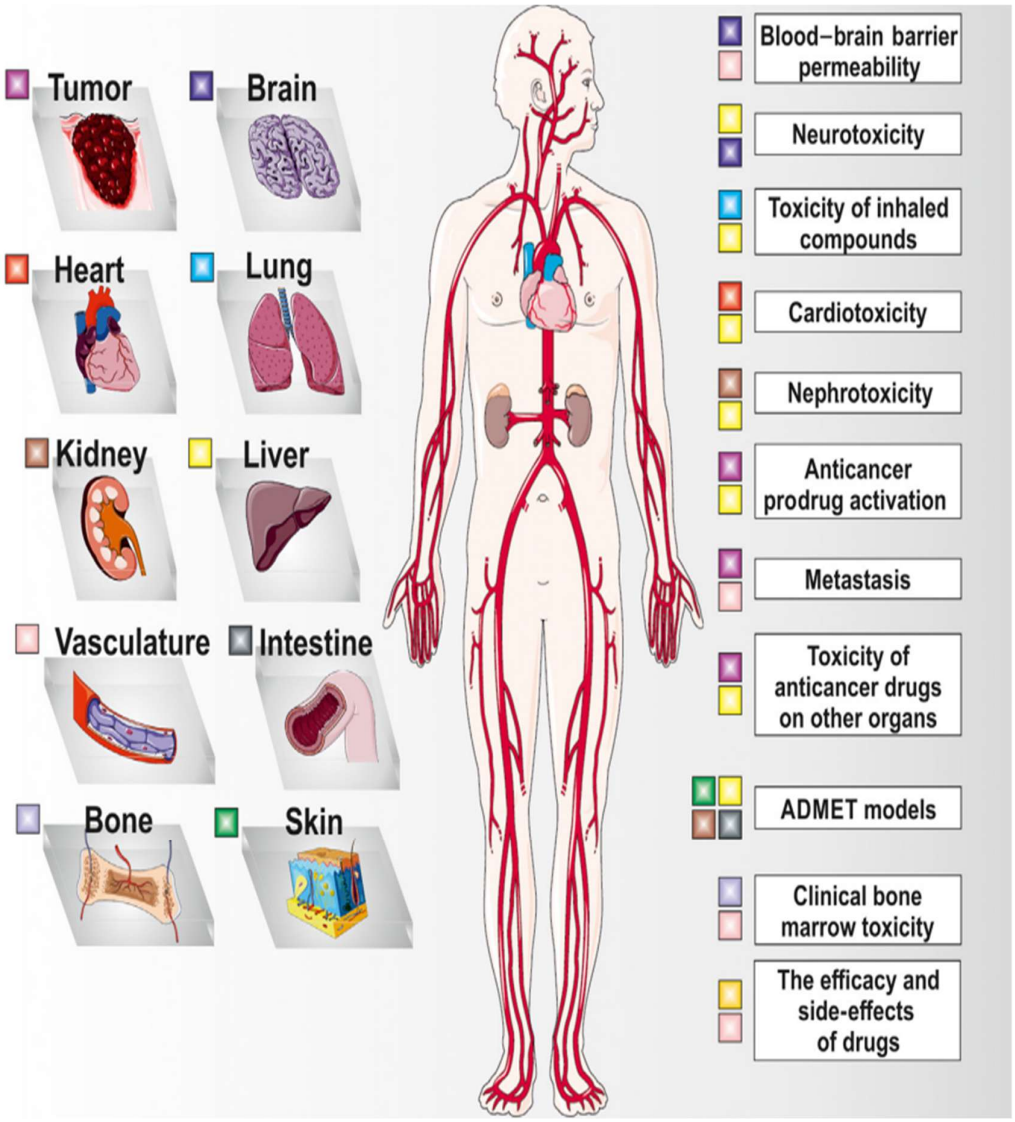

Figure 11. Multiple Organ on a chip[7]

The multiorgan system may attempt to integrate various organs and form a network to study the absorption, distribution, metabolism, and elimination of drugs in the body, such as liver-kidney and hepatoenteric diseases [4]. Many examples of integrated organ-on-a-chip models are emerging, including integrated abdominal, liver, female reproductive, and 8-OoC connectivity, culture, and application [15] . Many examples of integrated body-on-a-chip models are emerging, which include an integrated abdomen, liver, female reproductive system, and 8 bodies-on-a-chip with culture and standards [15].

Three organs, small intestine, liver and lungs, were simulated on a microfluidic chip. Preparation of organ junctions via microporous membranes and microchannels. Caco-2, HepG2, and A549 cells represent the small intestine, liver, and lung, respectively. Due to the perfusion medium and high oxygen permeability of polydimethylsiloxane (PDMS), the device is able to integrate three types of cells in less than 3 days. This model was used to study the pharmacokinetics

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1595-1607 www.ijprajournal.com ISSN: 2249-7781

of three antibiotics (epirubicin, ilintecan, and cyclophosphamide), and the results showed that the device was able to reproduce the chemical properties of the target-blocking drug [7].

II. CONCLUSION:

Organ-on-a-chip technology has revolutionized the field of biomedical research by providing a more accurate and efficient platform for studying human organs and their interactions. These miniature devices offer a glimpse into the complex dynamics of human physiology, allowing researchers to better understand disease mechanisms and test potential treatments. While significant efforts have been made to improve the performance, efficiency, and robustness of body-on-chip models, recent projects have pushed the technology forward. Take this to the next level by creating a variety of organ-on-chip targets. in simulating entire rare biological processes. One of the ultimate goals of Organ-on-a-Chip is to develop tumour models for animal and human experiments by simulating physiologically relevant environments by controlling data, dimensions, and microenvironmental variables (such as toxic humans and mechanical factors).With further advancements and integration of different organ systems, organ-on-a-chip holds immense promise in accelerating drug discovery, personalized medicine, and reducing reliance on animal models.

Future perspective:

The main goal of body-on-a-chip technology in toxicology is to improve the reproduction of results and compare them with clinical data. Advances in this technology can reduce the cost and time of the drug development process and improve the accuracy of breast cancer treatment. Organ-on-chip technology will help identify and develop new cancer cells/therapeutics for cancer applications. In the long term, this technology could pave the way for the development of personalized diagnostic tests based on existing breast cancer cells in patients with breast cancer. Future directions for the development of liver systems-on-a-chip include the integration of lentivirus-induced fluorescent biosensors for automatic readout of various cellular functions and finer structural control of liver microstructure. Creating a pancreas on a wafer that better demonstrates the complexity of islets as a tissue, or islets as another type of tissue, along with the various organs on the wafer- thin can reveal a blood cell model of diabetes and create a platform that can do this for clinical studies, particularly diabetes and immunotherapy. In Future by using the multiple Organ on a Chip, there will be the high possibilities that the Researchers will develop the artificial organ on a chip. It also helps to improve islet transplantation outcomes.

REFERENCES:

[1]. Beckwitt CH, Clark AM, Wheeler S, Taylor DL, Stolz DB, Griffith L, Wells Liver ‘organ on a chip’. Experimental cell research. 2018 Feb 1;363(1):15-25.

[2]. Danku AE, Dulf EH, Braicu C, Jurj A, Berindan-Neagoe I. Organ-on-a-chip: A survey of technical results and problems. Frontiers in Bioengineering and Biotechnology. 2022 Feb 10;10:840674

[3]. Kang S, Park SE, Huh DD. Organ-on-a-chip technology for nanoparticle research. Nano Convergence. 2021 Dec;8:1-5.

[4]. Cong Y, Han X, Wang Y, Chen Z, Lu Y, Liu T, Wu Z, Jin Y, Luo Y, Zhang

[5]. X. Drug toxicity evaluation based on organ-on-a-chip technology: a review. Micromachines. 2020 Apr 3;11(4):381.

[6]. Leung CM, De Haan P, Ronaldson-Bouchard K, Kim GA, Ko J, Rho HS, Chen Z, Habibovic P, Jeon NL, Takayama S, Shuler ML. A guide to the organ-on-a-chip. Nature Reviews Methods Primers. 2022 May 12;2(1):33.

[7]. Nathalie Picollet-D’hahan, Agnieszka Zuchowska,IrisLemeunier and Séverine Le Gac, Multiorgan-on-a-Chip: A Systemic Approach To Model and Decipher Inter-Organ Communication, Published by Cell press open Acess, Trend in Biotechnology, August 2022, Volume no. 29.

[8]. Deepanmol Singh, Ashish Mathur, Smriti Arora, Souradeep Roy, Neeraj Mahindroo, Journey of organ on a chip technology and its role in future healthcare scenario, Published by Elsevier, [31 March 2022]

[9]. Liu X, Su Q, Zhang X, Yang W, Ning J, Jia K, Xin J, Li H, Yu L, Liao Y, Zhang D. Recent advances of organ-on-a-chip in cancer modelling research. Biosensors. 2022 Nov 18;12(11):1045.

[10]. Choi, Y., et al., A micro engineered pathophysiological model of early-stage breast cancer. Lab on a Chip, 2015. 15(16): p. 3350-3357

[11]. Subia B, Dahiya UR, Mishra S, Ayache J, Casquillas GV, Caballero D, Reis RL, Kundu SC. Breast tumour-on-chip models: From disease modelling to personalized drug screening. Journal of Controlled Release. 2021 Mar 10;331:103-20.

[12]. http://ink.springer.com/article/10.1007/s10439-022-02902-7

[13]. Abadpour S, Aizenshtadt A, Olsen PA, Shoji K, Wilson SR, Krauss S, Scholz

[14]. Pancreas-on-a-chip technology for transplantation applications. Current diabetes reports. 2020 Dec;20:1-3. https://dailyevergreen.com/135347/news/researchers-develop-gut-on-a-chip-technology-to-study-e-coli-future-treatments/

[15]. Francis I, Shrestha J, Paudel KR, Hansbro PM, Warkiani ME, Saha SC. Recent advances in lung-on-a-chip models. Drug Discovery Today. 2022 Sep 1;27(9):2593-602.

[16]. Clapp N, Amour A, Rowan WC, Candarlioglu PL. Organ-on-chip applications in drug discovery: An end us er perspective. Biochemical Society Transactions. 2021 Aug 27;49(4):1881-90.

[17]. https://www.cambridge.org/core/journals/mrs-communications/article/abs/multiorgan-on-a-chip-for-personalized-precision-medicine/CC78A8DF36F173510F7A4E9A8AE1FAC3