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Bioreactors: A Potential Treatment for Chronic Illnesses That Necessitate Organ Transplantation

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Abstract
The process of turning raw materials into biological products and/or less undesirable byproducts takes place in vessels or tanks known as bioreactors.As the medical field continues to advance, the possibilities for bioreactor modifications and research gaps in organ growth are becoming more numerous. Bioreactorsare a type of laboratory equipment used to grow living tissue in a controlled environment by mimicking the natural environment of cells. The ability to create and modify bioreactors to grow organs in the labhas the potential to revolutionize organ transplantation and the treatment of numerous diseases. Further research into the possibilities of bioreactor modifications and organ growth can have a profound impacton the medical field, particularly for those with life-threatening conditions who desperately need transplanted organs. As such, exploring these possibilities can lead to better treatments and outcomes for patients in need. this review article gives an overview of the types of bioreactors and their implications.
Keywords:Bioreactors, Types of bioreactors, Research gaps, Modifications.

Introduction

Available types of bioreactors

1. **Stirred tank-type bioreactor**

Stirred-tank bioreactors are suitable for industrial production because of their many benefits. They enable the handling of animal cell cultures that are both anchorage-dependent and independent, simple scaling up, a homogeneous environment for cell growth and proliferation, and relatively simple control of product quality[1]. Consequently, they play a crucial role in the creation of biopharmaceuticals. However, stirred tanks also have some serious disadvantages. For instance, the cultivated cells may suffer damage as a result of the shear stress created by their mechanical motion. But such damage can be reduced by adjusting the impeller blade's shape and diameter, or by adding bovine serum albumin, serum, dextran, or the non-ionic surfactant Pluronic F68 to the culture medium[2].

2. **Airlift bioreactor**

In commercial procedures, airlift bioreactors are frequently used, and it has been reported that hybridoma cells were successfully cultivated in a 10,000-liter airlift bioreactor to manufacture monoclonal antibodies. This type of reactor's construction is considerably different from that of a stirred-tank bioreactor since both oxygenation and agitation occur simultaneously, with an oxygen flow that typically contains 5% CO2 in place of the stainless steel agitated system. As a result, it generates very little shear stress, and the grown cells rarely sustain damage. However, significant cell damage from aeration, particularly from bubbles smaller than 2 mm in diameter, can occur during high-density large-scale growth[3].

3. **Hollow fiber bioreactor**

It is more advantageous to employ a hollow fiber configuration because of its high surface-to-volume ratio, for membrane reactors. This ratio enables the production of a high biocatalyst density in a tiny volume of the reactor. Animal cell culture was first carried out in hollow fiber bioreactors, which are still

widely used today. This type of bioreactor's key advantage is that nutrients are continuously provided, minimizing nutrient limitation and the buildup of harmful metabolites. Such circumstances allow for a high cell density of 109 cells per milliliter[4].

4. Rotating wall vessel bioreactor

A rotating wall vessel bioreactor (RWVB), in which the culture vessel is made up of an inner and an outer cartridge, was used by NASA to build the rotary cell culture system (RCCS) in the 1990s. It is also referred to as a space bioreactor since the RCCS bioreactor can mimic the microgravity conditions of space. An RCCS bioreactor allows the direction of the cultures' gravitational pull to be randomly altered while it rotates, reducing the environment's gravity and simulating the microgravity of space. Animal cells cultivated in RCCS can develop in three dimensions in a standard tissue culture incubator because of reduced shear stress, high mass transfer, and the microgravity effect[5].

5. Wave bioreactor

A non-pathogenic defective parvovirus called adeno-associated virus (AAV) is one of the most promising vectors for delivering genes in human clinical trials. The current enrollment in rAAV clinic gene therapy studies appears to be a hint that this virus will be extensively studied in human diseases. The volume of rAAV production and the use of AAV vectors for commercial purposes are, however, constrained by the expansion and transfection of adherent cells. To produce an AAV vector, a wave bioreactor has been employed to cultivate suspended SF9 insect cells. Based on physical characteristics and physiological activity, the particles generated are identical to those made by 293 cells[6].

6. Shaking bioreactor

a bioreactor that shakes, comprising a shaker and a cylindrical vessel with a height-to-diameter ratio of 3:2, and a method for growing animal cells has been created.

7. Helical ribbon Impeller bioreactor

By the early 1990s, helical and double helical ribbon impellers (HRIs) were embedded in bioreactors to be well adapted for shear-sensitive suspension cultures. Despite the presence of surface baffles, which reduce power input, HRI bioreactors reduced shear damage and improved power dissipation, mixing rate, and OTR, particularly in viscous plant cell suspensions, by generating, re-dispersing, and entraining bubbles from the upper gas interface[7].

8. Membrane bioreactor

Technically, MBRs have a convenient in-situ separation capability that other types of bioreactors lack. Furthermore, MBRs provide complete cell retention as well as selective removal of products as well as harmful metabolites and by-products. Membranes are classified according to their geometries, which include ceramic capillaries, plate-and-sheet (flat), tubular, spiral-wound, and polymeric hollow-fiber modules[8].

9. Tubular membrane bioreactor

Tubular MRBs (TMBRs) with various membrane systems, such as hollow fibers or ceramic capillaries, have been designed with high surface-to-volume ratios for high-density plant cell cultures with low shear stress. TMBR has been used successfully to improve the extraction of betanin from beetroot (Beta vulgaris) and ajmalicine and yohimbine from Madagascar periwinkle (Catharanthus roseus) cells[9].

10. Silicone-tubing aerated bioreactor

In various types of bioreactors, silicon-based materials are replaced with polypropylene membranes. Bioreactors with silicone tubing provide a bubble-free oxygen supply, making them ideal for somatic embryo production. Surprisingly, the use of silicon tubing in STRs prevents foaming when the stirrer is set to low speed[10].

11. Slug bubble bioreactor

The rate of oxygen transfers and the appropriate mixing with a low shear force are critical issues in bioreactor systems for plant micro propagation[11].

12. Disposable bioreactor

Disposable bioreactors (DBRs), also known as single-use bioreactors, are made of single-use plastic bags that are suitable for plant cell suspension culture. DBRs save time and money by eliminating cross-contamination and reducing turnaround time between runs[12].

13. Bed bioreactor

Cell immobilization is used in bed bioreactors.These bioreactors are made up primarily of (a) fixed or packed bed (PBB) bioreactors and (b) fluidized bed bioreactors (FBB). A cellular or enzymatic biocatalyst is immobilized in or onto a solid support in an FBB, while a fluid (gas or liquid) is passed at high velocities through a solid granular material (usually a catalyst, possibly shaped as small spheres) to suspend the solid phase and allow it to function as a fluid. PBBs, on the other hand, are made of high- density packet micro carrier material (typically sphere particles ranging in size from 100 to 300 lm) that form a fixed bed. Circulating liquid nutrients across beds supplies nutrients and oxygen to cultured cells/tissues, as well as organ parameters to improve cell culture performance[13-15].

13. Mist/spray bioreactor

Mist bioreactors are gas-phase devices with the greatest potential for hairy root cultivation. Unlike in liquid bioreactors, roots grown in mist/ spray reactors are not oxygen limited even at high bed densities; and secondary metabolite production is often higher in mist bioreactors than in liquid phase reactors. A spinning disc, a compressed gas atomizer, or an ultrasonic droplet generator can all be used to disperse liquids. Furthermore, droplet size is an important consideration in mist reactors because smaller droplets have a higher surface-to-volume ratio, which facilitates gas transport into liquids. For root irrigation, the minimum applicable droplet size is approximately 1 ml[16].

14. Super-spinner bioreactor

Because they can reduce shear forces, super-spinner bioreactors with a low-speed central membrane stirrer are suitable systems for plant cell suspension culture[17].

15. Photo bioreactor

Photo bioreactor (PBR) systems generate biomass by cultivating phototrophic microorganisms such as plants, microalgae, and cyanobacteria in the presence of a light source. To that end, transparent material in a PBR constrains the culture. The compact PBR or compact tubular PBR, a new generation of PBRs, are efficient systems for supplying biofuel/electricity and synthesis of novel materials. Because of their high photosynthetic efficiency and salt tolerance when compared to field crops, microalgae are suitable cultures for PBRs[18].

16. TIS/Temporary immersion bioreactor

TIS originated in 1983 when scientists created an apparatus called "auxophyton" that combined aeration and liquid medium culture. Auxophyton rotated the culture containers on a wheel, exposing the experimental plants to air or liquid alternately. The carrot tissue weighed 2.6 times more after 20 days than the tissue cultured on agar medium. Previous attempts with carrot tissue culture failed due to a lack of oxygen, possibly. TIS-based bioreactors have been subjected to numerous changes since that time. All devices, however, meet the described requirements, including (a) no continuous immersion (b) sufficient mixing and OTR (c) consecutive medium changes automation (d) low shear stress, contamination, and costs[19].

Parts of the human body can be generated by a bioreactor.

- Lungs
- Kidney
- Liver
- Bones

Limitation

- The system must be small enough to fit in typical lab-grade incubators, flexible enough to accommodate different loading requirements, and simple enough to assemble and operate for a large audience.

- Longer culture times may be necessary for several applications, including the examination of radiation damage (from space radiation or other sources), normal and pathological growth mechanisms, and drug development applications. Therefore, adding methods to extend the length of culturing without reducing cellular viability presents another difficulty for future bioreactors.
- Finally, access to the tissue surface may be necessary for in-situ monitoring during long-term culturing.
- Limitations include bulky design, low shear stress, forced perfusion, interruption in perfusion during loading, restrictions in terms of tissue size and/or culture period, or a combination of these.
- Even though existing bioreactors have significantly contributed to our understanding of the functional and cellular activity assessment of bone tissue, these bioreactors have drawbacks.
- Additionally, the majority of lab-grade bioreactors are less flexible for use in business and healthcare because they are not intended for a larger audience or high throughput applications.
- To meet the need for a wide range of research and clinical application, the next-generation bioreactor must solve the limitations of the current system and offer an approachable and adaptable design[20].

Other functions of bioreactors

1. In creating and evaluating in-vitro model studies in DMPK studies.
2. Used in research and development of extracorporeal bio artificial organs.
3. Bioengineering of human organs.
4. Production of vaccines within the period.

Benefits of using bioreactors

The prospects of bioreactors in the organ growth field are exciting. By using bioreactors, we can create organs that are more similar to natural organs[21]. This could potentially help us to solve the organ shortage crisis.

The future of bioreactors in organ growth is looking very promising.

Some of the benefits of using bioreactors include:

- improved oxygenation
- improved nutrient delivery
- improved cell growth and viability
- reduced risk of infection

Potential modifications to bioreactors

Numerous modifications have been implemented in bioreactors since their development, but the most significant results in recent years have been the increasing use of bioreactors that are specially designed for growing larger pieces of tissue or even whole organs. The modifications of bioreactors to grow larger tissues or organs are made to improve the efficiency of the artificial organogenesis process and produce organs that are viable for transplantation or therapeutic applications[22]. The most significant modifications to bioreactors made to grow more prominent pieces of tissue or whole organs include

- increasing the volume of the bioreactor,
- optimizing oxygen levels,
- and improving the nutrient supply to the bioreactor.
- An increased volume of the bioreactor allows for a larger piece of tissue or organ to be placed in the bioreactor, which increases the amount of time it takes for an organ to be fully grown in the bioreactor.

  By using these modifications scientists have grown vital human organs such as kidneys, liver, bone, lungs, etc.,

Research gaps in organ growth

Though significant progress has been made in the fields of organ engineering and bioreactor research, there are still significant gaps in knowledge that must be addressed before fully functional organs can be grown by bioreactors. Researchers have not yet been able to determine

- the ideal conditions for organ growth in a bioreactor, including the optimal oxygen levels, temperature, pH levels, and nutrient concentrations for different types of organs.
- Another significant research gap in organ growth in bioreactors is the lack of an effective technique for organ transplantation after organ growth in a bioreactor.

Researchers are working to develop an effective method of transplanting organs grown in a bioreactor and ensuring that they successfully integrate with the body[23-25].

Conclusions and future implications

Bioreactors are a type of laboratory equipment used to grow living tissue in a controlled environment by mimicking the natural environment of cells. The ability to modify these bioreactors to grow organs in the lab has the potential to revolutionize organ transplantation and the treatment of numerous diseases. As the medical field continues to advance, the possibilities for bioreactor modifications and research gaps in organ growth are becoming more and more numerous. Modifications to bioreactors can lead to better treatments and outcomes for patients in need.

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