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A Comprehensive Study of 3D- Bioprinting by Hydrogel-Based Bio-Inks

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ABSTRACT

Biomaterials printing of three-dimensional (3D) type gives an excellent alternative in the production of allograft organs and tissues to overcome the incidences of organ shortages and donor scarcities. With the present shortage of readily viable and available organs for transplantation, the medical field is encountered with the shortage in supply and an increasing organs demand. In last decade, regenerative medicine and tissue engineering (TE) continue to give alternative methods for artificial organs and tissues. Current research presents those implying hydrogels as a bio-inks of cell laden type for the 3D tissue fabrication builds allows an immunogenicity lack, sine the bio-ink based on hydrogel is specific of patient and described from biopolymers which illustrate extraordinary biodegradability and biocompatibility, lowered rejection of organs, enhanced viability of organs, and increased the supply based on demand. Although enough evidence leads researchers and scientists to conclude the efficient and safe procedure of seeding biomaterials, cells, and biomolecules utilizing 3D bioprinting, there are several restrictions, that needs appropriate attention, such as integrity, strength of biomaterials, cost, and volumetric bioprinting, as well as multi-material and multicellular bioprinting. In this paper, we are providing the overview of various applications of hydrogels as bio-inks implied in 3D bio-printing. Moreover, article provides an efficient multidisciplinary application of hydrogel-based bio-inks.

Key words: Bio-inks, Biomaterials, Bio-printing, Hydrogels.

1. INTRODUCTION

The process of generating models of cell-laden into functional tissue and body organs utilized for transplantation and testing of drug, is known as the 3D bioprinting. The recent popularity and interest in 3D bioprinting prove the ability for technology of 3D bioprinting to decrease heavy burden of fabrication procedures in regenerative or reconstructive medicine [1]. 3D bioprinting gives researchers of tissue engineering with biomaterials based on bio inks to the structures of biologically relevant 3D print.Various biomaterials of these types have been illustrated an increase in durability and strength compared with the authentic organ or tissue. Although, bio inks are generally based on the frameworks of hydrogel. 3D bioprinting grants various advantages over traditional tissue implanting for tissue engineering. It permits for the accurate placement of biomaterials, cells, and biomolecules in a spatially predetermined 3D position. This type of printing having a variety of techniques such as selective inkjet, sintering, and extrusion bioprinting, that reduces the restrictions of traditional tissue engineering with integration of a computer-aided design (CAD) [2].

3D bioprinting might be utilized to generate structures of biomimetic based on estimated image of tomographic gathered from an injured or damaged human body organ and putting these data to a CAD system and it leads the generation of a specific structure of patient.While appropriate proof directs researchers to prove the efficient and safe procedure of seeding biomaterials, cells, and biomolecules utilizing 3D bioprinting, there are various restrictions, which needs appropriate attention, such as integrity, volumetric bioprinting, strength, and cost of biomaterials, as well as multi-material and multicellular bioprinting [3]. In this paper, the attention is on the considerations, limitations, and applications of hydrogels as bio inks utilized in 3D bioprinting.

2. METHODOLOGIES TO HYDROGEL BASED ON THE 3D BIOPRINTING FOR THE REGENERATION OF TISSUES

The initial method of 3D bioprinting is to give seeding of homogeneous cell and accurate implantation of cells to create structures of complex multifunctional. The implantation of cells includes placing cells onto a bio-degradable scaffold, which is necessary for the development and growth of cells for tissue engineering [4]. The traditional method to tissue engineering needs acquiring isolated cells onto a porous scaffold, that is then obeyed by into the implantation of vivo. Polyglycolic acid (PGA) has been utilized as a choice of polymer, owing to its biodegradability and thermoplastic [5]. This bioprinting method for tissue engineering has many limitations, which are as follows:

- Tissues and organs are the structures of multifunctional, containing an array of various species of cellular types which require appropriate location for effective functioning, which located a significant technical problems as traditional tissue engineering lacked the capacity to appropriate position tissues or cells [6].
- The choice of polymer is polyglycolic acid, lacks limit and contractability this implication for rheumatology [6].
- Cellular attachment, placement, and development need a scale of time from weeks to months. Placement of cellular lacks uniformity [6].
- Traditional volumetric tissue engineering is bounded by the lack of vascular structures [6].

Currently, these restrictions might be considered by utilizing 3D bioprinting as a method for tissue engineering. Computer aided design procedures are utilized to build a 3D system of living cells around a biodegradable temporary scaffold. This permits for fast volumetric printing and generation of complex organs of multicellular types. 3D bioprinting also permits for the concurrently scattering of cells and biomaterials, outcoming in the efficiency of seeding and the obstruction of distribution for non-homogenous cell becauseseeding of post fabrication [7].

3. 3D- BIOPRINTING METHODS FOR THE FABRICATION OF CELL-LADEN BASED ON THE HYDROGEL BIO INKS

3D bioprinting techniques are utilizing for the fabrications of cell laden through hydrogel-based bio inks. These bioprinting are of different types which are described in following types.

3.1 Inkjet Bioprinting

This type of bioprinting is the procedures of scattering droplets of picolitre of the bio inks, through a process of non-contact on to a substratum. The benefits of employing this type of printing scheme cell laden hydrogels contain enhanced speed of printing, which might be attributed to the capacity of printer nozzle to permit for parallel workflow, relatively decreased acquisition, and utilization costs, and high cell viability. Inkjet bioprinting might be described into two wide classes, based on the employed mechanism to develop the droplet for dispense.

3.2 ThermalInkjet Bioprinting

Comprises the electrical heating of the head of the printer, creating pulses of pressure, and impels excretion of the droplet size of 10-15 per liter. The necessary temperature for this method lies between 200 to 300^{o}C. Because of the duration of very short heating, there is just a fluctuation of 4 to 10^{o}C of the entire system; therefore, there is not appropriate harm to the biological substances [8]. Figure 1 demonstrates the complete structure of the functionalities of the 3D bioprinting working principle. This Figure provides an outstanding performance efficiency of the bioprinting system for the application of 3D imaging processes in various medical purposes.

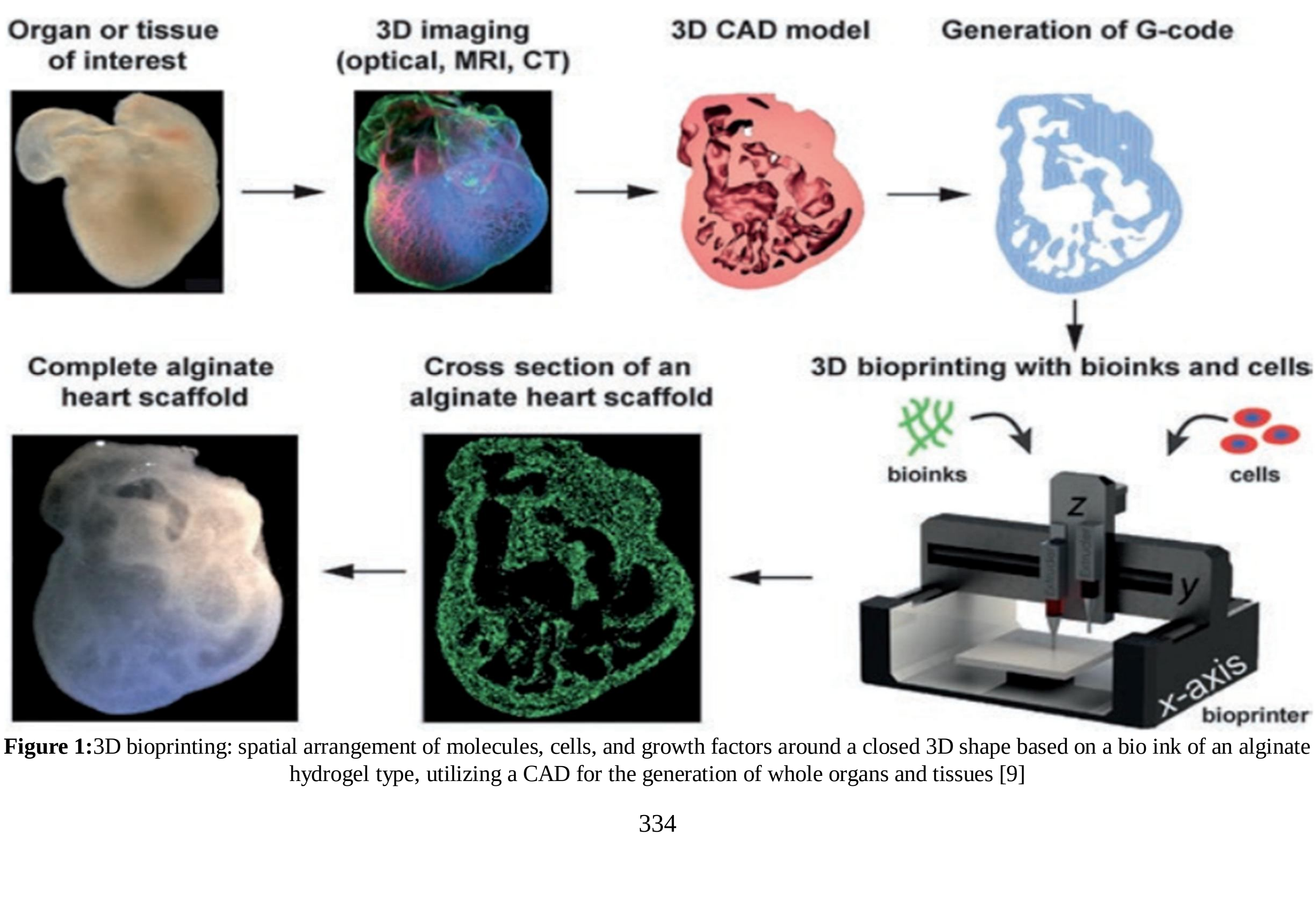

Figure 1:3D bioprinting: spatial arrangement of molecules, cells, and growth factors around a closed 3D shape based on a bio ink of an alginate hydrogel type, utilizing a CAD for the generation of whole organs and tissues [9]

3.3Micro Extrusion Bioprinting

This type of bioprinting includes a stage, that might move around planes of three orthogonal, XYZ; a cartridge with temperature-controlled dispensing; an area with fiber-optic light illuminated deposition; a video camera; and a humidifier. Micro extrusion creates constant biomaterial beads that means distributed in 2-dimensional area with the help of a CAD, unalike inkjet bioprinting, that discharge droplets. Everylayer of deposited area serves as a primary base for the following layer, while the printer or the stage directly moves along the Z-axis.

3.4 Laser-Assisted Bioprinting

Laser-assisted bioprinter (LAB) having components, which are given below:

- Sources of pulsed laser
- Ribbon which helps in the printing of biological materials
- Receiving platforms

The LAB inbuilt with multilayer ribbon having of a support. The transparent layer is known as the support relative to the wavelength of the laser radiation, which is then overspread with a layer of transfer, generally known as the bio ink. The bio inks optical properties or the laser wavelength leads whether that the layer of laser-absorbing addition between the bio ink and support will induce ejection [10].

Figure 2 illustrates the different types of the 3D bioprinting and it defines the complete process, principle of working and several applications of this type of printing scheme. Thus, this Figure shows the complete structure of 3D bioprinting.

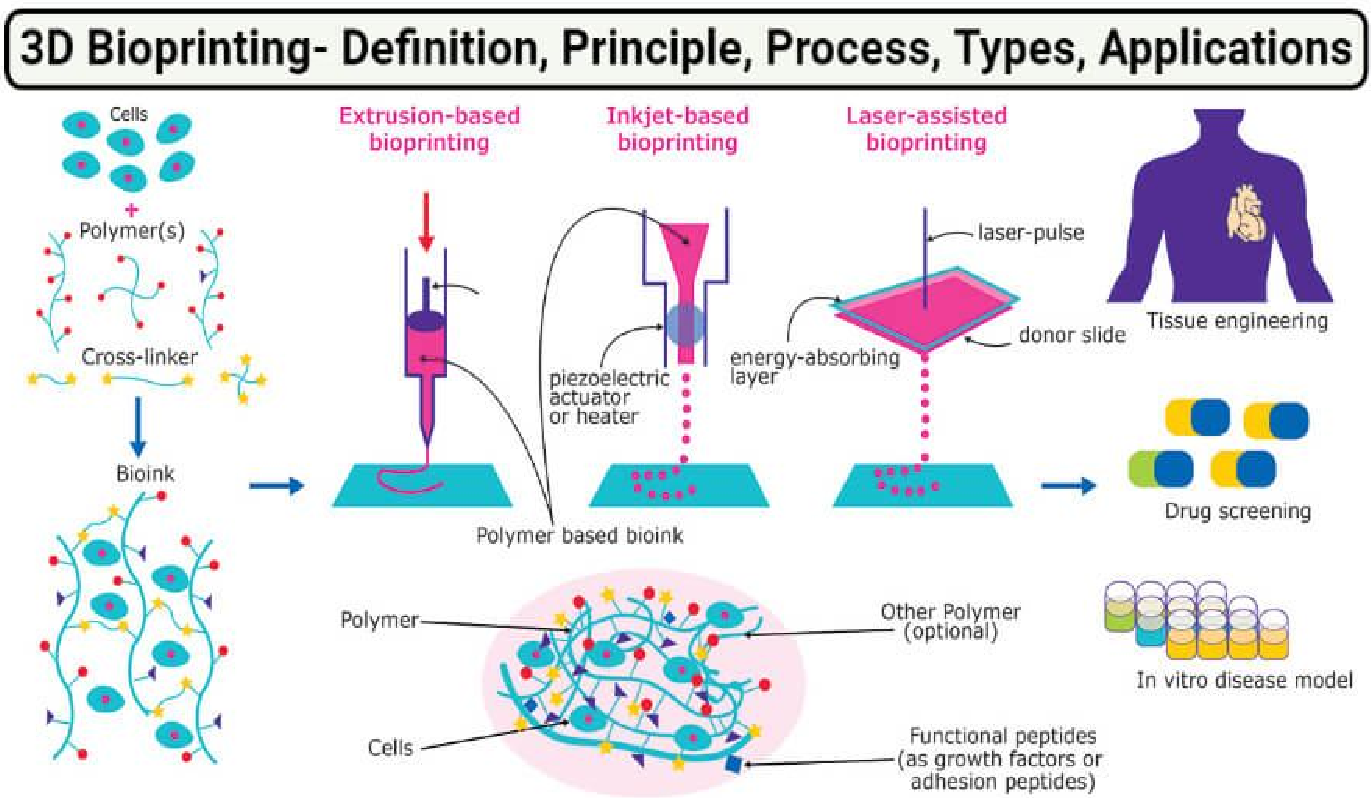

Figure 2: 3D- bioprinting definition, process, applications, and types [11]

4. CONSIDERATION OF HYDROGEL BASED BIO INKS FOR THE 3D BIOPRINTING

Currently, soft biomaterials utilized for enhancing the structures of cell-laden and giving a convenient environment for cellular development and growth are based on hydrogel. Hydrogel are described as networks of 3D consisting of polymer chains of crosslinked hydrophilic, distinguished by their biophysical properties of array and high-water content. Hydrogels might be printed and designed into several forms, shapes, and sizes to reach the final requirements of product. The efficient hydrogel properties are that it might be designed to copycat the microenvironment of extracellular tissue, allowing its application in medical fields as biosensors, technology of drug delivery, and scaffolds for the regeneration of tissue [12]. In tissue engineering hydrogels are attractive as cells, cancer research, and stem sell, considering to recent enhances in 3D bioprinting. Considerations should be delivered to the restrictions of certain hydrogels which, based on implantation, might introduce several side effects estimated by the residues of polymerization, such as catalysts, monomers, and reaction initiators. Residual monomer of methyl methacrylate, created during the poly polymerization, outcomes in death and cellular damage, skin and ocular irritation, and damage of central nervous system. The long-term discharge of these substances of toxic types are attributed to degradation and erosion of the polymer over time [13]. Figure 3 represents the different types of application of bio inks in the field of pharmacy.

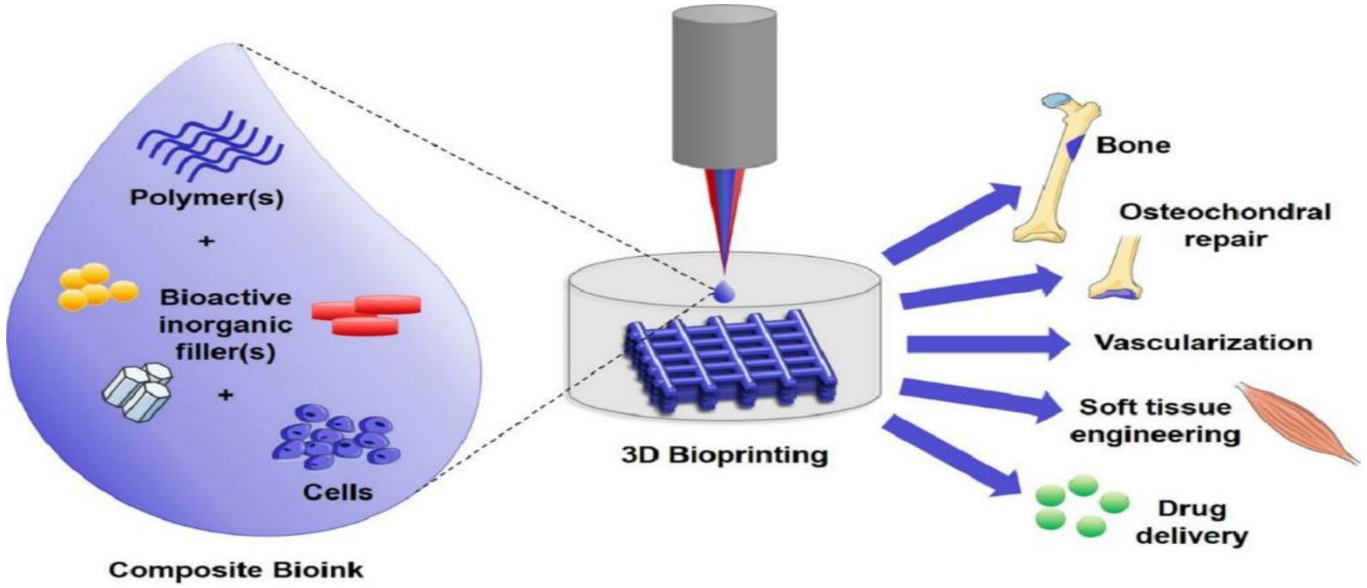

Figure 3: Illustration of pharmaceutical applications of 3D bioprinting [14]

5. REQUIREMENTS OF BIO INKS FOR DIFFERENT BIOPRINTING

Quality and quantity of the bio inks is mostly depending upon the types of the bioprinting. That means what types of the bio ink is available then on that basis we can decide the type of the bioprinting. Figure 4 demonstrates the requirements of the bio inks and modalities of the procedure of the bioprinting. It can describe in detail about the process of bioprinting in details together with the types of requirements of the bio inks requirements by that bioprinting.

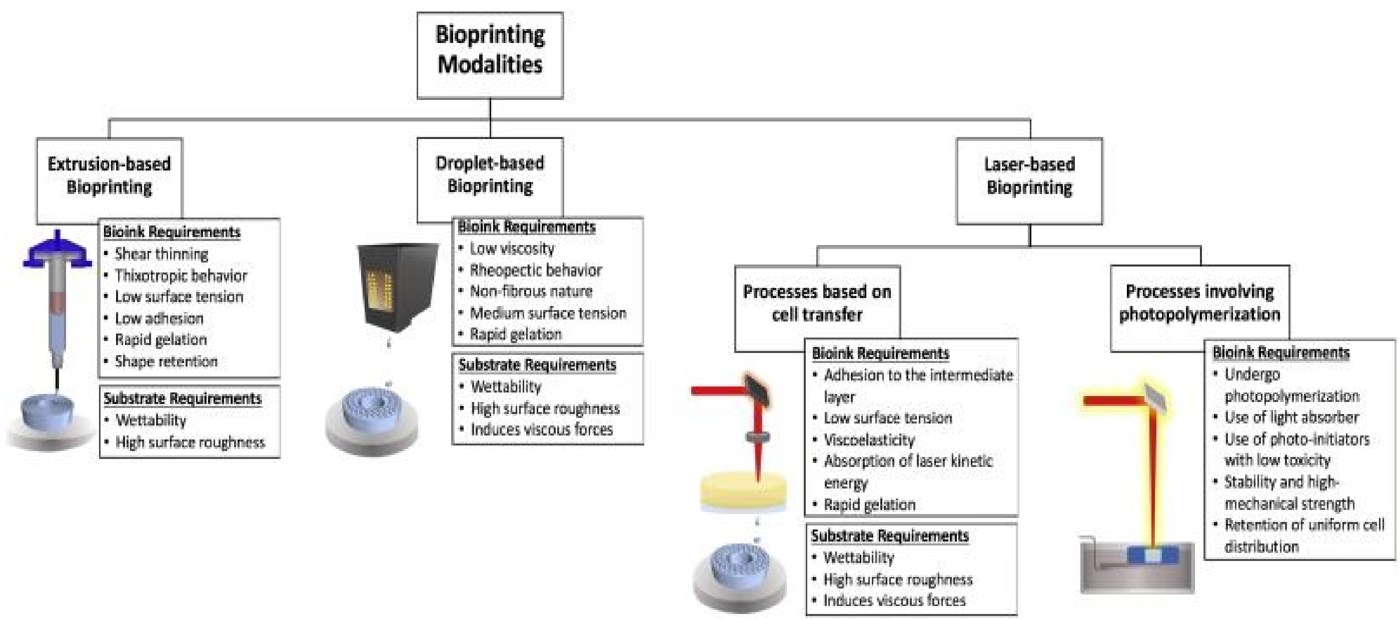

Figure 4: Requirements of the bio inks and modalities of the bioprinting [15]

6. FUTURE RESEARCH TRENDS

Despite the very high progress in the development of biomaterial for regenerative medicine and tissue engineering, relatively very small endeavors of research have been attention to the biomaterial's development for the processes of bioprinting. Most of the researchers of the biomaterial does not focus on the biomaterials refinement for utilize in bioprinting. Thus, future effort must be focused to novel bio printable material for engineering [15]. A novel area of study and research in the development and creation of new materials of bio ink is likely to come in the upcoming future. In near future, development of these bio ink materials, processes of compatible bioprinting must be initially recognized as every modality of bioprinting contains different requirements for the materials of bio inks. Most of the efforts have been focused to cells of engineering. Although, researchers must be focused on the improvement of the qualities of the bio inks.

6. CONCLUSIONS

This article presents the materials of bio inks utilized in the technology of 3D bioprinting, including cell aggregates, microcarriers, hydrogels and describes a detailed evaluation of comparative of these materials of bio inks under several metrics of performance. Future efforts in the materials of bio ink evolution require to collect regarding solutions that will strengthen the properties of mechanical to stabilize the construction of bioprinting, provide compounds of biology to permit better interactions of cellular, facilitate a significant environment to create physiologically relevant, tissues of function which are vascularized and might be integrated with the tissue host after implantation. This paper provides an appropriate overview of the hydrogel-based bio inks introduction, some major applications, major considerations, and future research trends. This article is best for the early-stage researchers, who wants to start their career in this field of study.

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