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Strategies To Enhance Biocompatibility of Bone Scaffold for Tissue Engineering Applications

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ABSTRACT

Tissue engineering (TE) is a modern approach to improve or restore tissues that has been diseased or damaged by combining the factors in growth signaling and appropriate cells to form compatible biomaterial scaffold. Bone repair has been a major global health challenge in recent decades. Bone transplantation is widely used as an effective clinical treatment for this purpose. However, there are several serious issues with transplantation, including a shortage of autologous bone, immune rejection, the risk of virus transmission with allogeneic bone, and postoperative complications. In recent years, scaffolds for bone tissue engineering have emerged as a promising alternative for bone repair. These scaffolds have porous structures that mimic the extracellular matrix, which can enhance the migration, proliferation, and differentiation of osteoblasts. This process accelerates the repair of bone defects.The usage of bioactive materials has become important tool in tissue engineering and regenerative medicine application as they are to mimic tissues mechanically, chemically, and physically. Polymeric scaffold provides numerous advantageous for tissue engineering since the physicochemical properties such as porosity, pore size, solubility and biocompatibility can be controlled. Therefore, research works were carried out to explore the potential of various materials in producing bone scaffolds in tissue engineering technology. As for both newcomers and experts, this review paper will help them to find information on various types of biomaterials in imparting or enhancing their biological properties such as biocompatibility, bacterial inhibition, tissue regeneration and cell growth, bio inertness, bioactive and resorbability for bone scaffold tissue engineering application.

Keywords: Tissue engineering; biomaterials; bioprinting; bioactivity; biocompatibility; antibiotic infusion

INTRODUCTION

The malfunctioning of organs and injured tissues of body had been human issues for decades. Unfortunately, today, elements together with inactivity, obesity, driving injuries, aging and the unfold of diverse styles of bone cancers have placed humans at threat for tissue damage. It has been reported that the bone is the second commonly transplanted tissue in the world (Naderi et al. 2020; Koons et al. 2020). Tissue engineering technique is proposed since the conventional scientific remedy techniques together with autografts and allografts resulted in some disadvantages. For instance, using bone allografts relates to a disease transmission risk from the donor material and using bone autografts affects in extra morbidity related to restoration of the donor site. Bioresorbable membranes are usually used due to the fact they do now no longer require a secondary surgical procedure to be eliminated after bone restoration (Zhang et al. 2020; Wei et al. 2019; Haasanajili et al. 2019). The demanding situations for reaching a research along with drug delivery with complicated biological surroundings encompass premature drug launch in blood, shorter time for blood circulation, loss of cytospecificity and inadequate renal clearance. Further, booming studies interest has additionally been proven in fabricating biomaterials for reaching cell encapsulation and growing tissue engineering scaffolds (Sood et al. 2021). Synthetic chemical compound scaffolds are normally utilized in bone tissue engineering (BTE) relating to their adequate mechanical properties and biocompatibility. However, lack of specific cell recognition sites and also hydrophobicity confined their utilisation (Dong et al. 2017). Bone is defined as body mineralized connective tissue which includes microstructures (like single trabeculae and osteons), macrostructures (consisting of cortical bone and cancellous), nano-structures (fibrillar collagen), submicrostructures (lamellae), and sub-nanostructures (collagen molecules and minerals). The bone natural component consists of collagen proteins, with type I collagen making up the majority (90%). Additionally, non-collagenous proteins such as osteocalcin, growth factors, osteopontin, and bone sialoproteins contribute to its composition. The inorganic component comprises calcium and phosphate ions, which play a crucial role in nucleating and forming small crystals of hydroxyapatite. Bone strength and stiffness are reciprocally proportional to porosity. (Dwivedi et al. 2019). With the important need of novel materials for biomedical applications, extensive research has been carried out creating progressed beneficial materials with good properties (Sood et al. 2021; Su et al. 2021). In this paper, we have discussed the strategies and goals to achieve enhanced bio properties of bone scaffold materials and the essential necessities for implant.

TISSUE ENGINEERING

Tissue engineering field is considered as the regenerative science top pick multidisciplinary the last three decade (Olguín, Y. et al. 2023). Tissue engineering consist of science practices, chemistry, material science, atomic biology, pharmaceutical and engineering. The combination of bioactive particles, biocompatible materials and the local cells are used to form a useful three-dimensional tissue scaffold to overcome issues such as tissue and organ damage. The main aim of tissue scaffolds are to generate porous morphological structures with surface proportion being expanded. The usage of biocompatible materials allows this in order to imitate extracellular matrix (ECM) of the native tissues and giving the cells an appropriate environment to attach, proliferate and to have certain biocompatibility level (Aydogdu et al. 2019; Gao et al. 2022). Tissue engineering scaffold considered to be among the imperative components in tissue engineering; until presently, numerous sorts of scaffolds have been outlined utilizing diverse biomaterials (Figure 1) (Zarrintaj et al. 2018; Pardeep et al. 2020).

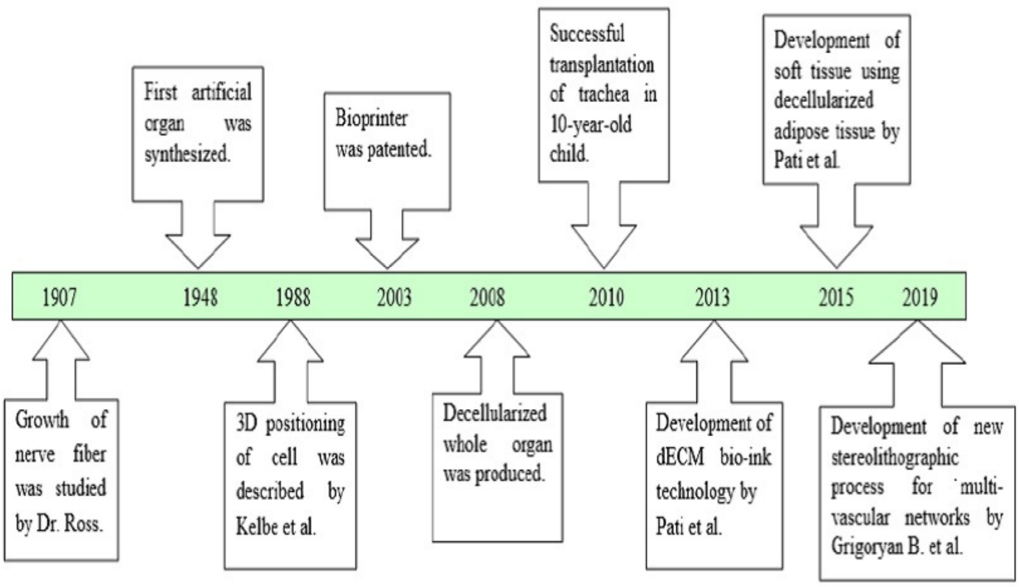

FIGURE 1. Tissue engineering milestone (Pardeep et al. 2020)

Tissue engineering technology is considered viable to ease the organ malfunction around the world by imitating organs and tissue. Commonly, three components are utilized by tissue engineering to create useful construct of tissue: i) only cells, ii) only biomaterials, iii) materials and cells combination within the scaffold shape (Unagolla *et al.* 2020). Tissue engineering scaffolds are being utilized broadly ever since Langer and Vacanti proposed in developing organs and tissues in vitro which gives the cells a three-dimensional (3D) microenvironment. Tissue and organs can continue to survive with the help suitable spatial dispersion and cells signaling. In expansion, they imitate capacities of ECM and permit the migration, attachment, differentiation and multiplication of seeded cells, together with the oxygen and supplements diffusion (Zhang, 2017; Asma, 2020; Fadaie, 2018). Tissue engineering is among the recently created bioengineering range with essential necessities need for implantation (Figure 2) in which different biomaterials are being utilized i.e., bioceramics, biopolymers, other bioinorganics etc. These biomaterials initiate the differentiation signals into distinctive configures transplanted surgically and improves the proliferation toward the tissue recovery within the favored site of the organs or infected/damaged regions in the body (Hasnain et al. 2019; Ranjit et al. 2021).

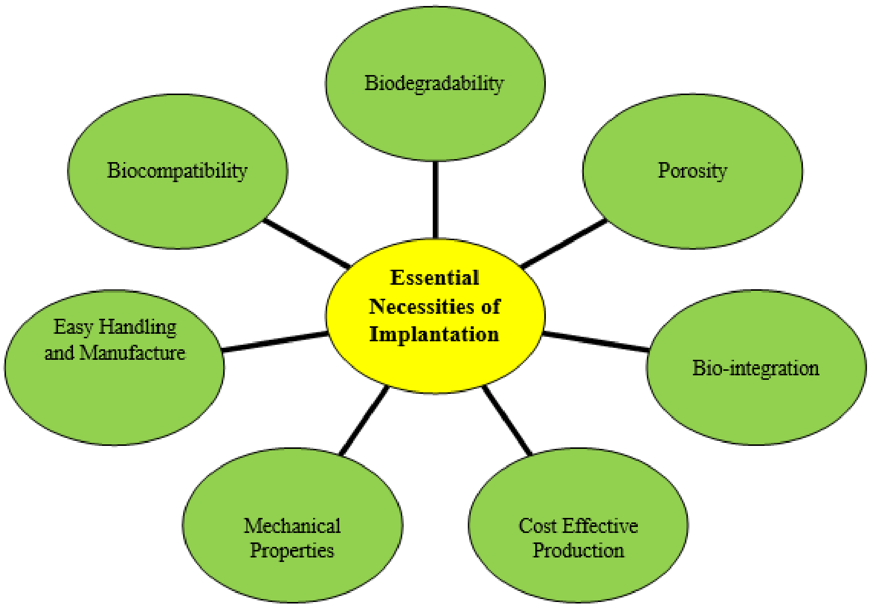

FIGURE 2. The essential necessities required for an implantation (Hasnain et al. 2019)

Materials strategies, engineering and cells are the tissue engineering combination, beside appropriate physiochemical and biochemical variables to supplant or progress biological tissues, including the cartilage, skin, blood vessels, bone and bladder. Advance in cell culture, cell choice and formulations of modern material has driven to more viable treatments for regenerative medication (TERM) and tissue engineering improvement. Different materials have been investigated for regenerative applications, including natural and synthetic materials (Cui et al. 2019).

BIOMATERIALS

Biomedical engineering involves the development of biomaterials, which are specially designed substances that interact with biological systems for medical purposes. These materials can serve therapeutic functions, such as treating, augmenting, repairing, or replacing tissue functions in the body, or they can be used for diagnostic purposes. Biomaterials encompass a variety of materials like metals, ceramics, polymers, and composites. They find wide application in areas such as joint replacements, dental implants, drug delivery systems, and tissue engineering (Mingyua S. et al. 2023)

The important matter in designing biomaterials is that they must be harmonious with their specific structure, physiological environment, function, degradation, and mechanical performance depending on different tissues and organs in reproductive tissue engineering (Liu et al. 2022). For the past few decades, a broad impulse in creating biologically active materials has been laid to design devices for medical applications like electrets, bone joints and scaffolds (Das et al. 2022). Biological tissues are profoundly energetic and viscoelastic. Biomaterials example poly (L-lactic acid) (PLLA) and poly (ε-caprolactone) (PCL) that has been utilized in regenerative medicine broadly do not imitate the native tissues elasticity and semi-crystalline (Wandel et al. 2021). Tissue engineering scaffolds basic parameters of the material are structural composition, surface roughness and wettability (Balavigneswaran et al. 2018).

Collagen could be and exceptionally common natural biomaterial and has been broadly utilized within tissue engineering field. Collagen fiber scaffolds with arrangements have numerous points of interest within the process of initiated repair of particular tissues. At present, there are 29 known types of collagens, among which type I collagen content is the foremost copious within the ECM, particularly in tendons and bones. Collagen in ECM considered to be the major component in human body. Collagen is in the shape of strands, and the arrangement of collagen fiber in several tissues is additionally distinctive, in arrange to meet the needs of distinctive mechanical properties of the body and give fitting living environment for cells. For example, collagen fiber parallel to a single direction are used for the most part that are found in tendons. Meanwhile, collagen strands with various leveled structure are found in cortical bones, and collagen strands in cornea are more often not organized in an orthogonal grid (Ma et al. 2021; Li et al. 2021).

At the time of bone formation and recovery, mesenchymal stem cells (MSCs) and osteoblasts have an important role. Is it known that hydroxyapatite (HA) and collagen (COL) both can initiate bone marrow mesenchymal stem cells (BMMSCs) to differentiate into osteoblasts. The composites with exogenous HA high substance can initiate the separation of MSCs into osteoblasts, whereas the composite with HA low substance can initiate cells to quickly multiply (Ou et al. 2021). Table 1 shows applications and methods of biomaterials in Tissue Engineering.

There are three primary categories of biomaterials namely bioinert, bioresorbable and bioactive materials. Bioinert are the materials that are not tolerant and unable to actuate any bond of biological interfacial between the host and embed tissue. Meanwhile, bioresorbable are the type of materials that are steadily absorbed again until they completely vanish and are entirely supplanted in vivo by new tissue. The bioactive materials on the other hand have the ability in collaborating with body tissue, biological or shaping chemical bonds and favors the improvement process, for example; embed fixation, tissue regeneration and colonization (Oladapo et al. 2019).

Biomaterials that been derived naturally such as cellulose, alginate, collagen, chitosan, silk fibroin and gelatin are generally known in having low immunogenic potential and chemical flexibility, and nearly boundless as resources (Kim et al. 2019). In orthopedic applications, the biomaterials aim is to reestablish the supplant or injured bone structural integrity. Designing scaffolds requires consideration in every biomaterial for example, suitability in the properties of mechanical (such as elastic modulus and particular weight), biocompatibility, great bio-stability (resistance to hydrolysis, oxidation and corrosion), osseo-integration (among the bone prosthetics case), high bio-inertness (non-toxic and non-irritant), high wear resistance, and surgical application ease (Figure 3). Success in tissue remodeling and cell proliferation of biomaterials have shown (Kumar et al. 2020).

TABLE 1. Applications and methods of biomaterials in Tissue Engineering.

Biomaterials	Technique	Application	Advantages	Reference
Hydroxyapatite	SLA, Cryogenic Printing, 3DP	Bone and Hard Tissue	Biocompatible	(Wang et al.2020); (Li et al. 2021); (Yang et al. 2021); (Iglesias-Mejuto et al. 2021); (Antoniac et al. 2021); (Feng et al. 2021); Yang, H. et al. 2023)
Collagen	Synchronous self-assembly, Freeze drying, 3DP, Hybridization	Bone, Cartilage Tissue	Biocompatible	(Liu et al. 2020); (Mosaddad et al. 2020); (Li et al. 2021); (Putri et al. 2020); (Antoniac et al. 2021)

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Chitosan	3DP, Freeze drying	Bone, Peripheral Nerve, Cartilage Tissue, Periosteal TE,	Natural biodegradable	(Hoemann et al. 2022); (Lu et al. 2021); (de Souza et al. 2020); (Cheng et al. 2021)
Gelatin	Freeze drying, Lyophilization, 3DP, Bioprinting, Freeze drying	Soft TE, Cartilage Tissue, Hard Tissue	Biocompatible, Viscosity allows for extrusion, can be used with cells to form hydrogel	(Indurkar et al. 2020); (Nooeaid et al. 2020); (Kreller et al. 2021); (Iranmanesh et al. 2021); (Cheng et al. 2021); (Zheng, J. et al. 2023)
Alginate	Bioprinting, 3DP, Freeze gelation	Soft & Hard Tissue, Cartilage Tissue, Bone Tissue, Pancreas Grafts, Fungal therapeutics	Biocompatible, Provides mechanical strength to cells	(Iranmanesh et al.2021); (Kreller et al.2021); (Iglesias-Mejuto et al. 2021); (Idaszek et al.2021); (Masood et al. 2022)

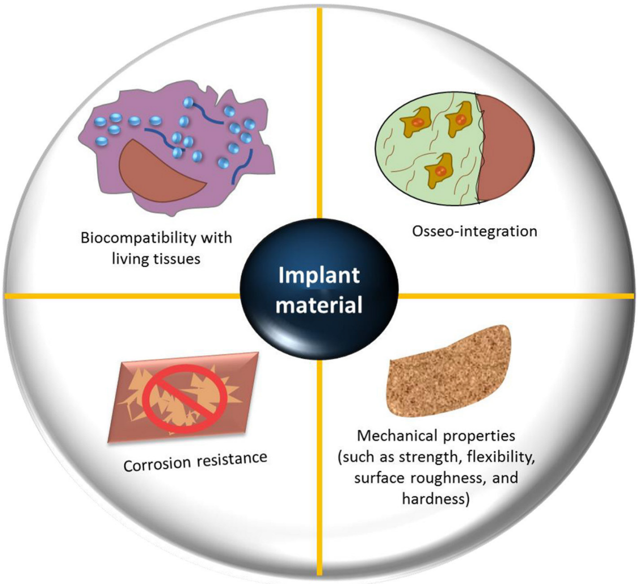

FIGURE 3. Design factors for implant material (Kumar et al. 2020).

Every biomaterial has particular chemical, physical and the ability to manage and manipulate the 3D forms and geometry, along with mechanical characteristics. The choice of fabrication method depends on the scaffold needs, material requirements, and machine parameters (Cámara-Torres et al. 2019).

Bone tissue engineering scaffolds are used to be prepared by various biomaterials including polymers and bioceramics. For instance, synthetic polymers like PCL, poly(lactic-co-glycolic) acid (PLGA), and poly(lactic acid) (PLA) exhibit excellent biocompatibility and suitable mechanical strength, making them well-suited for creating bone scaffolds using various techniques. Also, natural biopolymers like gelatin, chitosan, and collagen exhibit excellent biocompatibility and provide numerous cell recognition sites suitable for tissue engineering applications, but their mechanical properties often fall short, particularly in the context of bone tissue engineering. Apart from that, bone scaffolds also require a range of desired bioactivity for advancing stem cells osteogenic differentiation. Hydroxyapatite (HA), a primary inorganic constituent of natural bone, is expected to exhibit significant bioactivity and finds extensive application in the field of bone tissue engineering. Studies have found that bioactive glasses, glass-ceramics, HA and tricalcium phosphate (TCP) possess high compressive quality, great bone integration and osteoconductivity (Luo et al. 2018; Soundarya et al. 2018; Spiridon et al.2018; Safina et al. 2022). The biomaterials application in tissue engineering is significantly impacted by the morphology, mechanical strength, and surface properties. The cell capacities such as cell multiplication and attachment can be tuned by the surface topography on substrates like honeycomb pores (Shebi et al. 2018).

The major challenge in tissue engineering is the failure to scale biomaterials to build a 3D tissue with microenvironments that imitate its mechanical, chemical, and biological properties. The integration of biomaterial with the host vasculature in vivo or the vascularized organize in vitro is crucial for fundamental particles and supplements to maximize the transport. Additionally, the biomaterial must keep up its properties beneath physiological conditions without causing an immunological reaction within the host. On a very basic level, this factor is significant in clinical interpretation where biomaterial adequacy and patient safety are profoundly related (Nguyen et al. 2020).

BIOPRINTING

The distinction between "*3D printing*" and "*3D Bioprinting*" must be understood on clearly as these two terms being utilized in the scientific community interchangeably. A 3D object is being constructed in both processes layer by layer from a 3D model. In any case, 3D bioprinting includes the cell-laden bioinks utilization and other biologics to develop a living tissue whereas 3D printing advances not involving the utilization of biologics or cells. Porous polymeric scaffolds 3D printing for cell seeding ought to not be confused with cell-laden bioinks bioprinting (Vijayavenkataraman et al. 2018; Ashammakhi et al. 2019).

Bioprinting is defined as the strategic arrangement of living cells, along with other biological elements such as growth factors, through a computer-assisted layer-by-layer deposition process. This method is employed for the fabrication of organs and living tissues. Bioprinting is a rapid prototyping expanded application or a method of additive manufacturing to print layer-by-layer (LbL) materials that are bio-functional when implanted in cytocompatible biomaterials (Zhang,X. et al. 2023). This method involves designing and printing other biological properties or cells, specifically on a tissue culture dish or substrate through a system that automatically dispensed. This interesting advancement guarantees that the particular patient cells and other cell types are together bounded when extruded in biocompatible materials to create the intended 3D functional structures. The bioprinting techniques mechanisms involves (Figure 4) extrusion-based bioprinting, droplet-based bioprinting and laser-based bioprinting (Unagolla et al. 2020; Datta et al. 2018).

3D bioprinting method have the ability in fabricating engineered active organs/tissues with complex tissue design by using spatiotemporal dispersion of bioactive substances, encompassing cells, growth factors, and other elements, serve to enhance the precision of tissue regeneration guidance. It had been broadly utilized to make bone, cartilage, neural and vascularized tissues, cancer models and 4D transformative builds (Cui et al. 2018; Farhat et al. 2021). The material choices utilized in bioprinting may be a difficult work since the materials are frequently complex and opposing in nature. Bio-printing technology requirement consist of: viable cells, 3D printers and polymer solution (Aljohani et al. 2018; Godau et al.2022).

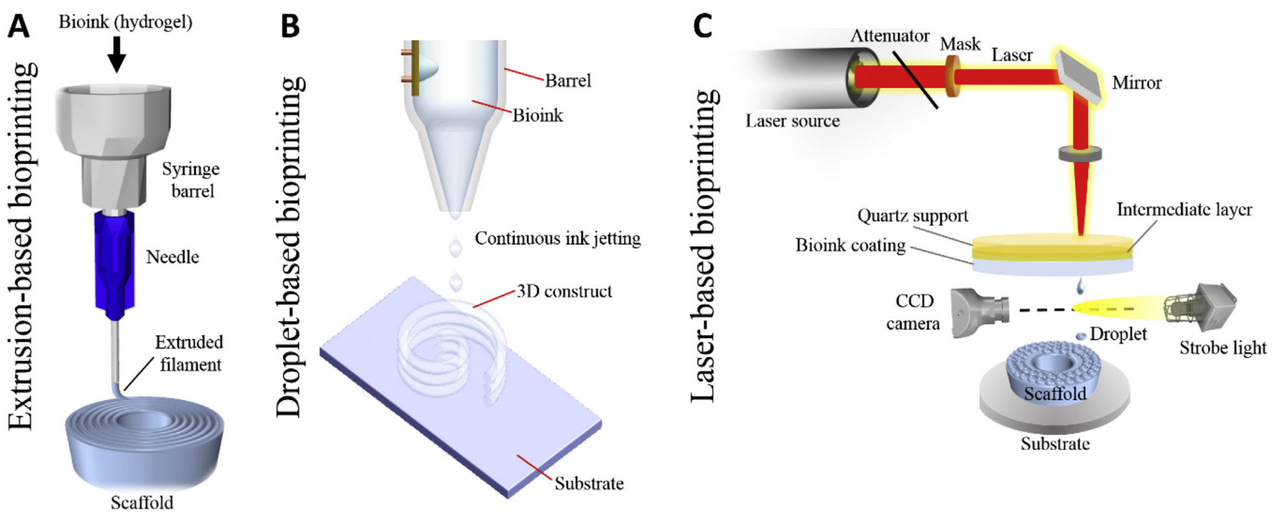

FIGURE 4. Bioprinting techniques mechanisms: A) extrusion-based bioprinting, B) droplet-based bioprinting, C) laser-based bioprinting. (Datta et al. 2018)

Biomaterials that include a foundational structure, cells, and other crucial components are referred to as 'bioinks.' Cell-based bioinks are systematically assembled into desired complex geometries and shapes, facilitating the creation of multifaceted 3D mimetic tissue constructs. This approach holds promise as a gateway for organ and tissue printing, allowing the generation of novel and functional 3D tissues using a cell source. (Matai et al. 2019, Singh et al. 2020). Biomaterials for live-cell printing is not practical if they need organic solvents and high temperature in their printing process. There are two bioinks category: scaffold-based bioinks and scaffold-free bioinks. To have progressed bioink, we must utilize distinctive strategies to extend cytocompatibility and printability.

For occurrence, during extrusion, shear thinning designed bioinks have distinctive properties like produced high shear rates lower viscosities and are able to exhibit with advanced bioinks as shown in (Figure 5) 1) multimaterial bioinks; enhances the functionality of the scaffold being printed, printability while keeping the mechanical strength desired and encapsulated cells incorporating ability, 2) stimuli-responsive bioinks; their function can be changed according to the external stimuli as the field of magnetic, 3) self-assembly bioinks; the element work for the larger constructs fabrication as building blocks in anatomical shapes, 4) biomolecular bioinks; they do not need crosslinkers and the surrounding gel can be degraded by them, they have similar conditions as the natural microenvironment, 5) nano engineered bioinks; contains more than one constituent materials which being additional to polymeric hydrogels that benefits in changes to different mechanical, physical properties and chemical (Mobaraki et al. 2020).

The requirement for exact, on demand, and high-throughput generation of cell-laden structures supports bioprinting`s developing its significance and relevance. This requirements for bioprinting is upheld by a few rising applications in tissue engineering and regenerative medication (Lepowsky et al. 2018, Wan et al. 2020). There are three fundamental variables required for extrusion bioprinting: 1) viscosity adjustability, 2) Pre-extrusion bioink state, and 3) the biofabrication window specific to the material. Viscosity can be shear thinning or temperature function and thus, need to be balanced for varied technique of printing. Furthermore, the bioink needs to be in a liquid state to prevent nozzle clogging. Nevertheless, not all biomaterials are conducive to the printing process, and even among those that are printable, they may not provide an extensive array of processing parameters. (Derakhshanfar et al. 2018; Im et al. 2022).

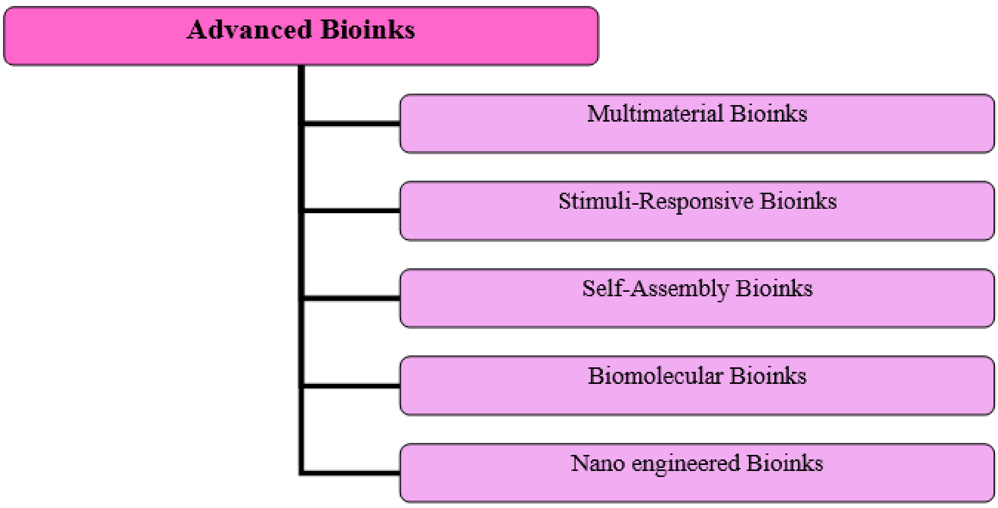

FIGURE 5. The advanced bioinks (Mobaraki et al. 2020)

In spite of being a moderately young whereas inventive technology of tissue engineering, 3D bioprinting faces a few challenges such as recognizable proof of biomimetic and biodegradable materials that are printable and enable prompt cell attachment and proliferation, the requirement for single-cell level of vascularization, complex pattern of heterocellular tissues and long-term functionality post-printing and keeping up cell viability and until regeneration and remodeling is done (Matai et al. 2020). Biological properties can be progressed by functionalizing the hydrogels.

For instance, a polysaccharide-based hydrogel that is broadly utilized in dispensing-based bioprinting, alginate is commonly employed due to its excellent biocompatibility, high printability, and low toxicity. (Naghieh et al. 2018; El-Husseiny et al. 2022).

BIOACTIVITY AND BIOCOMPATIBILITY

The perfect scaffold must have great biocompatibility, interconnected space, mechanical strength and osteoconductivity to supply the area for the multiplication of newly generated osteoblasts and providing an osteogenic microenvironment conducive to bone regeneration. (Sun et al. 2021; Haider et al. 2021). The biomedical molecules and materials play a vital part in tissue healing and regeneration by elective integration with other functional substances such as cells, exosomes, cell development factors, drugs, genes and etc (Wang et al. 2021; Przekora et al. 2019). The novel biomaterials design and development with two functions consisting simultaneous osteoinductive properties and antimicrobial for different orthopedic applications is profoundly interesting for the abandoned and infected bone treatment. Figure 6 shows some of the applications of the biomaterials in various orthopedic applications.

In this case, microbial contaminations are a huge challenge and burden for public and health society, driving in expanding healthcare costs. By adding the antibacterial properties into the fabrication, it can reduce the healing and treatment time. Moreover, the constraints in bone healing can be caused by the defect or bone damage localized infection. Presently, there are various materials with antibacterial properties such as cerium oxide nanoparticles (CeO_2NPs), silver nanoparticles (AgNPs), selenium nanoparticles (SeNPs), copper (Cu), polymers such as carbon nanostructures, antimicrobial peptides (AMPs) and chitosan are that could be used in tissue engineering (Afewerki et al. 2020).

Infections of bacteria can cause triggering of osteomyelitis, an inflammatory response in bone that leading to create biofilms and bone destruction or osteolysis, which brings the treatment of antibiotic a challenge (Cámara-Torres et al. 2021; Khan et al. 2021; Wang et al. 2021). One of the major considerations for creating an engineered tissue scaffold is to confer satisfactory bioactive properties to strengthen the regenerative process as well as in a tissue specific way. Several approaches like pharmaceutical compounds (anti-inflammatory, anti-microbial and antioxidant), different nanomaterials (such as bio-ceramics, metal/non-metal materials and bioactive glass), and growth components have been utilized broadly (Sheridan et al. 2022; Wei et al. 2022). As of now, tissue healing found to be a complex phenomenon and components such as bacterial infections, extreme inflammation and oxidative stress may basically delay the method. Looking into it, nanomaterials and/or pharmacological operators have been joined into tissue engineered scaffold to provide inflammatory, antioxidative and antimicrobial properties and encourage tissue regeneration (Agarwal et al. 2021; Abdelaziz et al. 2021; Vasconcelos et al. 2019). To define pro-regenerative and an antibacterial for surface for bone inserts, combinations of organically dynamic particles and polymers in one coating framework are being progressively explored (Rivera et al. 2021; Zhao et al. 2022).

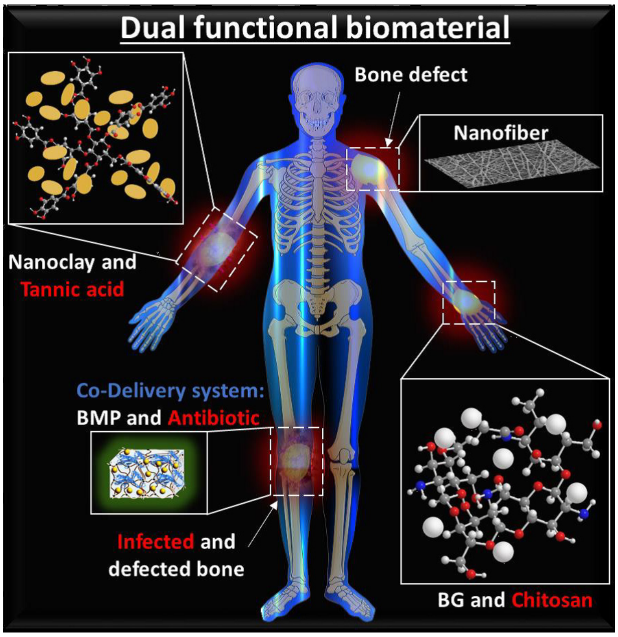

FIGURE 6. Examples of body components with osteoinductive and antibacterial properties (dual functional) for various orthopedic applications (Afewerki et al. 2020).

The few unwanted properties such as (genotoxicity, cytotoxicity, thrombogenicity, immunogenicity and mutagenicity) (Figure 7) as they might be reason in extreme inflammatory reaction and this causes dismissal by the body or reduce healing (Soundarya et al. 2018). Polymers biocompatibility refers to their ability to stay in direct contact without causing harmful impact or inciting immunogenic or allergic reaction with the living tissues.

Therefore, it must be properly managed by any biomaterials for applications in vitro. Essentially, for the applications of in vivo, biocompatibility is been referred to cells ECM integration and degradation potential without creating harmful by products or producing negative connections with the cells (Aljohani et al. 2018; Feroz et al. 2021). The medium within the pore may supply the supplements for cell development while the edge of pores may supply the areas for cell attachment (Lu et al. 2021).

Scaffolds designed for bone tissue engineering necessitate an interconnected structure. This structure should facilitate the exchange of oxygen and nutrients, promote the formation of new vessels through pores, and mimic the specific bone structure of an individual patient. Additionally, surface roughness is a crucial factor that can modify wettability, aiding in the transfer of oxygen and nutrients and enhancing the retention of proteins associated with biocompatibility. The formation of cadherin is being advanced by the higher calcium particle concentrations to improve osteodifferentiation which leads to needed biocompatibility (Dahong et al. 2021; Ruiz-Alonso et al. 2021).

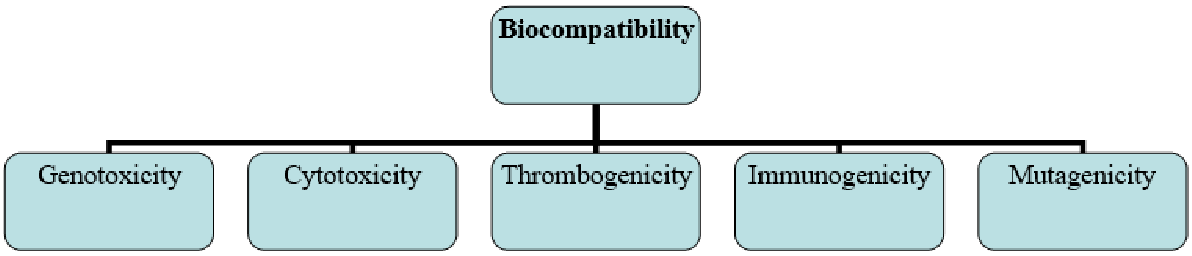

FIGURE 7. Biocompatibility unwanted Properties (Soundarya et al. 2018)

From the past decades, nature has been the major source of bioactive ingredients pharmaceutical advantages and therapeutic properties. Other than the biocompatibility, a perfect tissue scaffold ought to moreover have controlled feasibility and biodegradability for chairside control. The recovery of bone tissue engineering has three fundamental components which includes scaffolds for osteoconduction, cell and gene conveyance for osteoconduction and operators for differentiation/ growth induction. The second and third components can be gained through a variety of useful materials (Moghadam et al. 2021; Zhu et al. 2021).

Scaffolds made of single polyesters can give a sensible three-dimensional (3D) space for cell attachment, migration and proliferation, but an osteogenic induction environment is not offered by them as they need a biologically useful substances. In expansion to calcium particles, growth variables of bioactive osteogenic offers the osteoblasts or stem cells to capture and suitable microenvironment for the adhesion, driving to both in vivo or in vitro osteogenic separation. Bone morphogenetic protein2 (BMP2) may be a normal protein-based development figure, which is basic for stem cells osteogenic separation or osteogenic precursor cells. BMP2 has capable osteoinductive properties, and has in like manner been connected in bone recovery to initiate the stem cells separation into osteoblast (Rahman et al. 2021; Sheehy et al. 2021).

Despite these benefits, the restricted bioactivity presents a limitation to its application. The inadequate interfacial integration between the artificial implant and host bone tissue poses a substantial challenge in clinical practice, potentially resulting in issues such as interfacial loosening, weakness, and eventual failure. To impart bioactivity to PCL implants, various studies have been conducted, including the incorporation of bioceramics into the PCL matrix and surface modification of PCL scaffolds. (Feng et al. 2021). The viability and separation of cell, considered by an ALP activity, (i.e., by seeding the bottom scaffold surface on the cells) to look at the cell cytotoxic potential reaction and the separation of the cellular, respectively. The viability of cells is considered by evaluating the living cells, which the values appear measurable importance with regard to the cultivation time, though no importance between the scaffolds. The increase in ALP activity is essential with the time of culture, at an early stage of ALP activity shown for osteoblast phenotype (Pottathara et al. 2021).

SUMMARY AND FUTURE PERSPECTIVE

As a conclusion, bone tissue engineering is respected among the leading elective approach to the conventional bone joining methods due to different variables as there are numerous biomaterials involved in fabricating scaffold. The creation of scaffold can be done by employing an assortment of methods by taking into count the polymers nature, characteristics and implantation location conferring or improving their biological properties such as biocompatibility, cell growth and tissue recovery, bacterial inhibition, resorbability and bioactive. The methods in fabricating scaffold and the choices of polymer are the important factors to attain these objectives. Besides that, polymers and biomaterials in fabricating desired scaffolds need to have characteristics capacity for cell development support, adequately hold the printed develops shape, an implies for starting to preserve cellular phonotype or cell differentiation and biocompatibility. Whereas each method has its merits and demerits claim share, selecting an appropriate technique is crucial to meet the specific requirements of the tissue type that requires repair. The necessities of a perfect scaffold for bone tissue engineering application is complex, capable knowledge needed from the distinctive science areas for example material science, chemical engineering and biomedical engineering, etc. Another perspective is the bioprinting fabrication process. In order to have a coordinate impact on the ultimate result, suitable criteria of design needed to be choose such as determination, compatibility with cells and speed.

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DECLARATION OF COMPETING INTEREST

None

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