International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(REVIEW ARTICLE)

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Biomaterial scaffolds in tissue engineering: A review of natural, synthetic and hybrid polymers for regenerative constructs

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International Journal of Science and Research Archive, 2026, 18(01), 037-050

Publication history: Received 05 November 2025; revised on 18 December 2025; accepted on 20 December 2025

Article DOI: https://doi.org/10.30574/ijsra.2026.18.1.3260

Abstract

Tissue engineering relies on biomaterial scaffolds, which provide a bioactive three-dimensional structure that encourages cell adhesion, proliferation, and differentiation in order to repair injured tissues. Natural polymers (e.g., collagen, hyaluronic acid, and chitosan) have better biocompatibility and bioactivity than synthetic fossil-based polymers (e.g., PCL, PLA, and PVA), but their mechanical properties and degradation rates can be adjusted. Finally, hybrid materials, which combine polymers with bioceramics or other polymers, offer the best of both worlds. In this article, the authors go over the chemical, structural, and biological requirements for a scaffold to integrate and operate properly. Highlighting the crucial importance of material science in driving regenerative medicine towards clinically feasible and patient-specific therapeutic options, this study evaluates the benefits, limits, and particular uses of varied materials.

Keywords: Tissue Engineering; Scaffolds; Material Science; Medicine; Regenerative; 3D Structure

1. Introduction

Several factors may limit the body's ability to heal wounded tissue. These restrictions include tissue type, injury severity, function loss, and tissue abundance. However, the body can naturally repair injured tissue. Organ transplantation is the best way to regenerate large or complex tissues, however donor tissues and organs are few, making this process difficult to administer. Tissue engineering and regenerative medicine have showed great promise in repairing wounded tissues in recent years [1].

Tissue engineering combines chemistry, engineering, and biology. Its goal is to create biological substitutes for normal tissue that has been lost by significant injuries, accidents, or diseases [2]. To regenerate damaged tissue, tissue engineering uses three main strategies: (1) induced pluripotent stem cells (iPSC) or adult stem cells or genetically modified cells like CRISPR cas9 (productive), (2) biomaterial scaffolds as cell support systems (conductive), and (3) cell signalling molecules like growth factors, genes, or physical stimulus (inductive). Biomaterial scaffolds provide a three-dimensional milieu for cell adhesion, proliferation, and differentiation in tissue creation. The scaffold also stores signalling substances that drive cells to differentiate according to the tissue environment [3].

2. Scaffold features for tissue engineering

Despite the fact that various researches have reported on numerous breakthroughs in tissue engineering, the commercialisation of these newly found functionalities has substantially grown owing to the fact that these results have medicinal applications. Therefore, in order to enhance the acceptability of clinical applications of such technologies, it

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is vital to combine certain biological, clinical, and mechanical characteristics. These features are not only theoretical, but they may also play a role in the actual execution of the technology. In order to promote cell development, vascularization, proliferation, and host integration, an ideal scaffold must be able to mend human tissues with minimal needs. Furthermore, materials should be able to decay naturally either during or after the healing process. On the other hand, a scaffold has certain qualities that are associated with the biological aspect, structure, and chemical composition [4].

2.1. Biological Characteristics

Scaffold biological properties include biocompatibility and nontoxicity. Li et al. [5] state that scaffold-grown cells must be able to proliferate and distinguish without intervention to create a new matrix. Thus, a scaffold is suitable for tissue engineering if it can mimic tissue extracellular matrix (ECM) to accomplish faultless and complete regeneration. As said, the supporting cell's function depends on many factors. Choice of cell line, material underlying surface, surface characteristics, and scaffolding structure.

Rosetti et al. [4] recommend that the matrix not be toxic so the system may remove it without disrupting other members. Scaffold biological properties affect how they interact with organs and tissues, making them important modifiers. To increase cellular contact, migration or differentiation, tissue information, and host integration, bioactive scaffolds have been used. To prevent scarring, bioactive scaffolds are used. Because organic stuff cannot communicate well with its environment. Additionally, the scaffold must defend itself from host immunological responses. Immune-inert biomaterials have just recently been discovered to affect the immune system (reducing NK cell activity and T and B cell-mediated immunity) [4].

2.2. Structural Characteristics

Biological tissue contains sophisticated mechanical processes related to mass transfer in three dimensions. Thus, tissue engineering's main objective is to minimise tissue complexity and function by employing biological scaffolds to reconstruct tissue using cells, proteins, and genes. Biological materials and architectures cannot replicate complicated tissue settings. Many cell types interact with many cytokines to generate extracellular matrices in these situations. High nonlinearity and two-phase mechanical function are shown by these hierarchical matrices. Lack of vascular insufficiency causes ineffective osseo integration, making vascularised engineering scaffolds a major difficulty. Material choice affects scaffold physical properties [6, 4]. To assist cell proliferation, scaffold porosity is typically enhanced. The scaffold with the correct pore size promotes cell motility, water absorption, and oxygen mass transfer [7, 8].

2.3. Chemical Composition

Yang et al. [7] found that most scaffolds are constructed of polymers, bioceramics, and hybrid materials, whether natural or engineered. Biocompatibility, composition, and breakdown products of such matrices are affected by the scaffold's manufacturing ingredients. Despite extensive scaffold research, certain materials do not encourage cell growth. Natural and synthetic polymers are their categories. Biocompatible, osteoconductive natural polymers include hyaluronic acid, fibrin, chitosan, and collagen. Over their lifespan, they exhibit low mechanical stability and significant free degradation. Synthetic polymers including polypropylene fumarate (PPF), polyanhydride, polycaprolactone (PCL), polyphosphazene, PEEK, PLA, and PGA have controlled breakdown rates. Synthetic polymers can be mass-produced cheaply and last longer than natural polymers. According to several in vitro studies, the chemical might entirely degrade ex vivo tissue synthesis compared to actual tissue matrices. Immunogenicity, degradation duration, and degradation product effects may also affect in vivo regeneration [4].

3. Natural and bio-based polymers

Biopolymers, or natural polymers, are made from natural materials and ensure natural structure, biomimetic character, and bioactivity, according to Liu et al. [9]. Synthetic bio-based polymers may be made from biomass monomers. The extraction or transformation of biomass sources into monomers may be used to polymerise new polymers that do not exist in nature. Polylactic acid is a typical bio-based polymer. Biopolymers alone include polysaccharides such chitosan, alginate, and cellulose and polypeptides like gelatin, fibrin, and silk. They play several functions in nature. Natural polymers that mimic the extracellular matrix (ECM) and are biodegradable and bioresorbable are preferred for scaffolding in tissue engineering. New tissue synthesis and degradation should be balanced [10].

3.1. Collagen

Collagen, a biocompatible biopolymer, is easy to make and does not bother the immune system. Present is a porous structure with interconnected pores. The extracellular matrix's structural and biological integrity depends on it. Its

extreme biocompatibility and bioresorbability have helped skin, bone, the nervous system, and the vascular system grow and repair. Collagen fibrils are the main component of connective tissues. Seven types of collagen may generate fibrils. They include collagen types I–V, XI, XXIV, and XXVII. Type I fibrillar collagen is the most common in vertebrates, according to Siadat and Ruberti [11]. The modified collagen fibres (MCF) D-periodic spacing and orientation give open sites for mineral nucleation, proteoglycan binding, and crosslinking. In addition to increasing bone mechanical characteristics, collagen fibril organisation promotes mineral deposit simpler [12]. The properties outlined above allowed this polymer to be used in bone graft tissue engineering (Figure 1) [13].

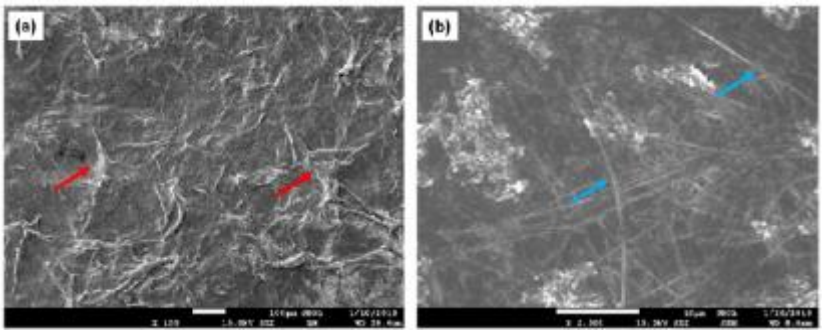

Figure 1 Collagen scaffold surface topography SEM pictures. (a) The scaffold's rough surface is made of collagen fibres (red arrows). Depicted design increases matrix surface area, allowing cell attachment; (b) thorough scaffold architecture study shows collagen fibres orientated unalignedly (blue arrows) (Source: [14])

3.2. Hyaluronic Acid (HA)

HA is a linear polyanionic polysaccharide made up of repeated glucuronic acid and N-acetylglucosamine units connected by alternating β-1,4 and β-1,3 glycosidic linkages. According to Necas et al. [15], this structure is prevalent in all living things and maintains tissue hydration. Since it is involved in mineralisation, it is a main extracellular matrix (ECM) component and may crosslink collagen fibrils [16]. HA is biocompatible, bioresorbable, and flexible in composition and structure within the body. It has been widely employed to make hydrogel composite materials for bone tissue engineering and oral disease therapy, according to Li [17]. The molecular weight of HA affects some physiological functions. High molecular weight HA controls cell proliferation and migration, whereas low molecular weight HA has a function in cell reproduction, according to Zhao et al. [18]. HA is typically treated with chemical groups like methacrylate to improve its mechanical properties as a hydrogel network in tissue engineering [19].

3.3. Chitosan, Fibrin

Other natural polymers being studied for tissue engineering include chitosan and fibrin. These polymers supplement collagen and HA. Polymers may form fibres or foams. Fibrin, an important component of the extracellular matrix (ECM), spontaneously produces gels and thrombuses during wound healing [20]. Chitosan, made from chitin, seems promising for articular cartilage repair. Chitosan's inability to dissolve in water under physiological conditions limits its utility in tissue engineering, according to Wu et al. [21]. The polymer's hydroxyl and amino groups provide many bioactive group derivatisation or grafting options. Chitosan's pH-dependent solubility allows gentle processing. Madihally and Matthew [22] state that this property is crucial when bioactive compounds are needed before developing the material's three-dimensional microstructure.

3.4. Polysaccharides

Polysaccharides are bioresorbable, biocompatible, easy to derivatise, and inexpensive to manufacture. They are ideal for tissue engineering because they resemble the extracellular matrix (ECM). Crab shells contain structural polysaccharide chitin. However, glycogen and starch are storage polysaccharides with similar functions. Due to branching, sequencing, and molecular weight dispersion, natural polymers are difficult to employ to generate homogenous scaffolds without affecting biorecognition and rheology [23].

New nanocomposite fibres for bioactive chemical transmission were made from chitosan and XG [24]. Crosslinked XG, a biocompatible natural substance, may become a soft hydrogel. The use of freeze-drying technology has made it easier and faster to create porous materials for spinal cord rehabilitation [25]. A freeze-drying process was utilised to build the gel scaffold. XG and graphene oxide were coupled via metal coordination and hydrogen bonding. A spinal cord-like scaffold is built using this method. It promotes cell growth and prevents tissue compression. The porous internal three-dimensional structure, analogous to the extracellular matrix (ECM), offers growth space and nutrition transport

pathways for spinal cord tissue regeneration. The electroconductive, porous, and soft gel scaffold proved biocompatible, reduced astrocyte development surrounding spinal cord injuries, and helped injured rats walk [26].

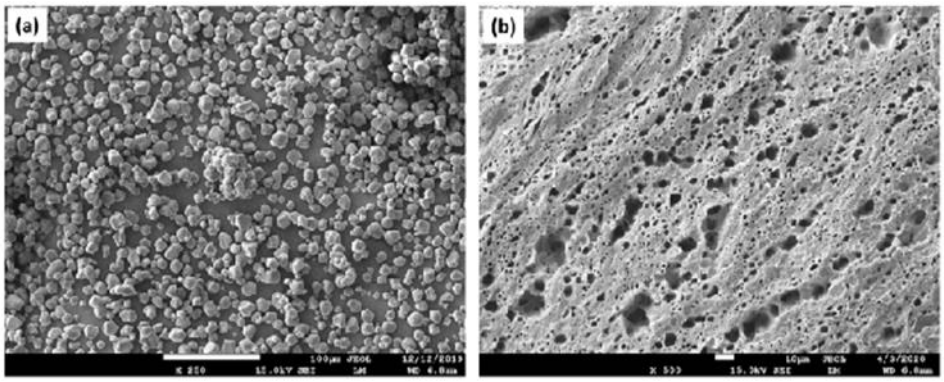

Figure 2 Scaffold engineering using starch. (a) Dispersed starch granules in SEM picture. (b) When added to a polymeric mix as a porogen, starch granules may form a porous structure and change scaffold topography and interior design (Source: [14])

3.5. Poly (Lactic Acid) (PLA)

PLA is a thermoplastic polymer with good biocompatibility, bioresorbability, and mechanical resilience [27]. Lactic acid (LA) becomes polylactic acid (PLA) by condensation polymerisation or ring opening. Due to its chirality and two asymmetric centres, LA may be generated in many ways. In addition to D, it has L, D, and D, L isomers [28]. More than 15% D monomers are employed to form amorphous polymers, whereas L monomers make PLA more crystalline. D, L-lactide forms the amorphous structure of poly (D, L-lactide), although highly pure L- and D-lactides generate semicrystalline polymers like PLLA and PDLA. Due to its many isomers and their distribution, Maadani and Salehinejad [29] state that PLA may be made in molecular weights.

PLA is bioabsorbable, hydrolytically degradable, and does not release harmful chemicals when broken down, making it suitable for scaffold-based implants in TE (Figure 3).

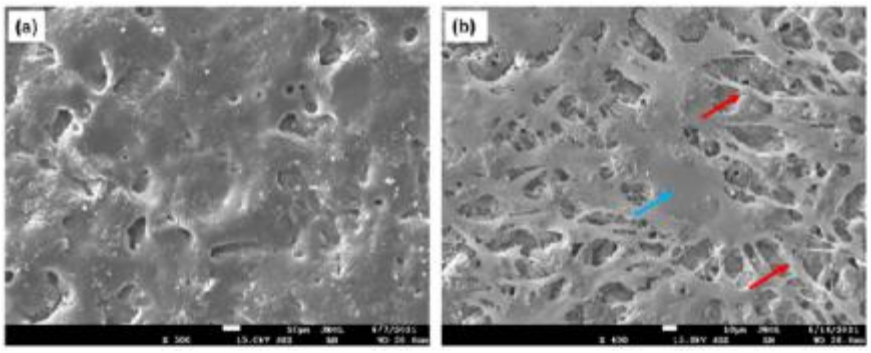

Figure 3 PLA scaffold. (a) Pressed PLA scaffold surface analysis (reference sample). SEM picture shows smooth, uniform cell attachment region; (b) PLA scaffold containing human cells (blue arrow). (Source: [30]).

3.6. Polyhydroxyalkanoates (PHAs)

Bacteria usually produce hydrophobic, bioresorbable linear polyesters called PHAs. A carboxylic acid, hydroxyl-alkanoic acid, produces polyhydroxyalkanoate. This acid is HO-R-COOH. They may have varied molecular weights, shapes, and contents depending on the microbe, growth circumstances, and polymer extraction procedure [31, 32]. These materials may change their morphology and crystal structure using additions including nucleating agents, plasticisers, and fillers. These additives are expected to affect the materials' thermal, mechanical, and bioresorbability [33]. Animal cell membranes include naturally occurring polyhydroxyalkanoates (PHAs). Human blood contains substantial levels of low-molecular-weight poly3-hydroxybutyrate (P3HB), and 3-hydroxybutyric acid (3HB) is a naturally occurring metabolite found in the heart, liver, brain, lungs, and muscle tissue [34]. PHB decomposes into 3HB, a non-toxic, naturally occurring metabolite present in many organs. The nanoparticle form of PHB may affect scaffold properties.

Crystallinity also affects seeded cell biology, notably proliferation [35]. Esmail et al. [36] also found that polyhydroxybutyrate (PHB) scaffold pore size affects cell attachment, proliferation, and differentiation.

PHBV is a popular microbial copolymer for scaffold tissue engineering due to its biocompatibility, bioresorbability, and wet electrospinnability. As blood components, PHBV's biodegradation products diminish tissue inflammation, making it beneficial. PHBV has been extensively studied as a pro-regenerative material for skin tissue engineering [37]. PHBV is commonly combined with ceramic particles to improve cell growth in vitro (bioactive glass, hydroxyapatite) or antibacterial activity (ZnO, TiO2). This is often done to attain aims. According to Kouhi et al. [38], a hybrid structure improves the mechanical properties of weak electrospun PHBV fibres. Living organisms break down PHBV to create hydroxybutyric acid, which the body may easily metabolise [39].

3.7. Hydrogels Based on Natural Polymers

Sheehy et al. [40] describe a hydrogel as a three-dimensional polymer network scaffold with an interconnected pore structure that can hold a lot of water and provide an extracellular matrix (ECM)-like environment for cell proliferation, differentiation, and growth. Polysaccharides (sodium alginate, gelatin, chitosan, hyaluronic acid, and proteins) hydrogels are biocompatible and bioresorbable [41]. For bioresorbable hydrogels, covalent bonds may be created via chemical synthesis or physical contact. Also, physical interactions may produce covalent bonds. Due of their chemical resistance, the first method is usually used. Irreversible chemical crosslinking causes bulk deterioration and local flexibility issues. Hydrogels and water-swollen polymers behave according to scaffolding component structural interactions. Hydrogen bonds, Van der Waals interactions, and electrostatic interactions dominate biological hydrogel interactions. Growing the network system allows them to be made. Guyot et al. [42] say adaptive design is the best technique to create realistic supramolecular hydrogel materials in three dimensions.

4. Fossil-based polymers

FBPs are fossil-based polymers made in a lab or factory from fossil raw materials, usually petroleum or natural gas. They are human-made and chemically bonded. In general, they have a controlled structure, no allergic reaction, and more processing flexibility. They can also enhance polymer structure synthesis and design. Using FBPs in regenerative medicine has several advantages. High-grade, pure products may be recreated. They also outperform natural polymers in heat resistance and mechanical properties [43]. TE uses FBPs extensively, and their chemical, physical, mechanical, and morphological properties (pore size and distribution, surface texture, typology, and crosslinking) can be tailored to the application (Figure 4) [44]. The chemical structure of FBPs determines their degradability and other important scaffold design properties. These polymers can build endless shapes and forms, which is useful. Hydrolysis breaks down polymers in tissue engineering. The breakdown rate may be changed by changing the polymer's composition, molecular weight, end groups, and device shape [45].

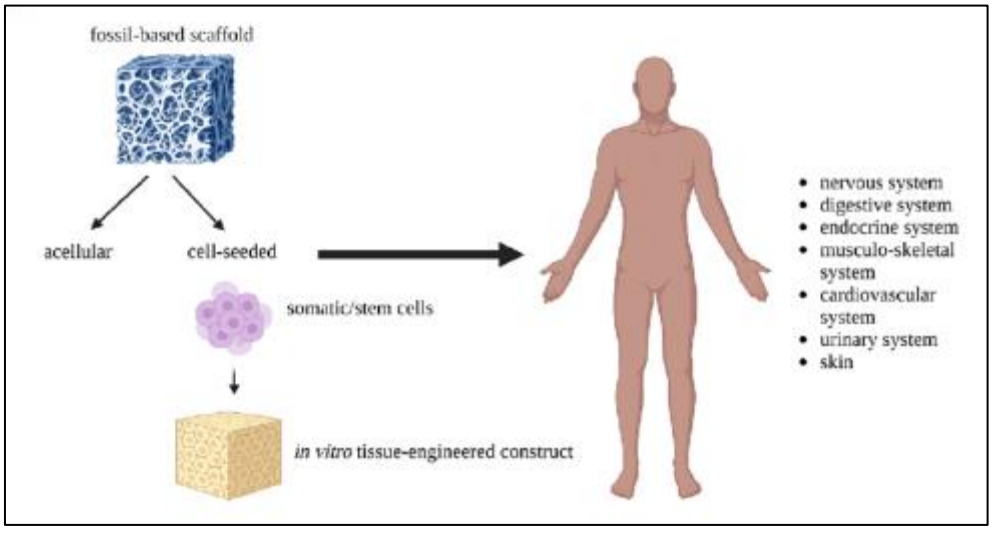

Figure 4 Fossil-based polymers as scaffolding material in tissue engineering (Source: [14]).

4.1. Poly(ε-caprolactone) (PCL)

Durable aliphatic polyester polyvinyl chloride (PCL) is employed in many biomedical applications. Repeating hexanoate units make it a polymer with a low melting point of 60°C. PCL possesses bioresorbability, mechanical elasticity, thermal stability, biocompatibility, rheological and viscoelastic properties, and high stiffness. It is cheap, flammable, non-toxic, and decomposes slowly. However, this synthetic biopolymer exhibits limited cell adhesion and slow disintegration. Polylactic acid (PLC) coupled with other polymers, such as PLA, creates a less hydrophobic, more mechanically efficient, and more degradable composition. It was done to reduce the limits indicated before. PCL is stable in vivo and does not degrade after six months [46]. PCL has been used to make bone, teeth, skin, liver, cartilage, ligaments, muscle, neurones, retina, and blood vessels. PCL is used in dentistry. According to studies, layer-by-layer PCL scaffold modelling is suitable for skin tissue engineering (TE). They are appropriate substrates for cell-colonized structures with epidermal and dermal skin layers [46].

4.2. Poly(vinyl) Alcohol (PVA)

PVA has several biomedical applications. Polyvinyl alcohol (PVA) is an exciting scaffold engineering polymer because to its biodegradability, biocompatibility, hydrophilicity, permeability, flexibility, and ability to mix with other biopolymers. It is commonly mixed with chitosan or polyhydroxy butyrate to make wound-healing nanofibers. Research has proven that electrospun PVA nanofibers can be re-epithelized. These nanofibers were mixed with gelatin and Carica papaya. A study found that the composite scaffold's damp environment caused this phenomenon [47]. They found that PVA nanofibers kill both gram-positive and gram-negative bacteria, including Staphylococcus aureus and E. coli. This action helps wounds heal and shows nanofibers' potential for wound healing. Polyvinyl alcohol (PVA) is also a unique substance since it can store a lot of water or biological fluids and serve as a cartilage-like lubricant [48]. Zhu et al. [49] advises combining PVA with other synthetic or natural materials to overcome these constraints. Because PVA is water-soluble, it must be crosslinked to reduce its solubility and improve its mechanical properties. Tissue engineering applications benefit from PVA-based scaffolds with a percentage above 85% [45].

4.3. Polyethylene Glycol (PEG)

PEG is polymer of ethylene oxide (PEO) or polyoxyethylene [46]. Zhao et al. [18] describe polyethylene glycol (PEG) as a water-soluble, non-ionic, biodegradable synthetic polymer. Its tissue engineering uses are diverse. According to Affar e et al. [1], polyethylene glycol (PEG)'s high mechanical stiffness may improve composite mechanical properties. PEG has low immunogenicity and nontoxicity. Additionally, polyethylene glycol (PEG) scaffolds have hydrated architectures that improve cytocompatibility [50]. Mechanical stiffness is a key property, as said. Chemical crosslinking is a technology that has the potential to increase this behaviour [1].

4.4. Polypropylene Fumarate (PPF)

Fumaric acid with propylene glycol form PPF, a linear polyester. Yang et al. [51] observed that crosslinking double bonds in this biodegradable polyester creates a polymeric network, which strengthens it. This makes it ideal for orthopaedics. It may be used with PEG, PLA, or PCL to make them hydrophobic [52]. Polypropylene fluoride breaks down by ester bond hydrolysis. Main chain molecular mass, crosslinkers, and crosslink density determine degradation rate [53]. PPF is widely employed in orthopaedics because to its incredible mechanical strength, biocompatibility, and osteoconductivity. Characteristics of PPF-based scaffolds dictate their applicability in bone tissue engineering. According to Javid-Naderi et al. [54], these matrices dissolve during bone healing and remodelling. Polypropylene (PPF) scaffolds have also been investigated for application in ophthalmic, cardiac, and neurological tissue engineering [53].

4.5. Polyurethane (PU) and Modified Polyurethanes (MPUs)

PU is an attractive tissue engineering framework material. Its high flexural strength, biodegradability, and biocompatibility make it unique among materials in its mechanical, physical, and biological qualities [55]. Elasticity and poly(ester-urethane) urea conversion are desirable features. Polyurethane (PU) has low cytotoxicity, interfacial tension, thrombo-resistance, oxygen permeability, and good mechanical properties for pharmaceutical and biological applications. Wound dressings, medication transporters, and antimicro bias filters are examples. Modified polyurethanes (MPUs) may increase the bioactivity of polyurethane (PU) scaffolds by adding biodegradable, electroactive, surface-functionalized products, ceramic, and natural polymers [56]. Naureen et al. [55] say PU and MPUs can construct soft and rigid tissues.

5. Hybrid biomaterials

Two or more polymers must be combined to create the polymer blend. The process permitted the creation of new materials with better physical properties. However, component miscibility affects blend quality. Miscibility also impacts separated phase morphology [57]. The three types of polymer mixtures are:

- Homogenous polymer blends, or thermodynamically miscible polymers, consist of equivalent chemical composition polymers. These techniques create single-phase mixes with one glass transition temperature;
- Compatible polymer blends: immiscible polymers with strong interphase interaction exhibit consistent physical features;
- Heterogenous polymer blends, or immiscible polymers, have unique phase structures and multiple glass transition temperatures [57].

The main reason these materials are popular is their ability to change and adapt to their application. Mixing several polymers lowers prices. Combining may minimise product costs and increase quality [58].

5.1. PCL-Based Blends

PCL-based composites are being studied and employed in more biomedical, medical, and pharmaceutical applications than PCL-based materials alone. Throughout the investigation, PCL mixes had better mechanical, thermal, and viscoelastic properties. PCL/PLA is one of the biodegradable polymer composite mixes extensively studied by researchers. Due to improved PCL mechanical and thermal properties. Several research groups are interested in manufacturing procedures [59], overall characterisation [60], and biodegradation. Many research efforts concentrate on PCL/PLA electrospinning [61]. Electrospinning is a common method for creating nanometre-sized continuous threads. Electrospun fibres may be employed in drug administration, wound healing, tissue engineering, and regenerative medicine, according to Bhattarai et al. [62].

PCL may be mixed with natural polymers. Collagen scaffolds, which generally lack mechanical properties, are used to make manufactured human skin. Combining PCL with collagen and electrospinning it into fibres strengthens collagen scaffolds. In dermatology [63, 64, 65, 66, 67, 68]. PCL/collagen mixes are promising materials for vascular tissue engineering [69, 70, 71].

5.2. PLA-Based Blends

PLA can be combined with many polymers to create tissue-specific scaffolds. Ritz et al. [72] examined endotoxins and biocompatibility of solid discs and PLA-cemented or collagen-filled porous three-dimensional structures. The study proved PLA is biocompatible and showed endotoxin contamination below FDA limits. In addition, PLA-printed discs helped osteoblasts, osteoblast-like cells, and human umbilical vein endothelial cells grow, spread, and proliferate. 3D printed scaffolds may become more hydrophilic, allowing cells to attach and migrate [73]. PLA and biocompatible ceramics (via composite fibre or ceramic coating on polymer scaffolds) can achieve this. Drug carriers were shown to be possible with PLA/PEG block copolymers in 1990. Zhu et al. [74] discovered that polymer composition could affect drug release and biodegradation. Nanomedicine applications like micelles are being studied using this material [75]. Nanomedicine treats, monitors, treats, and regenerates the human body using nanotechnology, which manipulates and manufactures materials or devices 1 to 100 nanometres (nm; 1 nm = 0.0000001 cm) in size [76]. A branch of medicine that uses nanotechnology is nanomedicine. Additionally, PLA/PEG may be used to create bone tissue. Its low melting point allows PEG to act as a plasticiser, which affects the blend's processing [77]. Salehi et al. [77], Serra et al. [78], and Asadollahi et al. [79] suggest that this material could be modified to accommodate 3D printing to create patient-specific bone grafts. Scaffaro et al. [80] performed PLA/PEG mix research. In this study, melt mixing a PLA/PEG blend with sodium chloride (NaCl) created three-layered scaffolds with pore size gradients. Pore diameters were adjusted using NaCl granulometry. The mixes' porogens (NaCl and PEG) were removed by selective leaching in boiling demineralised water. The researchers characterised 3D printed PLA/PHB items and found that they have good mechanical, thermal, and cell viability. PLA/PHB scaffolds lack the porosity needed for tissue engineering.

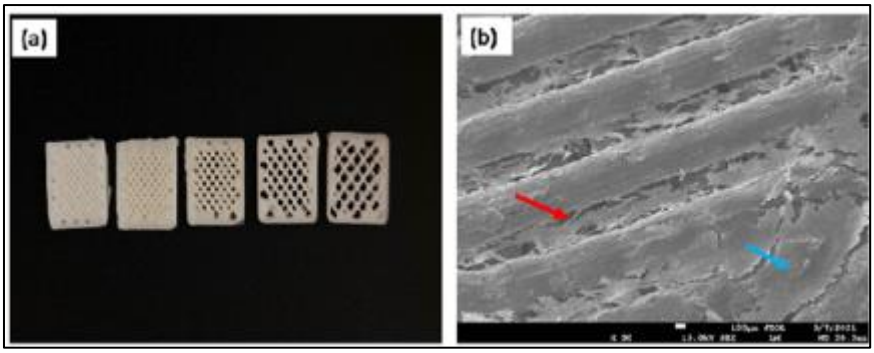

Figure 5 PLA/PHB 3D scaffolds: (a) Printed scaffolds with various designs; (b) SEM shot of adipose tissue-derived mesenchymal stem cells for scaffold colonisation (blue arrow) (Source: [14])

5.3. Polymer/Bioceramic Blends

Polymer scaffolds frequently lack mechanical strength, Young's modulus, and toughness. To overcome their weak bioactivity, ceramic materials including hydroxyapatite (HAp), tricalcium phosphate (TCP), and bioactive glasses may be added in the formulation. Ceramics develop strong bonds with hard and soft tissues via cellular activity. Ceramics interact with bodily fluids. Bio-ceramics and flexible polymers aid tissue regeneration [81]. Bio-ceramics are non-metallic inorganic ceramics. These ceramics repair and regenerate musculoskeletal and periodontal structures. Their biocompatibility, osteoinductivity, corrosion resistance, and compressive strength are excellent. However, their surface is brittle, fracture toughness is poor, mechanical dependability is low, elasticity is low, and stiffness is unnaturally high compared to human bone. Pina et al. [82] found that bioceramics are stronger in compression than tension. Ceramic biomaterials commonly employ inorganic calcium or phosphate salts. These salts promote bone growth and osteoblast differentiation with their osteoconductive and osteoinductive properties. In bone regeneration, hydroxyapatite (HAp, $Ca10(PO4)6(OH)2$), β-tricalcium phosphate (β-TCP, $Ca3(PO4)2$), and bioactive glasses are commonly used to create three-dimensional scaffolds [82].

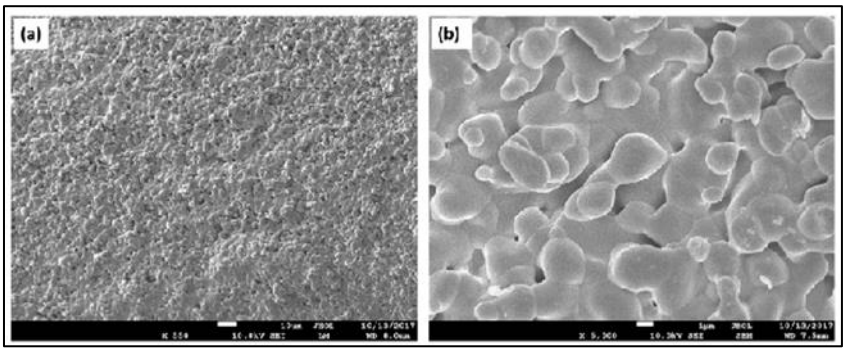

Figure 6 HAp-based scaffold SEM pictures. (a) Topography study shows matrix roughness; (b) shattered scaffold inner structure (Source: [14])

Polylactic acid (PLA) and bioceramics offer benefits, such as additive manufacturing for customisation [73, 83, 84, 85, 86, 87]. Wang et al. [88] study found that PLA/bioceramic mixes may be more biocompatible and osteogenic than pure PLA scaffolds. PLA and HAp have been extensively studied and can be processed using stable, low-cost fused deposition modelling (FDM) technology [84]. Adding PLA to HAp changes its mechanical properties from brittle to ductile. This technique significantly increases flexural and compressive strength. Nikpour et al. [26] studied nanostructured bioactive glass/dextran composite scaffolds for bone tissue engineering. The hydrogel matrix's mechanical strength increased significantly when bioactive glass nanoparticles were added. These scaffolds boosted reactivity with physiological fluids, creating active mineralisation sites, [26]. Dextran matrix included inorganic minerals such hydroxyapatite (HAp) [89].

6. Conclusion

Carefully conceived and executed biomaterial scaffolds drive tissue engineering. The molecular and architectural foundation of tissue regeneration is scaffolds. Natural polymers are biocompatible and bioactive like the extracellular

matrix, but synthetic polymers give unmatched control over mechanical strength, porosity, and breakdown kinetics. By combining materials into hybrid and composite scaffolds, tissue-specific mechanical, biological, and structural demands may be met. Intelligently blending materials like PCL or PLA with bioactive ceramics or other polymers can help researchers create next-generation constructs with improved osteoconductivity, vascularization potential, and patient-specific design using advanced manufacturing methods like 3D printing.

The successful translation of scaffold-based medicines from lab to clinic requires understanding the material's properties and how they interact with the host environment. We must continue to build intelligent, adaptable scaffolds that can direct cellular activity during healing via controlled signalling and dynamic adaptation in addition to passively supporting cells. As material science, biology, and engineering merge, sophisticated, off-the-shelf, and customised regenerative structures will enable tissue repair and organ regeneration.

Compliance with ethical standards

Acknowledgments

I would like to thank the Centre for Gas, Refining and Petrochemicals for the opportunity to have this successful study.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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