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Biodegradable Polymers as Scaffold Materials: Applications in Tissue Engineering

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Abstract. Biodegradable polymer scaffolds are an important research direction in the field of tissue engineering. Their temporary support, controlled degradation, and biocompatibility overcome the limitations of traditional implants, such as permanent retention. In the field of cardiac tissue engineering, BRS and PGS/PLA electrospun scaffolds have shown potential in myocardial repair and vascular regeneration, but balancing degradation rates and mechanical properties remains challenging. In the field of bone tissue engineering, interface-enhanced ternary blends and PCL/HA composite scaffolds enhance bone defect repair outcomes by optimising the strength-toughness balance and osteogenic differentiation capacity. For neural tissue engineering, fibrinogen-modified PCL and PLA-based scaffolds enhance cell adhesion and neural regeneration capacity, aiding in the treatment of neurological disorders. Such scaffolds, with PEDOT-POCO scaffolds as an example, also show application potential in bladder tissue engineering. Natural and synthetic polymers have their respective advantages and disadvantages as scaffold materials, making hybrid materials a key development direction. Future trends will lean toward biomimetic, intelligent, and personalised designs, but challenges remain in matching material properties with tissue requirements and achieving clinical translation.

Keywords: Biodegradable polymer scaffolds, Tissue engineering, Cardiac tissue repair, Bone tissue regeneration

1. Introduction

1.1. Tissue engineering

Traditional therapeutic approaches for tissue repair, typified by autografts (where patient's own healthy tissue is transplanted) and allografts (utilizing tissue from compatible donors), have long anchored clinical strategies for restoring damaged tissues across diverse anatomical sites [1]. Yet, at the macroscopic level, both methods inherently falter in recapitulating the intricate hierarchical structure (spanning cellular organization to tissue-scale architecture) and biomechanical properties that define native tissues, creating a persistent gap in fully restoring tissue function and long-term structural integrity.

To overcome these limitations in traditional therapeutic approaches, tissue engineering, which merges life sciences, materials engineering, and modeling to create functional scaffolds and artificial

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tissue constructs for biomedical applications, has emerged as a promising interdisciplinary solution [2]. At its essence, this multidisciplinary field seeks to address the unmet clinical need for replacing or regenerating damaged tissues caused by disease, congenital defects, or traumatic injuries. It offers a promising solution, with the potential to revolutionize patient care by enabling the regeneration of tissues ranging from individual organs to specific anatomical structures [3], such as adipose tissue for breast reconstruction following mastectomy [4].

1.2. Biodegradable polymers

1.2.1. What are biodegradable polymers

Biodegradable polymers are a class of macromolecules that can be broken down through enzymatic or hydrolytic processes within biological environment. The resulting degradation products are typically small molecules that can be readily metabolized or excreted by the body. Derived primarily from renewable resources, these polymers offer a sustainable alternative to conventional petroleum-based plastics [5]. Driven by growing concerns over resource depletion, population growth, and environmental pollution, the development and application of biodegradable polymers has accelerated in recent years.

1.2.2. Classification of biodegradable polymers

1.2.2.1. Natural degradable materials

Natural biodegradable polymers are derived directly from biological materials or processes. Starch-based polymers, derived from agricultural products such as corn and potato, are not only cost-effective but also fully biodegradable. Cellulose, the most abundant polymer on Earth, represents another important natural material, with applications ranging from paper production to biomedical scaffolds. Chitin and its derivative chitosan, obtained from crustacean shells and fungal cell walls, possess unique properties such as antibacterial activity and mucoadhesion, making them ideal for a variety of biomedical applications [6]. Protein-based materials, including gelatin and collagen, can mimic natural extracellular matrices and therefore have high biocompatibility and are widely used in tissue engineering. Other notable examples of natural biodegradable polymers include natural rubber and alginate [7].

1.2.2.2. Synthetic degradable polymers

Synthetic biodegradable polymers can be broadly classified into two categories based on their monomer sources: bio-based and petrochemical-based.

Bio-based polymers, such as Poly (Lactic Acid) (PLA), Polyhydroxyalkanoates (PHA), and Poly (Butylene Succinate) (PBS), are synthesized from renewable biomass sources. PLA, for instance, is derived from lactic acid monomers produced through the microbial fermentation of carbohydrates. PHAs are synthesized by microorganisms under specific growth conditions, and their properties can be tailored by varying the composition of the monomers.

Petrochemical-based synthetic polymers, including Polycaprolactone (PCL), Poly (Butylene Adipate-co-terephthalate) (PBAT), and Poly (Glycolic Acid) (PGA), are derived from petroleum-based monomers. In tissue engineering, these polymers show considerable promise. For example, PBAT combines the biodegradability of aliphatic polyesters (facilitating controlled degradation to support tissue remodeling) with the mechanical strength of aromatic polyesters (mimicking native

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tissue stiffness for structural integrity). This dual-funtionality makes it a versatile candidate for scaffolds in soft tissue repair (e.g., skin regeneration matrices) or even preliminary frameworks for load-bearing tissue pre-conditioning, bridging the gap between temporary mechanical support and biological integration critical to tissue engineering workflows.

1.2.2.3. Microbial construction

Microbially-synthesized polymers, primarily Polyhydroxyalkanoates (PHAs), represent a unique class of biodegradable materials that combine the advantages of natural and synthetic polymers. Produced by microorganisms as intracellular carbon/energy stores, PHAs boast excellent biocompatibility (minimizing immune responses in host tissue), tunable mechanical properties (adaptable to mimic soft/hard tissue mechanics), and complete biodegradability (ensuring resorption without long-term foreign material retention). In tissue engineering, these attributes position PHAs as ideal candidates for cell-seeded scaffolds (e.g., vascular grafts or cartilage repair templates) [8]. However, scaling production and cutting costs remain hurdles to unlock their full commercial potential in large-scale tissue reconstruction therapies.

1.3. Application areas of biodegradable polymer scaffold materials in tissue engineering

1.3.1. Reasons for choosing biodegradable polymer scaffolds

Biodegradable polymers are particularly well-suited for biomedical applications due to their tunable degradation rates, ease of processing, and chemical and biological similarity to native extracellular matrices (Figure 1).

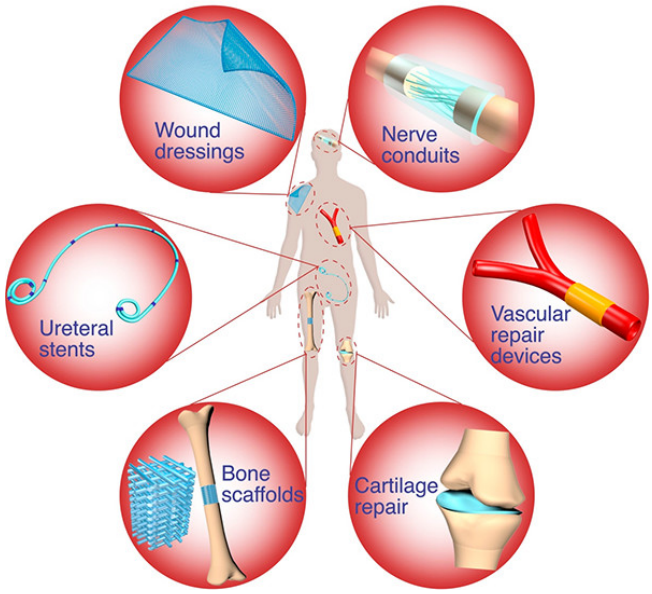

Figure 1. Main medical applications of biodegradable polymer scaffolds

Among them, a typical tissue engineering construct comprises three essential components: cells, a structural template (scaffold), and growth cues [9]. The scaffold, often fabricated from porous polymeric biomaterials, serves as a temporary extracellular matrix, providing a physical framework for cell attachment, proliferation, and tissue remodeling [1].

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In fact, scaffold materials, as a key component, serve multiple functions, including supporting cell proliferation, guiding tissue regeneration processes, regulating tissue structure and morphology, and mediating the release of bioactive factors. These characteristics make them one of the core elements determining the success or failure of tissue engineering technology. In recent years, biodegradable polymeric synthetic materials with excellent biocompatibility have been developed through optimised preparation processes to construct tissue engineering scaffolds with mimetic extracellular matrix topological structures, mechanical strength matching physiological requirements, and controllable release functions for bioactive substances. This has gradually emerged as a leading research direction in the field [10]. In the context of tissue engineering, the combination of living cells with biodegradable scaffolds represents a powerful strategy for regenerating damaged biological tissues. These scaffolds act as a temporary support structure, providing mechanical stability and biochemical cues to facilitate the healing process. Additionally, scaffold materials must possess suitable mechanical properties and be amenable to functionalization to meet the specific requirements of different tissues.

1.3.2. Clinically used for organs

The clinical applications of biodegradable polymer scaffolds are extensive, covering almost all major organ systems. In nerve repair, for example, these scaffolds can be fashioned into conduits to bridge gaps in damaged nerves, guiding axonal regeneration and promoting functional recovery [11]. In skin tissue engineering, they serve as advanced wound dressings, creating a moist environment that promotes epithelialization and accelerates the healing of acute and chronic wounds [12]. In cardiovascular applications, biodegradable polymer scaffolds are being explored for vascular grafts and cardiac tissue repair, offering the potential to overcome the limitations of traditional non-degradable materials [13]. In orthopedics, they are used for bone and cartilage repair, providing a three-dimensional framework for the ingrowth of new tissue [14].

This review will continue by listing some examples of the application of different types of biodegradable polymer scaffolds in these fields.

2. Main

2.1. Cardiac tissue engineering

2.1.1. Cardiovascular disease

Cardiovascular disease is one of the leading causes of death worldwide. Acute cardiovascular injury, such as Myocardial Infarction (MI), occurs when blood supply to the myocardium is blocked, leading to myocardial death, reduced cardiac function, and ultimately pathological remodeling of the heart, which permanently repairs tissue functional recovery [15]. Traditional metal stents and artificial vessels present clinical issues such as permanent retention and late thrombosis. Biodegradable polymer stents, with their temporary support and complete degradation properties, can partially deliver stem cells to promote the infiltration and remodeling of endogenous cells, making them a research hotspot in cardiovascular tissue engineering.

2.1.2. Example 1: Biodegradable Scaffold (BRS)

To overcome issues such as late thrombosis and vascular dysfunction associated with Drug-eluting Stents (DES), BRS provides temporary vascular support (6–9 months) before fully degrading,

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promoting positive vascular remodeling [16,17]. Professor Daniel Wee Yee Toong's team developed a polymer scaffold that combines conductivity, degradability, and regenerative properties, achieving synergistic optimization of mechanical and electrical properties through material composites (POCO+PEDOT), for use in myocardial repair and vascular regeneration. The mechanical strength of polymers such as PLLA and PCL is insufficient thus requires enhancement through crystallinity control (e.g., melt spinning to 70%) or composite fillers (e.g., $BaSO_4$ nanoparticles) [17,18]. The first-generation PLLA-based BVS failed clinically due to excessively thick scaffold beams (150 μm). The new generation of BRS (e.g., MeRes100, APTITUDE) optimised the process to reduce the thickness to 85–100 μm, significantly improving safety [19,20]. Magnesium-based BRS (e.g., Magmaris) demonstrate faster absorption (12 months) and lower thrombosis risk in clinical settings [21]. However, balancing degradation kinetics with mechanical performance remains a challenge for future development [22] (Figure2).

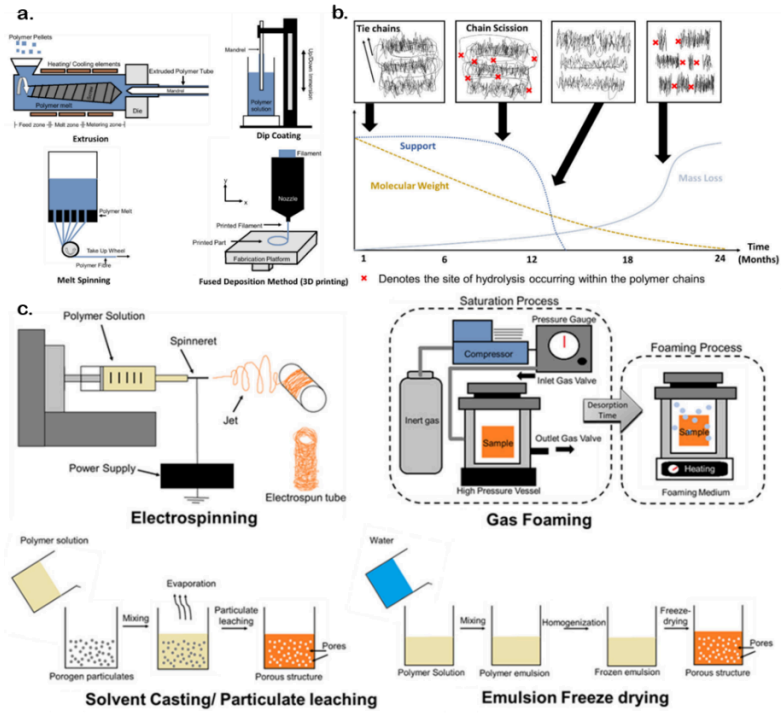

Figure 2. a. Preparation of BRS. b. Degradation process of aliphatic polylactic acid (PLA). c. Scaffold preparation method

2.1.3. Example2: PGS/PLA electrospun scaffolds

In 2020, Florence Flaig and her team successfully developed performance-optimized PLA:PGS composite scaffolds by incorporating 30% Polyglycerol Stearate (PGS) elastomer into Polylactic Acid (PLA), with scaffold performance closely related to processing parameters. The study employed mixed electrospinning technology to produce two different fiber specifications with diameters of 600 nm and 1300 nm, respectively, and achieved differentiated cross-linking density control through curing at 90°C or 120°C. Then this study systematically evaluated the biocompatibility, biodegradability, and chemical and mechanical properties of the scaffold. Results showed that the incorporation of PGS significantly enhanced the material's hydrophilicity, thereby promoting surface functionalization of the scaffold by common cell culture matrices such as Matrigel or laminin. After coating with Matrigel or laminin, the interaction between the PLA:PGS

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scaffold and cells was significantly enhanced. In cell culture experiments, cardiomyocytes seeded on the scaffold exhibited morphological characteristics similar to those of natural tissue, particularly on fibers with a diameter of 600 nm and higher PGS cross-linking density [23].

Animal experiments further validated the superior performance of the PLA:PGS scaffold. After transplantation into mouse hearts, the scaffold not only induced new blood vessel formation but also did not trigger inflammatory reactions or foreign body giant cell reactions. In summary, this thin PLA:PGS scaffold with excellent biocompatibility and the ability to effectively support cardiomyocyte development holds great potential as a biomaterial in the field of cardiac tissue engineering (Figure3).

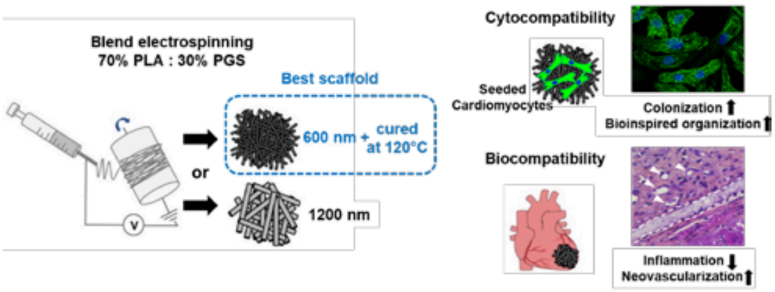

Figure 3. Design of electrospun scaffolds for cardiac tissue engineering based on PGS and PL

2.2. Bone tissue engineering

2.2.1. Bone diseases

Bone tissue performs functions such as support and protection, and its renewal process depends on the balance between osteoclasts and osteoblasts. Osteoporosis disrupts this metabolic balance, with a prevalence rate as high as 36% among the Chinese population aged 60 and above. Traditional bone implant materials struggle to repair damaged structures and often require surgical removal. Bone defects and non-union fractures are commonly caused by trauma or tumours, with defects exceeding 5 millimetres being difficult to heal spontaneously. Traditional bone implant materials struggle to repair damaged structures and often require surgical removal. Bone metastasis is relatively common, and reconstructing bone defects after tumour removal presents significant challenges. The application of biodegradable polymers in this field is becoming increasingly important.

2.2.2. Interfacial toughening-type ternary blend materials

Biodegradable polymers and composite materials are ideal implants for bone tissue engineering, but existing composite scaffolds face challenges in balancing strength and toughness. To address this, the research team proposed an interface toughening strategy, incorporating a third polymer into the mutually insoluble biopolymer matrix to improve compatibility. By utilizing weak chemical interactions and high-shear melt processing, the team achieved nanoscale dispersion of nanofillers, enabling polymer chain entanglement to produce silver streaks and shear yielding. The resulting ternary blends and composite materials exhibited an 11-fold increase in toughness without compromising stiffness or strength. A 3D-printed composite scaffold with a 70% porosity exhibits compressive strength comparable to that of cancellous bone [24]. In vitro experiments demonstrate that the scaffold exhibited high cell viability and effectively promotes osteogenic differentiation of human bone marrow mesenchymal stem cells, providing a practical strategy for the development of bone tissue regeneration materials (Figure4).

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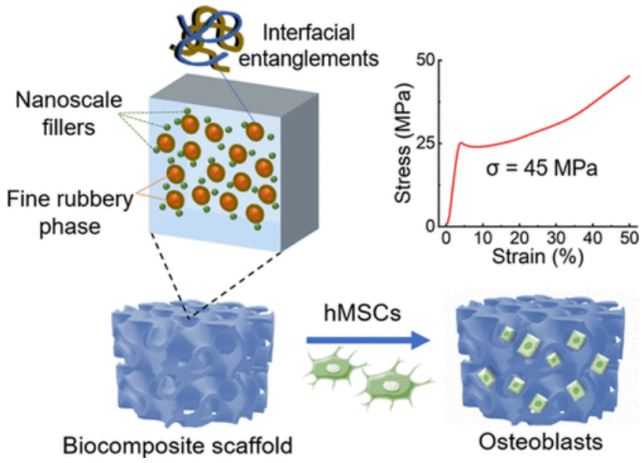

Figure 4. Preparation of biocomposites

2.2.3. Bionic structure PCL/HA composite scaffold

The research team led by Maria José da Silva Lima employed a combination of short-distance electrospinning and 3D printing technology to prepare PCL/HA composite scaffolds. SEM analysis revealed that the scaffolds exhibited a biomimetic porous nanofiber structure, while XRD, FTIR, and TGA analyses confirmed the uniform incorporation of HA into PCL. Mechanical testing demonstrated that the mechanical properties of the scaffolds matched those of cancellous bone. In vitro experiments showed that osteoblast-like cells proliferated and differentiated more effectively on the scaffold surface compared to the control group, demonstrating excellent biocompatibility and osteoinductive capacity [25]. In vivo rat cranial defect experiments revealed that after scaffold implantation, new bone grew rapidly in the defect area using the scaffold as a template, with a significant increase in bone volume fraction, and the scaffold degradation balanced with new bone formation. These findings further demonstrates that the composite scaffold exhibits excellent mechanical compatibility, biocompatibility, and osteogenic performance, and can be scaled up for production and subjected to long-term safety studies (Figure5).

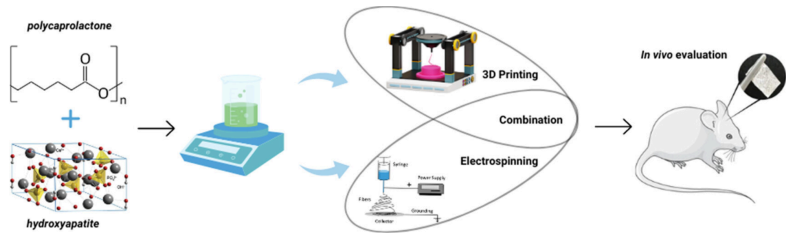

Figure 5. Manufacturing of PCL/HA scaffolds

2.3. Neural tissue engineering

2.3.1. Nervous system treatment

The nervous system is a vital component in living organisms. Injury or disease affecting the nervous system can disrupt bodily functions and even lead to death. Current manufacturing methods and the availability of a wide range of biodegradable polymers have made it possible to develop scaffolds with shapes and properties that support the treatment process, regulate biological signals, promote

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and guide axonal growth, and slow or inhibit the formation of scar tissue. The use of polymers to in the treatment of central nervous system diseases is a multidisciplinary challenge [26].

2.3.2. Fibrinogen-modified polycaprolactone scaffold

Parkinson's Disease (PD) is caused by the degeneration of Dopaminergic (DA) neurons. In vitro modelling using human-induced pluripotent stem cell-derived Neural Progenitor Cells (NPCs) is crucial for PD research, but the hydrophobicity of electrospun Polycaprolactone (PCL) scaffolds hinders cell adhesion. Salma P. Ramirez and colleagues optimised PCL scaffold performance using fibrin coating, characterised the scaffolds via SEM and FTIR-ATR techniques, seeded NPCs onto the coated scaffolds, and induced their differentiation. They analysed differentiation and electrophysiological activity using TH immunofluorescence, SEM, and microelectrode arrays [27]. The results showed that the fibrin coating increased the proportion of TH-positive cells by 37%, effectively promoting neurite outgrowth. Microelectrodes detected a discharge frequency of 12.5±2.3 Hz, with the 1:5 diluted fibrin coating yielding the optimal effect, increasing the differentiation rate by 2.1-fold. The scaffold had a porosity of 75% and a compressive modulus of 18.6 MPa, meeting application requirements. This research not only improves the performance of biodegradable polymer scaffolds but also provides a new technical platform for PD research and drug screening (Figure6).

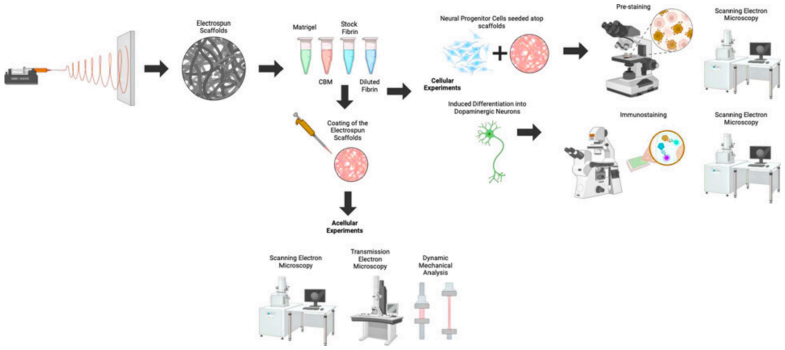

Figure 6. NPCs cultured on electrospun (ES) polycaprolactone (PCL) nanofibre scaffolds

2.3.3. Biodegradable PLA/PELA and PLA/PEG scaffolds

Lokesh Agrawal's team prepared PLA/PELA and PLA/PEG (50:50 w/w) biodegradable composite scaffolds for neural tissue engineering via electrospinning. Scanning electron microscopy revealed that the scaffolds had a nanofibre network of 100–500 nm, mimicking the extracellular matrix of nerve cells. PEG or PELA improved hydrophilicity, with the former causing surface erosion and the latter achieving degradation equilibrium. The PLA/PELA (2k) scaffold exhibited a fracture strain of 500%, making it highly compatible with the mechanical properties of nerve tissue. Neural stem cells exhibit high survival rates on the scaffold and successfully differentiated into functional networks. PLA/PELA scaffolds supplemented with growth factors also regulated bioelectric potentials to promote neural signal repair. This blended scaffold offers structural biomimicry, mechanical compatibility, and neural induction advantages, providing an ideal material solution for neural repair [28].

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2.4. Engineering of other tissues

Biodegradable polymer scaffolds hold significant clinical promise in bladder tissue engineering, primarily addressing bladder tissue regeneration issues caused by neurodegenerative diseases (such as spina bifida), cancer, and trauma [29].

In 2024, Rebecca L. Keate's team explored the feasibility of combining conductive polymers with biodegradable citrate-based elastomers (Figure7). Researchers employed in situ complexation and oxidative polymerisation techniques to prepare PEDOT-POCO composite scaffolds. This scaffold possesses unique advantages: it exhibits a uniform porous structure with pore sizes ranging from 500 to 700 nm (porosity of 78.3 ± 5.2%), with the PEDOT network fully integrated throughout the structure. It combines an electrical activity of 32.5 ± 4.1 C/cm² with the the antioxidant properties of POCO, and the POCO main chain is completely hydrolysed within 28 days [30]. Animal experiments further confirmed that the scaffold promotes urinary tract epithelial regeneration (thickness: 44.5±24.6 μm), induces an anti-inflammatory microenvironment (CD206+ cell proportion: 68±7%), and achieves outcomes comparable to those of cell-seeded scaffolds ($p>0.05$) [31].

In summary, the PEDOT-POCO composite scaffold offers an innovative and feasible solution for cell-free bladder regeneration [32].

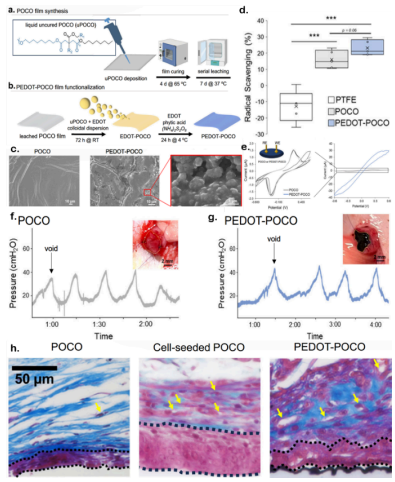

Figure 7. a. Schematic diagram of the cross-linking of a. uPOCO prepolymers to form a POCO film. b. In situ polymerisation process of PEDOT in the POCO matrix. c. SEM image of the PEDOT-POCO scaffold (scale bar 5 μm), showing a uniform porous structure with pore sizes of 500–700 nm, confirming the successful polymerisation of EDOT into a three-dimensional conductive network. d. PEDOT-POCO retains the antioxidant properties of POCO (scavenging rate of 92±3%), showing a significant difference compared to the PTFE control group (8±2%). e. Characteristic redox peaks (-0.2 V/+0.3 V) correspond to the doping process of PEDOT, with a charge storage capacity of 32.5±4.1 C/cm². f, g. Four-week postoperative urodynamic follow-up showed that the PEDOT-POCO group (blue) had a voiding curve similar to the normal group (black), significantly better than the POCO group (grey) (n=6 animals). h. Bladder tissue staining showed that the PEDOT-POCO group formed complete urinary epithelium (44.5 μm, marked with black dashed lines), with muscle layer (red) and collagen (blue) proportions similar to natural tissue (scale bar 100 μm)

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3. Discussion

3.1. Current status and comparison

Currently, biodegradable polymer scaffolds are developing rapidly in the field of tissue engineering. Natural polymers such as collagen and chitosan have excellent biocompatibility but suffer from poor mechanical strength and rapid degradation; synthetic polymers (such as PLA and PCL) offer superior mechanical properties and controllable structures but face limitations such as poor cell adhesion and lower biocompatibility. To overcome these shortcomings, researchers have developed hybrid materials with the advantages of different scaffolds, such as PGS blended with PLA for cardiac scaffolds, which match myocardial modulus and maintain structural integrity within 28 days; and PCL combined with gelatin via electrospinning to prepare bone scaffolds, significantly promoting cell proliferation. The application of technologies such as 3D printing and electrospinning has further enabled the fabrication of scaffolds with complex architectures.

3.2. Prospects and challenges

In the future, biodegradable polymer stents will evolve towards biomimetic, intelligent, and personalised directions, enhancing treatment outcomes by mimicking the extracellular matrix, achieving stimulus-responsive functions, and customising patient-specific stents. However, numerous challenges remain, such as the difficulty in precisely matching the mechanical properties and degradation rates of materials with tissue repair requirements, the challenges in vascularising large-sized tissue defects, and issues related to high production costs and low standardisation. Additionally, insufficient interdisciplinary collaborative innovation is hindering the translation of novel scaffolds from the laboratory to clinical applications.

4. Conclusions

In conclusion, biodegradable polymer scaffolds have emerged as a transformative force in tissue engineering, offering tailored solutions for cardiac, bone, neural, and other types of tissue repair. Their tunable degradation rates, excellent biocompatibility, and ease of functionalization address limitations of traditional therapies. For instance, PGS/PLA electro spun scaffolds enhance cardiac tissue regeneration, while PCL/HA composites facilitate bone repair. In neural tissue engineering, fibrin-modified PCL and PLA-based blended scaffolds show promise in treating Parkinson's disease. However, several challenges remain, including the need to balance mechanical properties with degradation rates, achieve large-scale vascularization, and reduce production costs. Future research should focus on interdisciplinary collaborations to optimize material design, scale up production, and accelerate clinical translation, thereby realizing the full potential of biodegradable polymer scaffolds in regenerative medicine.

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