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REVIEW

Harnessing the Power of Electroconductive Polymers for Breakthroughs in Tissue Engineering and Regenerative Medicine

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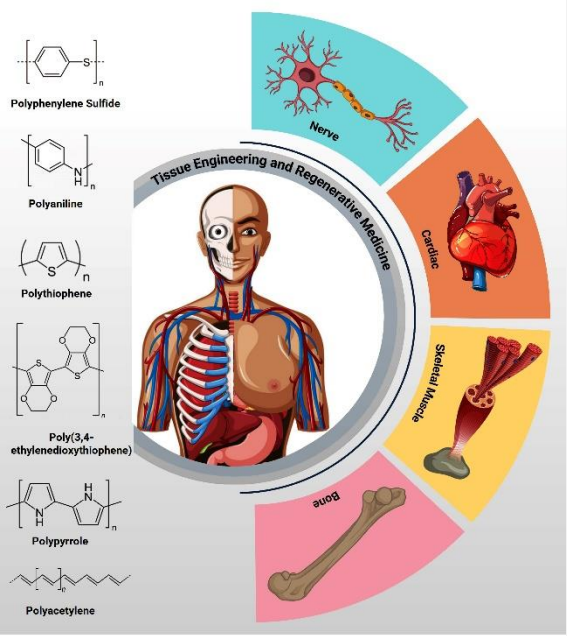
ABSTRACT

Electroconductive polymers (ECPs) have garnered increasing attention in the realms of tissue engineering and regenerative medicine due to their unique physicochemical properties, including their ability to conduct electrical signals. These polymers, with inherent conductivity mirroring that of native tissues, present a promising platform for scaffolds that can modulate cell behavior and tissue formation through electrical stimulation. The biocompatibility, tunable conductivity, and topographical features of ECPs enhance cellular adhesion, proliferation, and differentiation. Furthermore, their electrical properties have been shown to augment nerve regeneration, cardiac tissue repair, and musculoskeletal tissue formation. Combined with other biomaterials or biological molecules, ECP-based composites exhibit synergistic effects, promoting enhanced tissue regeneration. Moreover, the integration of ECPs with cutting-edge technologies such as 3D printing and microfluidics propels the design of sophisticated constructs for tissue engineering applications. This paper concludes with the challenges faced in the clinical translation of ECP-based scaffolds and provides perspectives on the future trajectory of ECPs in regenerative medicine. The synthesis of ECPs with emerging biotechnologies has the potential to revolutionize treatments, bridging the gap between traditional regenerative approaches and sophisticated bioelectronic remedies.



Keywords: Electroconductive polymers, tissue engineering, regenerative medicine, biomedical applications

1. Introduction

Tissue engineering and regenerative medicine represent the most exciting field in current biomedical research. Their goal, often intertwined, is to restore, maintain, or enhance the functionality of damaged or lost tissues and organs. These highly interdisciplinary domains bring together principles from biology, chemistry, physics, and engineering to develop innovative solutions to address some of today's most critical healthcare issues [1, 2].

A key element of both tissue engineering and regenerative medicine is the utilization of suitable biomaterials to support the growth, differentiation, and function of cells. These materials often need to replicate the intricate, dynamic nature of native tissue environments to effectively guide cellular processes, which is a challenging task. In recent decades, electroconductive polymers (ECPs) have garnered substantial interest in this regard [3, 4]. ECPs diverge

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considerably from traditional polymers due to their ability to conduct electricity. This property results from the delocalization of π electrons along the polymer backbone, allowing them to behave more like metals or semiconductors than typical insulating polymers. Applications for these materials span numerous domains, from flexible electronics and batteries to sensors and biomedical devices. Their significance in tissue engineering and regenerative medicine is particularly profound because many tissues, such as nerves, cardiac, skeletal muscle, and bone, depend on electrical signaling for their normal function [4-7].

Herein, we will delve into the underlying principles and properties of ECPs. Subsequently, we will discuss their application in tissue engineering and regenerative medicine. We will also provide an outlook on the prospects of ECPs in this field, emphasizing areas where we anticipate the most significant advances.

2. Electroconductive polymers (ECPs)

In the late 1970s, Alan J. Heeger, Alan G. MacDiarmid, and Hideki Shirakawa made a revolutionary discovery related to the conductivity of polymers. Before their research, polymers were typically viewed as insulators. However, these scientists demonstrated that polyacetylene (PA), a simple polymer based on the alkene group, could have its conductivity enhanced when doped with iodine. The doped polymer took on properties similar to metals, a truly groundbreaking finding. It challenged and expanded the conventional understanding of materials and blurred the lines between what were once thought to be distinct categories: insulating polymers and conductive metals. In acknowledgment of their monumental contribution to the field of chemistry, and by extension to materials science and electronics, they were awarded the Nobel Prize in Chemistry in the year 2000. Their discovery laid the foundation for various applications of conductive polymers, including their use in organic electronic devices, sensors, and more [8].

In the decades following this discovery, a wave of new ECPs, such as polyaniline (PANI), polypyrrole (PPy), and polythiophene (PT), were discovered and synthesized. These polymers cleverly combined the advantages of plastics, such as mechanical resilience and easy processability, with the electronic and optical properties typical of metals and semiconductors. This paved the way for their use in a wide variety of applications, spanning from flexible electronics to solar cells, and more recently, to biomedical applications [7, 9].

The unique electrical conductivity of ECPs is a product of their molecular structure. They are characterized by a series of alternating single and double bonds along the polymer backbone, forming a conjugated system (**Figure 1**). This conjugation allows π electrons, which are associated with the double bonds, to become delocalized, effectively enabling them to move freely along the length of the polymer chain, and hence conferring electrical conductivity [4, 10, 11]. Although, in their pristine state, these polymers are typically not highly conductive, their conductivity can be significantly boosted through a process known as doping. Doping involves the intentional introduction of impurities, which can either act as electron acceptors (p-type doping) or electron donors (n-type doping). These dopants interact with the conjugated system, either removing an electron (p-type doping) or supplying an electron (n-type doping) to it. This process generates mobile charge carriers within the polymer, dramatically increasing its ability to conduct electricity [12-15].

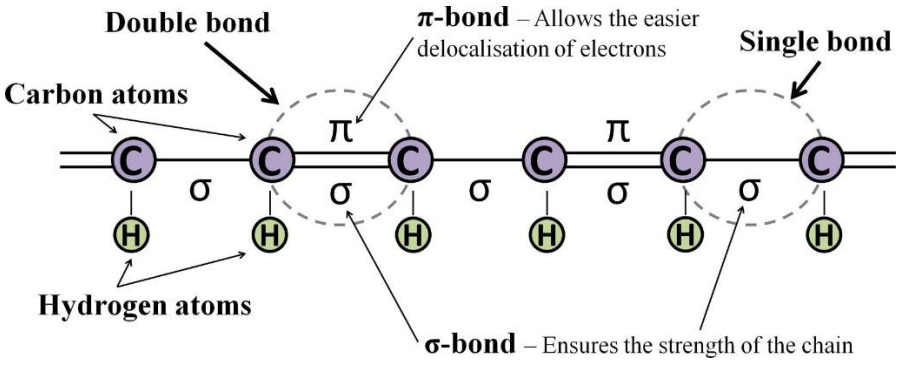

Figure 1. A basic diagram representing a conjugated backbone, which is a chain composed of alternating single and double bonds. Reproduced with permission from [4] Copyright 2014, Elsevier

Among the broad class of ECPs, a few of them have garnered particular attention due to their exceptional electronic properties, processability, and stability. For instance, PANI stands as one of the most extensively studied ECPs, primarily due to its high electrical conductivity, cost-effectiveness, low toxicity, low operational voltage, good chemical and thermal stability, and ease of synthesis. Intriguingly, it can exist in several oxidation states, each corresponding to a different level of conductivity, thereby providing a range of tunable electronic properties [16-20]. PPy, characterized by its excellent conductivity and straightforward polymerization process, has also found extensive use in the realm of biomedicine. Its inherent biocompatibility makes it an ideal candidate for biological and medical applications, from drug delivery systems to tissue engineering scaffolds [21, 22]. Another example of commonly used ECPs is PT. PT and its derivatives occupy a crucial space in the world of organic electronics. Their popularity arises from their high conductivity, excellent environmental and thermal stability, and reduced band gap energy [19, 23].

The capability of these ECPs to modulate cellular behavior through electrical stimulation offers a realm of opportunities for tissue regeneration. Moreover, the compatibility of these polymers with various biotechnologies, such as 3D printing and microfluidics, amplifies their potential in designing intricate tissue constructs that mirror native tissue dynamics.

3. Versatile properties of ECPs in biomedical applications

3.1. Antimicrobial activity

Infections caused by microorganisms like bacteria pose a significant threat to human health, and effective treatment is crucial [24]. However, with the last new antibiotic class being introduced in 2003, treating many infectious diseases has become increasingly challenging, particularly those caused by multidrug-resistant bacteria [25]. The post-antibiotic era, where previously responsive infections become resistant to even the most antibiotics, has led to a need for new strategies to fight microbial infections [26]. The Centers for Disease Control and Prevention in the US estimated that over 2 million infections and close to 23,000 deaths per annum were caused globally by antibiotic-resistant ESKAPE pathogens, including Staphylococcus aureus, Klebsiella pneumoniae, and Enterobacter species [27].

In combating these extensively drug-resistant pathogens, antimicrobial materials offer a promising microbial strategy [28]. Biomedical devices containing antimicrobial composites have received significant attention in both academia and the pharmaceutical industry [29]. These materials can be classified into those that are intrinsically antimicrobial, those that act as carriers for antimicrobial agents, and those that possess both functional properties.

One example of intrinsically antimicrobial materials is antimicrobial PANI composites [30, 31]. PANI has been applied in biomedicine, including electrotherapy, antimicrobial clothing, and electromagnetic devices for health monitoring [20]. PANI composites have been developed in combination with various antimicrobial agents, including silver nanoparticles, titanium oxides, and non-leachable compounds such as quaternary ammonium salts, to prepare several antimicrobial devices [32]. These devices show significant potential for use in biomedical applications to combat infections caused by multidrug-resistant bacteria. PANI-based compounds have been synthesized to control microbial contaminations, and their antimicrobial activity has been reported against both Gram-negative and Gram-positive bacteria [33]. Various nanomaterials, polymers, and other compounds have been added to PANI to enhance its antimicrobial activity, conductivity, and photocatalytic activity. For example, PANI-based composites consisting of different nanoarchitectures such as rods, spherical particles, tubes, and sheets have been developed and have shown promising results in biomedical applications [34].

PPy is another ECP that has been extensively studied for its antimicrobial properties. PPy exhibits excellent biocompatibility and has shown antimicrobial activity against a broad spectrum of microorganisms, including bacteria, fungi, and viruses [35-37]. PPy-based antimicrobial coatings have been developed for various biomedical applications, such as orthopedic implants, wound dressings, and catheters [37]. These coatings can prevent biofilm formation and bacterial adhesion, which are common causes of implant-associated infections. In addition, PPy nanoparticles have been shown to have the potential for use as an antimicrobial agent in various drug delivery systems [38]. The

antimicrobial mechanism of PPy is not well understood, but it is believed to involve the disruption of the bacterial membrane and the generation of reactive oxygen species (ROS). PPy can also interact with the bacterial DNA, resulting in the inhibition of bacterial growth [39]. Overall, PPy is a promising material for the development of antimicrobial coatings and drug delivery systems due to its biocompatibility, easy synthesis, and broad-spectrum antimicrobial activity. However, further research is needed to fully understand its antimicrobial mechanism and optimize its properties for specific biomedical applications.

3.2.Antioxidant activity

ECPs exhibit antioxidant activity, which means they can neutralize free radicals such as ROS, hydroxyl radicals, H_2O_2, superoxide anion radicals, and reactive nitrogen species by donating electrons or active hydrogen atoms [40]. Free radicals are not only produced in food samples (through lipid oxidation) and can affect food quality but they are also generated in cells through intracellular metabolism and are eliminated by intracellular antioxidant mechanisms to maintain homeostasis between intracellular oxidation and antioxidant effects [41]. However, if this balance is disrupted, a condition known as oxidative stress can occur, leading to cell damage and creating a favorable environment for the development of neurodegenerative disorders, various types of cancers, and cardiovascular diseases [42].

Antioxidants are essential due to the harmful effects of free radicals, such as tissue damage and the progression of diseases like inflammation, heart disease, cancer, and premature aging [43]. Antioxidants, as their name suggests, are substances that prevent the oxidation of other molecules. They play a crucial role in protecting both food and body tissues and reducing the risk of chronic diseases, thereby contributing to overall human health [44].

ECPs have shown promise in reducing the overexpression of reactive radical species and may be effective in treating tissues experiencing oxidative stress [45]. The antioxidant activity of ECPs can be assessed easily by their reaction with 1,1-diphenyl-2-picrylhydrazyl (DPPH), a free radical molecule, as a scavenger. This interaction involves the transfer of electrons and hydrogen from the polymers to DPPH to neutralize the scavenger. The resulting quenching of free radicals occurs in the microenvironment, causing a noticeable color change. Consequently, ECPs may provide a beneficial antioxidant effect to damaged tissues [46].

ECPs can be oxidized to generate positively charged centers on the polymer backbone, which can be balanced by the anionic form of DPPH or soluble anions, or DPPH may remove a proton from the polymer to form DPPH. The fact that several DPPH radicals are scavenged for each unit of aniline or pyrrole in ECPs suggests that additional reaction pathways may be involved in which the polymer distributes the charge into the surrounding solution [46]. PPy has been identified as a potent antioxidant that can counteract a variety of free radical species by donating electrons or active hydrogen atoms to the radicals, thereby preventing oxidative damage caused by free radicals [47].

3.3. Biocompatibility

Biocompatibility is an important consideration when developing materials for biomedical applications, including ECPs [48]. Cytotoxicity concerns are gaining attention as the intentional interaction of materials with cells has the potential to create adverse effects on the human body. Therefore, it is crucial to ensure that the materials used do not harm the body [49].

PPy and its composites have been used extensively in biomedical applications. It is important to identify the factors that affect their biocompatibility to evaluate their use in clinical trials. For instance, the half maximal inhibitory concentration (IC50) of PPy, which is a measure of its potency in inhibiting a specific biological function, is 0.77 mM [50]. This value indicates that PPy is partially cytotoxic, and the toxicity of PPy composites on normal cells is concentration-dependent.

Coating or surface modification of PPy with natural products can improve its biocompatibility [7]. Natural polymers such as chitosan, hyaluronic acid, and gelatin have been applied to enhance the safety profile of nanomaterials. For example, when dextran was used as a shell for PPy-based nano-assemblies, its biocompatibility was improved [51].

PANI and its composites are being investigated as promising materials for biomedical applications. As with other materials, the biocompatibility and cytotoxicity of PANI and its composites are important considerations for their use in medical applications [52]. Biocompatibility refers to the ability of a material to coexist with living tissue without

causing harm, while cytotoxicity refers to the toxic effects of the material on cells. The structures of PANI and its composites can affect both biocompatibility and cytotoxicity [53].

Studies have shown that the deprotonation-reprotonation cycles undertaken by PANI can decrease its cytotoxicity, but it is not expected to be toxic because it is insoluble and stable in aqueous solutions [54]. Low molecular weight compounds that result from byproducts with oligomers of aniline or from the acids that form PANI salts are the primary sources of cytotoxicity. The modification of PANI can significantly improve its biocompatibility and reduce cytotoxicity [55]. PANI is biocompatible in terms of dermal irritation and sensitization according to ISO 10993 standards [54]. Additionally, PANI composites have shown outstanding biocompatibility properties in the duration of dermal irritation [56].

Researchers have investigated the biocompatibility of PANI using various cell lines, including mouse embryonic fibroblast (NIH/3T3) cell lines and embryonic stem cells [57]. The results have shown that the correlation of cytotoxicity with impurity contents is not always strictly linear. Studies have found that PANI salts and PANI-based compounds have similar cytotoxicity levels [53]. However, further studies are necessary to better understand the biocompatibility and cytotoxicity of PANI and its composites for various medical applications.

4. ECPs in tissue engineering and regenerative medicine

Tissue engineering and regenerative medicine are interdisciplinary fields that aim to regenerate, repair, replace, or enhance the function of damaged or diseased tissues and organs. This is typically accomplished by combining cells with three-dimensional scaffolds that mimic the extracellular matrix, providing a supportive environment for cells to grow and differentiate [58]. Through conductive scaffolds, the normal bioelectric flow in the body could be linked, thereby enhancing tissue regeneration. Furthermore, external electrical stimulation can modulate cellular functions such as cell migration, DNA synthesis, and protein secretion [59].

ECPs have emerged as a promising class of materials for the design of advanced tissue engineering scaffolds. ECPs can be engineered to deliver electrical and biological cues that stimulate the body's repair mechanisms. For instance, electrical stimulation through conductive scaffolds can enhance cell migration and proliferation, aiding in wound healing and tissue repair [56, 60, 61]. For cell therapies and organ transplants, ECPs can be used to engineer highly functional, patient-specific tissues in the lab. They can enhance cell maturation and tissue formation, leading to improved graft survival and integration post-transplantation [4, 62]. Moreover, ECPs can be used to design smart drug delivery systems that respond to electrical signals, allowing for controlled and targeted release of therapeutic agents. Such systems can improve treatment efficacy and minimize side effects [11, 63]. ECPs have seen innovative use in the design of bioelectrodes for neuromodulation therapies, as biosensors for real-time monitoring of physiological signals, and as components of microdevices for minimally invasive therapies. Additionally, the advent of advanced fabrication techniques like 3D bioprinting has allowed for the creation of complex, patient-specific tissue constructs using ECPs. By integrating the electrical properties of ECPs with the strength, stability, and functionality of other polymers/biomaterials, these composites can simulate the electrical microenvironment of native tissues, particularly those that are electroactive like neural, muscular, and cardiac tissues [11, 64, 65]. **Table 1** presents the electrical conductivity values for various native tissues sourced from *in vivo* animal models, mostly from rats. As indicated in this table, to effectively engineer different tissues, researchers must consider these values, ensuring their engineered electroconductive scaffolds align with these electrical characteristics. However, these values are not absolute and different measurement systems and various factors can result in slight variations in the values obtained by different researchers [66].

Table 1. The range of electrical conductivity values for different native tissues [66].

Tissue	Nerve	Cardiac	Skeletal muscle	Bone	Lung	Liver
Electrical conductivity, S/m	0.08–1.3	0.005–0.16	0.04–0.5	0.02–0.06	0.04–0.2	0.05–1

In neural tissue engineering, ECPs can play a crucial role in promoting neurite outgrowth and enhancing neural signal transmission. These materials have shown potential in supporting the growth and differentiation of neural stem

cells, aiding in nerve injury repair, and the treatment of neurodegenerative diseases [7, 64, 67, 68]. Moreover, the heart's electroactive nature makes ECPs an attractive option for cardiac tissue engineering. These materials can enhance the maturation and electrophysiological functionality of cardiomyocytes, driving the formation of functional cardiac tissues for heart repair [4, 11, 64, 69, 70]. For musculoskeletal tissues, including bone, cartilage, and muscle, ECPs can support cell attachment, proliferation, and differentiation. For instance, these materials can guide osteogenic differentiation of stem cells, promoting bone regeneration [11, 71-75]. **Table 2** provides some examples of ECPs utilized in nerve, cardiac, skeletal muscles, and bone tissue engineering. The scaffolds used in these studies, such as hydrogels, electrospun nanofibrous scaffolds, 3D printed constructs, and nanostructured films and membranes were used as a replacement for native tissue's extracellular matrix, which provides an appropriate substrate for tissue mechanical integrity while facilitating cell adhesion, proliferation, and differentiation.

Numerous innovations have been made in the design and application of ECPs for tissue engineering. These include the development of composites with tailored conductivity, mechanical properties, and bioactive cues; the fabrication of complex 3D scaffold structures using techniques like 3D printing; and the design of electrically responsive systems for on-demand delivery of growth factors or genes. These advancements demonstrate the potential of ECPs in creating more sophisticated and effective tissue engineering strategies. Nevertheless, several challenges persist, such as ensuring optimal biocompatibility, adjusting degradation rates, managing the controlled release of bioactive molecules, and maneuvering through the regulatory framework for clinical application. Despite these hurdles, the progress in this field paints a promising picture for the future of tissue engineering and regenerative medicine [11, 76, 77]. While promising, the use of ECPs in regenerative medicine also faces challenges, such as ensuring long-term stability and performance in the physiological environment, understanding the *in vivo* response to these materials, and meeting regulatory requirements for safety and efficacy. However, continued research and technological advancements hold the promise of overcoming these challenges and realizing the full potential of ECPs in regenerative medicine [4, 11, 60].

Table 2. Examples of ECPs employed in tissue engineering.

Tissue	ECP	Composite	Cell type	Animal model	Outcome	Ref
Nerve	PPy	PPy/PCL	hESC-NCSCs	N/A	hESC-NCSCs differentiation to peripheral neurons on the scaffolds	[59]
		PPy/Chitosan	Schwann cells	N/A	Cell adhesion, spreading, and proliferation on the membranes	[78]
	PEDOT	PEDOT NPs/SF	BJ fibroblast cells/Schwann cells	N/A	Prevention of scar tissue formation in the lumen with no toxicity	[79]
		PEDOT NPs/ Chitin/CRGD	Schwann cells	Sciatic nerve defect rat model	Attachment and proliferation enhancement of Schwann cells and angiogenesis	[67]
Cardiac	PANI	PANI/PLA	H9c2 cardiomyoblast/ RNCMs	N/A	Promoting effect on the differentiation of H9c2 cardiomyoblasts in terms of maturation index and fusion index; Improvement of the cell-cell interaction, maturation, and spontaneous beating of primary CMs	[80]
		PANI/PGS	C2C12 cells	N/A	Improvement of electrical conductivity	[81]
	PPy	PPy/SF	Primary RNCMs/hiPSC-CMs	N/A	Elongation and anisotropically orientation of primary RNCMs on PPy/SF with locally	[82]

					organized sarcomeric striations; Strong contractions of hiPSC-CMs on PPy/SF	
		PPy NPs/ GelMA/PEGDA	RNCMs	MI rat models	Functionalization enhancement of the CMs; Excellent synchronous contraction by increasing the expression of α-actinin and connexin-43; Improvement of the cardiac function *in vivo*	[69]
		PPy/PCL	HL-1 atrial myocytes	N/A	Improvement of formation of connexin-43 to enhance cell-cell communication, resulting in higher velocities for calcium wave propagation, and reducing calcium transient duration	[83]
		PPy NPs/BC	Cardiac fibroblasts/ H9c2	N/A	Increase in the expression of functional cardiac markers in H9c2 cells	[84]
Skeletal Muscle	PANI	PANI/ Chitosan/Dextran	Mouse C2C12 myoblast/AdMSCs	N/A	Promotion of cell proliferation on the scaffolds	[85]
		PANI/PAN	hMSCs	N/A	Support of cell growth; promote hMSCs differentiation into muscle-like cells (gene expression and immumocytochemistry)	[86]
		PANI/PCL	Mouse C2C12 myoblast	N/A	Promotion of cell growth, orientation, and myotube formation	[87]
		PANI/Gelatin	Mouse C2C12 myoblast	N/A	Enhancement of myogenesis, myotube maturation	[88]
		PANI/PCL/SF	Mouse C2C12 myoblast	N/A	Promotion of cell growth, elongation, and myotube formation	[89]
		PANI/PAN	Mouse satellite cells	N/A	Promote differentiation	[90]
		PANI/PAN/CSA/G	Mouse satellite cells	N/A	Promote proliferation and differentiation	[91]
	PPy	PPy/GG/SLH	Mouse C2C12 myoblast	N/A	Support of cell adhesion and spreading	[92]
	PEDOT	PEDOT/PU	NG108-15 neuron cells/Mouse C2C12 myoblast	N/A	Support of cell adhesion and spreading	[93]
		PEDOT NPs/PCL	Rat muscle cells	N/A	Good cytocompatibility	[94]
Bone	PANI	PANI/PCL	AdSCs	N/A	Exhibition of suitable conductivity for bone tissue engineering applications and cytocompatibility	[95]
		PANI-TiO_2 NPs/PCL	MC3T3-E1 cells	N/A	Formation of hydroxyapatite layer on the surface of the nanofibrous webs in SBF	[96]
		PANI/TNTs	MC3T3-E1 cells	N/A	Enhancement in proliferation of pre-osteoblast cells	[55]
		PDA-modified PVA/PU-PANI	Rat BMSCs	N/A	Support of the formation of hydroxyapatite-like crystals; Higher expression of alkaline phosphatase and secretion of Collagen I under the electrical field indicating the applicability	[97]

				of modified electroconductive scaffolds as a reconstructive bone substitute	
PEDOT	PEDOT/Fe_3O_4/PLGA	MC3T3-E1 cells	N/A	Improve in cell proliferation; Induce cell alignment arrangement.	[98]
	PEDOT:PSS/Gelatin/BG	DPSCs	Rabbit skull defect model	Enhancement in cell; New bone formation *in vivo*	[75]
PPy	PPy NPs/PCL	MC3T3-E1 cell	N/A	Increase in SBF-biomineralization; Enhancement of MC3T3-E1 cell adhesion, proliferation, and differentiation in electrical stimulation conditions	[99]

Abbreviations: AdMSCs: adipose-derived mesenchymal stem cells; AdSCs: adipose-derived stem cells; BC: Bacterial nanocellulose; BG: Bioactive glass; BMSCs: Bone marrow mesenchymal stem cells; CMs: Cardiomyocytes; CRGD: Cell adhesive tetrapeptide Cys–Arg–Gly–Asp; CSA: Camphor sulfuric acid; DPSCs: Dental pulp stem cells; ECP: Electroconductive polymers; Fe_3O_4: Iron oxide; G: Graphene; GelMA: Gelatin methacryloyl; GG: Gellan gum; hESC-NCSCs: Human embryonic stem cell-derived neural crest stem cells; hiPSC-CMs: Human induced pluripotent stem cell-derived cardiomyocytes; hMSCs: Human mesenchymal stem cells; MI: Myocardial infarction; NPs: Nanoparticles; PAN: Polyacrylonitrile; PANI: Polyaniline; PCL: Poly(ε-caprolactone); PDA; Polydopamine; PEDOT: Poly(3,4-ethylenedioxythiophene); PEGDA: Poly(ethylene glycol)diacrylate; PGS: Poly(glycerol-sebacate); PLA: Poly(l-lactic acid); PLGA: Polylactic-co-glycolic acid; PPy: Polypyrrole; PSS: Poly(4-styrene sulfonate); PU: Polyurethane; PVA: Polyvinyl alcohol; RNCMs: Rat neonatal cardiomyocytes; SBF: Simulated body fluid; SF: Silk fibroin; SLH: Spongy-like hydrogels; TNTs: Titanium oxide nanotubes

5. Challenges and future perspectives

While the potential of ECP composites in tissue engineering and regenerative medicine is clear, several challenges remain that need to be addressed. For instance, ensuring the biocompatibility of these materials is critical, as any adverse immune or inflammatory responses could compromise their performance and safety. In addition, controlling the biodegradability of these materials to match the tissue regeneration rate is a complex task that requires further research [7, 72]. Moreover, there is a substantial gap between laboratory research and clinical applications. The scalability, reproducibility, and cost-effectiveness of producing the ECP composites are issues that need to be resolved. Furthermore, these materials must meet strict regulatory requirements regarding their safety and efficacy before any clinical use [4, 72].

Despite these challenges, the field of ECPs is rich with opportunities, and continued research and innovation in this area are expected to drive significant advancements in tissue engineering and regenerative medicine including (i) Advanced Material Design: Future research will likely focus on the design of novel ECPs with enhanced electrical, mechanical, and biological properties. For instance, incorporating bioactive molecules within these materials can provide additional functionality, (ii) Innovative Fabrication Techniques: The development of new fabrication techniques, such as advanced 3D printing technologies, could enable the creation of more complex and patient-specific structures, offering significant improvements in the treatment of a variety of medical conditions; (iii) Integrated Systems: Looking forward, there is an exciting potential for the development of integrated systems that combine ECPs with other technologies, such as microelectronics, optogenetics, and wireless technology. Such integrated systems could offer unprecedented control over tissue regeneration and repair processes.

In conclusion, while significant challenges remain, the future of ECPs in tissue engineering and regenerative medicine is promising. As we continue to expand our understanding of these materials and develop new ways to manipulate their properties, they will undoubtedly play a central role in the evolution of the generation of biomedical treatments.

6. Conclusion

The advent of ECPs has ushered in a new era in the fields of tissue engineering and regenerative medicine. By leveraging the beneficial properties of these unique materials, researchers have unlocked unprecedented opportunities

to tackle some of the most complex medical challenges, ranging from the treatment of neurodegenerative diseases to cardiac repair and bone regeneration.

A significant advantage of ECPs is their ability to mimic the natural electrical microenvironment of various tissues. Despite the promising progress and the multitude of applications demonstrated so far, a clear understanding of the challenges, including issues related to biocompatibility, biodegradability, fabrication techniques, and regulatory hurdles, is crucial. The successful clinical translation of these ECPs can only be achieved through concerted efforts to address these challenges. Peering into the future, the adaptability of ECPs, combined with ongoing advancements in material creation and manufacturing methods, suggests a bright horizon for their expanded use in tissue engineering and regenerative medicine. It is anticipated that ongoing research in this vibrant field will yield more sophisticated systems, capable of treating a broad spectrum of health conditions, thereby improving the quality of life for patients around the globe. In conclusion, although the exploration of ECPs' full potential continues, the advancements so far underscore their significant potential to revolutionize tissue engineering and regenerative medicine. The ongoing synergy between materials science and biology is expected to inspire a plethora of innovative solutions in the forthcoming years.

Authors' contributions

All authors contributed to drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Declaration of competing interest

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