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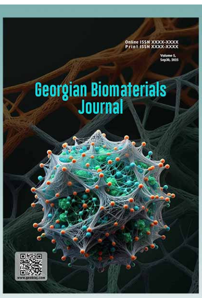

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Review Article

Exploring conductive polymers in biomaterials for electroactive wound dressings and controlled drug release

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A B S T R A C T

This study examines how conductive polymers integrated into biomaterials can create electroactive wound dressings and systems for controlled drug delivery. These polymers, with electrical conductivity similar to human skin and possessing antioxidant and antibacterial qualities, promote better wound healing through electrical stimulation and targeted drug release. Different fabrication techniques lead to various structures like films, nanofibers, hydrogels, and foams, all of which support cell growth and tissue repair. Their electroactive properties enable electrically controlled therapeutic agent release, enhancing treatments for acute, chronic, infected, and diabetic wounds. Additionally, this technology allows for real-time wound monitoring and responsive therapy, tackling current wound care challenges. The review covers recent developments, mechanisms, and future outlooks for multifunctional conductive biomaterials used in skin tissue engineering and regenerative medicine.

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1. Introduction

Incorporating conductive polymers into biomaterials represents a significant breakthrough for next-generation medical devices, especially in wound healing and drug delivery [1, 2]. Unlike conventional polymers, conductive types such as polyaniline (PANI), polypyrrole (PPy), and poly(3,4-ethylenedioxythiophene) (PEDOT) can conduct electricity, allowing them to interact actively with biological tissues and transmit electrical signals to cells [3, 4]. This electrical functionality offers new opportunities for creating smart biomaterials that can participate in healing and respond to physiological signals [1, 5].

Electroactive wound dressings mark a major advancement in wound care [6, 7]. Utilizing the electrical properties of these polymers, they can activate cellular functions, speed up tissue healing, and enable real-time healing monitoring [8]. The capacity to produce or relay bioelectrical signals at the wound improves fibroblast movement, collagen formation, and new blood vessel growth, all essential for effective wound healing [8, 9].

Meanwhile, the use of conductive polymers in controlled drug release systems provides precise, on-demand delivery of therapeutic agents [10, 11]. These materials can be designed to release drugs in response to external electrical signals, enabling spatial and temporal control over dosage and reducing side effects [12, 13]. This level of control is especially beneficial in

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treating chronic wounds and localized infections, where tailored therapy can greatly improve patient outcomes [12].

Although promising, challenges persist in enhancing the mechanical properties, biocompatibility, and durability of conductive polymer-based biomaterials [14, 15]. Current research aims to improve composite materials, modify polymer surfaces, and optimize fabrication processes to overcome these issues and fully realize the capabilities of electroactive platforms in medical applications [2].

This review investigates the current state of conductive polymers in biomaterials, emphasizing their use in electroactive wound dressings and controlled drug delivery. It underscores key material characteristics, biological interactions, and the challenges and future opportunities in this quickly advancing field.

2. Conductive Polymers: An Overview

Conductive polymers are a type of organic polymers that can conduct electricity, combining the mechanical traits of plastics with electrical conductivity usually linked to metals or semiconductors [16-18]. This special feature comes from their molecular structure, especially the presence of conjugated double bonds along their backbone, which enables the delocalization of π-electrons and helps facilitate charge transport [19].

2.1. Types of Conductive Polymers

Conductive polymers can be categorized according to their molecular structure, conduction mechanism, and applications. Fig. 1 and Table 1 illustrated the primary types.

2.2. Mechanisms of Electrical Conductivity

Electrical conductivity in materials mainly results from the movement of charge carriers, such as electrons or ions, depending on the material [36]. In metals, free electrons near the Fermi level are responsible, as they can move easily through the crystal lattice. These electrons are loosely bound to atoms and can flow freely under an electric field, leading to high conductivity [37]. Band theory explains this by showing how electrons occupy energy bands; in metals, partially filled bands near the Fermi level provide numerous states for electrons to jump between, enabling conduction [38]. Conversely, insulators and semiconductors have filled bands separated by energy gaps, which restrict electron mobility and lower conductivity [39]. Electrical conductivity involves electron and ionic conduction, with ions in materials like rocks and electrolytes acting as charge carriers [40]. It depends on charge carriers' number, charge, and mobility. Factors such as lattice vibrations and impurities affect conductivity by scattering carriers [41]. At microscopic levels, quantum effects influence charge movement, especially in nanoscale materials, impacting high-tech devices [42, 43]. Overall, it is determined by the material's atomic structure, charge carrier presence and mobility, and external factors like temperature and impurities [36, 44].

2.3. Biocompatibility and Degradability

Conductive polymers are increasingly seen as promising materials for biomedical uses because they uniquely combine electrical conductivity with potential biocompatibility [45, 46]. However, traditional intrinsically conducting polymers (ICPs) such as PEDOT, PPy, and PANI often have low or no biodegradability, limiting their application in temporary implants or tissue engineering scaffolds where material resorption is necessary [22, 47]. To overcome this, recent developments focus on designing polymers that are both biodegradable and biocompatible [48]. Methods include doping with biodopants or chemically modifying monomers to improve cellular compatibility, as well as creating block copolymers by linking electroactive oligomers with degradable ester bonds or copolymerizing conductive monomers with biodegradable polyesters such as poly(lactic acid) (PLA) or polycaprolactone (PCL). These strategies aim to refine the polymers' chemical and physical features to support cell growth while allowing controlled degradation in body environments [49]. Enhancing the degradability of conductive polymers, such as PEDOT with hydrolyzable side chains, allows for their gradual breakdown under physiological conditions [50]. These bioerodible polymers disintegrate into fragments suitable for renal clearance, reducing toxicity. Their erosion is pH-dependent and can be tailored for a specific lifetime, making them ideal for transient biomedical devices, such as implanted rechargeable batteries [2, 50]. Studies verify their cytocompatibility with various cell types, supporting safe biological integration. Overall, merging electrical functionality with biodegradability and biocompatibility promotes smart biomaterials for tissue engineering, biosensing, and implants [51].

3. Conductive Polymers for Electroactive Wound Dressings and Drug Delivery

Conductive polymers have emerged as a groundbreaking class of materials in biomedical fields, particularly for electroactive wound dressings and controlled drug delivery systems. Their unique combination of electrical conductivity, biocompatibility, and tunable properties makes them ideal for developing advanced biomaterials that can respond to physiological signals and external stimuli [2, 52].

3.1. Mechanisms of Action in Wound Healing

Conductive polymers have electrical conductivity similar to human skin, enabling them to deliver electrical stimulation directly at the wound site [53, 54]. Electrical stimulation has been demonstrated to promote wound healing by enhancing cellular activities such as fibroblast attachment, spreading, proliferation, migration, and angiogenesis [55]. For example, PPy-based composite films, especially when combined with electrical stimulation, can modulate cytokines like IL-6 and IL-8, along with growth factors such as FGF-1 and FGF-2, which are essential for tissue regeneration and myofibroblast transdifferentiation [56]. Additionally, conductive polymers can be engineered to release drugs in an electrically controlled manner, further increasing their therapeutic potential in wound care. Incorporating bioactive molecules and doping agents into CPs can improve biocompatibility, cellular adhesion, and growth, while their antioxidant properties help neutralize reactive oxygen species (ROS), protecting tissues from oxidative damage and infection during healing [57]. In addition to their electrical capabilities, conductive polymers aid wound healing by creating a supportive microenvironment that promotes cellular activities vital for tissue repair. They form a moist, three-dimensional matrix that encourages cell migration and growth, crucial for re-epithelialization and extracellular matrix reconstruction [58]. The surface hydrophilicity of the polymers can be adjusted to enhance cell attachment, and their antimicrobial properties help prevent infections, a major obstacle to healing. Research shows that conductive hydrogels made from CPs like PANI combined with biopolymers such as chitosan not only distribute electrical currents evenly but also function as drug delivery systems, releasing therapeutic compounds like vitamin D to speed up recovery [59, 60]. The combined benefits of electrical stimulation, antioxidant effects, antimicrobial activity, and controlled drug release position conductive polymers as a versatile, multifunctional platform for advanced wound dressings and skin tissue engineering [22, 61]. Fig. 2. shows schematic illustration of conductive polymers in wound healing and skin tissue engineering, illustrating their various structural forms (films, hydrogels, nanofibers, and scaffolds), and diverse applications including electroactive wound dressings and tissue scaffolds for enhanced healing and regeneration [56].

3.2. Integration of Conductive Polymers in Drug Release

Integrating conductive polymers into drug delivery systems offers a promising method for achieving controlled and targeted drug release [10, 62, 63]. Conductive polymers like polypyrrole, polyaniline, and polythiophene derivatives have distinctive electrical properties that allow them to respond to external stimuli, such as electrical fields [1, 64]. This ability can be utilized to finely control the release of therapeutic agents [65].

Table 1. Summary Table of Common Conductive Polymers

Polymer Type	Examples	Characteristics & Applications	References
Intrinsically Conductive	Polyaniline, Polypyrrole, Polythiophene, PEDOT:PSS, Polyacetylene	Conjugated polymers, doped for conductivity, used in sensors, electronics, energy devices	[20-24]
Composite Conductive	Polymer + Carbon black, metals	Conductivity via fillers, good mechanical stability	[25-30]
Ionically Conductive	Polymer electrolytes	Ion conduction, used in batteries, fuel cells	[31, 32]
Charge Transfer Polymers	Doped poly(vinyl carbazole), triarylamine doped polymers	Charge transfer mechanism, xerography applications	[33, 34]

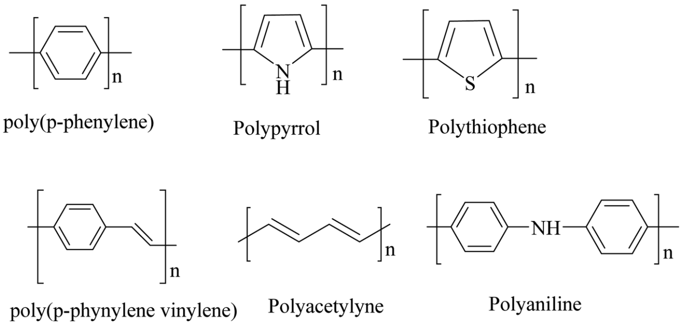

Fig. 1. Structural illustration of some Intrinsically conducting polymers [35].

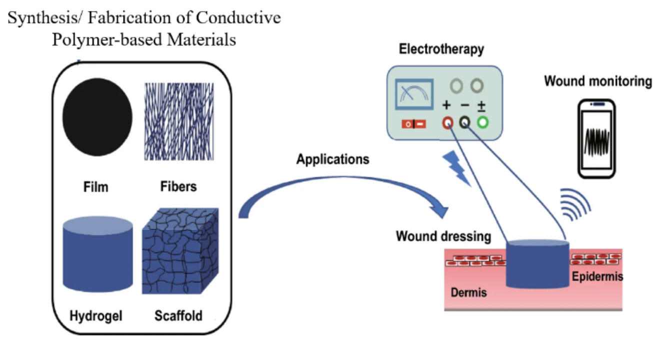

Fig. 2. Schematic depicting conductive polymers for wound healing and skin tissue engineering, showcasing various structural formats and practical applications [56].

In drug delivery, these polymers are typically designed as matrices or coatings that contain pharmaceutical agents. When an electrical stimulus is applied, the conductive polymer experiences redox reactions, resulting in modifications to its structure and porosity. These alterations help in releasing the encapsulated drug, enabling on-demand or pulsatile drug delivery [66]. This approach provides notable benefits over traditional systems by offering precise control over time and place, minimizing side effects, and enhancing treatment effectiveness [67]. Additionally, the biocompatibility and adjustable features of conductive polymers make them ideal for combining with different drugs and biomedical devices. Recent developments have concentrated on improving polymer synthesis, drug loading efficiency, and release kinetics to customize these systems for particular clinical applications [68]. The integration of electrical regulation with polymer chemistry marks a major progress in smart drug delivery, opening avenues for more personalized and adaptive therapies.

4. Future Directions and Challenges

The future directions and challenges of conductive polymers in electroactive wound dressings and controlled drug release focus on enhancing their multifunctional abilities while overcoming various technical and biological obstacles [68]. Despite the advantages of conductive polymers, precisely controlling drug release continues to be a significant challenge [69, 70]. For instance, while single-layer polypyrrole polymers have shown controlled release with minimal burst and passive diffusion, bilayer systems still encounter issues like burst release and the unintended release of polymer residues. This shows the need for further material refinement and a deeper understanding of drug-polymer interactions to ensure safety and effectiveness.

Another important approach involves combining conductive polymers with non-conductive materials to develop composite electroactive dressings that mimic the electrical properties of human skin, while also providing antibacterial and antioxidant benefits [56]. These composites can be produced as films, hydrogels, nanofibers, or foams to cater to different wound types and levels of severity [71, 72]. Applying electrical stimulation along with conductive polymers has shown to enhance cellular responses and gene activity related to wound healing, highlighting the promise of integrating material science with bioelectrical therapies [6]. Moreover, future research should prioritize creating intelligent wound dressings that can both deliver drugs in a controlled way and monitor healing progress directly within the body [73]. Achieving this will require advancements in biosensing technologies combined with conductive polymers to offer real-time feedback and allow for adaptive treatment [6].

Additionally, efforts must be made to overcome challenges like ensuring long-term biocompatibility, preventing cytotoxic effects from polymer breakdown products, and scaling up manufacturing processes without compromising quality, all essential steps to move these innovations from lab studies to clinical use [52].

5. Conclusion

In summary, the use of conductive polymers in biomaterials offers a highly promising avenue for creating electroactive wound dressings and systems for controlled drug release. These materials provide electrical conductivity similar to human skin and possess excellent biocompatibility, antibacterial, and antioxidant properties, which together promote faster wound healing by stimulating electrically responsive cells and enabling targeted drug delivery. Advances in fabrication methods like electrospinning enable precise control over the physical characteristics and drug release behavior of these dressings, helping to minimize issues such as burst release and systemic side effects. Although challenges remain, such as optimizing drug release profiles and ensuring all components are biocompatible, ongoing research into single- and bilayer conductive polymer systems and composite materials continues to improve their therapeutic potential. Incorporating conductive polymers into smart bandages holds great promise for personalized, effective treatment of chronic and complex wounds, representing a significant advancement in tissue engineering and regenerative medicine.

Author Contributions

Farzin Emami: Conceptualization, Writing – original draft, Writing – review & editing; **Elham Barati:** Writing – original draft, Writing – review & editing. All authors read and approved the final version of manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data is available.

Ethical issues

The authors confirm full adherence to all ethical guidelines, including the prevention of plagiarism, data fabrication, and double publication.

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