

RESEARCH ARTICLE

A Self-Powered Dressing Based on a Zn-Mo Galvanic Cell for Accelerated Wound Repair

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ABSTRACT

Acute wounds are a prevalent clinical concern, and their management requires strategies that actively support tissue regeneration. Electrical stimulation (ES), which mimics endogenous bioelectric cues, has emerged as a promising approach for promoting wound repair. However, many existing electroactive dressings depend on external power sources or non-degradable electronic components, limiting their practicality and long-term biocompatibility. To address these challenges, we developed a self-powered electroactive dressing (ES-GP/ZIM) integrating a biodegradable Zn–Mo galvanic cell within a trilayer electrospun scaffold loaded with icariin (ICA). In the physiological wound environment, the Zn–Mo galvanic couple generates continuous localized electrical stimulation, while the intermediate layer provides sustained ICA release to regulate inflammation and angiogenesis throughout the healing process. In a full-thickness skin wound model, ES-GP/ZIM markedly accelerated tissue repair, achieving ~85% wound closure by day 7 and near-complete epithelialization by day 14. Mechanistic studies further revealed that the combined action of ES and ICA effectively modulates key cellular processes, including inflammation, fibroblast migration, collagen deposition, and neovascularization. Collectively, this biodegradable and self-powered dressing provides a simple yet effective platform for active wound management and regenerative tissue repair.

1 | Introduction

Surgical wound healing remains a major clinical challenge, as the quality and rate of tissue repair directly affect postoperative recovery and patient outcomes. Despite continuous advances in surgical techniques and infection control strategies, complications such as wound dehiscence, surgical site infection (SSI), and delayed healing remain common and continue to impose a substantial healthcare burden worldwide [1]. Wound repair is a highly coordinated biological process involving hemostasis, inflammation, proliferation, and remodeling. These phases

overlap rather than occur independently, and successful healing depends on the precise regulation of biochemical, mechanical, and electrical cues within the wound microenvironment [2]. Conventional wound dressings, including paraffin gauze, hydrogels, and polymer membranes, primarily provide physical protection, moisture retention, and exudate management [3, 4]. Although these materials are effective in maintaining a favorable wound environment, they play a largely passive role and cannot actively restore the regulatory signals disrupted by tissue injury. Among the various factors involved in wound repair, endogenous bioelectricity has emerged as an important regulator of tissue

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regeneration. Intact skin maintains a transepithelial potential (TEP), and disruption of tissue integrity generates endogenous electric fields (EFs) that guide the migration of keratinocytes, fibroblasts, and other reparative cells toward the wound site [5]. However, these endogenous electrical signals can be weakened by excessive exudate, persistent inflammation, and tissue damage. As a result, electrical stimulation (ES) has attracted increasing attention as a strategy to supplement endogenous bioelectrical cues and promote wound healing [6, 7].

Recent studies have shown that electroactive dressings and conductive biomaterials can enhance wound repair by promoting cell migration, collagen deposition, and angiogenesis [8–11]. However, most reported systems depend on external power supplies, rigid electronics, or conductive components that are not fully integrated with the degradable wound-contact matrix. These features can reduce conformability, complicate device design, and often require removal after treatment. Advances in multifunctional wound dressings, including smart bioadhesives, now allow simultaneous integration of adhesion, antibacterial activity, stimulus responsiveness, sensing, wireless communication, and on-demand drug release. Electrospun nanofibrous scaffolds are particularly attractive, as they mimic the extracellular matrix (ECM), provide high porosity and large surface area, and can be loaded with bioactive molecules or conductive agents [9, 12, 13]. Such scaffolds offer a promising route to multifunctional electroactive wound dressings capable of actively guiding tissue regeneration. Full-thickness surgical wounds present additional challenges. An ideal transient dressing should maintain close contact with the wound bed, provide mechanical support during early healing, deliver localized therapeutic cues, and degrade safely after fulfilling its function. These requirements emphasize the need for a self-powered and biodegradable wound-contact system rather than conventional passive dressings or reusable external patches.

Despite the encouraging progress of electroactive wound dressings, several challenges still limit their practical application. Conductive dressings powered by external electrical sources can provide effective stimulation, but the need for wired or wireless power systems inevitably increases device complexity and may reduce patient comfort and mobility [14]. Self-powered platforms based on piezoelectric or triboelectric nanogenerators offer an attractive alternative [15]; however, their electrical output is closely associated with body motion and therefore often fluctuates with patient activity [16]. Battery-integrated bioelectronic dressings can deliver more stable electrical stimulation, yet many reported designs remain rigid or semi-rigid and show limited conformability to irregular wound surfaces. In addition, therapeutic functions such as controlled drug delivery are rarely incorporated into these systems. As wound healing is a dynamic process that requires coordinated biological regulation at different stages, an ideal electroactive dressing should not only provide continuous self-powered electrical stimulation, but also offer structural support, controlled therapeutic delivery, and safe biodegradation within a single platform. Such a multifunctional system may be particularly beneficial for the treatment of complex surgical wounds, large tissue defects, and poorly vascularized wounds, where sustained regulation of both the biological and electrical microenvironment is required throughout the healing process.

Electrical stimulation alone cannot fully address the complex biological requirements of wound healing. In addition to bioelectrical regulation, biochemical cues also play a critical role in controlling inflammation, angiogenesis, and tissue remodeling throughout the repair process. Among various bioactive molecules, icariin (ICA), a natural flavonoid isolated from *Epimedium* species, has attracted considerable attention due to its anti-inflammatory and pro-angiogenic activities [17–21]. Previous studies have shown that ICA can suppress excessive inflammatory responses by regulating NF- κ B and MAPK signaling pathways while enhancing antioxidant defense through Nrf2 activation [22, 23]. At the same time, ICA promotes endothelial cell proliferation and neovascularization through activation of the PI3K/Akt/eNOS pathway and enhanced VEGF secretion [24]. These biological activities make ICA particularly attractive for wound-healing applications, where early control of inflammation and subsequent vascular regeneration are both required. Therefore, integrating ICA delivery with localized electrical stimulation may provide complementary therapeutic effects during different stages of wound repair.

To achieve sustained and autonomous therapeutic action, self-powered electroactive materials have emerged as an attractive strategy for wound management. Unlike conventional bioelectronic systems, these materials can provide localized electrical stimulation without external power sources and may safely degrade after completing their therapeutic function, thereby reducing the need for secondary intervention [25]. Among biodegradable metals, zinc (Zn) is particularly attractive because of its favorable electrochemical activity, good conductivity, high theoretical volumetric capacity, and established biological safety as an essential trace element [26–28]. In physiological environments, Zn can act as an active anode and continuously generate mild electrical stimulation through electrochemical reactions. When coupled with a conductive cathode such as molybdenum (Mo), a localized micro-electric field can be established at the wound interface [29]. Previous studies have demonstrated the feasibility of electrochemical stimulation for tissue repair using battery-integrated or self-powered bioelectronic platforms. However, most reported systems focus primarily on electrical stimulation or wound monitoring, while the integration of biodegradable galvanic stimulation, ECM-mimicking structural support, and controlled therapeutic delivery remains limited.

To highlight the current design gap, representative self-powered wound dressings are compared in Table 1. Existing systems generally emphasize either electrical regulation or monitoring functions, whereas few platforms simultaneously combine a biodegradable galvanic couple, an ECM-inspired nanofibrous architecture, and localized delivery of bioactive therapeutics within a single transient dressing. This unmet need motivated the development of the ES-GP/ZIM system.

Building on these considerations, we sought to develop a wound-contact system capable of providing localized electrical stimulation while simultaneously regulating the biological microenvironment throughout the healing process (Figure 1). To this end, a self-powered and fully biodegradable electroactive dressing, designated ES-GP/ZIM, was constructed based on a Zn–Mo galvanic architecture integrated within a multilayer electrospun scaffold.

TABLE 1 | Comparison of Representative Self-Powered Wound Dressings.

Dressing	Power Source	Drug Delivery	ECM-Mimicking Structure	Biodegradability	Main Function	In Vivo Performance
ES-GP/ZIM (This work)	Zn–Mo galvanic cell	ICA sustained release	Trilayer electrospun scaffold	Yes	ES + anti-inflammation + angiogenesis	~85% closure (D7); nearly complete healing (D14)
P-E-PGP [7]	Exudate-driven streaming potential	No	Nanofiber membrane	Partial	ES	23.6% improvement in wound healing
TGC dressing [30]	Thermogalvanic effect	No	Hydrogel-based	Yes	ES + monitoring	20.6% improvement (D14)
Zn–Mo battery [31]	Zn–Mo galvanic cell	No	No	Yes	Long-term bioelectric stimulation	Nerve regeneration model

Unlike conventional battery-assisted devices in which the power source is physically separated from the wound-contact material, the Zn and Mo components were directly incorporated into the scaffold structure to enable localized electrical stimulation under physiological conditions.

Specifically, the bottom GP/Z layer and the top GP/M layer contain Zn and Mo nanoparticles, respectively, forming a biodegradable galvanic couple capable of generating a localized micro-electric field in the wound environment. Positioned between these two electroactive layers, the GP/I layer functions both as a physical separator and as a reservoir for sustained icariin (ICA) release. The scaffold matrix, composed of gelatin (Gel) and polycaprolactone (PCL), provides a biocompatible and degradable nanofibrous network with structural features resembling the native extracellular matrix (ECM), thereby supporting cell adhesion, proliferation, and migration [32].

This integrated design enables localized electrical stimulation and controlled ICA delivery within a single biodegradable platform, allowing regulation of macrophage polarization, angiogenesis, and extracellular matrix remodeling throughout the healing process. Compared with previously reported electroactive wound dressings, ES-GP/ZIM was designed to address four persistent challenges in active wound management: (i) dependence on external power supplies, (ii) limited integration between electroactive components and biodegradable wound-contact matrices, (iii) insufficient incorporation of phase-matched therapeutic delivery, and (iv) the lack of a unified platform capable of providing both electrical and biochemical regulation.

To evaluate the respective roles of the scaffold matrix, ICA, and galvanic stimulation, GP-b, GP/I-S, ES-GP/ZM, and ES-GP/ZIM were included as control groups. Comprehensive materials characterization, electrochemical evaluation, degradation and drug-release studies, cellular experiments, macrophage polarization assays, and full-thickness wound-healing studies were subsequently performed to assess the therapeutic performance of ES-GP/ZIM and investigate its underlying mechanism of action.

2 | Results and Discussion

2.1 | Comprehensive Characterization and Performance Analysis of the ES-GP/ZIM Scaffold

The ES-GP/ZIM scaffold was fabricated via sequential electrospinning to establish a functionally stratified three-dimensional fibrous network [9, 34]. Scanning electron microscopy (SEM) analysis (Figure 2a,b) revealed that the non-crosslinked scaffold consisted of randomly oriented filaments with smooth surfaces and uniform diameters. Upon EDC/NHS crosslinking, pronounced fiber adhesion and the formation of interconnection points were observed, yielding a more compact and robust three-dimensional architecture; this morphological evolution is critical for enhancing the scaffold's mechanical properties and structural integrity. Macroscopic observations (Figure 2c) showed that the scaffold exhibited a uniform grayish-white hue, attributable to the homogeneous incorporation of Zn and Mo nanoparticles, while simultaneously demonstrating exceptional flexibility. The material maintained its structural coherence even under manual bending, underscoring its favorable adaptability for clinical handling.

Fourier transform infrared spectroscopy (FT-IR, Figure 2g) further corroborated the successful integration of all constituent components. The spectrum of ICA displayed a broad absorption band between 3200 and 3400 cm^{-1} , attributed to O–H stretching vibrations, alongside a characteristic peak near 1500 cm^{-1} associated with aromatic ring skeletal vibrations. Gel exhibited a broad feature spanning 3200 to 3500 cm^{-1} , indicative of overlapping N–H and O–H stretching vibrations typical of proteinaceous materials, while PCL showed distinct absorption peaks at 2945, 2854, and 1725 cm^{-1} , corresponding to C–H and C=O stretching modes. Analysis of the crosslinked GP (cGP) spectrum revealed the coexistence of the broad Gel band (3200–3500 cm^{-1}) and the characteristic PCL peaks (2945, 2854, and 1725 cm^{-1}). The absence of significant shifts in peak position, intensity, or shape relative to the individual precursors indicated effective composite formation between Gel and PCL, with the crosslinking process preserving the intrinsic functional group structures of the raw materials. Similarly, the spectrum of the non-crosslinked GP/I

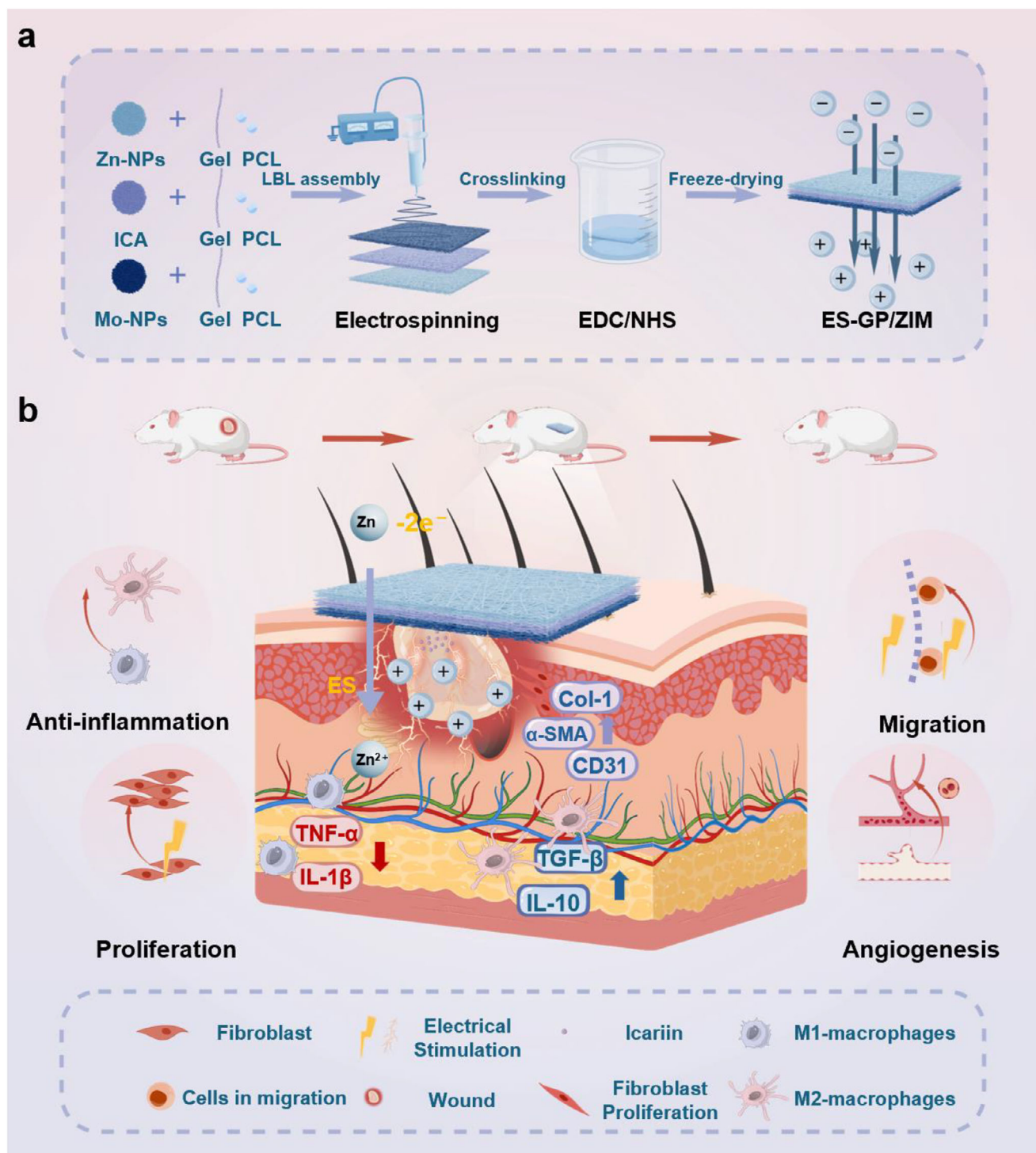


FIGURE 1 | (a,b) Preparation and application of ES-GP/ZIM, Created with BioGDP.com [33].

composite scaffold retained the diagnostic peaks of Gel, PCL, and ICA without noticeable displacement, confirming the successful encapsulation of ICA within the Gel/PCL matrix.

X-ray diffraction (XRD) analysis (Figure 2j, Figure S1) of the ES-GP/ZIM scaffold yielded diffraction patterns featuring characteristic peaks corresponding to Zn, Mo, and ICA. These results further substantiated the successful incorporation and uniform distribution of both the metallic nanoparticles and

the therapeutic agent within the composite fibers. Collectively, these spectroscopic and diffractometric findings confirm the effective integration of ICA, Gel, and PCL, thereby validating the successful establishment of the ES-GP/ZIM composite system.

Thermogravimetric analysis (TGA) of the GP/M fibrous membrane was performed under an air atmosphere, with samples heated from 30°C to 800°C at a rate of 10.0°C/min. The resulting thermogram (Figure S2) exhibited a slight weight loss between

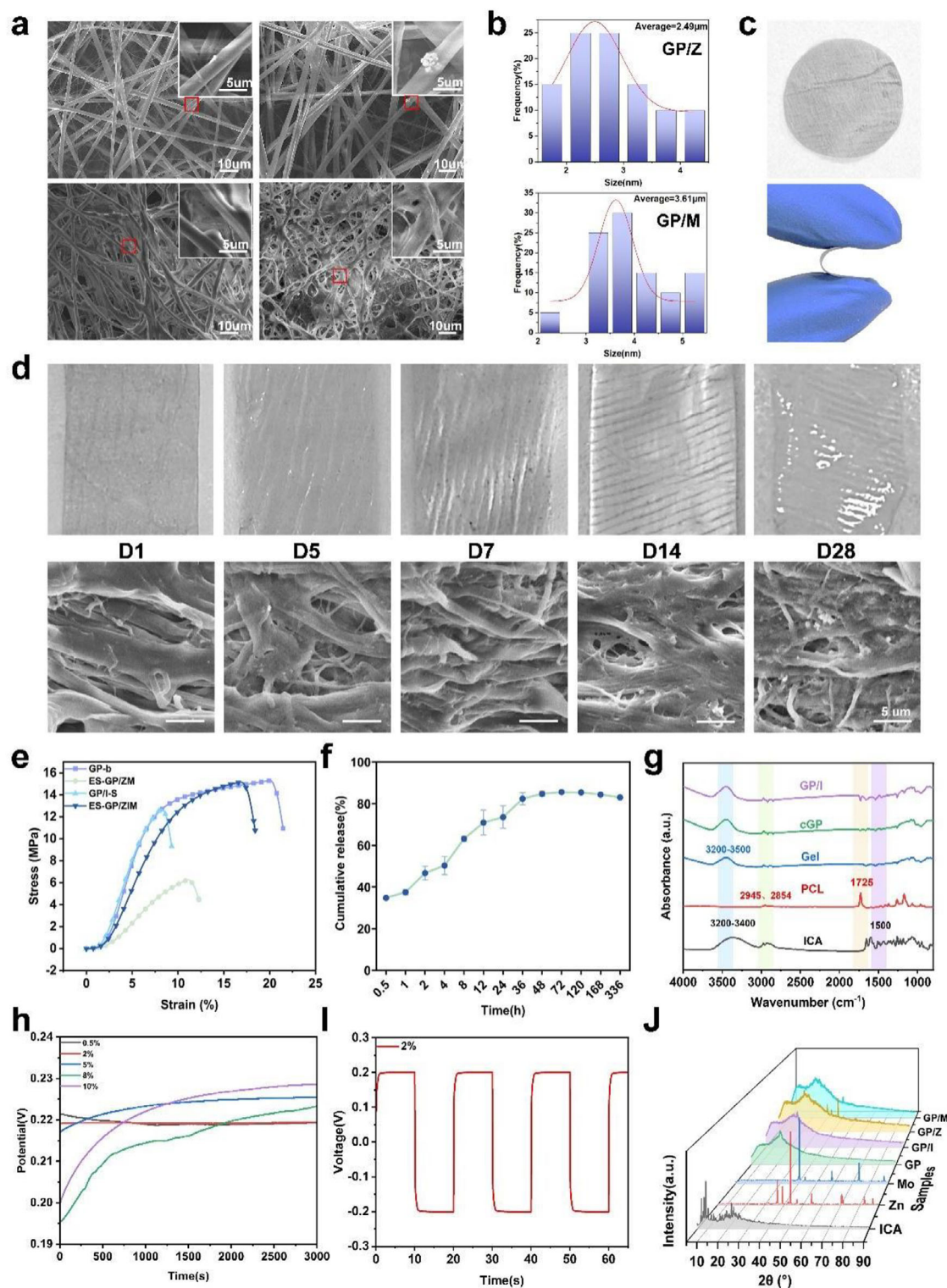


FIGURE 2 | Structural Characterization and In Vitro Performance of the ES-GP/ZIM Trilayered Composite Fibrous Scaffold. (a) SEM images of both surfaces of the ES-GP/ZIM scaffold (magnification: 1000×). The left panel shows the top GP/Z layer (loaded with Zn NPs), and the right panel shows the bottom GP/M layer (loaded with Mo NPs). Insets display higher magnification views (5000×) highlighting the morphological differences in the fibrous network before and after crosslinking. (b) Corresponding fiber diameter statistics of the uncrosslinked scaffolds. (c) Optical photographs of the ES-GP/ZIM scaffold demonstrating its integrated structure, flexibility, and handling capability. (d) In vitro degradation behavior of the scaffold in PBS at different time points (day 1, 5, 7, 14, and 28): Top row shows macroscopic photographs; middle row shows corresponding SEM images (magnification: 2000×). (e) Stress–strain curves of different materials, comparing the mechanical properties of the ES-GP/ZIM scaffold with those of single-component scaffolds. (f) Cumulative release profile of ICA from the ES-GP/ZIM scaffold over time at 37 °C. (g) FT-IR spectra. (h) Open circuit potential (OCP) versus time curves of electrospun fiber scaffolds with different Zn and Mo doping ratios. (i) Galvanostatic charge–discharge (GCD) curves of electrospun scaffolds with 2% Zn and Mo doping. (j) XRD patterns of individual components and the composite scaffold. Data are presented as mean ± SD ($n = 3$).

30°C and 150°C, primarily attributed to the evaporation of adsorbed and bound water within the fibrous matrix. A pronounced mass reduction occurred between 200°C and 400°C, corresponding to the thermal degradation of the Gel macromolecular backbone, while the temperature range of 400°C–500°C represented the stage of deep thermo-oxidative decomposition of the PCL matrix. Above 500°C, the mass progressively stabilized, yielding a final char residue of approximately 22% at 800°C, composed mainly of thermally stable inorganic Mo and its oxide derivatives. These findings indicate that Mo doping effectively enhances both the thermal stability and high-temperature char yield of the fibrous membrane, thereby ensuring robust structural integrity during subsequent fabrication processes and in vivo applications.

An ideal acute wound dressing must maintain structural integrity for 7–14 days, degrading only after complete epithelialization is achieved. By integrating macroscopic photography, SEM imaging, and mass retention curves obtained at various time points, we systematically evaluated the in vitro degradation behavior of the ES-GP/ZIM trilayered composite fibrous scaffold (Figure 2d,e). The results revealed a mild and controllable multi-stage degradation profile under simulated physiological conditions. During the initial phase (1–7 days), macroscopic observations showed the scaffold surface transitioning from a smooth, uniform state to one exhibiting slight wrinkling and localized swelling. Concurrently, SEM images revealed a loosening of the fibrous network accompanied by the fracture of finer fibers. Correspondingly, the mass retention rate dropped rapidly from 100% to approximately 40%, driven primarily by the hydrolysis of surface-exposed Gel and the release of loaded functional small molecules, including ICA. In the middle-to-late stage (7–28 days), macroscopic photographs displayed noticeable surface depressions and the accumulation of degradation residues. SEM analysis indicated further thinning of the fibrous network, characterized by fiber adhesion and pore formation in specific regions. During this phase, the rate of mass loss slowed significantly, decreasing only from 40% to approximately 28%. Degradation in this period was predominantly governed by the hydrolysis of PCL ester bonds and the gradual breakdown of crosslinked Gel.

This degradation kinetics aligns closely with the typical 2–4 week healing cycle of cutaneous wounds. The rapid initial degradation facilitates the timely release of anti-inflammatory and pro-angiogenic functional components (ICA, Zn, and Mo) while enabling the prompt initiation of electrical stimulation effects via the generated micro-electric field. Conversely, the subsequent slow degradation phase provides sustained physical support for nascent tissue, preventing premature scaffold collapse and ensuring microenvironmental stability conducive to tissue regeneration. Furthermore, EDC/NHS crosslinking not only enhanced the mechanical integrity of the scaffold but also retarded the rapid hydrolysis of Gel, thereby optimizing the overall degradation profile. This modification establishes a structural foundation for the sustained release of bioactive agents and the long-term maintenance of electrical stimulation efficacy. Moreover, this mild degradation pattern mitigates the burst release of acidic by-products, reducing the risk of local inflammation and complementing the scaffold's inherent anti-inflammatory design. Additionally, as degradation progresses, the fibrous network transitions from a dense to a porous architecture.

This structural evolution promotes cell infiltration and nutrient exchange, while the remaining three-dimensional fibrous skeleton preserves continuous electrical conduction pathways. Consequently, the combined therapeutic effects of electrical stimulation and bioactivity are maintained throughout the entire degradation process. Collectively, these findings validate that the ES-GP/ZIM scaffold achieves an optimal balance between structural stability and degradability, providing a critical rationale for its potential long-term application in wound healing therapies.

Given the dual pharmacological properties of ICA, encompassing both anti-inflammatory and pro-angiogenic activities, its release kinetics are of paramount importance. Under simulated physiological conditions, ICA exhibited a characteristic biphasic release profile (Figure 2f). The initial 0–24 h period represented a rapid burst-release phase, with cumulative release reaching approximately 45% within 2 h and increasing to about 70% by 24 h. This behavior was primarily attributed to the rapid dissolution and diffusion of ICA loaded on the scaffold surface and within superficial layers, coupled with the hydrolysis of non-crosslinked surface Gel. Subsequently, from 24 h to 336 h, the system transitioned into a slow sustained-release phase characterized by a significantly reduced release rate. A plateau of approximately 85% was reached around 120 h and remained stable, maintaining a release level of roughly 83% up to 336 h. This sustained phase relied on the gradual degradation of the crosslinked Gel network and the slow hydrolysis of PCL, facilitating the continuous release of deeply embedded ICA. The cumulative ICA release plateaued at approximately 83%, whereas the scaffold mass retention decreased to approximately 28%. This difference likely arises because a fraction of ICA remained physically entrapped within the crosslinked Gel/PCL network or associated with degradation residues, while partial degradation of ICA during prolonged incubation may further reduce the measurable cumulative release.

This “fast-then-slow” release pattern effectively addresses the temporal demands of wound healing: the early burst release supplies a high concentration of anti-inflammatory agents during the inflammatory phase, while the subsequent sustained release provides pro-angiogenic bioactive substances throughout the proliferative phase, aligning with the staged requirements of cutaneous wound repair.

Correlating the drug release behavior with the scaffold's degradation kinetics and design objectives reveals a close correspondence between scaffold degradation, ICA release, and the intended therapeutic timeline. During the initial degradation stage (1–7 days), the rapid hydrolysis of non-crosslinked surface Gel not only reduced mass retention to approximately 40% but also drove the initial burst release of ICA. The rapidly released ICA exerts anti-inflammatory effects during the wound inflammatory phase, while the exposed Zn and Mo nanoparticles establish an endogenous micro-electric field, initiating electrical stimulation to modulate cell behavior. These responses create a favorable microenvironment for subsequent tissue repair. In the middle-to-late degradation stage (7–28 days), the slow hydrolysis of the crosslinked Gel network and PCL further reduced mass retention to approximately 28%, corresponding to the sustained-release phase of ICA. The continuously released ICA maintains its pro-angiogenic and cell-proliferative effects during the

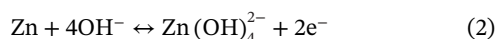
wound proliferative phase. Meanwhile, the preserved three-dimensional fibrous skeleton maintains electrical conduction pathways, allowing the micro-electric field generated by nano-Zn/Mo and sustained ICA release to remain active throughout the tissue repair process. This provides stable physical support and functional regulation for nascent tissue, preventing premature scaffold collapse. These observations underscore the critical role of EDC/NHS crosslinking, which not only optimized the scaffold's degradation kinetics but also regulated the release rhythm of ICA, ensuring full compatibility with the 2–4 week healing cycle of skin wounds. Furthermore, the mild degradation pattern mitigates the burst release of acidic by-products, forming a dual safeguard alongside ICA's anti-inflammatory effects to minimize the risk of local inflammation. Finally, the structural evolution of the fibrous network from dense to porous promotes cell infiltration and nutrient exchange while preserving electrical conduction pathways, ultimately supporting long-term electrical and biological regulation throughout wound healing.

Appropriate mechanical properties are essential for effective wound treatment and recovery [35]. The stress–strain curves (Figure 2e, Figure S4) demonstrate that the ES-GP/ZIM group exhibits optimal mechanical adaptability, effectively balancing strength, extensibility, and flexibility. This group achieved a tensile strength of 15.16 MPa, an elongation at break of 18.42%, and a tensile elastic modulus of 196.43 MPa. These metrics indicate sufficient mechanical integrity to withstand potential damage during clinical handling and wound movement, moderate extensibility to accommodate dynamic skin deformation, and a relatively compliant elastic modulus that minimizes mechanical irritation to the wound site. In comparison, while the GP-b group displayed slightly higher tensile strength (15.30 MPa) and elongation at break (21.46%), its elastic modulus reached 280.52 MPa, suggesting a relatively rigid material that could restrict skin movement and induce discomfort. Conversely, the GP/I-S group exhibited an elongation at break of only 8.02%, reflecting insufficient extensibility to adapt to dynamic wound stretching. Furthermore, the ES-GP/ZM group showed a tensile strength of merely 6.26 MPa, indicating inadequate mechanical support and a potential risk of rupture during clinical application. Collectively, these findings confirm that the ES-GP/ZIM scaffold possesses mechanical properties that are superiorly aligned with the clinical requirements for advanced wound dressings.

In a simulated physiological environment utilizing PBS as the electrolyte, the electrochemical behavior of the Zn–Mo micro-battery is governed by the following reactions: Zn, acting as the active anode, undergoes oxidation to release electrons and generate Zn ions (Reactions 1).



Concurrently, Zn may undergo parasitic reactions with hydroxide ions (OH^-) in the solution to form zincate ions or Zn oxide (Reactions 2 and 3). These by-products exhibit limited solubility in PBS and do not significantly impede the electrode reactions.



At the cathode, two primary reactions occur: the hydrogen evolution reaction (Reaction 4) and the oxygen reduction reaction (Reaction 5), with the latter serving as the dominant process under physiological conditions.



Electrospun fiber scaffolds containing different Zn and Mo doping ratios (0.5%, 2%, 5%, 8%, and 10%) were systematically evaluated by electrochemical impedance spectroscopy (EIS), open circuit potential (OCP), galvanostatic charge–discharge (GCD), and cyclic voltammetry (CV) measurements to identify an appropriate composition for constructing the self-powered electroactive dressing.

EIS Nyquist plots (Figure S5a) revealed that the 2% Zn/2% Mo scaffold exhibited the lowest charge transfer resistance and a well-balanced electrochemical profile and the steepest low-frequency slope. These features indicate the lowest charge transfer resistance and the most efficient charge transfer and ion diffusion kinetics at the electrode–electrolyte interface. In contrast, the 0.5% Zn/0.5% Mo scaffold exhibited the largest high-frequency semicircle and the highest impedance, primarily attributed to insufficient metal nanoparticle loading, which compromised electrical conductivity and ion transport capacity. Conversely, in the high-doping groups (5%, 8%, and 10%), the high-frequency semicircle diameter progressively increased, and the low-frequency slope decreased as the doping ratio rose. This trend suggests that excessive metal loading disrupts the fibrous microstructure and intensifies side reactions at the electrode–electrolyte interface, leading to a marked increase in interfacial impedance.

OCP measurements (Figure 2h) revealed that all scaffolds generated stable potentials within the range of 0.21–0.23 V. Although higher doping ratios produced slightly higher equilibrium potentials, the 2% Zn/2% Mo scaffold reached a stable plateau rapidly with minimal fluctuation, suggesting favorable electrochemical stability under physiological conditions. To further evaluate the environmental adaptability of the Zn–Mo galvanic system, OCP measurements were conducted under different pH conditions (pH 5, 7, and 9) (Figure S5b). The scaffold maintained a stable potential of approximately 0.21 V under physiological pH conditions. Under acidic conditions (pH 5), the potential gradually increased, which may be attributed to enhanced Zn oxidation and accelerated galvanic activity. In contrast, the potential decreased under alkaline conditions (pH 9), likely due to the formation of passivating zinc hydroxide/oxide layers. Nevertheless, measurable electrochemical activity was maintained across the entire tested pH range, indicating that the scaffold possesses sufficient environmental tolerance for wound-healing applications.

GCD tests conducted within a biocompatible potential window of −0.3 to 0.3 V (Figure 2i) showed that the 2% Zn/2% Mo scaffold possessed excellent reversibility and stable charge–discharge profiles with distinct plateaus. This characteristic supports the delivery of continuous, gentle microcurrent stimulation to the

wound site while avoiding tissue damage associated with excessive voltage.

CV (Figure S5c) measurements demonstrated typical quasi-rectangular profiles for all groups, indicating capacitive behavior. The 2% Zn/2% Mo scaffold exhibited a well-maintained CV shape with a relatively large enclosed area, reflecting an appropriate balance between charge-storage capability and electrochemical reversibility.

Although the 5–10% groups generated slightly higher equilibrium potentials, excessive nanoparticle loading may adversely affect fiber morphology, increase structural heterogeneity, and potentially compromise long-term stability and biocompatibility. Therefore, the 2% Zn/2% Mo composition was selected as the optimal formulation by balancing electrochemical activity, scaffold integrity, and biological applicability.

Collectively, these results demonstrate that the scaffold can spontaneously generate a continuous micro-electric field via electrochemical reactions between nano-Zn and nano-Mo in the physiological environment, eliminating the need for an external power supply. This endogenous electrical signal effectively compensates for the bioelectric deficits during wound healing, regulating cell migration, proliferation, and differentiation, thus laying a direct electrical foundation for electrostimulation-mediated tissue regeneration. Specifically, pairing the 2% Zn/2% Mo scaffold with a Zn anode constructs a Zn–Mo galvanic cell that integrates spontaneous microcurrent generation (galvanic effect) with reversible capacitive charge storage and release. This dual mechanism supports the functional requirements of self-powered electrostimulatory wound dressings. In summary, the complementary data from EIS, OCP, GCD, and CV confirm that a 2% doping ratio for both Zn and Mo achieves an optimal balance among charge transfer efficiency, interfacial stability, and energy storage capacity, rendering this scaffold an appropriate candidate for next-generation self-powered wound therapy.

2.2 | In Vitro Biocompatibility of ES-GP/ZIM

In the realm of biomaterials, particularly for wound dressing applications, exceptional biocompatibility is a fundamental prerequisite for clinical translation, while the targeted modulation of the inflammatory microenvironment is pivotal for accelerating acute wound healing. In this study, human skin fibroblasts (HSFs) served as the cellular model to systematically evaluate the effects of the ES-GP/ZIM scaffold on fibroblast migration, viability, and proliferation via scratch assays, live/dead fluorescence staining, and CCK-8 proliferation assays. These experiments comprehensively elucidate the respective contributions of electrical stimulation and ICA, as well as their effects when applied together, on key cellular behaviors essential for wound repair, thereby establishing a cytological basis** for the scaffold's application in acute wound treatment.

The cell scratch assay results (Figure 3a,b) visually demonstrated the differential regulatory effects of the various treatment groups on HSF migration capacity. At 12 h of culture, the ES-GP/ZIM

group exhibited a cell migration rate of approximately 65%, which was significantly higher than that of the blank control (~30%) and the pure matrix group (GP-b, ~28%), and markedly superior to both the drug-only group (GP/I-S, ~45%) and the drug-free electrical stimulation group (ES-GP/ZM, ~35%). These findings confirm that the ES-GP/ZIM scaffold substantially promotes the directional migration of fibroblasts. Moreover, the group receiving both electrical stimulation and ICA exhibited a stronger promotive effect on cell migration than either treatment alone, aligning with the physiological requirement for rapid fibroblast recruitment to the wound center during tissue repair.

Live/dead fluorescence staining (Figure 3c) further corroborated the cytocompatibility of the scaffold. Across all treatment groups, live cells (labeled with Calcein-AM, green fluorescence) were overwhelmingly predominant, with negligible numbers of dead cells (labeled with PI, red fluorescence) observed. Notably, the ES-GP/ZIM group displayed a significantly higher density of viable cells compared to other experimental groups. This indicates that the ES-GP/ZIM scaffold exhibits no apparent cytotoxicity and supports cell adhesion and growth.

Quantitative data from the CCK-8 proliferation assays (Figure 3d) revealed that cell viability in all groups increased over the culture period from day 1 to day 3, with the most pronounced enhancement observed in the ES-GP/ZIM group. By day 3, the optical density (OD) value for this group reached approximately 1.9, higher than the GP-b group and the ES-GP/ZM group. Further quantitative analysis of relative cell viability (Figure 3e), normalized to the control group, showed that at day 3, the ES-GP/ZIM group achieved a viability value of approximately 1.7. This significantly exceeded the values for the GP-b group (~1.2), ES-GP/ZM group (~1.4), and GP/I-S group (~1.5). These findings are consistent with the CCK-8 assay results, further confirming the ability of the ES-GP/ZIM scaffold to promote fibroblast proliferation.

Integrating the results from the scratch assays, fluorescence staining, and CCK-8 analyses, it is evident that the ES-GP/ZIM scaffold, which provides both localized electrical stimulation and ICA delivery, enhances fibroblast proliferation and migration while maintaining good cytocompatibility. These two cellular behaviors form the core cytological basis for granulation tissue formation and epidermal regeneration during wound healing. Collectively, these results demonstrate the favorable in vitro biocompatibility and regenerative potential of the ES-GP/ZIM scaffold.

2.3 | In Vitro Regulation of Macrophage Polarization

The endogenous bioelectric field serves as a pivotal physiological cue that guides cell migration and modulates the inflammatory response during wound healing. Following skin injury, a direct current electric field (100–200 mV/mm) is naturally established between the wound center and its periphery; the absence of this signal significantly impedes the healing process. Leveraging its self-powering capability, the ES-GP/ZIM scaffold mimics and supplements this endogenous electric field. When combined

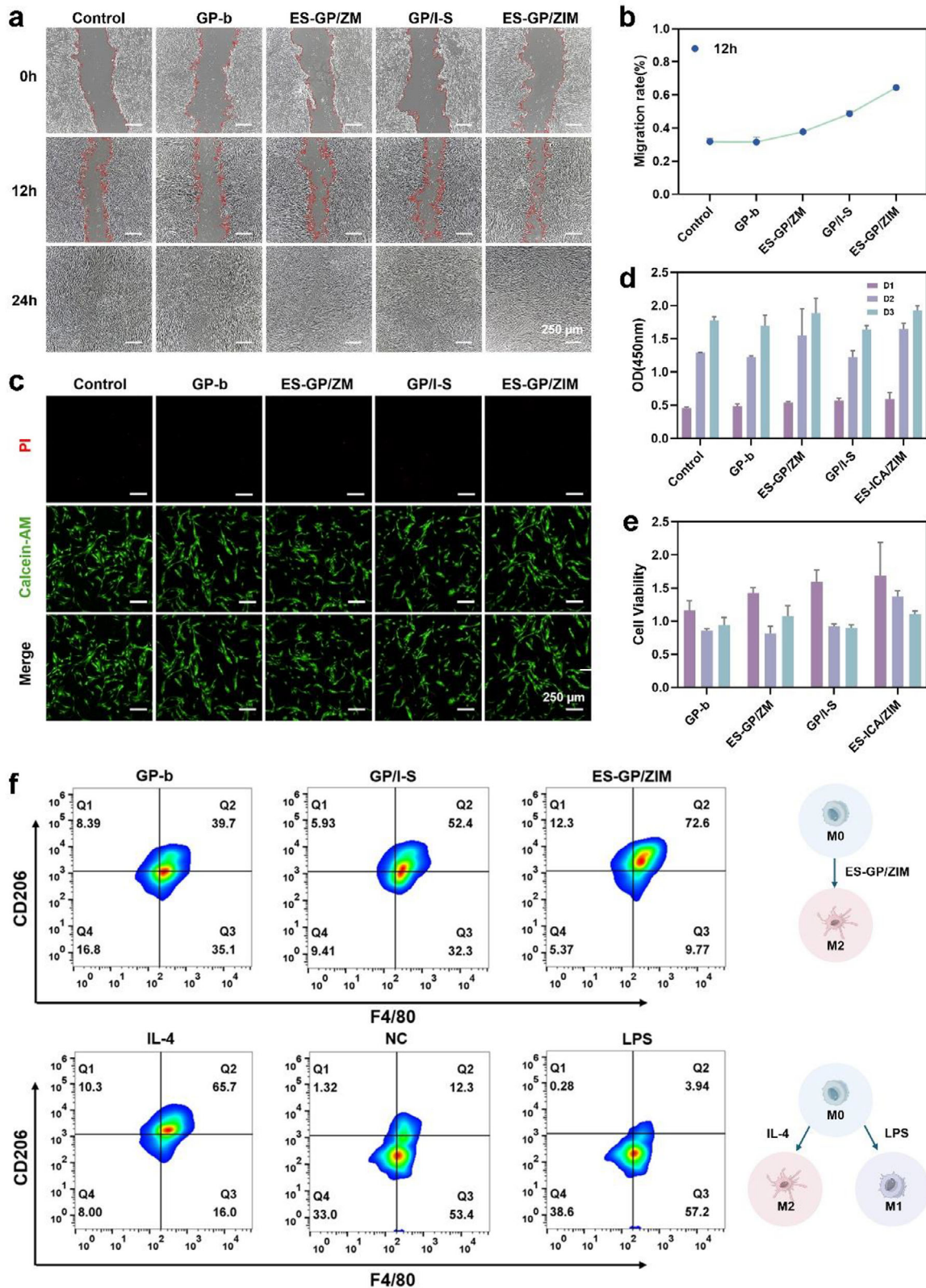


FIGURE 3 | In Vitro Biocompatibility and Anti-Inflammatory Performance Evaluation of the ES-GP/ZIM Scaffold. (a) Representative microscopy images of wound healing in human skin fibroblasts (HSFs) under different treatment groups at 0, 12, and 24 h. Scale bar = 250 μ m. (b) Quantitative analysis of scratch wound closure rates in HSFs at 12 h. (c) Live/dead fluorescence staining images of HSFs after exposure to different treatment groups (live cells: Calcein-AM, green; dead cells: PI, red). Scale bar = 250 μ m. (d) CCK-8 assay assessing the proliferative capacity of HSFs under different treatment groups at days 1, 2, and 3. (e) Quantitative analysis of HSF viability after exposure to different treatment groups. (f) Flow cytometry analysis of the co-expression levels of macrophage surface markers CD206 and F4/80. Data are presented as mean $\pm$ SD ($n = 3$).

with the pharmacological effects of ICA, it achieves precise regulation of the inflammatory microenvironment. To evaluate the scaffold's capacity to regulate macrophage polarization, this study focused on RAW264.7 cells, examining morphological changes and quantitatively assessing the expression of the M2-specific marker CD206 via flow cytometry. This approach aimed to elucidate the individual effects of electrical stimulation and ICA, as well as their influence when applied together, on key cells involved in wound repair, providing a cytological basis for the application of this scaffold in acute wound management. The experimental design included a blank control (NC), an IL-4 positive control, an LPS-induced inflammatory group, and treatment groups comprising GP-b, GP/I-S, and ES-GP/ZIM.

Morphological observations (Figure S6) revealed that untreated M0 macrophages exhibited a rounded or short spindle-shaped morphology with distinct boundaries. Following LPS induction, cells significantly increased in size, adopted irregular shapes, and extended numerous pseudopodia-like protrusions, indicative of a typical pro-inflammatory M1 phenotype. In contrast, IL-4-induced M2 macrophages were characterized by an elongated, spindle-shaped morphology, dispersed growth, and abundant pseudopodia [36]. Notably, the cell morphology in the ES-GP/ZIM group closely resembled that of the IL-4 group, predominantly exhibiting an elongated spindle shape. This finding preliminarily suggests the scaffold's potential to drive macrophage polarization toward the M2 phenotype.

Macrophage polarization levels were quantitatively assessed by analyzing the co-expression of CD206 (an M2-specific marker) and F4/80 (a pan-macrophage marker) using flow cytometry (Figure 3f). The IL-4-treated M2 positive control group showed a CD206-positive rate of 65.7%, validating the reliability of the experimental system. In the GP-b group, the CD206-positive rate was 39.7%, indicating that the scaffold matrix itself exerts only a minor influence on M2 polarization. The GP/I-S group exhibited a CD206-positive rate of 52.4%, demonstrating that ICA alone can induce a moderate level of M2 polarization. Significantly, the ES-GP/ZIM group achieved a CD206-positive rate of 72.6%, substantially higher than both the GP/I-S and GP-b groups, and even exceeding the IL-4 positive control. This result suggests a stronger anti-inflammatory response in the group receiving both electrical stimulation and ICA. As a negative control for M2 expression (representing M1 induction), the LPS-treated group showed markedly suppressed CD206 expression, with a positive rate of only 3.94%, significantly lower than that of the NC group (12.3%). This finding not only validates the successful establishment of the M1 induction model but also confirms the specificity of the CD206 antibody used.

Collectively, the morphological and phenotypic analyses demonstrate that the ES-GP/ZIM scaffold promotes macrophage polarization toward the anti-inflammatory M2 phenotype in the presence of both electrical stimulation and ICA. This shift toward M2 polarization establishes a critical foundation for subsequently modulating the functions of fibroblasts and vascular endothelial cells, thereby creating a pro-healing microenvironment.

2.4 | In Vivo Implantation of the ES-GP/ZIM Scaffold

Acute wounds, characterized by a sudden loss of skin integrity due to external insults such as surgery, trauma, or burns, represent one of the most prevalent clinical challenges. While their healing typically progresses through the orchestrated phases of inflammation, proliferation, and remodeling, the trajectory and quality of repair are profoundly influenced by the local microenvironment, concurrent infections, and the patient's systemic health. Suboptimal management can precipitate chronic non-healing wounds or complications such as hypertrophic scarring and functional impairment, thereby severely compromising patient quality of life and exacerbating the healthcare burden. Electrical stimulation (ES) therapy, which mimics or augments the endogenous wound electric field, has emerged as a potent physical intervention capable of guiding directional cell migration, promoting angiogenesis, and modulating inflammatory responses to accelerate acute wound repair. By replicating physiological electrical cues to regulate cellular behavior, ES acts additively with the anti-inflammatory and pro-regenerative properties of ICA, providing support for the healing process.

Building upon the promising efficacy demonstrated in our preceding *in vitro* studies, this study established a standardized murine model of full-thickness skin defects (Figure 4a). Specific pathogen-free (SPF) mice underwent a six-week acclimatization period prior to experimentation. On day 0, circular full-thickness skin defects with a diameter of 10 mm were surgically created, followed by the immediate application of dressings corresponding to the various treatment groups. Animals were euthanized on postoperative days 3, 7, and 14 to capture the inflammatory, proliferative, and remodeling phases, respectively. Tissue samples were harvested for comprehensive multi-parameter analysis spanning macroscopic evaluation, molecular profiling, histological examination, and protein expression assessment. To systematically elucidate the individual and combined effects of electrical stimulation and ICA, multiple control groups—including Control, GP-b, ES-GP/ZM, GP/I-S, and ES-GP/ZIM—were employed. This rigorous comparative experimental design provides a solid foundation for evaluating the therapeutic potential of the dressing and supports its future clinical translation.

Macroscopic evaluation of wound healing phenotypes across distinct time points (Figure 4b), complemented by quantitative image analysis using ImageJ (Figure 4c), vividly illustrated the dynamic disparities in repair trajectories among the experimental groups. On postoperative day 3, all groups exhibited characteristics typical of the inflammatory phase; while the ES-GP/ZIM group displayed marginally superior wound contraction compared to controls, these differences did not yet reach statistical significance. By day 7, however, wounds treated with ES-GP/ZIM demonstrated pronounced epithelialization, featuring well-defined margins and extensive coverage by newly formed tissue. In stark contrast, the GP-b group remained dominated by granulation tissue proliferation with substantial residual wound areas. Although the ES-GP/ZM and GP/I-S groups showed evident contraction, their healing rates lagged significantly behind that of the ES-GP/ZIM group. By day 14, the ES-GP/ZIM group achieved near-complete epithelialization

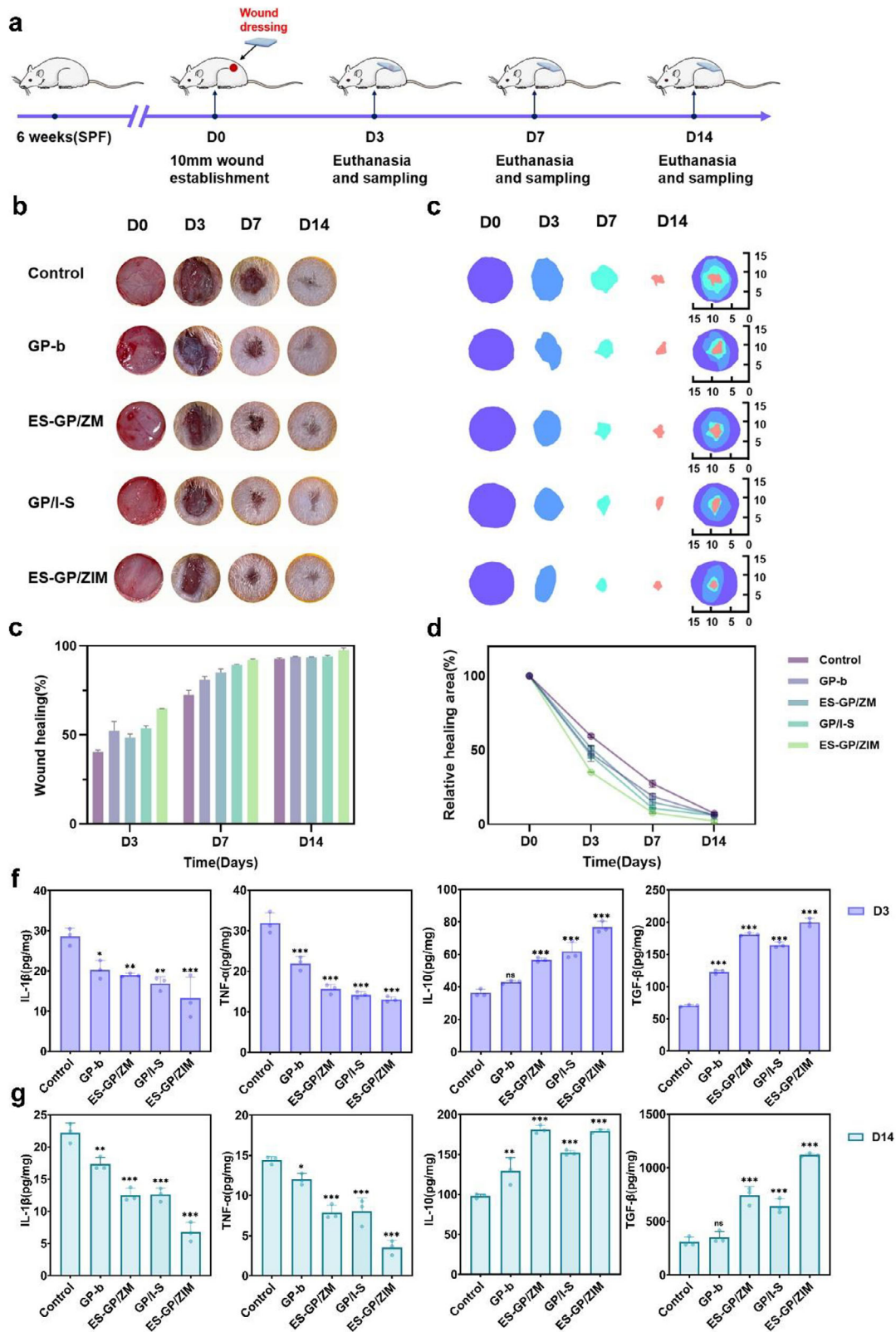


FIGURE 4 | Wound Healing Efficacy of ES-GP/ZIM in Full-Thickness Skin Defects. (a) Schematic illustration of the murine full-thickness wound model and experimental timeline. (b,c) Representative macroscopic images of wounds from each group on day 0, 3, 7, and 14, accompanied by quantitative analysis of wound area using ImageJ. (d,e) Statistical comparison of wound closure rates among different groups on day 3, 7, 14, and 21 ($n = 6$). (f,g) Expression levels of pro-inflammatory cytokines (TNF- α , IL-1 β) and anti-inflammatory/regenerative cytokines (TGF- β , IL-10) across groups on day 3 (f) and day 14 (g). Data are presented as mean $\pm$ SD ($n = 6$). Statistical analysis was performed using one-way ANOVA. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

with a smooth surface and no observable hypertrophic scarring, whereas the control groups—particularly GP-b—still presented with unclosed lesions, indicative of significantly delayed healing progression.

Quantitative assessment of wound closure rates (Figure 4d) further corroborated these observational trends. On day 3, the ES-GP/ZIM group exhibited a healing rate of approximately 64%, showing limited divergence from other groups. By day 7, the healing rate in the ES-GP/ZIM group surged to roughly 90%, significantly outperforming the GP-b (72%), GP/I-S (88%), and ES-GP/ZM (84%) groups. By day 14, the ES-GP/ZIM group approached 100% closure, confirming that the combined treatment strategy markedly accelerates both wound contraction and epithelialization. Furthermore, the relative wound area kinetics (Figure 4e) reinforced the superiority of the ES-GP/ZIM scaffold; this group consistently maintained the highest rate of area reduction, demonstrating sustained regenerative momentum particularly during the critical proliferative window from days 7 to 14. This temporal profile aligns precisely with the physiological requirements for optimal acute wound healing.

Precise modulation of the wound inflammatory response is a pivotal determinant of healing quality. While excessive or persistent inflammation exacerbates tissue damage and impedes repair, a balanced anti-inflammatory microenvironment fosters the activation of reparative cells and facilitates tissue regeneration. In this study, enzyme-linked immunosorbent assay (ELISA) was utilized to quantify the expression levels of key cytokines at the wound site on postoperative day 3 (inflammatory phase) and day 14 (remodeling phase), thereby elucidating the immunomodulatory mechanisms of ES-GP/ZIM at the molecular level.

On postoperative day 3 (Figure 4f), the ES-GP/ZIM group exhibited significantly suppressed levels of pro-inflammatory cytokines (TNF- α and IL-1 β) compared to all control groups. Specifically, TNF- α concentrations in the ES-GP/ZIM group were approximately 15 pg/mg, markedly lower than those in the Control (30 pg/mg) and GP-b (22 pg/mg) groups. Similarly, IL-1 β levels were reduced to approximately 15 pg/mg, representing a significant decrease relative to other cohorts. Concurrently, the expression of anti-inflammatory and repair-associated cytokines (TGF- β and IL-10) in the ES-GP/ZIM group showed a robust upward trend, surpassing levels observed in both the GP-b and Control groups. These findings indicate that ES-GP/ZIM effectively curtails the excessive release of pro-inflammatory mediators during the early inflammatory phase while simultaneously initiating anti-inflammatory repair programs. This dual action prevents secondary tissue damage induced by hyper-inflammation and establishes a favorable foundation for subsequent reparative processes.

By postoperative day 14 (Figure 4g), the ES-GP/ZIM group showed further reduction in pro-inflammatory cytokines (TNF- α and IL-1 β), remaining lower than those in all control groups. This indicates effective resolution of the inflammatory response. Conversely, the expression of anti-inflammatory and reparative factors (TGF- β and IL-10) was sustained at elevated levels, significantly exceeding those in the ES-GP/ZM and GP/I-S groups. This suggests that ES-GP/ZIM continuously modulates the immune microenvironment to promote granulation tissue maturation

and collagen remodeling while mitigating hypertrophic scarring. Comparative analysis with single-function control groups revealed that both the suppression of pro-inflammatory factors and the upregulation of anti-inflammatory/reparative factors were significantly more potent in the ES-GP/ZIM group than in the ES-GP/ZM (electrical stimulation only) or GP/I-S (drug-loaded only) groups. These results suggest that the combined application of electrical stimulation and ICA contributes substantially to the regulation of the wound immune microenvironment.

2.5 | Multidimensional Validation of the in Vivo Wound Healing Efficacy of ES-GP/ZIM

Histomorphological staining and quantitative analysis (Figure 5) further elucidated the pro-healing mechanisms of ES-GP/ZIM at the structural level. Hematoxylin and eosin (H&E) staining (Figure 5a) clearly delineated tissue repair characteristics across distinct healing phases. On postoperative day 3, the ES-GP/ZIM group exhibited a significantly reduced infiltration of inflammatory cells compared to the control groups. By day 7, this group demonstrated accelerated directional migration of epithelial cells, denser granulation tissue formation, and preliminary reconstruction of the dermal architecture. By day 14, wounds in the ES-GP/ZIM group had formed an epidermal layer with a thickness approaching that of normal skin, accompanied by a well-organized dermal papillary layer. In contrast, control groups displayed thinner epidermal layers and loosely arranged dermal tissue. Quantitative analyses (Figure 5c,e) corroborated these observations, revealing that the ES-GP/ZIM group possessed significantly increased epidermal thickness and the lowest proportion of inflammatory area among all cohorts. These histological findings align closely with the ELISA results, which showed early suppression of pro-inflammatory cytokines (TNF- α , IL-1 β) and sustained upregulation of anti-inflammatory and repair-associated cytokines (TGF- β , IL-10), thereby clarifying the core mechanism by which electrical stimulation and the pharmacological agent additively regulate the inflammatory microenvironment. Furthermore, quantification of the residual unhealed wound area (Figure 5d) validated the superior repair efficacy; by day 14, the proportion of unhealed area in the ES-GP/ZIM group approached zero, demonstrating statistically significant improvements compared to all control groups.

Masson's trichrome staining (Figure 5b) coupled with quantitative analysis of collagen fibers (Figure 5f) revealed that by day 14, the ES-GP/ZIM group exhibited the highest degree of collagen deposition and the most densely organized fiber arrangement, higher than all other groups. These findings underscore the dressing's capacity to effectively promote collagen maturation and tissue remodeling, thereby enhancing the overall quality of wound repair. To further evaluate the in vivo biosafety of the ES-GP/ZIM dressing, H&E staining of major organs (heart, liver, spleen, lungs, and kidneys) was conducted on postoperative day 14 (Figure S7). The results demonstrated intact tissue architecture in both the ES-GP/ZIM treatment and control groups, with no observable pathological alterations or inflammatory infiltration in myocardial fibers, hepatic lobules, splenic white pulp, alveolar structures, or renal tubules. The absence of significant differences between the groups indicates that the ES-GP/ZIM

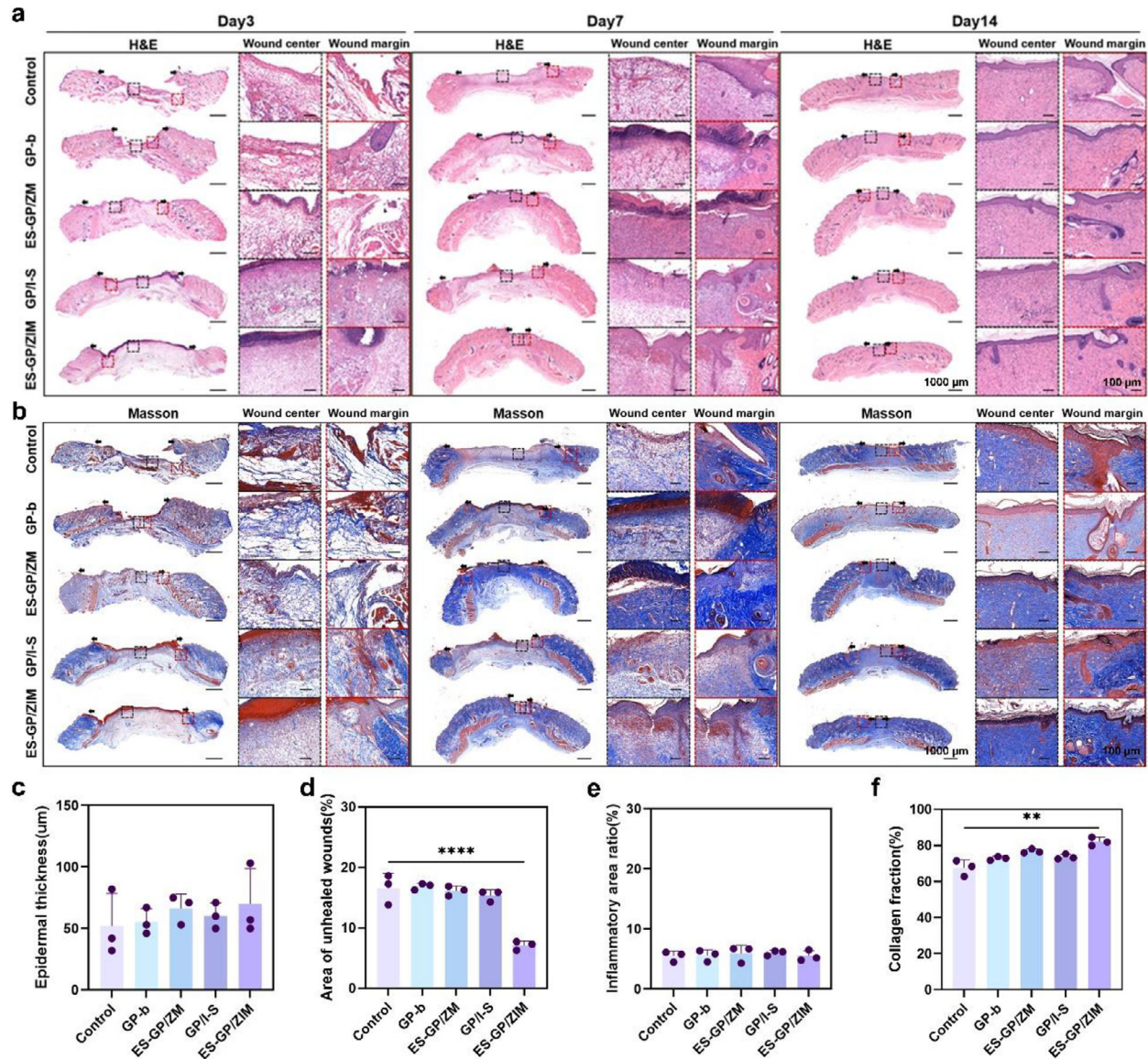


FIGURE 5 | Regulatory Effects of the ES-GP/ZIM Electroactive Dressing on Wound Histomorphology and Collagen Remodeling. (a) H&E staining sections of wound tissues from different treatment groups on days 3, 7, and 14 (Scale bar = 1000 μm), with magnified views of the wound center and edge regions on the right (Scale bar = 100 μm). (b) Masson's trichrome staining sections at corresponding time points (blue: collagen fibers; red: muscle fibers and cytoplasm). (c–f) Quantitative analysis on day 14 of (c) epidermal thickness, (d) percentage of unhealed wound area, (e) percentage of inflammatory area, and (f) collagen fraction (deposition) across all groups. Data are presented as mean ± SD ($n = 6$). Statistical analysis was performed using one-way ANOVA. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

dressings induces no evident systemic toxicity during in vivo application, exhibiting favorable biosafety profiles that provide a critical safety foundation for its subsequent clinical translation. In summary, the ES-GP/ZIM-electroactive dressing leverages the coordinated interplay between electrical stimulation and pharmacological delivery to precisely modulate the inflammatory response, accelerate re-epithelialization and angiogenesis, and enhance collagen deposition and maturation. Collectively, these effects significantly improve both the efficiency and quality of acute wound healing while mitigating the risk of pathological scarring, all while maintaining excellent in vivo biosafety.

Immunohistochemical staining and quantitative analysis (Figure 6) elucidated the molecular targets through which

ES-GP/ZIM promotes wound healing at the cellular functional level, focusing on three core repair processes: collagen synthesis, wound contraction, and angiogenesis.

Type I collagen (Col-1), a critical structural protein for dermal repair, serves as a direct indicator of collagen remodeling efficiency (Figure 6a,d,e). On postoperative days 7 and 14, the proportion of Col-1-positive staining area in the ES-GP/ZIM group both reached over 80%, respectively, representing the highest values among all cohorts. These positive signals were predominantly concentrated within the dermis and exhibited significantly enhanced staining intensity. Quantitative analysis confirmed that Col-1 expression in this group was markedly superior to that in both control and single-function groups,

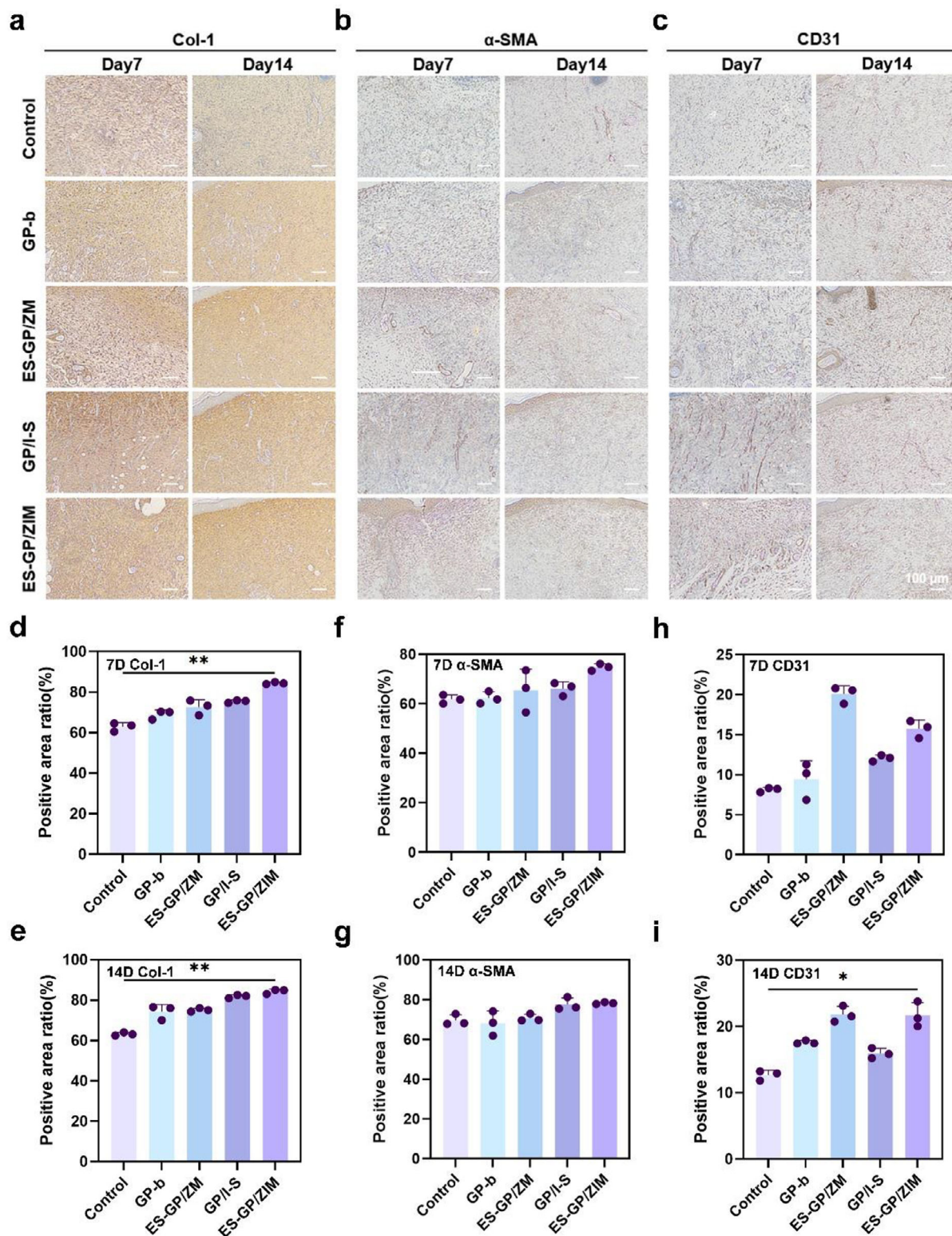


FIGURE 6 | Regulatory Effects of the ES-GP/ZIM Electroactive Dressing on the Expression of Key Proteins Involved in Wound Repair (Immunohistochemical Analysis). (a) Immunohistochemically stained sections for type Col-1 in different treatment groups on days 7 and 14. Scale bar = 1000 μm. (b) Immunohistochemically stained sections for α-SMA at corresponding time points. Scale bar = 1000 μm. (c) Immunohistochemically stained sections for CD31 at corresponding time points. Scale bar = 1000 μm. (d) Quantitative analysis of the Col-1-positive area percentage in each group on day 7. (e) Quantitative analysis of the Col-1-positive area percentage in each group on day 14. (f) Quantitative analysis of the α-SMA-positive area percentage in each group on day 7. (g) Quantitative analysis of the α-SMA-positive area percentage in each group on day 14. (h) Quantitative analysis of the CD31-positive area percentage in each group on day 7. (i) Quantitative analysis of the CD31-positive area percentage in each group on day 14. Data are presented as mean ± SD ($n = 6$). Statistical analysis was performed using one-way ANOVA. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

indicating that ES-GP/ZIM potently activates collagen synthesis in fibroblasts, thereby accelerating dermal structural reconstruction and tissue repair.

α -Smooth muscle actin (α -SMA), a specific marker for myofibroblasts, reflects wound contraction capacity (Figure 6b,f,g). The proportion of α -SMA-positive area in the ES-GP/ZIM group was approximately 75% on day 7 and increased to 80% by day 14, significantly exceeding levels in other groups. With positive signals primarily distributed at the interface between granulation tissue and the dermis, these findings demonstrate that ES-GP/ZIM effectively induces myofibroblast activation, enhancing wound contractility and providing the mechanical foundation necessary for rapid closure.

Platelet endothelial cell adhesion molecule (CD31), a specific marker for vascular endothelial cells, directly reflects angiogenic potential (Figure 6c,h,i). The CD31-positive area in the ES-GP/ZIM group accounted for approximately 15% on day 7 and 22% on day 14; notably, these signals displayed a reticular distribution within the granulation tissue, indicative of a well-formed microvascular network. Quantitative analysis revealed that CD31 expression in this group was significantly superior to controls, confirming that ES-GP/ZIM promotes vascular endothelial cell proliferation and neovascularization. This continuous improvement in wound perfusion ensures adequate nutritional and oxygen support throughout all repair phases.

Integrating these multidimensional analyses, the ES-GP/ZIM electroactive dressing achieves precise and comprehensive regulation of acute wound healing through the combination effects of electrical signal modulation and bioactive release. Its core mechanism operates sequentially: during the early inflammatory phase, it suppresses excessive inflammation via coordinated action to remodel an anti-inflammatory microenvironment; during the proliferative phase, it activates fibroblast-mediated collagen synthesis, myofibroblast-driven contraction, and endothelial neogenesis to accelerate granulation tissue formation and epithelialization; and during the remodeling phase, it promotes organized collagen deposition to enhance healing quality. Consequently, this dressing enhances the efficiency of acute wound healing. It also improves the overall quality of tissue repair.

3 | Conclusions

This study presents the successful development and validation of ES-GP/ZIM, a novel self-powered electroactive wound dressing that integrates a biodegradable Zn–Mo galvanic microcurrent source with a trilayered, ECM-mimicking nanofibrous scaffold and spatiotemporally controlled icariin (ICA) release within a single platform. Unlike previously reported self-powered wound dressings that mainly provide electrical stimulation alone, ES-GP/ZIM provides localized electrical stimulation together with controlled biochemical regulation throughout the wound-healing process.

By delivering sustained electrical stimulation and biphasic ICA release, the system addresses limitations in conventional wound care, offering a biodegradable platform for active wound man-

agement. The dressing demonstrated a controlled multi-stage degradation profile and enabled rapid anti-inflammatory regulation during early wound healing, followed by sustained support for angiogenesis and tissue repair in later stages, despite ~11% of ICA remaining physically bound or unreleased.

Comprehensive in vitro evaluations confirmed biocompatibility and promoted fibroblast migration, viability, and proliferation, without cytotoxic effects. Compared with single-factor control groups, the ES-GP/ZIM dressing produced more pronounced effects on cellular responses associated with wound repair, including macrophage polarization toward the M2 phenotype. In vivo studies in acute wound models demonstrated accelerated closure (~85% by day 7) and near-complete re-epithelialization by day 14. Mechanistic investigations revealed early suppression of pro-inflammatory mediators (TNF- α , IL-1 β) and sustained upregulation of reparative factors (TGF- β , IL-10), while histological analyses confirmed enhanced collagen deposition, improved fiber organization, and increased neovascularization.

Although the present study establishes proof-of-concept efficacy in standardized full-thickness skin defects, the modular design of ES-GP/ZIM—incorporating self-powered electrical stimulation, phase-matched ICA delivery, and ECM-mimicking architecture—may provide a framework for future investigation in more complex wound environments, including diabetic, infected, and large-area wounds [10]. The potential influence of dynamic skin motion has been discussed qualitatively as future work, acknowledging in vitro limitations in replicating mechanical deformation in vivo.

Overall, ES-GP/ZIM establishes a biodegradable self-powered wound dressing capable of providing localized electrical stimulation and controlled therapeutic delivery within a single platform. These findings support the potential of integrating electroactive materials and bioactive regulation strategies for wound repair and may contribute to the development of next-generation electroactive wound dressings.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supporting File: smll74388-sup-0001-SuppMat.docx.