Research Progress on FGF1-Mediated STFS in Skin Wound Repair

Lufan Guan[1], Zhimin Li[1], Zhengwu Li[2]
[1]School of Biotechnology, East China University of Science and Technology, Shanghai 200237, China
[2]Shanghai Tenry Pharmaceutical Co., Ltd., Shanghai 201412, China

Corresponding author: Zhimin Li (e-mail: lzm15176180389@163.com)

ABSTRACT Skin wound repair remains a major challenge in regenerative medicine, particularly for chronic wounds requiring sustained bioactive regulation and intelligent therapeutic intervention. Recent advances in smart textile fiber scaffolds (STFS) have provided versatile platforms for localized drug delivery and responsive biomedical applications, with increasing relevance to wearable sensing and electromagnetic-assisted healthcare systems. This review systematically summarizes the biological functions of fibroblast growth factor 1 (FGF1) in inflammation modulation, angiogenesis, extracellular matrix remodeling, and epithelial regeneration, while discussing recent progress in STFS design, including material selection, hierarchical architectures, and FGF1 loading and controlled-release strategies. Particular attention is given to the synergistic interactions between scaffold biomimicry and growth factor delivery, highlighting how structural optimization and smart release mechanisms improve microenvironment regulation and tissue regeneration. Current advances in covalent immobilization, heparin-mediated specific binding, and stimulus-responsive release systems are critically evaluated together with their limitations and future prospects. By integrating functional textile engineering with precision drug delivery, FGF1-mediated STFS provide a promising platform for next-generation wound dressings and offer valuable insights for intelligent biomedical devices, wearable sensing technologies, and electromagnetic-responsive therapeutic systems that require reliable signal interaction and adaptive material functionality.

INDEX TERMS FGF1, smart textile fiber scaffolds, controlled drug delivery, wearable biomedical sensing, electromagnetic-responsive biomaterials

I. INTRODUCTION

As the largest surface barrier of the human body, skin spans approximately 1.5–2.0 m^2 and performs vital physiological functions including protecting internal organs, regulating body temperature, defending against microbial invasion, and sensing external stimuli [1]. According to World Health Organization statistics, over 120 million people worldwide suffer from skin wounds annually due to trauma, burns, diabetes, and other factors, with chronic wounds accounting for 15–20% of these cases [2]. In China, the annual incidence rate of chronic wounds is approximately 0.45%, affecting over 6 million people, with related medical expenditures exceeding 30 billion yuan annually [3]. Compared to acute wounds, chronic wounds often exhibit healing stagnation at the inflammatory stage due to microenvironmental imbalances (pH acidification, heightened oxidative stress, abnormal protease activation), prolonged inflammatory responses, and impaired angiogenesis. This manifests as persistent non-healing, recurrent infections, and in severe cases, limb dysfunction or even amputation, significantly diminishing patients' quality of life [4].

Traditional wound dressings (e.g., gauze, oil-soaked gauze, hydrocolloid dressings) merely provide basic functions like physical coverage and exudate absorption, lacking the ability to actively regulate the healing process. Consequently, their efficacy in treating chronic wounds remains limited [5]. With the convergence of regenerative medicine and materials science, "active healing-promoting" wound dressings have emerged as a research focus. Their core design principle involves achieving targeted delivery and controlled release of active components—such as growth factors and antimicrobial agents—through biomimetic structural engineering and functional modification of carrier materials. This approach regulates the wound healing microenvironment at cellular and molecular levels [6].

Growth factors are key bioactive molecules regulating cell proliferation, differentiation, and extracellular matrix (ECM) synthesis, playing a central role throughout all stages of wound healing [7]. As the prototypical member of the fibroblast growth factor (FGF) family, FGF1 was the first factor discovered with angiogenic activity, making its clinical potential highly sought after [8]. However, FGF1's protein characteristics present significant challenges: its small molecular weight (approximately 17 kDa) and high structural flexibility make it susceptible to degradation by matrix metalloproteinases (MMPs) in the wound microenvironment, resulting in an in vivo half-life of only 3–5 hours. Additionally, its high water solubility causes it to leach out with wound exudate during direct topical application, making it difficult to maintain effective therapeutic concentrations [9]. Therefore, developing an efficient FGF1 delivery system is crucial to overcoming these application bottlenecks.

STFS, with their highly ECM-mimetic network structure, large specific surface area, and tunable functional properties, have emerged as ideal carriers for FGF1 delivery [10]. Their advantages include: 1 Bionic structures provide "anchorage points" for cell adhesion and proliferation, guiding cell growth along fiber orientations; 2 The porous structure facilitates nutrient exchange and exudate absorption, maintaining a moist wound microenvironment; 3 Active groups can be chemically introduced onto the fiber surface to achieve specific binding and smart controlled release of FGF1 [11]. This review explores FGF1's wound healing mechanisms, the design and fabrication of STFS, FGF1 loading and controlled release strategies, and their synergistic wound-promoting mechanisms, providing references for related research.

II. WOUND HEALING MECHANISMS AND APPLICATION BOTTLENECKS OF FGF1

A. MOLECULAR CHARACTERISTICS AND WOUND HEALING MECHANISMS OF FGF1

FGF1 is a single-chain polypeptide composed of 140 amino acid residues, with a molecular weight of approximately 17 kDa and an isoelectric point of 9.6, exhibiting basicity [12]. Its molecular structure contains two primary functional domains: one for binding to the fibroblast growth factor receptor (FGFR) on the cell surface, and another for binding to heparin or heparan-like glycosaminoglycans (HSPGs) [13]. The wound healing effects of FGF1 are not regulated by a single target but rather exert synergistic control across multiple signaling pathways during the inflammatory, proliferative, and remodeling phases of wound healing.

Compared with other mainstream growth factors (VEGF, PDGF, EGF), FGF1 has unique advantages in chronic wound repair: First, it exhibits multi-stage regulatory capabilities, acting throughout the inflammatory, proliferative, and remodeling phases—unlike VEGF (focused solely on angiogenesis) or EGF (limited to epithelialization)—and excels at improving the inflammatory microenvironment of chronic wounds. Second, it possesses high heparin binding affinity ($K_a = 10^8$ M^{-1}), a "strong binding" level that enables seamless integration with heparin-mediated smart release systems for wound-targeted delivery, while VEGF and PDGF have only 1/10–1/5 of this binding capacity. Third, it has low cytotoxicity, with concentration-dependent saturated proliferation promotion that avoids excessive scar formation, unlike EGF which may induce abnormal epithelial cell proliferation at high concentrations.

1) Regulation During the Inflammatory Phase: Mitigating Prolonged Inflammation to Lay the Foundation for Healing Initiation

During the initial wound formation phase, inflammatory cells (neutrophils, macrophages) infiltrate extensively to clear necrotic tissue and pathogens while releasing inflammatory mediators to initiate the healing process [14]. However, chronic wounds exhibit excessive and prolonged inflammatory responses. The persistent presence of inflammatory mediators (e.g., TNF-α, IL-6) inhibits cell proliferation and angiogenesis, impeding healing [15]. FGF1 regulates the inflammatory response through two pathways: 1 Directly modulating inflammatory cell activity: FGF1 binds to FGFR on macrophage surfaces, promoting their polarization from M1 (pro-inflammatory) to M2 (anti-inflammatory/repair) types, reducing pro-inflammatory factor release and increasing anti-inflammatory factor expression (e.g., IL-10) [16]; 2 Inhibiting inflammatory signaling pathways: FGF1 activates the PI3K/Akt pathway and downregulates NF-κB signaling activity, thereby suppressing the transcription and release of inflammatory mediators [17]. Studies confirm that exogenous FGF1 reduces inflammatory infiltration in chronic wounds by 40% and shortens the inflammatory phase by 3–5 days [18].

2) Proliferative Phase Regulation: Promoting Cell Proliferation and Angiogenesis to Accelerate Granulation Tissue Formation

The proliferative phase is the core stage of wound healing, primarily involving processes such as fibroblast proliferation, collagen synthesis, endothelial cell migration, and angiogenesis [19]. FGF1's regulatory effects in this phase are manifested as follows: 1 Promoting fibroblast proliferation and activation: FGF1 binds to FGFR1/2 on fibroblast surfaces, activating the MAPK/ERK signaling pathway to promote cell cycle progression from G0/G1 to S phase, thereby accelerating proliferation; Simultaneously, it upregulates the expression of type I collagen (Col-I), type III collagen (Col-III), and fibronectin, providing the structural foundation for granulation tissue formation [20]; 2 Accelerating angiogenesis: FGF1 is a potent angiogenic factor that binds to FGFR on endothelial cell surfaces, activating the PLCγ/PKC signaling pathway to promote endothelial cell migration, proliferation, and lumen formation. Concurrently, FGF1 upregulates vascular endothelial growth factor (VEGF) expression, synergistically enhancing angiogenesis [21]. Studies indicate that FGF1 increases neovascular density by 67% and enhances granulation tissue thickness by 50% in wounds [22].

3) Remodeling Phase Regulation: Optimizing Collagen Remodeling to Improve Healing Quality

The Role and Regulatory Mechanisms of FGF1 in Accelerating Wound Healing Phases As shown in Table 1:

The remodeling phase primarily facilitates the transition of wound tissue from granulation tissue to mature skin

TABLE 1. The Role and Regulatory Mechanisms of FGF1 in Accelerating Wound Healing Phases

Wound Healing Phases	Key Processes	Regulatory Mechanisms of FGF1	Supporting Evidence [Reference]
Initial Inflammatory Phase	Massive infiltration of inflammatory cells (neutrophils, macrophages); clearance of necrotic tissue and pathogenic microorganisms; release of inflammatory factors to initiate healing; excessive and prolonged inflammation in chronic wounds (sustained presence of TNF-α, IL-6); inhibition of cell proliferation and angiogenesis	1) Directly regulates inflammatory cell activity: FGF1 binds to FGFR on macrophages, promoting their polarization from M1 (pro-inflammatory) to M2 (anti-inflammatory/repair) phenotype, reducing pro-inflammatory factor release and increasing anti-inflammatory factor (e.g., IL-10) expression. 2) Inhibits inflammatory signaling pathways: FGF1 activates the PI3K/Akt pathway and downregulates NF-κB pathway activity, thereby suppressing transcription and release of inflammatory factors	Reduces inflammatory infiltration in chronic wounds by 40% and shortens the inflammatory phase by 3–5 days
Proliferative Phase	Proliferation of fibroblasts; collagen synthesis; migration of endothelial cells; angiogenesis; granulation tissue formation	1) Promotes fibroblast proliferation and activation: FGF1 binds to FGFR1/2 on fibroblasts, activates the MAPK/ERK pathway, accelerates cell cycle transition from G0/G1 to S phase, and upregulates the expression of Col-I, Col-III, and fibronectin. 2) Enhances angiogenesis: FGF1 binds to FGFR on endothelial cells, activates the PLCγ/PKC pathway to promote endothelial cell migration, proliferation, and vascular lumen formation; upregulates VEGF expression to synergistically enhance angiogenic activity via paracrine effects	Increases neovascular density by 67% and granulation tissue thickness by 50%
Remodeling Phase	Degradation and rearrangement of collagen fibers; transformation of granulation tissue into mature skin tissue; scar formation reduction; imbalanced collagen metabolism in chronic wounds (excessive and disorganized Col-III expression leading to hypertrophic scars)	1) Regulates MMPs/TIMPs balance: downregulates MMP-2 and MMP-9 expression to reduce excessive collagen degradation; upregulates TIMP-1 expression to inhibit MMPs activity. 2) Guides ordered collagen fiber arrangement along stress directions to improve mechanical properties of wound tissue. 3) Promotes fibroblast differentiation into myofibroblasts to accelerate wound contraction	Optimizes collagen remodeling and reduces scar formation

through collagen fiber degradation and rearrangement, while minimizing scar formation [23]. In chronic wounds, imbalanced collagen metabolism—characterized by excessive Col-III expression and disordered arrangement—leads to excessive scar tissue proliferation [24]. FGF1 optimizes collagen remodeling by regulating the balance between matrix metalloproteinases (MMPs) and their inhibitors (TIMPs): 1 Downregulating MMP-2 and MMP-9 expression to reduce excessive collagen degradation; 2 Upregulates TIMP-1 expression to inhibit MMP activity; 3 Guides collagen fibers to align orderly along stress directions, enhancing wound tissue mechanical properties [25]. Additionally, FGF1 promotes fibroblast differentiation into myofibroblasts, accelerating wound contraction and further improving healing quality [26].

B. APPLICATION BOTTLENECKS OF FGF1

Despite its potent wound-healing activity, clinical application of FGF1 faces several challenges, primarily manifested in the following aspects:

(1) Poor Stability: As a protein molecule, FGF1's spatial structure is susceptible to denaturation and inactivation by factors such as temperature, pH, and proteases. The wound microenvironment contains abundant MMPs that degrade FGF1's peptide bonds, rendering it biologically inactive with an in vivo half-life of only 3–5 hours [27].

(2) Low Bioavailability: FGF1's high water solubility causes it to leach away with wound exudate during direct topical application, making it difficult to maintain effective therapeutic concentrations (typically 10–100 ng/mL) at the wound site, resulting in limited therapeutic efficacy [28].

(3) Low delivery efficiency: Conventional delivery methods (e.g., gels, sprays) fail to achieve targeted delivery and controlled release of FGF1, necessitating frequent administration that increases patient discomfort and infection risk [29].

Therefore, developing an efficient FGF1 delivery system capable of stable loading, targeted delivery, and on-demand release is the core challenge to overcome its application limitations.

When administered via traditional gels, FGF1 reaches a peak local concentration of $\sim$120 ng/mL at 2 hours post-application but drops below 10 ng/mL within 4 hours, failing to maintain effective therapeutic levels. In contrast, smart textile fiber scaffolds (STFS) achieve stable FGF1 release at 25–80 ng/mL for 10–14 days through sustained-release design.

III. RESEARCH PROGRESS ON STFS FOR WOUND REPAIR

STFS refer to fiber materials prepared through techniques such as electrospinning, meltblowing, and weaving. They feature biomimetic structures capable of responding specifically to wound microenvironment stimuli (e.g., pH, temperature, enzymes, ROS) to achieve controlled release of active components or dynamic adjustment of structural properties [30]. In wound healing, these STFS mimic the ECM through structural biomimicry, providing an optimal microenvironment for cell growth. Concurrently, functional modifications enable efficient loading and intelligent controlled release of FGF1, synergistically promoting wound healing.

Research primarily focuses on two core aspects: material selection and structural design.

A. MATERIAL SELECTION FOR SCAFFOLDS

The choice of scaffold material directly determines its biocompatibility, mechanical properties, degradation rate, and functionalization potential, forming the foundation of smart textile fiber scaffold design. Currently, materials used for wound repair primarily include natural polymers, synthetic polymers, and composite polymers. The characteristics and application statuses of each material category are as follows:

1) Natural Polymers

Derived from plants, animals, or microorganisms, natural polymers exhibit excellent biocompatibility, high biological activity, and degradability. Their molecular structures often contain cell adhesion sequences (e.g., RGD sequences), providing an optimal signaling environment for cell growth. Common natural polymers used in wound repair scaffolds include gelatin, collagen, chitosan, and sodium alginate.

Gelatin, a hydrolyzed product of collagen, retains the RGD cell adhesion sequence of collagen. It offers excellent biocompatibility, abundant sources, and low cost, making it an ideal raw material for wound repair scaffolds. For example, Li et al. prepared electrospun scaffolds from gelatin, which effectively promoted fibroblast adhesion and proliferation, with a 50% higher cell adhesion rate compared to PLA scaffolds. However, gelatin scaffolds suffer from poor mechanical properties and excessively rapid degradation rates (in vivo degradation cycle of 1–2 weeks), making them unsuitable for long-term structural support in wound repair.

Chitosan, the deacetylated product of chitin, exhibits excellent antibacterial activity, biocompatibility, and degradability. Its amino groups on the molecular chain can be chemically modified to introduce functional groups for functionalization. Chen et al. developed a chitosan/gelatin composite electrospun scaffold exhibiting 95% antibacterial efficacy against Staphylococcus aureus while promoting fibroblast proliferation, significantly enhancing wound healing in infected areas. However, chitosan's poor solubility—requiring dissolution in acidic solutions—limits optimization of the spinning process.

Natural polymer materials offer high biological activity but exhibit poor controllability in mechanical properties and degradation rates. Their use alone often fails to meet the complex demands of wound repair, necessitating composite use with synthetic polymers.

2) Synthetic Polymer Materials

Synthetic polymer materials, prepared through chemical synthesis, exhibit stable mechanical properties, controllable degradation rates, and excellent processability. Their performance can be optimized by adjusting parameters such as molecular weight and crystallinity to meet diverse wound repair requirements. Common synthetic polymer materials used in wound repair scaffolds include polycaprolactone (PCL), polylactic acid (PLA), poly(glycolic acid) (PGA), and polylactic-poly(glycolic acid) copolymer (PLGA).

PCL is a semi-crystalline polyester exhibiting outstanding mechanical properties (tensile strength of 5–10 MPa) and controllable degradation rates (in vivo degradation cycles of 6–12 months). It possesses good biocompatibility, degrades into carbon dioxide and water without cytotoxicity, and is a common raw material for wound repair scaffolds. Wang et al. prepared PCL electrospun scaffolds that maintained structural integrity even after 4 weeks of degradation, providing long-term structural support for cell growth. However, PCL exhibits weak biological activity and lacks surface cell adhesion sites, necessitating surface modification or natural polymer composites to enhance its bioactivity.

PLGA, a copolymer of PGA and PLA, allows degradation rate adjustment by varying the PGA/PLA ratio (higher ratio accelerates degradation). It exhibits excellent biocompatibility and has received FDA approval for clinical use. Zhang et al. prepared PLGA electrospun scaffolds. By adjusting the PGA/PLA ratio, they matched the scaffold degradation cycle with the wound healing cycle (2–4 weeks), significantly promoting the repair of full-thickness skin defects in rats. However, PLGA scaffolds exhibit poor hydrophilicity, hindering cell adhesion and the loading of active components.

Synthetic polymers offer controllable mechanical properties and degradation rates but exhibit weak biological activity, necessitating functionalization to enhance cell interaction.

Before loading FGF1, hydrophobic synthetic polymers like PCL/PLGA require surface activation to improve hydrophilicity and active sites: 1 Plasma treatment: Low-temperature plasma bombardment introduces hydroxyl/carboxyl groups, reducing PCL's contact angle from 110° to $< 50^\circ$ and increasing FGF1 loading efficiency by 30%–40%; 2 Chemical oxidation: Mild oxidation with potassium permanganate or hydrogen peroxide creates active sites for FGF1 adsorption/coupling; 3 UV grafting: UV-initiated grafting of hydrophilic monomers (e.g., acrylic acid) forms a hydrophilic coating to enhance loading stability. Activated PCL/PLGA can be synergistically used with natural polymers—for example, plasma-activated PCL combined with gelatin increases FGF1 loading efficiency by 25% compared to unactivated PCL.

PLGA degrades into lactic acid and glycolic acid—human metabolic intermediates—but local high-concentration accumulation may cause a transient pH drop (0.3–0.5 units), potentially exacerbating chronic wound acidification. Mitigation strategies include: 1 Composite modification with alkaline biomaterials (chitosan, hydroxyapatite) to neutralize acidity, maintaining wound pH at 5.8–6.2; 2 Regulating degradation rate via PGA/PLA ratio (e.g., 50:50) to match the 2–4 week wound healing cycle; 3 Porous structure design (porosity $\geq$80%) to facilitate degradation product diffusion and reduce local concentration.

3) Composite Polymers

Single polymers struggle to simultaneously meet scaffold requirements for mechanical strength, biological activity, and degradation rate, making composite polymers a research focus. By combining natural polymers with synthetic polymers, complementary properties can be achieved, balancing structural stability and biological activity in scaffolds. Classification and Characterization of Polymer-Based Scaffolds for Wound Healing Applications As shown in Table 2:

The PCL/gelatin composite system is one of the most extensively studied composite materials. PCL provides excellent mechanical support and structural stability, while gelatin confers good biological activity and hydrophilicity. For instance, Zhang et al. prepared PCL/gelatin (2:1 by weight) electrospun composite scaffolds exhibiting tensile strength of 8.5 MPa and elongation at break of 120%. Additionally, fibroblast adhesion rates on the scaffold surface increased by 60% compared to pure PCL scaffolds. Li et al. controlled the degradation rate of scaffolds to 2–4 weeks by adjusting the PCL/gelatin mass ratio, perfectly matching the wound healing cycle and significantly improving chronic wound healing outcomes.

Beyond PCL/gelatin, composite systems such as PLGA/collagen and chitosan/PLA have also been extensively studied. For instance, Zhao et al. developed PLGA/collagen composite scaffolds where collagen incorporation substantially increased hydrophilicity—reducing contact angle from 105° to 45°—while boosting endothelial cell proliferation by 45%. These composite polymers offer complementary properties, expanding possibilities for designing STFS.

B. STRUCTURAL DESIGN OF SCAFFOLDS

Scaffold structure directly influences cell-scaffold interactions, active ingredient loading and release efficiency, and wound healing outcomes. With advancements in textile technology, scaffold structures have evolved from simple mesh frameworks to “function-oriented” precision architectures, primarily including oriented structures, core-shell structures, and multilevel structures.

1) Oriented Structures

Natural skin ECM fibers exhibit oriented arrangements that guide cell growth along fiber directions, enabling skin’s mechanical properties and functions. Oriented scaffold structures mimic the fiber alignment of natural ECM to direct cell growth and migration, promoting ordered collagen fiber arrangement and reducing scar formation.

Oriented scaffold structures are typically prepared using electrospinning technology, where fiber alignment is achieved by adjusting the rotational speed of the receiving device (e.g., a rotating drum). For instance, Wang et al. used a rotating drum (2000 rpm) to prepare an oriented PCL/gelatin composite scaffold with 85% fiber orientation. Fibroblasts grew along the fiber orientation, achieving 40% higher collagen fiber orderliness compared to random-structure scaffolds and reducing scar area by 35%. Li et al. prepared oriented PLGA/collagen scaffolds that guided endothelial cell migration along fiber directions, promoting vascular growth with 75% orientation of neovascularization and significantly enhancing wound blood supply.

Oriented scaffold structures offer advantages in guiding cell-directed growth and tissue remodeling while reducing scar formation, making them suitable for applications requiring targeted repair such as skin wounds and nerve injuries.

2) Core-Shell Structures

Core-shell scaffolds are fabricated via coaxial electrospinning, comprising a shell layer and a core layer. The shell typically consists of mechanically stable polymeric materials, while the core loads drugs or growth factors. This architecture enables physical encapsulation of active components, preventing inactivation during preparation, and facilitates controlled degradation of the shell for sustained release.

For instance, Zhao et al. developed a core-shell electrospun scaffold using PLA as the shell layer and gelatin/FGF2 as the core layer. The physical barrier function of the shell layer preserved 85% of FGF2’s biological activity, representing a 50% improvement over physically mixed scaffolds. In vitro release experiments demonstrated that this scaffold enabled sustained FGF2 release, achieving a cumulative release rate of 75% over 14 days and significantly promoting chronic wound healing. Zhang et al. prepared PCL/gelatin (shell)/VEGF (core) core-shell scaffolds, where VEGF release spanned 21 days, increasing neovascular density in wounds by 60% compared to controls.

The advantage of core-shell scaffolds lies in their efficient encapsulation and sustained release of bioactive components, preserving their biological activity. They are suitable for loading easily inactivated bioactive substances such as growth factors and antibiotics.

3) Multilevel Structures

Natural ECM possesses a complex multilevel architecture (micrometer-scale fiber networks and nanometer-scale collagen fibers), providing a multi-tiered spatial environment for cell growth. Multilevel scaffolds mimic the hierarchical architecture of natural ECM, integrating advantages across different scales to achieve multifunctionality encompassing “structural support-cell regulation-active delivery.”

Multilevel scaffolds are typically fabricated using composite spinning techniques. For instance, Li et al. developed a “micrometer-scale PCL fibers-nanoscale gelatin fibers” multilevel scaffold, where micrometer PCL fibers provide mechanical support while nanoscale gelatin fibers load FGF1. This scaffold achieved tensile strength of 10 MPa, with FGF1 loading efficiency reaching 80%. It demonstrated a 90% wound closure rate at 14 days, significantly outperforming single-scale scaffolds. Wang et al. developed a “nanoscale PLGA fiber-micron hydroxyapatite particle” multilevel scaffold, where nanofibers loaded drugs while microparticles provided osteoconductivity, enabling simultaneous repair of skin and bone tissues.

TABLE 2. Classification and Characterization of Polymer-Based Scaffolds for Wound Healing Applications

Category of Scaffold Materials	Definition & Key Characteristics	Common Types	Performance Advantages	Limitations
Natural Polymer Materials	Derived from animals, plants, or microorganisms; excellent biocompatibility, high bioactivity, biodegradable; molecular structure often contains cell adhesion sequences (e.g., RGD sequence) to provide a favorable signal transduction environment for cell growth.	Gelatin; collagen; chitosan; sodium alginate	High bioactivity; contains natural cell adhesion sites; good biodegradability; low cost and wide availability.	Poor mechanical properties; uncontrollable degradation rate; limited processability (e.g., poor solubility of chitosan).
Synthetic Polymer Materials	Prepared via chemical synthesis; stable mechanical properties, controllable degradation rate, excellent processability; performance can be optimized by adjusting molecular weight, crystallinity, etc., to meet the repair needs of different wounds.	Polycaprolactone (PCL); polylactic acid (PLA); polyglycolic acid (PGA); poly(lactic-co-glycolic acid) (PLGA)	Stable mechanical support; adjustable degradation rate; good processability; non-cytotoxic degradation products (e.g., CO_2 and H_2O for PCL).	Weak bioactivity; lack of natural cell adhesion sites; poor hydrophilicity (e.g., PLGA).

The advantage of multi-level structural scaffolds lies in integrating functions across different scales to achieve multidimensional wound healing regulation, making them suitable for treating complex wounds such as deep burns and exposed bone injuries.

Selection of scaffold structure should balance repair needs and performance trade-offs: oriented structures for scar reduction, core-shell structures for growth factor protection, and multilevel structures for complex wounds like deep burns.

IV. LOADING AND CONTROLLED RELEASE STRATEGIES FOR FGF1 IN STFS

The loading and controlled release of FGF1 are central to the design of STFS, directly impacting their bioavailability and wound-healing efficacy. An ideal loading and release strategy should meet the following criteria: 1 High loading efficiency to ensure sufficient FGF1 dosage within the scaffold; 2 High bioactivity retention to prevent FGF1 inactivation during loading; 3 Smart controlled release to achieve on-demand FGF1 delivery at the wound site. Currently, FGF1 loading and controlled release strategies primarily include physical loading methods and chemical conjugation methods. Among these, chemical conjugation methods have become a research hotspot due to their high loading stability and excellent controlled release performance.

A. PHYSICAL LOADING METHODS

Physical loading methods incorporate FGF1 into scaffolds through physical interactions (e.g., adsorption, encapsulation). These methods are simple to operate and require no chemical modification. However, they exhibit low loading efficiency, poor stability, and a tendency toward FGF1 burst release. Based on loading mechanisms, physical loading methods can be categorized into surface adsorption and internal encapsulation.

1) Surface Adsorption Method

This technique involves immersing the scaffold in an FGF1 solution, where FGF1 adsorbs onto the surface via electrostatic interactions, hydrogen bonds, and other physical forces. While operationally simple and gentle on FGF1's biological activity, this method suffers from low loading efficiency and susceptibility to FGF1 loss through wound exudate.

For instance, Han et al. immersed PLGA electrospun scaffolds in FGF1 solution to achieve surface adsorption via electrostatic interactions, yielding only 35% loading efficiency. In vitro release experiments showed an 80% burst release rate within 72 hours, making it difficult to maintain sustained effective concentrations at the wound site. To enhance adsorption efficiency, researchers typically improve scaffold hydrophilicity to strengthen interactions with FGF1. For instance, Li et al. enhanced PCL scaffold hydrophilicity via plasma treatment, reducing contact angle from 110° to 50° and increasing FGF1 adsorption efficiency to 55%, though burst release issues persisted.

Surface adsorption offers advantages of simplicity and minimal impact on FGF1 activity, but suffers from low loading efficiency and stability, making it suitable for short-term wound repair or scenarios requiring rapid FGF1 release.

2) Internal Encapsulation Method

Internal encapsulation involves directly mixing FGF1 into the spinning solution and encapsulating it within fibers via electrospinning. This method enables uniform distribution of FGF1 throughout the scaffold and achieves higher loading efficiency than surface adsorption. However, factors such as organic solvents and high-voltage electrostatic forces during spinning can cause FGF1 denaturation and inactivation. For instance, Zhang et al. incorporated FGF1 into PLA spinning solutions and achieved internal encapsulation via electrospinning, reaching a loading efficiency of 70%. However, the use of trifluoroethanol during spinning resulted in only 30% retention of FGF1's biological activity. To protect FGF1's biological activity, researchers commonly blend it with lyophilization protectants (e.g., mannitol, trehalose) to reduce structural damage from organic solvents. For instance, Wang et al. blended FGF1 with mannitol (1:10 mass ratio) before incorporating it into PCL spinning solutions, increasing FGF1's bioactivity retention to 65%. However, this still falls short of clinical requirements.

The internal encapsulation method offers advantages in high loading efficiency and uniform FGF1 distribution, but it significantly degrades FGF1's biological activity. It is suitable for loading growth factors with higher stability, such as EGF.

While microsphere encapsulation avoids direct FGF1 damage from electrospinning's high voltage and organic solvents, common microsphere synthesis methods (emulsification-solvent evaporation) have inherent limitations: residual organic solvents (e.g., dichloromethane) can damage FGF1's secondary structure, and high-speed emulsification shear force may reduce bioactivity—only increasing FGF1 activity retention by 10%–15%.

Improvement directions include: 1 Adopting mild preparation processes (low-temperature spray drying, ionic gelation) to avoid organic solvents and high shear force; 2 Adding protective agents (bovine serum albumin, trehalose) inside microspheres to enhance FGF1 stability during preparation, increasing activity retention from 65% to over 80%.

B. CHEMICAL CONJUGATION METHODS

Chemical conjugation methods introduce active groups onto the scaffold surface through chemical modification. These groups form covalent bonds or specific interactions with FGF1's amino acid residues, achieving stable FGF1 loading. This method offers high loading efficiency and stability, enabling smart controlled release of FGF1 by adjusting binding site properties. It is currently the most extensively studied loading strategy. Based on binding mechanisms, chemical conjugation methods are categorized into covalent conjugation and specific conjugation.

1) Covalent Binding

Covalent binding employs chemical methods such as EDC/NHS cross-linking or amidation reactions to form covalent bonds between active groups on the scaffold surface (e.g., carboxyl, amino groups) and amino acid residues of FGF1 (e.g., amino group of lysine, carboxyl group of aspartic acid), achieving stable FGF1 loading. This method offers high loading stability, effectively preventing FGF1 burst release and loss. However, the chemical reaction may damage FGF1's active sites, reducing its biological activity.

For example, Chen et al. employed EDC/NHS crosslinking to form amide bonds between gelatin scaffold carboxyl groups and FGF1 amino groups, achieving 85% loading efficiency. In vitro release experiments demonstrated a 70% cumulative release rate over 14 days, with 60% bioactivity retention of released FGF1. To preserve FGF1's biological activity, researchers typically employ mild reaction conditions (e.g., low temperature, low crosslinker concentration) and select amino acid residues distant from the active site for binding. For instance, Li et al. targeted the non-active terminal region of FGF1 for covalent coupling, increasing the bioactivity retention rate to 80%.

The advantage of covalent conjugation lies in its high loading stability, enabling sustained release of FGF1. However, it significantly impacts FGF1's biological activity, necessitating optimized reaction conditions to protect its active site.

2) Specific Conjugation

Specific conjugation leverages specific interactions between biomolecules (e.g., heparin-FGF1, antigen-antibody) to achieve stable FGF1 loading. This method involves mild coupling that does not compromise FGF1's biological activity. Furthermore, the coupling exhibits environmental sensitivity, enabling intelligent controlled release of FGF1, making it the most ideal loading strategy currently available. Among these, heparin-mediated specific coupling has become a research hotspot due to the strong interaction between heparin and FGF1 and its pH sensitivity.

Heparin, a strongly negatively charged sulfated glycosaminoglycan, forms electrostatic interactions and hydrogen bonds between its sulfate groups and the basic amino acid residues (e.g., arginine, lysine) of FGF1, constructing a stable heparin-FGF1 complex. This complex not only protects the spatial structure of FGF1 and inhibits protease degradation but also enhances its binding affinity to FGFR receptors, thereby increasing its biological activity. More importantly, the interaction between heparin and FGF1 exhibits pH sensitivity: under the acidic microenvironment of chronic wounds (pH 5.5–6.5), the sulfate groups on the heparin molecular chain become protonated, weakening electrostatic interactions and leading to rapid FGF1 release. whereas in normal physiological conditions (pH 7.4), the two molecules bind tightly, resulting in slow FGF1 release. This mechanism enables "wound-targeted" smart delivery. For instance, Yang et al. immobilized heparin onto PLGA scaffold surfaces via EDC/NHS crosslinking. Leveraging the specific interaction between heparin and FGF1, they achieved 90% FGF1 loading efficiency with 85% bioactivity retention. In vitro release experiments demonstrated that at pH 5.5 (simulating wound conditions), the 24-hour FGF1 release rate reached 45%, whereas at pH 7.4 (normal physiological conditions), it was only 15%, confirming wound-targeted release. In vivo studies showed that this scaffold reduced chronic wound healing time by 40% in rats and increased neovascular density by 67%. Comparison of Covalent and Specific Binding Strategies for FGF1 Immobilization on Scaffolds As shown in Table 3:

Beyond heparin, researchers have explored other specific binding systems, such as antibody-antigen interactions. For instance, Zhang et al. immobilized monoclonal antibodies against FGF1 onto PCL scaffold surfaces, leveraging antigen-antibody specificity to achieve 88% loading effi-

TABLE 3. Comparison of Covalent and Specific Binding Strategies for FGF1 Immobilization on Scaffolds

Chemical Binding Method	Definition	Core Mechanism	Key Advantages	Limitations
Covalent Binding Method	A method to achieve stable loading of FGF1 by introducing active groups on the scaffold surface through chemical modification, which form covalent bonds with amino acid residues of FGF1 via chemical reactions such as EDC/NHS crosslinking and amidation.	Scaffold surface active groups (e.g., carboxyl, amino) form covalent bonds with FGF1's amino acid residues (e.g., amino of lysine, carboxyl of aspartic acid), realizing stable immobilization of FGF1.	High loading stability; effectively avoids burst release and loss of FGF1; enables sustained release of FGF1.	Chemical reactions may damage the active sites of FGF1, reducing its bioactivity.
Specific Binding Method	A method to stably load FGF1 by utilizing specific biomolecular interactions (e.g., heparin-FGF1, antigen-antibody), enabling intelligent controlled release of FGF1 due to environment-sensitive binding.	Heparin-mediated binding: sulfate groups on heparin form electrostatic interactions and hydrogen bonds with basic amino acid residues (e.g., arginine, lysine) of FGF1, forming stable heparin-FGF1 complexes. In acidic chronic-wound microenvironments (pH 5.5–6.5), sulfate groups are protonated, weakening interactions and triggering rapid FGF1 release; in physiological environment (pH 7.4), tight binding ensures slow release.	High loading efficiency; high bioactivity retention (mild binding without damaging FGF1); enables environment-responsive intelligent controlled release; heparin-mediated method has low cost and good efficacy.	Antigen-antibody binding system has high cost, limiting large-scale application.

ciency. However, this approach carries high costs, limiting its scalability.

The advantages of specific conjugation methods lie in their high loading efficiency, high retention of biological activity, and the ability to achieve smart controlled release, representing the future direction for FGF1 loading

strategies. Among these, heparin-mediated specific conjugation holds broad clinical application prospects due to its low cost and excellent efficacy.

V. HEALING PROMOTION MECHANISM AND APPLICATION PROSPECTS OF FGF1-MEDIATED STFS

A. SYNERGISTIC HEALING PROMOTION MECHANISM

FGF1-mediated STFS achieve efficient wound repair not through simple FGF1-scaffold superposition, but via the synergistic interaction of "scaffold structural biomimicry-factor controlled release-microenvironment regulation." Their synergistic healing promotion mechanism primarily encompasses the following aspects:

1) Structural Support and Microenvironment Optimization

The porous structure (70%-90% porosity) of the smart textile fiber scaffold effectively absorbs wound exudate, maintaining a moist wound microenvironment and preventing cell apoptosis caused by wound desiccation. Simultaneously, the scaffold's physical barrier function isolates external pathogenic microorganisms, reducing infection risk. Moreover, the scaffold's mechanical properties align with the stress demands of wound tissues, preventing excessive contraction that leads to scar formation. For instance, the tensile strength of PCL/gelatin composite scaffolds reaches 12 MPa, effectively supporting wound tissues and reducing contraction rates by up to 30%.

2) Regulation of Cell Adhesion and Proliferation

The scaffold's biomimetic structure provides "anchorage points" for cells. Bioactive components on its surface (e.g., RGD sequences in gelatin, heparin) bind to cell surface receptors, promoting cell adhesion and spreading. Simultaneously, the scaffold's slow release of FGF1 activates intracellular signaling pathways, stimulating cell proliferation and differentiation. For instance, FGF1-mediated PCL/gelatin scaffolds increased fibroblast proliferation by 42% and endothelial cell proliferation by 58%.

3) Inflammation Regulation and Angiogenesis Enhancement

FGF1 released from the scaffold modulates inflammatory cell polarization, promoting the transition of macrophages from M1 to M2 type and reducing inflammatory responses. Simultaneously, FGF1 activates intracellular signaling pathways in endothelial cells, promoting their migration, proliferation, and lumen formation, thereby enhancing blood supply to the wound site. Additionally, FGF1 upregulates VEGF expression via paracrine effects, synergistically boosting angiogenesis activity. Studies indicate that FGF1-mediated STFS increase neovascular density by 67% and reduce inflammatory cell infiltration by 40% at wound sites.

4) Optimization of Collagen Synthesis and Tissue Remodeling

FGF1 released from the scaffold promotes fibroblast synthesis of collagen proteins such as Col-I and Col-III while regulating the balance between MMPs and TIMPs to optimize collagen remodeling. Furthermore, the scaffold's oriented structure guides collagen fibers to align orderly along stress directions, enhancing the mechanical properties of wound tissue and reducing scar formation. For instance, an oriented FGF1/PCL/gelatin scaffold increased collagen fiber order by 40% and reduced scar area by 41%.

B. APPLICATION PROSPECTS

FGF1-mediated STFS exhibit broad application potential in wound repair due to their superior healing-promoting properties, primarily manifested in the following aspects:

(1) Chronic Wound Treatment: Chronic wounds often fail to heal due to prolonged inflammation and impaired angiogenesis. FGF1-mediated STFS can effectively promote healing by regulating inflammatory responses and enhancing angiogenesis. For diabetic wounds, this scaffold reduces healing time by 40% and increases healing rates by 50%.

(2) Deep Burn Wound Repair: Deep burn wounds often involve full-thickness skin defects requiring structural support and bioactive regulation. FGF1-mediated STFS promote granulation tissue formation and epithelialization, reducing the need for skin grafts.

(3) Treatment of Chronic Wounds: For difficult-to-heal wounds such as radiation ulcers and pressure ulcers, this scaffold achieves efficient wound repair by continuously regulating the wound microenvironment through sustained, stable release of FGF1.

VI. CONCLUSIONS

The research on FGF1-mediated STFS highlights a promising avenue for advanced skin wound repair, moving beyond passive dressings to active, intelligent wound management. These scaffolds, prepared through techniques like electrospinning and utilizing materials ranging from natural (gelatin, chitosan) to synthetic (PCL, PLGA) and their composites, are engineered for structural biomimicry of the native extracellular matrix (ECM). Crucially, the development centers on achieving intelligent controlled release of FGF1, with chemical conjugation methods, particularly heparin-mediated specific conjugation, emerging as the most effective strategy for ensuring high loading efficiency, maximized bioactivity retention, and wound-targeted delivery (e.g., pH-sensitive release in chronic wounds). The scaffolds promote healing through a powerful synergistic mechanism involving structural support, cell regulation, anti-inflammatory effects, enhanced angiogenesis (up to 67% increase in neovascular density), and optimized collagen synthesis, ultimately leading to faster healing, reduced contraction, and lower scar formation, showing significant potential for treating chronic wounds and deep burns.

AUTHOR CONTRIBUTIONS

Conceptualization –Lufan Guan, Zhimin Li and Zhengwu Li; methodology – Lufan Guan, Zhimin Li and Zhengwu Li; investigation – Lufan Guan and Zhimin Li; writing-original draft preparation – Lufan Guan, Zhimin Li and Zhengwu Li. All authors have read and agreed to the published version of the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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