Chinese Journal of Plastic and Reconstructive Surgery xxx (xxxx) xxx

Contents lists available at ScienceDirect

Chinese Journal of Plastic and Reconstructive Surgery

journal homepage: www.sciencedirect.com/journal/chinese-journal-of-plastic-and-reconstructive-surgery



Review Article

Spinning a new future: The resurgence of silk fibroin biomaterials in oral and maxillofacial surgery

Gayathri Priyadharshini[a,*], Indra Kumar[b]

[a] Department of Periodontology, Vivekanandha Dental College for Women, Ellayampalayam, Tiruchengodu, 637205, Tamil Nadu, India
[b] Department of Oral and Maxillofacial Surgery, Vivekanandha Dental College for Women, Ellayampalayam, Tiruchengodu, 637205, Tamil Nadu, India

ARTICLE INFO

Keywords:
Silk fibroin
Biomaterials
Oral surgery
Bone regeneration
Tissue engineering
Guided bone regeneration

ABSTRACT

Oral and maxillofacial surgery (OMFS) continuously seeks biomaterials capable of meeting the complex regenerative requirements of the craniomaxillofacial region, which includes both hard and soft tissue repair. Historically valued for its textile applications, silk—particularly the protein silk fibroin (SF) derived from the *Bombyx mori* silkworm—has emerged as a highly biocompatible polymer. Upon removal of the immunogenic sericin coating, SF demonstrates excellent mechanical strength, tunable biodegradation rates, and the capacity to support stem cell differentiation. This review highlights the current landscape of SF applications in OMFS and identifies existing gaps in its utilization. Specifically, it discusses SF-based bone tissue engineering scaffolds, barrier membranes for guided bone regeneration, vehicles for drug and growth factor delivery, and adjuncts for soft tissue and nerve repair. Finally, the review addresses translational challenges that must be overcome before SF can become a standard-of-care material in clinical practice. Overall, SF represents an economical and minimally invasive biomaterial that promotes facial and intraoral harmony and can be seamlessly integrated into advanced dental practice.

1. Introduction

The reconstruction of osseous defects resulting from trauma, pathology, congenital deformities, or tooth loss remains a cornerstone of oral and maxillofacial surgery (OMFS).[1] The primary objectives of regenerative medicine in OMFS are the restoration of form and function following trauma, congenital anomalies, pathology, or tooth loss.[1,2] The ultimate goal is regenerative, rather than reparative, healing—thereby restoring the original form and function.[2,3] The oral cavity represents a unique and challenging environment characterized by continuous mechanical stress, a complex microbiome, and the requirement for esthetic outcomes. Consequently, there is an increasing demand for biomaterials that can endure these conditions while actively promoting tissue regeneration.[3]

Although autogenous grafts remain the "gold standard" for many procedures, they are limited by donor-site morbidity and restricted availability.[4] Consequently, tissue engineering strategies incorporating scaffolds, cells, and signaling molecules have gained significant research attention. Ideal scaffolds for OMFS should be biocompatible and osteoconductive, possess mechanical strength appropriate for the load-bearing jaw environment, and exhibit a degradation rate compatible with new bone formation.[4]

Synthetic alternatives (such as metallic alloys or synthetic polymers) often lack bioactivity or degrade too rapidly.[5] Natural polymers, including collagen and chitosan, have been widely employed due to their inherent bio-recognition properties. However, collagen frequently exhibits rapid enzymatic degradation and insufficient mechanical stability upon hydration.[4,5]

In this context, silk fibroin (SF) has gained significant attention. SF, a protein polymer obtained by degumming silk from the *Bombyx mori* silkworm, has emerged as a promising alternative material.[6] Unlike traditional silk sutures, which often elicited adverse reactions due to the presence of the sericin coating, purified fibroin is highly biocompatible. Once limited to surgical sutures, SF is now recognized as a versatile protein-based biopolymer.[7] Its distinctive combination of mechanical strength, slow biodegradation rate, and excellent biocompatibility makes it particularly appealing for OMFS applications ranging from alveolar ridge preservation to complex craniofacial reconstruction.[7,8] The ability of SF to be processed into diverse forms—including three-dimensional (3D) porous sponges, electrospun membranes, and hydrogels—and its controllable biodegradation profile over months to years make it a unique and adaptable biomaterial.[8–11]

* Corresponding author.
E-mail address: dregayathripriyadharshini@vdcw.ac.in (G. Priyadharshini).

https://doi.org/10.1016/j.cjprs.2026.02.003
Received 20 December 2025; Received in revised form 1 February 2026; Accepted 21 February 2026
Available online xxxx
2096-6911/© 2026 China Medical Cosmetology Press Co. Ltd. Publishing services by Elsevier B.V. on behalf of KeAi Communications Co. Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Please cite this article as: Priyadharshini G, Kumar I, Spinning a new future: The resurgence of silk fibroin biomaterials in oral and maxillofacial surgery, Chinese Journal of Plastic and Reconstructive Surgery, https://doi.org/10.1016/j.cjprs.2026.02.003

Although numerous narrative reviews exist, there remains a need to quantitatively synthesize the available evidence regarding SF's performance in bone repair models relevant to the craniomaxillofacial complex. A systematic search was conducted in PubMed, Embase, and the Cochrane Library for articles published up to October 2025. The search employed combinations of the following keywords: ("silk fibroin" OR "*Bombyx mori*") AND ("bone regeneration" OR "alveolar ridge augmentation" OR "guided bone regeneration" OR "maxillofacial" OR "mandibular defect" OR "calvarial defect"). The inclusion criteria for this systematic search comprised controlled *in vivo* animal studies or human clinical trials; studies reporting quantitative histomorphometric data on new bone formation; and studies investigating SF use in craniofacial or oral bone sites, as well as relevant narrative reviews. Data regarding study design, animal species, defect size, SF scaffold type (e.g., porous sponge or electrospun mat), follow-up duration, and percentage of new bone formation (mean and standard deviation) were extracted. Based on the available evidence, this review summarizes the properties of SF, its expanding roles in oral surgical applications, and the translational challenges that must be addressed before SF can become a standard-of-care material in clinical practice.

2. Silk fibroin: From textile to biomaterial

Silk derived from the domestic silkworm *Bombyx mori* consists of two primary proteins: fibroin and sericin.[11] Fibroin forms the structural core of the silk fiber, whereas sericin serves as a glue-like coating that binds the fibers together. Early medical uses of unprocessed ("virgin") silk were frequently associated with hypersensitivity reactions, later found to result from the presence of sericin.[12] Modern biomedical silk undergoes a "degumming" process—typically boiling in an alkaline solution—to remove sericin and yield highly biocompatible fibroin.[13]

Degumming represents the critical initial step in converting raw *Bombyx mori* silk into a biocompatible scaffold for tissue engineering. Its primary objective is to eliminate sericin—the adhesive protein responsible for inflammatory reactions—while preserving the structural integrity of the fibroin core. The most commonly employed degumming techniques are summarized in Table 1, which illustrates different degumming processes of SF and their respective clinical applications.[13–16]

2.1. Alkaline hydrolysis (sodium carbonate)

This method is regarded as the "gold standard" for laboratory-scale SF extraction because of its reliability and efficiency. The fabrication process includes the following steps: first, the silk cocoons are boiled in a dilute sodium carbonate (Na_2CO_3) solution, typically at a concentration of 0.02 M, for 20–60 min. The high pH cleaves the peptide bonds and polar side chains of sericin, rendering it water-soluble. The main advantage of this technique is its ability to remove nearly 100% of sericin with consistent and reproducible outcomes. However, prolonged boiling may cause fibroin fibril degradation, reducing molecular weight and consequently diminishing the mechanical strength of the final material.[14–16] This processing technique is considered highly efficient in the biomedical field and particularly effective in modifying and enhancing the functional properties of SF microfibers and hydrogels.[15,16]

2.2. Enzymatic degumming

Enzymatic degumming represents a more "gentle" biological approach that employs specific enzymes to selectively remove sericin. The fabrication process proceeds as follows: first, proteolytic enzymes—most commonly papain or Alcalase—are applied in a temperature-controlled bath (typically 50 °C–60 °C). These enzymes specifically catalyze the hydrolysis of sericin without disrupting the crystalline regions of fibroin. The principal advantages of this technique are its environmental friendliness, energy efficiency, and the significantly reduced mechanical damage to fibroin fibers compared to boiling methods. However, the higher cost of enzymes and the challenge of completely removing residual enzyme from the silk may affect downstream biocompatibility.[14,15] This processing technique is regarded as superior to alkaline hydrolysis because it represents an eco-friendly approach that preserves the structural integrity and molecular weight of SF.[14,15]

2.3. High-temperature high-pressure (autoclaving)

This method relies on thermal energy and pressure rather than chemical reagents. The fabrication process involves submerging the silk in deionized water and placing it in an autoclave at approximately 121 °C for 30–60 min. The intense heat and pressure enhance sericin solubility, facilitating its diffusion into the aqueous phase. The main advantage of this method is that it is entirely chemical-free ("green" synthesis), making it ideal for medical implants where chemical residues are undesirable. The major drawback is that excessive pressure can cause random cleavage of fibroin chains, leading to inconsistent secondary structures, particularly in β-sheet formation.[14–16] Overall, this processing method is considered superior to both alkaline hydrolysis and conventional degumming because it preserves the structural integrity of fibroin, improves mechanical properties, and effectively removes the sericin layer without chemical agents.[14,15]

2.4. Organic acid degumming

Although used less frequently in high-tech silk synthesis, this method is more common in textile refinement processes. The fabrication process proceeds as follows: first, the silk is treated with weak organic acids such as citric acid or tartaric acid. The acid protonates the sericin, thereby

Table 1
Different degumming methods of silk fibroin and their clinical applications.

S. No.	Method	Reagent	Impact on fibroin	Clinical significance
1	Alkaline hydrolysis	Na_2CO_3	High (degradation)	Fastest preparation method; Used for the production of SF microfibers and hydrogels; Effective in modifying and enhancing the functional properties of SF for biomedical applications.
2	Enzymatic degumming	Papain/Alcalase	Low (preservation)	Superior to alkaline hydrolysis; Eco-friendly technique that preserves the structural integrity and molecular weight of SF; Widely applied in the fabrication of high-strength scaffolds.
3	High-temperature high-pressure (autoclaving)	H_2O	Moderate	Superior to both alkaline hydrolysis and conventional degumming, as it preserves structural integrity and improves mechanical properties; Effectively removes the sericin layer without chemical reagents.
4	Organic acid degumming	Citric acid/ Tartaric acid	Severe (partial removal)	Incomplete sericin removal may trigger immunogenic responses when used *in vivo*.

SF, silk fibroin.

Table 2
Summary of the advantages of silk fibroin in oral and maxillofacial surgery.

Feature	Clinical benefit in maxillofacial surgery
Biocompatibility	Minimizes the risk of graft rejection and chronic inflammation
Mechanical strength	Maintains structural stability and space within defect sites under functional load
Controlled degradation rate	Ensures synchronized resorption with new bone formation
Versatility	Enables precise adaptation to complex anatomical contours

disrupting its bonds with the fibroin core. The primary advantage of this technique is that it is less aggressive than sodium carbonate treatment. However, its main limitation is that it frequently results in residual "sericin skin" due to incomplete removal, which can induce immunogenic reactions when applied *in vivo*.[14–16]

2.5. Critical considerations for synthesis

Regardless of the chosen method, degumming time represents the most critical parameter influencing SF quality. Excessive degumming produces short-chain fibroin, which forms brittle films, whereas insufficient degumming leaves residual sericin that may induce cell death or inflammation in biological applications.[16]

3. Structure and properties

SF is a fibrous protein primarily composed of the amino acids glycine, alanine, and serine. Its exceptional mechanical strength arises from the formation of highly ordered β-sheet crystalline structures.[17] By adjusting processing parameters such as temperature, pH, and solvent type, researchers can modulate the ratio of crystalline to amorphous regions, thereby controlling the material's degradation rate and mechanical stiffness to suit specific tissue requirements.[18–20]

The key advantages of SF in oral and maxillofacial surgery include the following:

3.1. Biocompatibility

Processed SF exhibits low immunogenicity. When properly purified to remove sericin—a glue-like protein capable of triggering allergic or inflammatory reactions—SF induces only a minimal immune response in host tissues. It also promotes cell adhesion, proliferation, and differentiation, making it an optimal scaffold for osteoblasts and mesenchymal stem cells in bone regeneration applications.[18–20]

3.2. Robust mechanical properties

SF demonstrates remarkable tensile strength and toughness due to its β-sheet crystalline structure. In comparison with other natural polymers such as collagen and synthetic alternatives like polylactic acid (PLA), SF offers superior structural stability. This property is particularly critical in maxillofacial applications, where scaffolds must endure masticatory forces during healing.[18–20]

3.3. Tailorable biodegradation

Unlike many synthetic polymers that degrade through hydrolysis—often causing a localized decrease in pH—SF undergoes gradual enzymatic degradation by proteases such as protease XIV. The degradation rate can be precisely controlled by modulating crystallinity during processing. Consequently, SF scaffolds can remain stable for extended periods, supporting new tissue maturation before complete resorption occurs.[18–20]

3.4. Versatile processing

SF can be fabricated into a wide range of physical formats from an aqueous regenerated silk solution. Common morphologies employed in surgical applications include hydrogels, used for the injectable delivery of drugs or cells; 3D porous sponges, utilized for bone volume augmentation; films and membranes, applied in guided bone regeneration (GBR); and nanofibers, designed to replicate the extracellular matrix. Fig. 1 illustrates the different structural forms of SF used in OMFS.[18–20]

4. Applications of silk fibroin in oral and maxillofacial surgery

SF has emerged as a leading biomaterial in maxillofacial surgery because of its excellent biocompatibility, tunable mechanical properties, and controllable degradation rate (see Table 2). Within the complex anatomy of the head and neck, SF functions not only as a structural support but also as a bioactive platform that can be customized for both hard and soft tissue regeneration. Table 3 summarizes the diverse applications of SF within the maxillofacial region.

4.1. Silk fibroin in bone tissue engineering

The reconstruction of osseous defects in the jaws caused by cysts, tumors, periodontal disease, or trauma remains a major challenge in OMFS. SF is increasingly investigated as a scaffold material for bone regeneration.[21] Unlike rapidly degrading synthetic polymers, SF provides a protein-based scaffold with sufficient mechanical integrity to support the gradual process of osteogenesis in jaw and craniofacial

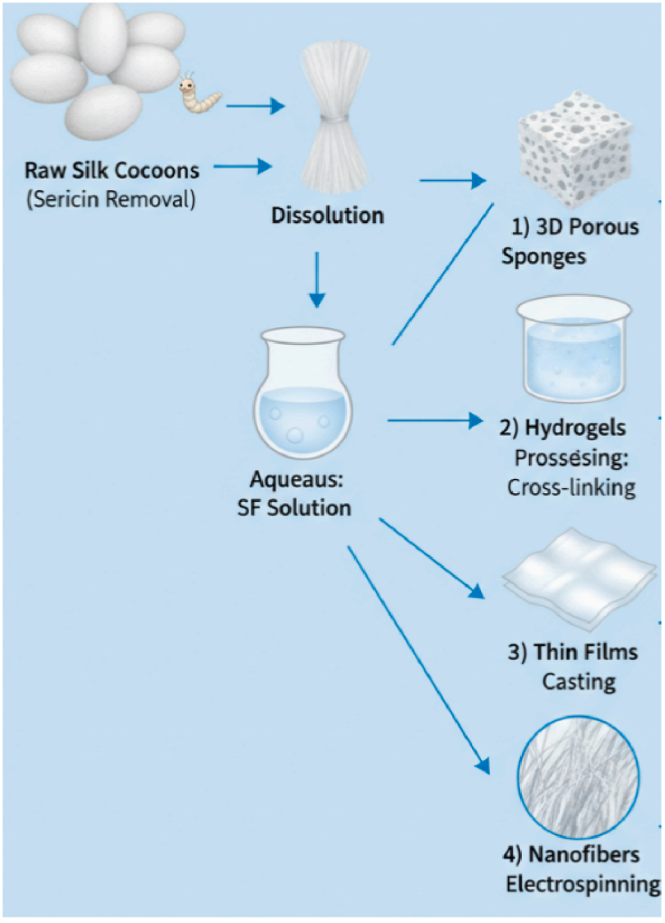


Fig. 1. Different structural forms of silk fibroin used in oral and maxillofacial surgery
SF, silk fibroin; OMFS, oral and maxillofacial surgery.

Table 3
Diverse applications of silk fibroin in the maxillofacial region.

Application area	Primary function and form	Key advantages
Bone tissue engineering and 3D scaffolds	Porous 3D structures—such as sponges or 3D-printed lattices—designed for large defect repair	Exhibits high compressive strength to withstand masticatory forces; promotes osteoblast adhesion and inward bone regeneration
Growth factor delivery	Carrier matrices for BMP-2, VEGF, or TGF-β in hydrogel or microsphere form	Enables slow and localized release of proteins; prevents systemic side effects while maintaining bioactivity of the incorporated factors
Guided bone regeneration	Thin, semi-permeable membranes produced by electrospinning or solvent casting	Functions as a barrier against soft tissue invasion into bone defects; resorbable, eliminating the need for secondary surgical removal
Soft tissue and mucosal healing	Bioactive films or hydrogels applied to oral mucosal defects	Maintains a moist wound environment; promotes rapid re-epithelialization of the oral lining and enhances patient comfort
Wound dressing	Antimicrobial-loaded mats or non-woven silk fibroin sheets	Conforms flexibly to irregular facial contours; reduces inflammation and efficiently absorbs exudate
Nerve regeneration	Nerve guidance conduits for peripheral facial or lingual nerve repair	Protects regenerating axons from compression; provides a structural bridge for Schwann cell migration; minimizes fibrotic scarring

3D, three-dimensional; VEGF, vascular endothelial growth factor; TGF-β, transforming growth factor-beta.

defects.[21] Its versatility enables fabrication into multiple forms—such as hydrogels, porous sponges, and 3D printed mats—that closely replicate the extracellular matrix of natural bone.[22] To improve therapeutic outcomes, researchers frequently functionalize SF scaffolds with bioactive agents such as hydroxyapatite or bone morphogenetic proteins (BMPs), thereby enhancing osteoconductivity and tissue integration.[22] Consequently, SF represents a promising alternative to traditional autografts, offering a biologically compatible solution that avoids donor-site morbidity while effectively supporting alveolar ridge preservation and bone augmentation procedures.[21,22]

4.2. Silk fibroin in 3D porous scaffolds

The application of SF as a 3D scaffold marks a significant advancement in reconstructive OMFS, particularly for repairing critical-sized defects in the mandible and maxilla.[23] These 3D architectures provide an interconnected porous network that facilitates nutrient diffusion, vascularization, and cellular infiltration—all of which are essential for regenerating dense craniofacial bone.[23] Furthermore, the slow degradation rate of SF enables the scaffold to maintain structural space, allowing osteoblasts to deposit mineralized matrix before the material is resorbed. When biofunctionalized with inorganic components such as nanohydroxyapatite, these scaffolds exhibit improved osteoconductivity and represent a promising, off-the-shelf alternative to autogenous bone grafts for complex alveolar ridge augmentation and corrective jaw reconstruction.[22,23] To promote effective bone regeneration, a scaffold must exhibit sufficient porosity to permit cellular infiltration and vascular ingrowth, as well as mechanical strength to withstand functional loading. SF scaffolds, commonly fabricated using freeze-drying or salt-leaching techniques, demonstrate excellent osteoconductive capacity.[23] They support the adhesion, proliferation, and differentiation of mesenchymal stem cells and osteoblasts.[24]

However, pure SF is not inherently osteoinductive. To enhance its bone-forming potential, SF is frequently combined with bioactive ceramics such as hydroxyapatite or tricalcium phosphate. These composite scaffolds mimic the natural inorganic–organic architecture of native bone, improving mechanical stiffness and accelerating mineral deposition and maturation.[24,25]

4.3. Silk fibroin in growth factor delivery for bone regeneration

Although SF is widely recognized for its role as a structural scaffold, its true clinical potential lies in its capacity to function as a bioactive reservoir for essential growth factors.[26] In bone grafting and alveolar ridge augmentation, fibroin-based matrices are frequently enriched with BMP-2 and vascular endothelial growth factor (VEGF) to accelerate osteogenesis and angiogenesis, respectively.[27] These growth factors are released in a controlled and sustained manner, thereby overcoming the common challenge of rapid "burst" release associated with many synthetic polymer carriers.[26,27]

Moreover, the residual presence of sericin or the incorporation of transforming growth factor-beta (TGF-β) within the fibroin matrix enhances soft tissue healing and periodontal ligament regeneration.[28] This synergy between the crystalline structure of silk and the embedded signaling molecules promotes cellular adhesion and proliferation, which are critical for the success of dental implants and reconstructive procedures.[28] By mimicking the biochemical and mechanical features of the native extracellular matrix, growth factor-augmented SF effectively bridges the gap between mechanical stability and biological integration in complex craniofacial defects.[27,28]

The protein structure of SF also enables the encapsulation and controlled release of bioactive molecules. Researchers have incorporated BMP-2 and BMP-7 into SF scaffolds, demonstrating sustained and localized delivery profiles. Unlike conventional collagen sponges that often release BMPs rapidly—sometimes leading to undesired ectopic bone formation—SF-based carriers provide a prolonged release, potentially reducing the required dosage while enhancing targeted bone regeneration.[26–28]

4.4. Silk fibroin in guided bone and tissue regeneration (GBR/GTR) membranes

In implant dentistry and periodontology, GBR and GTR are essential techniques for restoring lost bone around teeth or preparing sites for dental implants.[29] These approaches employ barrier membranes that prevent the rapid proliferation of soft tissues—such as the gingival epithelium and connective tissue—from invading the defect, thereby allowing slower-growing osteogenic cells to occupy the regenerative space.[29,30]

Collagen membranes are currently the most widely used barriers; however, they frequently collapse into the defect due to insufficient space maintenance and often degrade prematurely. In contrast, non-resorbable polytetrafluoroethylene (PTFE) membranes maintain their architecture but require a second surgical procedure for removal.[29–31]

SF membranes are emerging as a promising alternative. They possess superior wet tensile strength compared with collagen, are easier to handle intraoperatively, and retain their structural integrity for extended periods (approximately 4–6 months), which corresponds well with the typical timeline of human bone healing. Studies have demonstrated that SF membranes integrate effectively with host tissues and elicit minimal inflammatory responses, functioning as efficient barriers while simultaneously promoting bone regeneration beneath the membrane.[31,32]

4.5. Silk fibroin in soft tissue and mucosal healing

The oral mucosa differs from skin in that it heals rapidly but remains continuously exposed to saliva, mechanical stress, and microbial challenges.[33] SF demonstrates a remarkable ability to promote mucosal repair while maintaining its structural stability under masticatory

Table 4
Comparison of biomaterials used in maxillofacial reconstruction.

Material type	Examples	Key advantages	Major limitations
Natural protein (silk)	Silk fibroin	Tunable degradation rate; high tensile strength; low immunogenicity; can be fabricated into versatile forms such as hydrogels, films, and sponges	Exhibits slower initial cell adhesion if not functionalized (e.g., with RGD peptides)
Natural protein (collagen)	Bio-Gide®, collagen plugs	Excellent bioactivity; rapid cell recognition and attachment	Undergoes fast and sometimes unpredictable degradation; exhibits low mechanical strength; prone to collapse in large defects
Synthetic polymers	Polylactic acid, polyglycolic acid, and polycaprolactone	Highly reproducible; suitable for 3D printing; predictable degradation kinetics	Hydrophobic nature results in poor cell attachment; acidic degradation byproducts may cause localized inflammation
Bioceramics	Hydroxyapatite, tricalcium phosphate	Highly osteoconductive; chemically similar to native bone mineral	Brittle and mechanically weak; difficult to shape into complex maxillofacial contours.
Metals	Titanium	Exceptional strength for load-bearing applications; supported by decades of clinical success	Non-resorbable; may induce stress shielding; can cause imaging artifacts due to radiopacity

3D, three-dimensional.

forces.[33] Its slow and controllable biodegradation rate ensures scaffold persistence long enough to support guided tissue regeneration without inducing a chronic inflammatory response.[33] Researchers are increasingly exploiting the versatile processing properties of SF to develop films, hydrogels, and electrospun membranes specifically designed for socket preservation and intraoral wound coverage. Incorporation of bioactive molecules or growth factors into these silk-based matrices further accelerates re-epithelialization and minimizes postoperative scarring.[33] Ultimately, SF represents a sustainable and biologically advanced alternative to synthetic polymers, offering significant potential for improving clinical outcomes in complex oral reconstructive procedures.[33]

4.6. Silk fibroin in wound dressings

SF films and hydrogels are currently being explored for oral wound healing applications, such as covering free gingival graft donor sites on the palate. SF hydrogels maintain a moist wound environment, facilitate gas exchange, and protect the wound bed from bacterial contamination.[34,35] As a protein-based polymer, SF creates a protective yet breathable microenvironment that significantly accelerates re-epithelialization and mucosal regeneration.[34] Unlike conventional wound dressings, SF scaffolds provide a bioactive matrix that promotes fibroblast migration and collagen synthesis—both essential for closure of defects in the moisture-rich oral cavity. Recent clinical studies have demonstrated that SF-based films and hydrogels effectively reduce postoperative pain and exudate levels while eliciting minimal inflammatory responses.[34]

Furthermore, SF can be functionalized with antimicrobial agents such as silver nanoparticles or bioactive growth factors, enhancing protection against secondary infections in bacteria-dense environments.[35] Its tunable degradation rate ensures that the dressing maintains structural support throughout the critical healing phase before naturally resorbing. Ultimately, SF represents a sustainable and biologically advanced alternative to synthetic membranes, providing predictable and improved clinical outcomes in complex oral soft tissue repair.[34,35]

4.7. Silk fibroin in nerve regeneration within the maxillofacial region

Injury to the inferior alveolar or lingual nerves during procedures such as third molar extraction, orthognathic surgery, or facial trauma can result in debilitating paresthesia. When direct neurorrhaphy is not feasible, nerve guidance conduits are employed to bridge the neural gap.[36]

SF-based nerve conduits have shown considerable promise as alternatives to autologous nerve grafts. These SF tubes guide axonal sprouting across nerve gaps, providing a biocompatible and mechanically stable environment. The material is non-cytotoxic to Schwann cells and can be functionalized with nerve growth factors to further enhance axonal regeneration. The slow degradation profile of SF ensures conduit integrity throughout the regenerative phase until the nerve gap is fully bridged.[36,37]

4.8. Comparison of silk fibroin with commonly used biomaterials

In OMFS, the selection of a biomaterial depends on the specific mechanical and biological requirements of the target site—whether it involves the load-bearing mandible, the delicate oral mucosa, or a neural pathway. SF is frequently evaluated against conventional "gold-standard" materials such as titanium, collagen, and synthetic polymers. Table 4 summarizes the comparative advantages and limitations of SF relative to these commonly used biomaterials.

5. Regulatory pathways and clinical translation

The regulatory pathway of SF in tissue regeneration represents a complex interplay between the material's structural characteristics and the cellular microenvironment. When SF is introduced as a scaffold, its degradation products—particularly small peptides and amino acids—serve as biochemical cues that modulate the PI3K/Akt and MAPK/ERK signaling pathways.[38] These pathways are essential for promoting cellular proliferation, migration, and differentiation. Moreover, SF can influence the TGF-β/Smad signaling cascade, which plays a pivotal role in orchestrating the transition from the inflammatory to the proliferative phase of wound healing. By modulating integrin expression on the cell surface, SF enhances cell–matrix interactions, effectively directing mesenchymal stem cells toward lineage-specific differentiation such as osteogenesis or vasculogenesis, depending on the mechanical stiffness and secondary structure (β-sheet content) of the silk matrix.[38,39]

5.1. Regulatory mechanisms

Three principal regulatory mechanisms are involved in the bioactivity of SF: (1) Mechanotransduction, wherein the physical architecture of fibroin translates mechanical stimuli into intracellular biochemical signals through the activation of the Yes-associated protein pathway; (2) angiogenic modulation, which involves the upregulation of VEGF expression to promote neovascularization; and (3) immune regulation, characterized by the polarization of macrophages from a pro-inflammatory M1 phenotype to a pro-regenerative M2 phenotype.[37–39]

5.2. Regulatory approval for clinical translation

The regulatory approval of SF for clinical translation represents a critical bridge between material science and regenerative medicine, marking its transformation from a traditional textile fiber to an advanced biomedical material.[40] Historically, silk possesses a well-established clinical record as a U.S. Food and Drug Administration

(FDA)–approved biomaterial for non-absorbable surgical sutures—a precedent that has facilitated the subsequent approval of more complex SF-based devices, such as the Seri® Surgical Scaffold, used for soft tissue repair.[39,40] The primary regulatory challenges involve standardizing extraction and purification methods—particularly the complete removal of sericin, a secondary protein known to elicit inflammatory responses—to ensure the production of highly purified, medical-grade fibroin.[40] Regulatory authorities require comprehensive characterization of batch-to-batch consistency, inherent to naturally derived silkworm fibroin, and long-term studies on biodegradation kinetics to verify that degradation byproducts are both non-toxic and metabolically cleared.[40] As of 2026, the global regulatory framework is moving toward harmonized standards for bioinks and smart scaffolds, emphasizing controlled-environment sericulture to meet the stringent safety, efficacy, and reproducibility benchmarks essential for broad clinical implementation and commercial scalability. Table 5 summarizes the key regulatory components associated with SF-based biomaterials.[39,40]

5.3. FDA 510(k)-approved silk-based products

The clinical translation of SF represents a critical convergence between material science and regenerative medicine, reflecting its evolution from a traditional textile fiber to a clinically validated biomaterial.[38,39] Historically, silk has maintained a well-documented clinical record as an FDA-approved material for non-absorbable surgical sutures—a foundation that enabled the subsequent clearance of more advanced SF-based medical devices, such as the Seri® Surgical Scaffold, designed for soft tissue repair. Despite this established precedent, extending SF applications to advanced platforms such as injectable hydrogels, drug delivery systems, and 3D-bioprinted constructs requires navigating stringent regulatory pathways, including the FDA's premarket approval process and the European Medicines Agency guidelines for biological medicinal products.[38]

The major regulatory challenges involve standardizing extraction and purification procedures—particularly ensuring the complete removal of sericin, a secondary protein known to induce inflammatory responses—to produce high-purity, medical-grade fibroin.[38–40] Regulatory authorities also require detailed characterization of batch-to-batch consistency, which is inherently variable among silkworm sources, and long-term biodegradation studies to verify that degradation byproducts are non-toxic and fully metabolized.[38] By 2026, global regulatory efforts are aligning toward harmonized standards for bioinks and smart scaffolds, emphasizing controlled-environment sericulture to meet the stringent safety, efficacy, and reproducibility benchmarks necessary for broad clinical translation and commercial scalability.[38–40]

Although the approval process for SF-based products remains demanding, several notable silk-derived devices have successfully obtained FDA 510(k) clearance by demonstrating substantial equivalence to previously approved surgical materials. These regulatory achievements have established a benchmark for the translation of natural protein-based biomaterials into medical-grade implants.[38–40] Table 6 summarizes key FDA-cleared SF products that mark significant milestones in the clinical translation of SF.

5.4. Manufacturing scalability

The manufacturing scalability of SF-based medical products presents distinct challenges that require rigorous regulatory oversight to achieve clinical clearance[40]: (1) "Suture" predicate: Most SF-based devices leverage the well-established safety record of traditional silk sutures. However, while sutures are categorized as non-absorbable, modern SF scaffolds are engineered to be resorbable. Consequently, manufacturers must submit comprehensive data demonstrating the metabolic fate of the fibroin protein and its degradation byproducts to regulatory authorities.[39,40] (2) Biocompatibility focus: In the case of the Silk Voice® injectable, the FDA required specific validation of the purification and sterilization processes to confirm complete sericin removal—a critical factor in preventing granuloma formation and chronic inflammation, particularly within delicate laryngeal tissues.[38–40] (3) Material characterization: Unlike synthetic polymers such as PLA, SF requires submission of a master file that documents sericulture parameters, including silkworm strain, diet composition, and environmental conditions. This documentation ensures batch-to-batch reproducibility and establishes traceability of the raw material, which are prerequisites for regulatory approval.[40]

6. Human trials

Zhang et al.[41] in China developed a novel wound dressing based on physically cross-linked SF. Both preclinical evaluations and a clinical trial involving 71 participants demonstrated that SF significantly accelerated wound healing while reducing adverse reactions such as inflammation. In comparative analyses, the SF dressing outperformed established commercial products including Suprathel® and Sidaiyi®. The technology has since been commercialized as SeriSkin®, produced by Zhejiang Xingyue Biotechnology Co., Ltd., and has obtained National

Table 5
Key regulatory components for silk fibroin.

Phase	Focus area	Regulatory requirement
Sourcing	Raw material control	Implementation of standardized sericulture practices and verified species identification of *Bombyx mori*
Processing	Degumming and purification	Validation of complete sericin removal and quantification of residual solvent content
Characterization	Physicochemical properties	Comprehensive documentation of molecular weight distribution, β-sheet crystallinity, and secondary structure confirmation
Preclinical	Biocompatibility	Compliance with ISO 10993 standards, including tests for cytotoxicity, sensitization, and implantation response
Clinical	Efficacy and safety	Demonstration of consistent degradation kinetics and validated functional tissue regeneration outcomes

Table 6
Commercially available silk fibroin-based medical products with FDA 510(k) clearance.

Product name	Manufacturer	FDA 510(k) number	Clinical indication	Key feature
Seri® Surgical Scaffold	Sofregen Medical (formerly Allergan)	K123128	Soft tissue support and repair, including use in plastic and reconstructive surgery	Bioresorbable knitted silk mesh providing immediate mechanical strength and long-term tissue remodeling
Silk Voice®	Sofregen Medical	K180631	Vocal fold medialization and correction of vocal fold insufficiency	First injectable silk fibroin–hyaluronic acid composite scaffold used as a bulking agent to improve phonation
Sylke®	Sylke Medical	K222533	Topical skin closure and wound management	Medical-grade silk mesh designed to reduce skin tension and promote non-invasive wound closure
Silk surgical sutures	Various manufacturers (e.g., Teleflex, Ethicon)	Multiple	General soft tissue approximation and ligation	Historical predicate device for silk-based biomaterials; classified as a Class II non-absorbable surgical material

FDA, Food and Drug Administration.

Medical Products Administration approval in China for managing skin-graft donor sites.[40,41]

Kim et al.[42] conducted a prospective, split-mouth randomized clinical trial involving 25 patients with bilaterally impacted mandibular third molars. An SF membrane and a high-density polytetrafluoroethylene (dPTFE) membrane were applied to opposite extraction sockets. The outcomes confirmed that GBR using the SF membrane achieved comparable results to GBR with the dPTFE membrane.

Bele et al.[43] performed a systematic review assessing the efficacy of silk-based biomaterials compared with conventional bone grafts in bone regeneration and osseointegration around dental implants. The authors concluded that silk biomaterials exhibited greater efficiency than traditional bone grafts in promoting osseointegration and bone formation, without the risk of secondary infection. Moreover, silk was noted to be simple to use and cost-effective.

Only a limited number of high-quality human randomized controlled trials have been conducted using SF. The existing evidence base relies predominantly on animal studies which, although valuable for proof-of-concept, do not fully replicate human oral physiology, microbiome composition, or functional occlusal loading. Furthermore, several available investigations assessed SF composites (e.g., SF combined with hydroxyapatite), complicating efforts to isolate the specific biological effects of fibroin alone.

7. Hurdles of silk fibroin

A considerable gap persists between laboratory innovation and clinical translation for SF. Although extensive research demonstrates promising biological outcomes, only a limited number of SF-based products have successfully advanced through clinical trials to establish efficacy in human subjects.[44] This translational bottleneck is primarily driven by several major commercialization challenges.

7.1. Regulatory and raw material constraints

Unlike flexible laboratory-scale sourcing, medical-grade SF must comply with stringent biosafety and quality-control standards, including defined limits on endotoxins, viral particles, and bacterial contaminants. This high regulatory threshold results in a limited number of certified raw-material suppliers, often delaying the transition from experimental development to market readiness.[44,45]

7.2. Complexity versus scalability

Many experimental SF scaffolds incorporate secondary bioactive components to enhance therapeutic performance. However, such structural and compositional complexity frequently complicates large-scale manufacturing and regulatory approval. Generally, as the architectural or chemical sophistication of a scaffold increases, the pathway to commercialization becomes progressively more challenging.[44,45]

Despite these obstacles, there is growing clinical demand for SF-based hydrogel dressings, as hydrogels closely emulate the native extracellular matrix and are particularly advantageous for promoting skin regeneration. To bridge this “valley of death” between academic research and clinical application, stronger collaboration between material scientists, clinicians, and regulatory agencies is essential to develop streamlined and commercially scalable SF hydrogel technologies.[46,47]

8. Challenges and future directions

Despite encouraging research outcomes, several obstacles continue to hinder the widespread clinical translation of SF in OMFS.

8.1. Standardization

The properties of raw silk vary significantly depending on the silkworm species, diet, and environmental conditions. Establishing standardized sourcing and degumming protocols is essential to ensure the production of consistent, pharmaceutical-grade SF suitable for medical applications.[40,48]

8.2. Regulatory pathways

Although silk sutures have long been approved by the FDA, newer formats such as 3D scaffolds and drug-eluting membranes remain subject to stringent regulatory scrutiny. Key considerations include sterilization validation, long-term biodegradation kinetics, and the safety of degradation byproducts in bulk-manufactured quantities.[40,48]

8.3. Advanced fabrication

The future development of SF lies in its integration with advanced manufacturing technologies. 3D bioprinting using SF-based bioinks is currently being explored to fabricate patient-specific scaffolds derived from cone-beam computed tomography data for complex craniofacial reconstruction.[40] To translate SF from a promising experimental material to a clinical mainstay in OMFS, future investigations should prioritize: (1) The execution of well-designed human randomized controlled trials, particularly comparing SF membranes with collagen membranes in alveolar ridge preservation and GBR procedures. (2) The standardization of SF extraction and fabrication methods to ensure reproducible clinical performance.[40,48]

9. Conclusion

SF has undergone a remarkable transformation from a traditional textile fiber into a sophisticated biomaterial with broad potential in OMFS. Its unique combination of mechanical resilience, controllable biodegradation, and biological compatibility addresses many of the limitations associated with existing synthetic and natural polymers. From durable membranes used in GBR to bioactive scaffolds designed for complex craniofacial reconstruction, SF is emerging as a cornerstone material in regenerative oral surgery. Continued focus on process standardization and the execution of high-quality clinical trials will be critical for fully realizing its potential in patient-centered care.

CRediT authorship contribution statement

Gayathri Priyadharshini: Conceptualization, Data curation, Formal analysis, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Indra Kumar:** Formal analysis, Data curation, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Ethics approval and consent to participate

Not applicable.

Declaration of competing interests

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

References

1. Latimer JM, Maekawa S, Yao Y, et al. Regenerative medicine technologies to treat dental, oral, and craniofacial defects. *Front Bioeng Biotechnol*. 2021;9:704048. https://doi.org/10.3389/fbioe.2021.704048.
2. Hung M, Sadri M, Katz M, et al. A systematic review of stem cell applications in maxillofacial regeneration. *Dent J*. 2024;12(10):315. https://doi.org/10.3390/dj12100315.
3. Tatullo M, Marrelli M, Paduano F. The regenerative medicine in oral and maxillofacial surgery: the most important innovations in the clinical application of mesenchymal stem cells. *Int J Med Sci*. 2015;12(1):72–77. https://doi.org/10.7150/ijms.10706.
4. Elsalanty ME, Genecov DG. Bone grafts in craniofacial surgery. *Craniomaxillofacial Trauma Reconstr*. 2009;2(3):125–134. https://doi.org/10.1055/s-0029-1215875.
5. Zhao R, Yang R, Cooper PR, et al. Bone grafts and substitutes in dentistry: a review of current trends and developments. *Molecules*. 2021;26(10):3007. https://doi.org/10.3390/molecules26103007.
6. Shao Z, Vollrath F. Surprising strength of silkworm silk. *Nature*. 2002;418(6899):741. https://doi.org/10.1038/418741a.
7. Wang F, Guo C, Yang Q, et al. Protein composites from silkworm cocoons as versatile biomaterials. *Acta Biomater*. 2021;121:180–192. https://doi.org/10.1016/j.actbio.2020.11.037.
8. DeBari MK, King 3rd CI, Altgold TA, et al. Silk fibroin as a green material. *ACS Biomater Sci Eng*. 2021;7(8):3530–3544. https://doi.org/10.1021/acsbiomaterials.1c00493.
9. Johari N, Khodaei A, Samadikuchaksaraei A, et al. Ancient fibrous biomaterials from silkworm protein fibroin and spider silk blends: biomechanical patterns. *Acta Biomater*. 2022;153:38–67. https://doi.org/10.1016/j.actbio.2022.09.030.
10. Rockwood DN, Preda RC, Yücel T, et al. Materials fabrication from Bombyx mori silk fibroin. *Nat Protoc*. 2011;6(10):1612–1631. https://doi.org/10.1038/nprot.2011.379.
11. Vepari C, Kaplan DL. Silk as a biomaterial. *Prog Polym Sci*. 2007;32(8-9):991–1007. https://doi.org/10.1016/j.progpolymsci.2007.05.013.
12. Inoue K, Arikawa H, Fujii K, et al. Viscoelastic properties of oral soft tissue. 1. A method of determining elastic modulus of oral soft tissue. *Dent Mater J*. 1985;4(1):47–53. https://doi.org/10.4012/dmj.4.47.
13. Wöltje M, Kölbel A, Aibibu D, et al. A fast and reliable process to fabricate regenerated silk fibroin solution from degummed silk in 4 hours. *Int J Mol Sci*. 2021;22(19):10565. https://doi.org/10.3390/ijms221910565.
14. Feng Y, Lin J, Niu L, et al. High molecular weight silk fibroin prepared by papain degumming. *Polymers*. 2020;12(9):2105. https://doi.org/10.3390/polym12092105.
15. Kim HJ, Kim MK, Lee KH, et al. Effect of degumming methods on structural characteristics and properties of regenerated silk. *Int J Biol Macromol*. 2017;104(Pt A):294–302. https://doi.org/10.1016/j.ijbiomac.2017.06.019.
16. Gaviria A, Jaramillo-Quiceno N, Motta A, et al. Silk wastes and autoclaved degumming as an alternative for a sustainable silk process. *Sci Rep*. 2023;13(1):15296. https://doi.org/10.1038/s41598-023-41762-6.
17. Zhou K, Yuan T, Wang S, et al. Beyond natural silk: bioengineered silk fibroin for bone regeneration. *Mater Today Bio*. 2025;33:102014. https://doi.org/10.1016/j.mtbio.2025.102014.
18. Wei S, Wang Y, Sun Y, et al. Biodegradable silk fibroin scaffold doped with mineralized collagen induces bone regeneration in rat cranial defects. *Int J Biol Macromol*. 2023;235:123861. https://doi.org/10.1016/j.ijbiomac.2023.123861.
19. Zhou Z, Cui J, Wu S, et al. Silk fibroin-based biomaterials for cartilage/osteochondral repair. *Theranostics*. 2022;12(11):5103–5124. https://doi.org/10.7150/thno.74548.
20. Xu L, Wu C, Lay Yap P, et al. Recent advances of silk fibroin materials: from molecular modification and matrix enhancement to possible encapsulation-related functional food applications. *Food Chem*. 2024;438:137964. https://doi.org/10.1016/j.foodchem.2023.137964.
21. Mao Z, Bi X, Yu C, et al. Mechanically robust and personalized silk fibroin-magnesium composite scaffolds with water-responsive shape-memory for irregular bone regeneration. *Nat Commun*. 2024;15(1):4160. https://doi.org/10.1038/s41467-024-48417-8.
22. Lyu Y, Liu Y, He H, et al. Application of silk-fibroin-based hydrogels in tissue engineering. *Gels*. 2023;9(5):431. https://doi.org/10.3390/gels9050431.
23. Zuluaga-Vélez A, Quintero-Martinez A, Orozco LM, et al. Silk fibroin nanocomposites as tissue engineering scaffolds - a systematic review. *Biomed Pharmacother*. 2021;141:111924. https://doi.org/10.1016/j.biopha.2021.111924.
24. Shuang FF, Wang CC, Zhu WJ, et al. Preparation of a robust silk fibroin scaffold with a reinforced concrete structure constructed with silk nanofibers as the skeleton based on a CaCl2-formic acid solution and freeze-drying method. *Polym Test*. 2022;111(7):107599. https://doi.org/10.1016/j.polymertesting.2022.107599.
25. Amirian J, Wychowaniec JK, Amel Zendehdel E, et al. Versatile potential of photo-cross-linkable silk fibroin: roadmap from chemical processing toward regenerative medicine and biofabrication applications. *Biomacromolecules*. 2023;24(7):2957–2981. https://doi.org/10.1021/acs.biomac.3c00098.
26. Qi Y, Wang H, Wei K, et al. A review of structure construction of silk fibroin biomaterials from single structures to multi-level structures. *Int J Mol Sci*. 2017;18(3):237. https://doi.org/10.3390/ijms18030237.
27. Lujerdean C, Baci GM, Cucu AA, et al. The contribution of silk fibroin in biomedical engineering. *Insects*. 2022;13(3):286. https://doi.org/10.3390/insects13030286.
28. Holland C, Numata K, Rnjak-Kovacina J, et al. The biomedical use of silk: past, present, future. *Adv Healthcare Mater*. 2019;8(1):e1800465. https://doi.org/10.1002/adhm.201800465.
29. Gao Y, Shao W, Qian W, et al. Biomineralized poly (l-lactic-co-glycolic acid)-tussah silk fibroin nanofiber fabric with hierarchical architecture as a scaffold for bone tissue engineering. *Mater Sci Eng C Mater Biol Appl*. 2018;84:195–207. https://doi.org/10.1016/j.msec.2017.11.047.
30. Deng L, Hou M, Lv N, et al. Melatonin-encapsuled silk fibroin electrospun nanofibers promote vascularized bone regeneration through regulation of osteogenesis-angiogenesis coupling. *Mater Today Bio*. 2024;25:100985. https://doi.org/10.1016/j.mtbio.2024.100985.
31. Akdag Z, Ulag S, Kalaskar DM, et al. Advanced applications of silk-based hydrogels for tissue engineering: a short review. *Biomimetics*. 2023;8(8):612. https://doi.org/10.3390/biomimetics8080612.
32. Ferraz MP. An overview on the big players in bone tissue engineering: biomaterials, scaffolds and cells. *Int J Mol Sci*. 2024;25(7):3836. https://doi.org/10.3390/ijms25073836.
33. Kim SH, Lee YJ, Chao JR, et al. Rapidly photocurable silk fibroin sealant for clinical applications. *NPG Asia Mater*. 2020;12(1):46. https://doi.org/10.1038/s41427-020-0227-6.
34. Schäfer S, Smeets R, Köpf M, et al. Antibacterial properties of functionalized silk fibroin and sericin membranes for wound healing applications in oral and maxillofacial surgery. *Biomater Adv*. 2022;135:212740. https://doi.org/10.1016/j.bioadv.2022.212740.
35. Lu Y, Huang X, Yuting Luo, et al. Silk fibroin-based tough hydrogels with strong underwater adhesion for fast hemostasis and wound sealing. *Biomacromolecules*. 2023;24(1):319–331. https://doi.org/10.1021/acs.biomac.2c01157.
36. Wang C, Jia Y, Yang W, et al. Silk fibroin enhances peripheral nerve regeneration by improving vascularization within nerve conduits. *J Biomed Mater Res*. 2018;106(7):2070–2077. https://doi.org/10.1002/jbm.a.36390.
37. Kuihua Z, Chunyang W, Cunyi F, et al. Aligned SF/P(LLA-CL)-blended nanofibers encapsulating nerve growth factor for peripheral nerve regeneration. *J Biomed Mater Res*. 2014;102(8):2680–2691. https://doi.org/10.1002/jbm.a.34922.
38. Park YR, Sultan MT, Park HJ, et al. NF-κB signaling is key in the wound healing processes of silk fibroin. *Acta Biomater*. 2018;67:183–195. https://doi.org/10.1016/j.actbio.2017.12.006.
39. Gao K, Xie Y, Xu F, et al. Silk fibroin promotes H3K9me3 expression and chromatin reorganization to regulate endothelial cell proliferation. *APL Bioeng*. 2024;8(2):026115. https://doi.org/10.1063/5.0203858.
40. Bassani GA, Vincoli V, Biagiotti M, et al. A route to translate a silk-based medical device from lab to clinic: the silk biomaterials srl experience. *Insects*. 2022;13(2):212. https://doi.org/10.3390/insects13020212.
41. Zhang W, Chen L, Chen J, et al. Silk fibroin biomaterial shows safe and effective wound healing in animal models and a randomized controlled clinical trial. *Adv Healthcare Mater*. 2017;6(10). https://doi.org/10.1002/adhm.201700121, 10.1002/adhm.201700121.
42. Kim JW, Jo YY, Kim JY, et al. Clinical study for silk mat application into extraction socket: a split-mouth, randomized clinical trial. *Appl Sci*. 2019;9(6):1208. https://doi.org/10.3390/app9061208.
43. Bele R, Thombre B, Barabde A, et al. Comparative analysis of efficacy of silk biomaterial and conventional bone graft on bone regeneration and osseointegration in and around implants: a systematic review. *J Dent Res Rev*. 2023;10(4):194–201. https://doi.org/10.4103/jdrr.jdrr_130_22.
44. Sánchez-Cid P, Jiménez-Rosado M, Romero A, et al. Novel trends in hydrogel development for biomedical applications: a review. *Polymers*. 2022;14(15):3023. https://doi.org/10.3390/polym14153023.
45. Chaudhari AA, Vig K, Baganizi DR, et al. Future prospects for scaffolding methods and biomaterials in skin tissue engineering: a review. *Int J Mol Sci*. 2016;17(12):1974. https://doi.org/10.3390/ijms17121974.
46. Dimatteo R, Darling NJ, Segura T. *In situ* forming injectable hydrogels for drug delivery and wound repair. *Adv Drug Deliv Rev*. 2018;127:167–184. https://doi.org/10.1016/j.addr.2018.03.007.
47. Tavakoli S, Klar AS. Advanced hydrogels as wound dressings. *Biomolecules*. 2020;10(8):1169. https://doi.org/10.3390/biom10081169.
48. Yu Y, Wang J. Recent advances and challenges in silk fibroin-based small-caliber vascular grafts: a review. *Int J Biol Macromol*. 2025;322(Pt 3):146930. https://doi.org/10.1016/j.ijbiomac.2025.146930.