Am J Transl Res 2026;18(4):2808-2825
www.ajtr.org /ISSN:1943-8141/AJTR0168962

Review Article

Clinical progress and prospects of biodegradable intestinal stents

Keyu Li*, Sijun Wang*, Qiong Wang, Fenglin Zhang, Xinpu Yuan*, Chaojun Zhang*

*Department of Colorectal Surgery, Chinese People's Liberation Army General Hospital, Beijing, China. *Equal contributors.*

Received September 22, 2025; Accepted February 14, 2026; Epub April 15, 2026; Published April 30, 2026

Abstract: Anastomotic leakage and stricture after colorectal surgery are severe complications in gastrointestinal surgery, with their incidence rates reaching as high as 5%-30% and 10%-20%, respectively. Traditional self-expanding metal stents (SEMS) have limited clinical applications due to such drawbacks as non-degradability and the requirement for secondary surgical removal. In recent years, biodegradable intestinal stents have become a research hotspot due to their temporary support and degradable properties. Among them, silk fibroin-based stents have stood out for their excellent biocompatibility and mechanical adaptability. This article systematically reviews the clinical indications, material classification, latest advances, clinical challenges, and prospects of degradable intestinal stents, and focuses on discussing the value of silk fibroin-based stents in preventing intestinal anastomotic leakage and stricture.

Keywords: Biodegradable, intestinal stent, silk fibroin, anastomotic leakage

Introduction

Studies have shown that colorectal cancer is the third most common cancer worldwide, and surgical treatment remains the most effective therapeutic approach for this disease [1]. However, anastomotic leakage and stricture are common postoperative complications. Although traditional metal stents can temporarily alleviate obstruction or leakage, their non-degradable nature gives rise to the risk of secondary surgery, long-term foreign body reactions, and stent migration, which severely limit their clinical application [2]. With the rapid development of biomaterials science and tissue engineering technology, biodegradable intestinal stents have gradually become the research focus for replacing traditional therapeutic methods, relying on their characteristics of "temporary support - sealing leaks - synchronous degradation". Not only can biodegradable intestinal stents provide mechanical support for anastomosis and isolate intestinal contents to promote tissue regeneration, but they can also avoid foreign body residue through degradation, thereby reducing the risk of infection and inflammation.

In recent years, the application of various biodegradable materials (such as magnesium-based alloys, synthetic polymers, and natural polymers) in stent design has been continuously expanded. **Table 1** summarizes the research content related to biodegradable intestinal stents in recent years. Among them, silk fibroin-based stents have stood out due to their unique biocompatibility, regulable degradation kinetics, and multifunctional modification potential. Silk fibroin can match the intestinal healing cycle by regulating its degradation time and achieve synergistic anti-inflammatory, antibacterial, and anti-tumor effects through a drug-loading system, thereby providing a novel strategy for the prevention and treatment of post-colorectal surgery complications. However, numerous challenges still exist in the translation from laboratory research to clinical practice, including the precise matching of degradation rate with tissue repair, the dynamic adaptation of stent mechanical properties, and the requirements for personalized design.

https://doi.org/10.62347/DFWD4447

Table 1. Examples of a biodegradable intestinal stent

Author	Materials	Technology	Structure	Feature
Wang et al. [87]	PLGA	Electrospraying	Doxycycline drug-loaded covered stents	Biocompatibility Degradability Control of doxycycline loading and distribution, helps inhibit local MMPs, reduce collagen degradation, and maintain the strength of the anastomosis.
Sun et al. [16]	Mg-Zn-Y-Nd alloy	Extrusion molding Dip coating process	Mg-Zn-Y-Nd alloy was used as the base material, and the surface was coated with MAO layer and PLLA layer in turn, and the outermost layer was loaded with paclitaxel.	Biocompatibility Degradability The corrosion resistance is stronger, and the degradation rate is relatively slow. It significantly inhibited the proliferation of intestinal cells.
Wang et al. [9]	1,3-propanediol, 1,2-propanediol, and sebacic acid	Injection molding Extrusion molding	The shape of the stent was tubular, and the ends were fixed with the assistance of traction sutures and polyglycolic acid sutures.	Biocompatibility Degradability
Pérez et al. [7]	PDO	Weft-knitting	The stent was a tubular stent with a diameter of 31/25/31 mm and a length of 6-8 cm. It is divided into two types: polyethylene inner coating (coated) and uncoated	Biocompatibility Degradability Fixation was performed with cyanoacrylate, hemostatic clips, or a combination of the two.
Fathi et al. [23]	PCL/PDO	3D Printing	The scaffolds were thin-walled cylinders with a minimum external diameter of 30 mm and different thicknesses (1 mm, 0.75 mm, 0.25 mm, etc.), four equally spaced 1 mm diameter holes were designed at both ends.	Biocompatibility Degradability Based on the CT image data of the patient, the 3D model was generated by CAD technology, and then the scaffold was prepared by 3D printing for personalized customization.
Zhang et al. [88]	PTMC/PHA	Electrospinning	The scaffold has a bilayer structure, and the inner layer is PTMC/PHA nanofiber layer. The outer layer is PVA co-spun with OHA and added with gentamicin sulfate.	Biocompatibility Degradability Antibacterial Properties Chemical stability
Ren et al. [24]	PTMC	Electrospinning	The scaffold was tubular and electrospun to form a three-dimensional pore structure.	Biocompatibility Degradability The antibacterial properties of the scaffold were increased by the addition of TCS.
Xie et al. [48]	PDO/SF	Weft-knitting	The scaffold is tubular with a nanofibrous membrane loaded with CUR and 5-FU.	Biocompatibility Degradability It can inhibit the growth of intestinal tumor cells and exert synergistic anti-tumor effects. Sustained drug release characteristics
Son et al. [22]	PLGA/Gelatin	Electrospinning	The scaffold was tubular and electrospun to form a three-dimensional pore structure.	Biocompatibility Adjustable degradability Hydrophilic.

Huson et al. [30]	PVA/SIS	Unknown	The overall length of the stent was 6 cm, the diameter was 3.5 cm, and the wall thickness was 1.5 mm. The PVA was used as the core, and the outer eight layers of SIS were wrapped around the PVA.	Biocompatibility Degradability Effective prevention of anastomotic leakage
Feng et al. [49]	SF/PCL	Electrospinning	The scaffold was a tubular structure supported by an internal PDO braided scaffold and covered with PCF-loaded SF/PCL composite fibrous membrane.	Biocompatibility Degradability Drug sustained release characteristics Hydrophilic
Chen et al. [52]	SF/Chitosan	Electrospinning	The scaffold has a double-layer structure, and the inner layer is woven degummed silk. The outer layer was freeze-dried from SF/CS short fibers loaded with CUR/5-ASA to form a porous structure.	Biocompatibility Degradability High water absorption and porosity Good mechanical properties Anti-inflammatory
Chantarojanasiri et al. [57]	SF/PDO	Weft-knitting Dip coating process	The stent has a double-layer structure, with the inner layer being a manually woven PDO tubular structure, and the outer layer consisting of a coating film formed by surface treatment with a 0.5% concentration of silk fibroin.	Biocompatibility Degradability Moderate hydrophilicity Stable mechanical properties

Note: PLLA: poly-L-lactic acid; PDO: polydioxanone; SF: silk fibroin; PLA: polylactic acid; PCL: polycaprolactone; PLGA: poly(lactic-co-glycolic acid); MMPs: matrix metalloproteinases; MAO: micro arc oxidation; PTMC: Poly(trimethylene carbonate); TCS: triclosan; CUR: curcumin; 5-FU: 5-fluorouracil; SIS: small bowel submucosa; PVA: polyvinyl alcohol; PCF: Psoralea corylifolia formula; CS: Chitosan; 5-ASA: 5-aminosalicylic acid; PHA: polyhydroxyalkanoate.

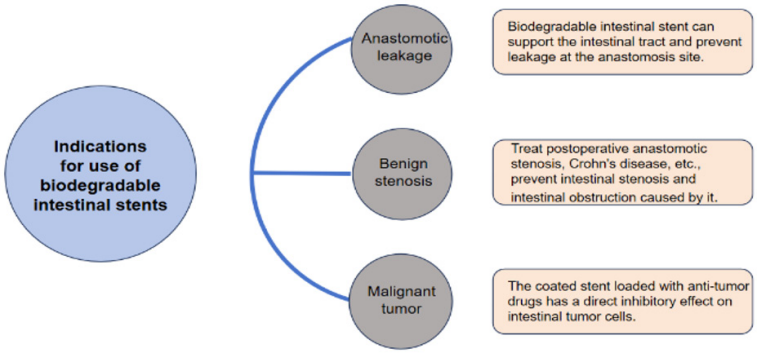

Figure 1. Biodegradable intestinal scaffolds are suitable for benign and malignant gastrointestinal diseases.

Based on the current research progress, this research systematically analyzes the clinical value of biodegradable intestinal stents in the management of anastomotic leakage, benign strictures and malignant tumors, further explores the performance differences and optimization strategies of different biomaterials, and focuses on the breakthrough advances of silk fibroin-based stents in terms of mechanical adaptability, drug-loading functionality and biosafety. Meanwhile, this review proposes an in-depth analysis of the molecular biological behaviors such as the degradation mechanism of silk fibroin, combined with cutting-edge technologies including 4D printing and artificial intelligence, so as to provide theoretical support and technical enlightenment for promoting the advancement of biodegradable intestinal stents towards practical clinical application.

Clinical Indications

Biodegradable intestinal stents come in a variety of types, with distinct functions and clinical applications. For instance, they can be used to prevent anastomotic leakage during surgery, to treat benign intestinal strictures under endoscopy, or for the palliative management of malignant tumors. **Figure 1** demonstrates the applications of biodegradable stents in the gastrointestinal field.

Anastomotic leak

Anastomotic leakage after colorectal surgery is a crucial factor leading to increased morbidity and mortality in patients, and traditional treatment requires ostomy, which increases patient suffering and medical costs. In a recent nationwide study, the incidence of anastomotic leakage was as high as 30%; more importantly, the leakage-related mortality rate after gastrointestinal resection and reconstruction has reached 60% [3]. Anastomotic leakage can lead to a series of severe consequences, such as peritonitis, abdominal abscess, intestinal necrosis, acute mesenteric ischemia, and intestinal obstruction; in severe cases, it can even cause multiple organ failure, acute lymphoblastic leukemia, and septic shock [4, 5]. In recent years, the introduction of biodegradable intestinal stents has provided a novel approach for preventing anastomotic leakage. By providing mechanical support to the anastomosis and isolating intestinal contents, they can effectively promote tissue healing. Previous studies have shown that the application of endoluminal biodegradable stents has gradually expanded from esophageal and gastric surgeries to the colorectal field, demonstrating remarkable clinical potential. For example, the Tsereteli team found in a pig model that after implantation of a 21 mm Polyflex self-expandable covered polyester stent, no anastomotic leakage or infection occurred in the experimental group within 2 weeks postoperatively; in contrast, 63% of the control group developed intra-abdominal infections (abscesses or fistulas), and 86% were complicated with severe intestinal adhesions. This confirms the key role of stents in reducing the risk of complications [6]. In further clinical explorations, Pérez et al. applied the SX-ELLA polydioxanone (PDO) stent in 10 patients with colorectal anastomotic leakage who had failed conservative treatment; the stents successfully closed the fistulas in 9 cases (with 1 case of recurrence), and no stent-related severe adverse reactions were observed, which highlights the advantages of PDO materials in terms of biocompatibility and functional reliability [7]. Meanwhile, another research team optimized the structural design of PDO stents. The researchers used PDO monofilaments as the stent substrate and prepared tubular stents via weft knitting technology. This stent can be disassembled by pulling the monofilaments without surgical removal, and can maintain more than 60% of its

original radial force within 12 weeks, which significantly improves the radial support force of the stent [8]. In addition, a novel biodegradable stent developed by Wang et al., synthesized from 1,3-propanediol, 1,2-propanediol, and sebacic acid, exhibited excellent safety in a porcine rectal anastomosis model. Compared with traditional manual suturing, it not only shortened the surgical time but also eliminated intestinal obstruction and anastomotic leakage, laying a solid foundation for clinical translation [9]. Despite the positive progress achieved in existing studies, large-sample clinical trials are still needed in the future to verify the long-term efficacy. Targeting challenges such as stent migration and matching between degradation rate and tissue repair process, in-depth research on material modification and structural optimization needs to be further carried out.

Benign intestinal stricture

For benign intestinal strictures such as postoperative anastomotic strictures and Crohn's disease-related strictures, traditional treatment modalities, including endoscopic dilation and metal stents, have difficulty avoiding high recurrence rates and harbor the risk of reoperation, thus exhibiting significant limitations in clinical application. Degradable stents avoid foreign body retention through in vivo degradation and have gradually emerged as a potential alternative. Jain *et al.* reviewed six international studies and explored the current application status of biodegradable stents in the treatment of benign intestinal strictures. The results indicated that these stents have a relatively high technical success rate, whereas there is considerable variability in the stent migration rate across different studies [10]. Currently, biodegradable intestinal stents are still in the preclinical stage of material development and animal validation. In terms of the treatment of benign intestinal strictures, there are only a few studies which lack high-level clinical evidence, and there is no standardized therapeutic protocol in clinical practice guidelines. In addition, stent migration is an important factor affecting clinical efficacy. Most intestinal stents reported so far have been modified from esophageal stents, and it is necessary to optimize their structural design and fixation methods to adapt to the intestinal physiological environment. Future studies should clarify the factors associated with stent migration and explore their role in preventing postoperative anastomotic strictures. In summary, biodegradable intestinal stents remain a reasonable therapeutic option for patients with intestinal strictures who have surgical contraindications or for those who refuse surgery.

Malignant tumors

Based on their functional characteristics, biodegradable intestinal stents are mainly categorized into two major types: bare stents and drug-eluting covered stents. Bare stents are mostly fabricated into a reticular structure by weaving metallic or polymeric materials. Although such stents can effectively dilate the strictures caused by tumor masses via radial supporting force, their uncovered design predisposes them to the invasive ingrowth of tumor tissues into the stent meshes, which in turn leads to secondary stricture and obstruction. This limitation has restricted the clinical development and application of bare stents. In contrast, drug-eluting covered stents can achieve physical isolation of intestinal contents through their outer drug coatings, thereby preventing anastomotic leakage. Importantly, these stents can be loaded with anti-tumor, antiproliferative and anti-inflammatory drugs, which serves to inhibit the local proliferation of tumor cells as well as reduce inflammatory responses and intestinal fibrosis.

Types of biodegradable materials

Currently, global research into biodegradable stents has stepped into an entirely new phase. The primary classifications of biodegradable stents consist of biodegradable alloy stents, polymer stents and natural polymer stents. **Figure 2** lists all the types of degradable scaffold materials.

Degradable alloys

In the past, metals have been the primary choice for intestinal stents, such as nitinol shape-memory alloy self-expandable stents and stainless-steel stents. However, both fall into the category of non-degradable metallic stents: their high rigidity predisposes them to intestinal perforation, and they may also interfere with magnetic resonance imaging (MRI).

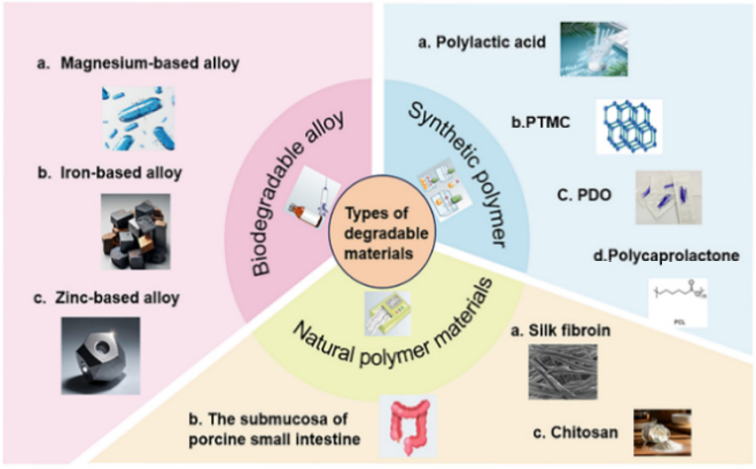

Figure 2. Biodegradable intestinal scaffolds are mainly divided into three categories: alloys, synthetic polymers, and natural polymers.

Nowadays, biodegradable alloys have gradually emerged as a promising new direction in the field of metallic intestinal stents, by virtue of their excellent mechanical properties, controllable degradation performance and favorable biocompatibility. Current research has demonstrated that biodegradable alloys primarily fall into three main categories: magnesium-based, zinc-based and iron-based alloys. These alloys possess an average elastic modulus of approximately 35-45 GPa, a value close to that of human bone (10-30 GPa), and a tensile strength ranging from 180 to 300 MPa, rendering their mechanical properties significantly superior to those of polymeric stents (e.g., polylactic acid (PLA) with a tensile strength of 50-80 MPa). In vivo, these alloys undergo chemical corrosion, and their degradation products are essential trace elements for the human body that exert no adverse effects on bodily tissues [11-13].

Early studies have indicated that the addition of 1~3 wt.% zinc (Zn) and 1 wt.% manganese (Mn) to magnesium alloys can significantly refine the alloy grains (with the grain size reduced from 200 μm to 50 μm). After extrusion treatment, the yield strength of the alloy is enhanced to 246 MPa with an elongation of 10%. In terms of the degradation mechanism, zinc addition facilitates the formation of a compact passive film, which can effectively inhibit the infiltration of Cl^- and improve the corrosion resistance of the material surface. However, the local pH value rises significantly following the degradation of this alloy, which disrupts the structural integrity of erythrocyte membranes and results in a high hemolysis rate of 65.75%. This finding suggests that surface modification techniques are required to improve its hemocompatibility [14]. Based on the magnesium-zinc-yttrium-neodymium (Mg-Zn-Y-Nd) alloy, Wang et al. fabricated a bilayer biodegradable intestinal stent via micro-arc oxidation (MAO) and poly-L-lactide (PLLA) coating, with the high-efficiency antiproliferative drug paclitaxel loaded onto the scaffold. In animal experiments, it was found that compared with the uncoated group, this coating reduced the content of phosphorus (P) and calcium (Ca) in corrosion products by 66% and 91%, respectively. This result confirmed that the coating technology improved the intestinal corrosion resistance of the magnesium alloy. Furthermore, immunohistochemical results demonstrated a significant downregulation of Bcl-2 expression in the intestinal tissues of the composite stent group, which could effectively inhibit the excessive proliferation of intestinal epithelial cells [15]. Based on the above studies, the research team conducted an in-depth investigation into the degradation process and antiproliferative molecular mechanism of the identical stent. Sun et al. established an in vitro simulated intestinal corrosion system using human feces. Scanning electron microscopy (SEM) observations revealed that only a small amount of intestinal contents adhered to the stent surface at 14 days, with no obvious corrosive cracks detected. In vivo experiments, the stent underwent complete degradation at 12 days post-implantation due to the action of the complex active organic microenvironment in the body. Importantly, the corrosion degree at the stent joints was significantly higher than that at the non-joint regions. This indicates that stress concentration is a critical factor accelerating the corrosion of magnesium alloy stents. At the molecular mechanism level, the implantation of the bilayer composite scaffold resulted in a significant decrease in proliferating cell nuclear antigen (PCNA) expression and a marked

increase in Caspase-3 expression in intestinal tissues. Meanwhile, both α-SMA expression and the quantity of collagen fibers were significantly lower in the bilayer composite stent group than in the bare stent group. Although the composite coating significantly delayed the degradation time, the stent collapsed completely within 12 days in vivo and lost its mechanical supporting function. This degradation rate failed to match the natural healing cycle of intestinal tissues, which typically requires 2-4 weeks [16]. Therefore, an excessively fast degradation rate remains the core challenge faced by Mg-Zn-Y-Nd alloy intestinal stents. In contrast to magnesium alloys, iron-based alloys exhibit a markedly slower degradation rate. For instance, Lin et al. developed a drug-loaded coated stent with a zinc barrier layer, which achieved precise regulation of the degradation rate of iron-based stents [17].

In summary, most biodegradable alloy materials exhibit excellent biocompatibility and mechanical properties, yet their degradation time fails to match the healing cycle of the intestinal tract. Therefore, biodegradable alloys can meet the practical clinical requirements for intestinal stents through strategies such as the continuous improvement of alloy elemental compositions and the fabrication of biodegradable polymer coatings.

Synthetic polymers

Synthetic polymeric scaffolds have overcome the bottleneck of non-degradability associated with traditional metal scaffolds, while simultaneously possessing excellent biocompatibility and sufficient mechanical support properties. Currently, commonly used synthetic polymeric materials include polylactic acid (PLA), poly (lactic-co-glycolic acid) (PLGA), poly-L-lactic acid (PLLA), polydioxanone (PDO), polycaprolactone (PCL), and polytrimethylene carbonate (PTMC), each with distinct advantages and limitations. For example, the degradation product of PLA is lactic acid, which offers high metabolic safety. However, its degradation rate is relatively slow (typically 6-12 months), and it exhibits high brittleness, making it difficult to meet the mechanical requirements of the dynamic intestinal environment. By adjusting the ratio of lactic acid to glycolic acid (e.g., 75:25 or 50:50), PLGA allows for the modulation of its degradation cycle and possesses excellent mechanical strength (e.g., the tensile strength of PLGA/gelatin 5/5 composite can reach 1.60 ± 0.06 MPa). Nevertheless, its acidic degradation products tend to induce local inflammation (with pH dropping below 5.0), which limits its long-term application. PLLA is suitable for long-term support due to its high crystallinity and prolonged degradation cycle, yet its hydrophobicity and acidic by-products may still lead to tissue necrosis. In contrast, PDO has shown potential for intestinal scaffold applications owing to its superior flexibility and moderate degradation cycle (with approximately 20% mass loss within 20 days). Nonetheless, its low mechanical strength (radial force only 0.4-0.6 N/cm) makes it difficult to withstand the peristaltic pressure of the intestine [18-21].

To overcome the drawbacks of single-component materials, the composite material strategy has been widely adopted. For example, Son *et al*. fabricated PLGA/gelatin fibrous tubes via electrospinning technology. In vitro experiments demonstrated that these fibrous tubes exhibited a low swelling ratio and a controllable degradation rate, with 71% degradation observed within 360 hours. Furthermore, by adjusting the gelatin proportion, the hydrophilicity and cell adhesion capacity were significantly enhanced, as evidenced by the increased proliferation rate of IEC-18 cells with the rise in gelatin content. In a rat model, the scaffold degraded completely 14 days after implantation. No inflammatory response was observed in the surrounding intestinal tissues, and the need for secondary surgery was eliminated, which verified the advantages of the composite material in terms of short-term support and biocompatibility [22]. On the other hand, the PCL-PDO composite material developed by Fathi *et al*. achieved the precision fabrication of personalized scaffolds via 3D printing technology. With an elastic modulus of 211 MPa, the scaffold can withstand an intraintestinal pressure of 1,765 Pa and exhibits excellent in vivo biocompatibility in a porcine model. However, the scaffold exhibits a slow degradation rate, with only 20% degraded within 20 days, which may lead to long-term foreign body reactions. Additionally, scaffold migration or intestinal obstruction occurred in some experiments. The above results suggest that further optimization of the design is required, such as adding suture holes

or adjusting the size, to improve clinical applicability [23]. In recent years, tubular stents based on PTMC have broken through the performance limitations of traditional polymer-based stents. Owing to the unique flexibility of PTMC, such stents can be sutured inside the intestinal tract, which effectively addresses the issue of stent migration. For instance, Ren et al. fabricated a PTMC-based scaffold via electrospinning and loaded it with the antibacterial agent triclosan (TCS), which promoted regeneration of the intestinal epithelium. In mechanical characterization, the stents exhibited an elastic modulus of 20.11 MPa and a tensile strength of 16.08 MPa. In vitro degradation studies revealed a mass loss of 40% and a length reduction of 50% over 28 days, with no acidic byproducts generated during the process. In a rat cecal model, the incidence of intestinal fistula was significantly reduced from 30% in the control group to less than 5%, and the occurrence of intestinal obstruction was effectively decreased. Furthermore, by sustaining the release of the antibacterial agent triclosan, the scaffold further inhibited bacterial infection and exhibited excellent biocompatibility. Specifically, the viability rate of L929 cells was over 90%, and the hemolysis rate was below 0.1%, demonstrating favorable functionality and biosafety [24]. However, the long-term mechanical stability of PTMC scaffolds still needs to be verified. Although their degradation rate is superior to that of PCL-PDO materials, it is still necessary to balance the support period and the risk of foreign body reactions. Eisenach *et al*. further evaluated the tissue inflammatory response of PCL/PTMC blended materials as grafts. The results indicated that this biodegradable polymer exhibits good biological inertness. Meanwhile, the level of high-sensitivity C-reactive protein is significantly correlated with the dynamic changes of local inflammation, which can serve as an effective indicator for evaluating post-implantation tissue reactions. This finding provides a new reference basis for the material screening and biocompatibility evaluation of biodegradable scaffolds [25].

Synthetic polymer materials have demonstrated significant advantages in the field of scaffold materials, providing an effective approach to address the limitations of metal scaffolds. They play a crucial role in tissue engineering applications, with numerous research achievements obtained, especially in intestinal scaffolds. However, these polymer scaffolds still have some existing issues at present; for instance, some scaffolds may cause complications such as intestinal obstruction and migration, which require further optimization.

Natural polymer materials

Natural polymer materials refer to materials fabricated based on macromolecular compounds existing in nature. They are widely sourced, possess numerous unique advantages, and have been extensively applied in various fields. Common natural polymer materials include polysaccharides (e.g., cellulose, starch), proteins (e.g., silk fibroin, collagen), and extracellular matrices such as small intestinal submucosa (SIS).

Submucosa of the Small Intestine (SIS): SIS has been used in human applications for more than 20 years and has established a favorable safety record in diverse fields ranging from fistula repair to dural substitution. As an extracellular matrix, SIS has been proven to contain a range of bioactive components, including basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), and transforming growth factor-β (TGF-β). Moreover, compared with the pro-inflammatory phenotype induced by some synthetic materials, SIS can induce the polarization of macrophages toward a pro-regenerative phenotype [26, 27]. At present, SIS has been successfully applied in clinical treatment. For patients with cervical esophageal perforation, porcine small intestinal submucosa matrix mesh was used for repair, and postoperative outcomes showed that the patients recovered well without complications such as inflammation or foreign body reactions [28]. Based on the excellent biological properties of SIS including favorable biocompatibility, biodegradability and low immunogenic rejection, the Hoeppner team verified the feasibility of SIS as an anastomotic sealant by establishing a porcine model of anastomotic leakage [29]. SIS has gradually expanded its application from biological patches to biodegradable scaffolds. However, intestinal scaffolds solely based on SIS are relatively soft and do not provide sufficient radial support to resist intestinal pressure. To address this issue, researchers

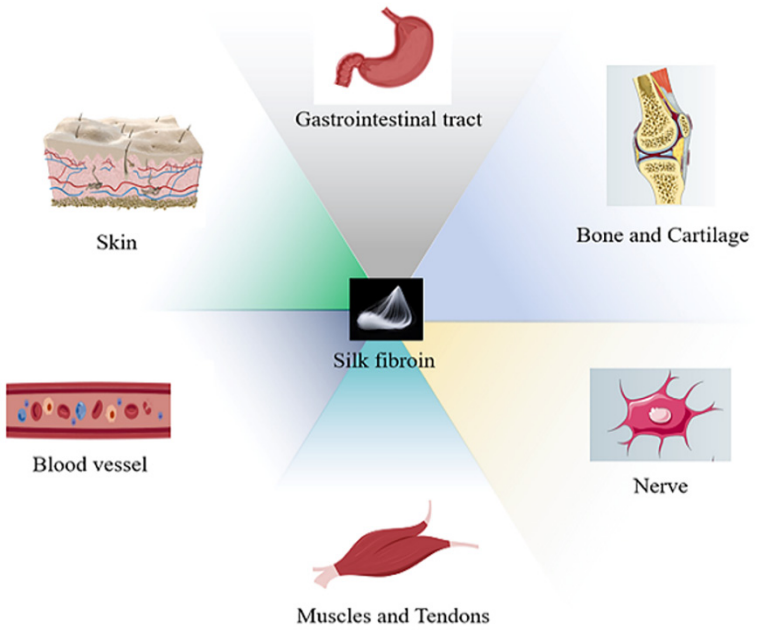

Figure 3. The applications of silk fibroin in the medical field.

have compounded SIS with other polymer materials to develop novel intestinal scaffolds. This type of composite scaffold has shown potential in preventing anastomotic leakage and stenosis, but it still needs to possess adequate radial and circumferential mechanical properties to cope with intra-abdominal and intestinal pressures, and its degradation rate must match the healing cycle of intestinal tissue. For instance, Huson *et al*. developed a novel scaffold using polyvinyl alcohol (PVA) and an SIS framework to prevent colorectal anastomotic leakage in pigs. This scaffold features a core of fully biodegradable, low-absorbable, and non-toxic PVA - a material already FDA-approved for multiple medical applications - with an outer layer encapsulated by eight layers of SIS. Researchers selected 10 healthy 6-month-old Yucatan female pigs, which underwent colectomy for scaffold implantation, during which a 2 cm intestinal wall defect was created. The experimental results showed that all 10 pigs survived until the end of the study, with no clinical symptoms such as obstruction, infection, leakage, fistula, wound complications, or hemorrhage. Postoperative intestinal function recovered normally, and the average weekly weight gain was 0.81 kg. Furthermore, histological examination revealed an intact layered structure of the intestinal wall and the formation of scar tissue at the anastomotic site. Regeneration of the intestinal wall layers was observed at the defect area both 2 and 4 weeks postoperation. When applied in porcine colon anastomosis with intestinal wall defects, the PVA-SIS scaffold did not induce anastomosis-related complications, which initially demonstrates the safety of this scaffold [30]. This study did have certain limitations, such as not setting up a control group and only using female pigs in the experiment. Future studies are needed that establish a control group to further verify the scaffold's efficacy and systematically evaluate the adaptability of scaffolds with different diameters, lengths, and morphologies in the intestinal environment. This will further promote the clinical application, which is expected to reduce the incidence of anastomotic leakage in colorectal surgery and decrease the need for temporary stomas.

Silk fibroin: Silk fibroin has unique advantages over degradable alloys and synthetic polymeric materials, including its excellent mechanical properties, superior biocompatibility, low immunogenicity, adjustable biodegradability, and versatile processing capabilities. It is widely used in tissue engineering and regenerative medicine. **Figure 3** lists the main applications of silk fibroin. Silk fibroin is primarily extracted from the silk of the domestic silkworm, with a molecular weight of 50-400 kDa. Its β-sheet structure provides high mechanical strength, with tensile strength greater than 100 MPa, and a degradation time of 2-12 weeks, which matches the healing cycle of gastrointestinal anastomoses [31-33]. Silk fibroin possesses mechanical properties, surface modifications, and cell affinity that no other synthetic fiber can replace. Therefore, silk fibroin can serve as an ideal material for intestinal scaffolds.

In the application of biodegradable intestinal stents, silk fibroin promotes cell adhesion and migration, thereby accelerating the healing of intestinal anastomoses. Basic research has

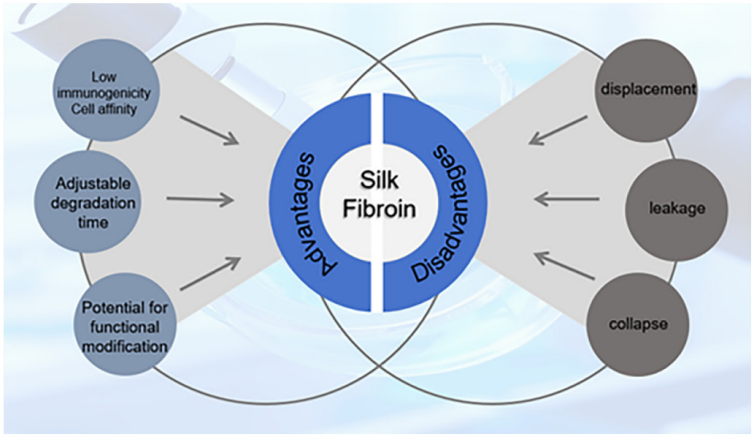

Figure 4. The advantages and disadvantages of silk fibroin protein as a biodegradable scaffold.

demonstrated that a porous foam composite with a dense membrane constructed from silk fibroin significantly enhances the attachment efficiency of intestinal epithelial cells and provides structural support for tissue repair [34]. To address the challenge of mechanical performance in wet environments, Chen et al. incorporated nano-silica and the silane coupling agent KH560 into silk fibroin composites, which enhanced the wet-state tensile strength by 40% and effectively mitigated the softening issue commonly encountered with conventional scaffolds in bodily fluid conditions [35]. In further functionalization studies, Rodriguez-Nogales *et al*. crosslinked RGD peptides onto the surface of silk fibroin nanoparticles via glutaraldehyde, achieving inflammation-targeted delivery. This approach improved the mucosal repair rate by 65% and reduced the risk of stenosis in colitis models, highlighting the anti-inflammatory and tissue repair potential of silk fibroin [36]. In terms of preventing and treating postoperative complications of colorectal surgery, the drug-loading capacity of silk fibroin has been extensively explored. For instance, Fuster *et al*. utilized silk fibroin nanoparticles to load naringenin, a hydrophobic drug, which increased its bioavailability by 3.2-fold and enhanced its anticancer activity [37]. In addition, Zhang et al. addressed the limitations in the mechanical properties of silk fibroin and fabricated a sustained drug release system with pH-responsive release characteristics. The researchers incorporated curcumin-loaded shellac nanoparticles into a double network hydrogel composed of gelatin methacrylate (GelMA) and silk fibroin methacrylate (SilMA). This drug delivery system achieved an 82% increase in the local drug concentration via colon-targeted curcumin release. Meanwhile, the SilMA component effectively enhanced the mechanical properties of the hydrogel, with an elastic modulus exceeding 15 kPa [38]. However, current research still needs to overcome three major clinical adaptation bottlenecks: blending silk fibroin with synthetic materials (e.g., PCL, PDO) to regulate flexibility for fitting the intestinal wall, precisely controlling the degree of crosslinking to match the degradation cycle with the epithelial regeneration rate, and designing suture-compatible microporous structures to prevent scaffold migration.

Although biodegradable intestinal scaffolds hold broad clinical prospects, their practical application still relies on appropriate material selection. Among various biomaterials, silk fibroin-based scaffolds exhibit significant advantages due to their unique comprehensive properties. The following section will focus on elaborating the advantages and challenges of the stents in clinical applications, which are briefly summarized in **Figure 4**.

Clinical advantages and challenges of silk fibroin-based scaffolds

Advantages

Low immunogenicity and cell affinity: The human immune system serves as a barrier against exogenous substances. When biological materials are implanted, proteins from tissue fluids adhere to the material's surface, thereby triggering immune system activation and causing various inflammatory responses. Over time, under the influence of multiple cytokines (such as tumor necrosis factor-alpha (TNF-α), interleukin-4, interleukin-6, interleukin-8, interleukin-13, and monocyte chemoattractant protein-1), acute inflammation dominated by neutrophils gradually transitions to chronic inflammation dominated by macrophages [39]. Eventually, fibrotic tissue replaces the

original tissue. Therefore, for intestinal scaffolds, implant materials need to have low immunogenicity to prevent the occurrence of fibrotic stenosis in the intestine. Studies have shown that silk fibroin plays a crucial role in influencing cell activity after implantation and helps achieve effective tissue regeneration [40].

As a natural polymer material, silk fibroin exhibits excellent biocompatibility and low immunogenicity, supporting the adhesion and proliferation of various cells, such as intestinal epithelial cells and fibroblasts. It has been widely applied in tissues including bone, cartilage, blood vessels, nerves, eyes, skin, and intestines. Silk fibroin possesses a relatively stable secondary structure, such as β-sheet conformation, and undergoes slow degradation in vivo. Its degradation products are usually small-molecule peptides or amino acids, which can be metabolized and utilized by the body, thereby reducing the immune response between the graft and the host [41, 42]. For instance, the immune inertness of silk fibroin has been demonstrated in a study by Panilaitis *et al*.: the extracted silk fibroin fibers can effectively inhibit the activation of mouse macrophages in both short-term and long-term cultures [43]. In a biocompatibility comparison between silk fibroin and PGA scaffolds, Seo et al. observed that while both macrophages and multinucleated giant cells were present around PGA scaffolds, only macrophage infiltration was detected surrounding silk fibroin scaffolds. These two studies highlight that the in vivo immune response induced by silk fibroin is milder and more controllable [44]. The biocompatibility of implanted materials is of critical importance, as their interaction with the host may elicit inflammatory reactions. Silk fibroin exhibits immunoinert properties, thereby mitigating the host immune response to a certain extent. This low immunogenicity, combined with its excellent cytocompatibility, demonstrates the considerable potential of silk fibroin in the field of intestinal stents.

Tunable degradability: Silk fibroin is a slowly degradable material, with its structure containing numerous anti-parallel β-sheets formed by repeating GAGAGX amino acid sequences in the crystalline regions of the heavy chains. These structures impart high stability, crystallinity, and hydrophobicity to silk fibroin, which in turn hinders its degradation [45]. Therefore, by altering the structure, morphology, crosslinking degree, and sterilization methods of silk fibroin, its degradation time can be controlled. In a study by Lv et al., a hybrid scaffold composed of silk fibroin and PCL was coated with basement membrane proteins and implanted into the esophagus. In vivo experimental results showed that mucosal regeneration was observed at the scaffold site 45 days post-implantation, and the scaffold partially degraded into fragments after 80 days. The degradation rate of this scaffold was compatible with the 6-8 weeks healing cycle of intestinal anastomoses [46]. Thus, although silk fibroin degrades slowly, its degradation profile can be modulated through blending and cross-linking strategies. Importantly, its degradation products are fully metabolized by the body, exhibiting no toxicity or sensitization - a notable biosafety advantage over many synthetic polymers.

Potential for functional modification: Silk fibroin can serve as a drug delivery carrier to achieve the integration of protection and therapy, thus advancing the clinical development of gastrointestinal scaffolds. Hudita et al. developed a silk fibroin-based nano-drug delivery system loaded with 5-fluorouracil (5-FU). In vitro experiments and mouse models demonstrated that this nanosystem could effectively induce apoptosis of HT-29 cells by activating Caspase-3/7, triggering DNA damage, and elevating reactive oxygen species (ROS) levels, thereby demonstrating significant antitumor activity in vitro. This system also efficiently alleviated the toxic side effects induced by 5-FU, as evidenced by reduced serum transaminase levels, alleviated intestinal pathological damage, preserved the integrity of mucosal structures, increased goblet cell counts and mucin expression; thereby protecting the ultrastructure of the intestinal mucosa [47]. With the in-depth research on silk fibroin-based drug delivery systems, a series of breakthroughs have been achieved in the fields of synergistic therapy for colorectal cancer and functional design of their composite scaffolds. For instance, in terms of dual-drug combination strategies, Xie *et al*. aimed at addressing the issue of easy drug resistance associated with 5-FU monotherapy for colorectal cancer. For this purpose, they innovatively co-loaded curcumin and 5-FU into silk fibroin and polyethyl-

ene glycol (PEG) nanofibrous membranes at gradient ratios (0.15/0.25 to 0.45/0.75 wt%) and constructed a sustained-release system via electrospinning technology. Characterization results revealed that the drug-loaded membranes maintained the stable secondary structure of silk fibroin while achieving sustained drug release over 400 hours (tending to stabilize after an initial burst release within 72 hours). Moreover, the dual-drug system synergistically induced tumor cell apoptosis via the Stat3 and NF-κB signaling pathways. The researchers further coated the drug-loaded membranes onto the surface of PDO scaffolds, achieving a sustained increase in local drug concentration and reversal of drug resistance, while also providing mechanical support for the intestine, thus avoiding intestinal obstruction and other issues caused by tumor recurrence [48].

Building on the concept of dual-drug synergy, research has extended toward multifunctional composite scaffolds. For instance, Feng *et al*. loaded the Chinese herbal compound extract of *Psoralea corylifolia* (PCF) into silk fibroin/PCL fibrous membranes. The study revealed that PCF not only regulated the formation of β-sheet structures in silk fibroin but also endowed the drug release with a "fast-slow" biphasic pattern: 60%-70% of the drug was released within 50 hours, followed by complete release at 400 hours. Cell experiment results demonstrated that the inhibitory activity of this system against rectal cancer cells was significantly higher than that against normal cells, exhibiting promising selective anticancer potential [49]. To address the risk of postoperative infection, Rahman *et al*. developed zeolitic imidazole framework-8 (ZIF-8)-loaded silk fibroin/PCL nanofibrous scaffolds. At a ZIF-8 loading content of 1%, the scaffold exhibited excellent antibacterial activity (with an antibacterial rate >90%) while maintaining favorable cytocompatibility, providing a novel strategy for the repair of infected intestinal anastomoses. In another approach, Vaseghi et al. fabricated a propolis (Ps)-loaded silk fibroin-chitosan aerogel scaffold via a sol-gel method. The scaffold exhibited pH-responsive drug release properties: the drug release rate increased by 2.1-fold in an acidic environment, with an eradication rate exceeding 85% for both *Escherichia coli* and *Staphylococcus aureus*. These combined features allowed the scaffold to simultaneously suppress local infection and effectively promote fibroblast proliferation, thereby facilitating wound healing [50, 51]. In response to clinical demands for intestinal mechanical support, Chen et al. designed a silk fibroin/chitosan composite scaffold capable of co-loading curcumin and 5-aminosalicylic acid. The scaffold exhibited compressive strengths of 12.28 N in the dry state and 3.08 N in the wet state, with a deformation recovery rate exceeding 92%. This mechanical robustness ensures structural stability during intraoperative implantation, while its dual pharmacological effects of anti-inflammation and wound healing promotion offer the potential to shorten the postoperative healing cycle [52]. Current research is evolving from single-drug delivery toward multidimensional functional synergy encompassing "mechanical adaptation, antibacterial activity, anti-tumor efficacy, and tissue regeneration", marking a crucial step toward the clinical translation of silk fibroin-based scaffolds. In summary, silk fibroin can achieve antibacterial, anti-inflammatory, and wound healing-promoting effects, among others, through functional modification or blending with other polymers, thereby meeting diverse clinical needs in the gastrointestinal field.

Clinical challenges

Over the past decade, silk fibroin-based biomaterials and medical devices have been proven to possess high biocompatibility in clinical research. In the field of gastroenterology, silk fibroin also holds enormous potential due to its numerous advantages, yet its further clinical translation still faces several key challenges.

First, the degradation rate of an ideal intestinal stent should match the growth rate of tissue cells. However, silk fibroin contains many antiparallel β-sheets, and these structural characteristics endow silk fibroin with high stability, crystallinity, and hydrophobicity, thereby impeding its degradation. Its in vitro degradation time can be as long as one year, which far exceedes the intestinal tissue healing time [53, 54]. The degradation of silk fibroin occurs primarily through protease hydrolysis mediated by the foreign body reaction, and its degradation rate is significantly affected by its crystallinity and morphology, including factors such as surface area to volume ratio, porosity, and pore size

[33, 54-56]. These complexities render it challenging to precisely control the degradation rate of silk fibroin, thereby limiting its application in the complex intestinal microenvironment. However, the complete healing of intestinal tissue requires a specific time window: an excessively fast degradation rate of the stent may lead to premature loss of mechanical support, resulting in lumen collapse or anastomotic leakage; in contrast, an excessively slow degradation rate may impede cell infiltration and tissue remodeling, and even trigger chronic inflammation or fibrous encapsulation. Recent studies have demonstrated that silk fibroin coating can delay the degradation rate of PDO stents, prolong their morphology retention time and provide radial support force, thereby enabling them to meet the clinical requirement of 6-8 weeks of stent implantation. However, the data of this study were derived from in vitro experiments, which may lead to inconsistencies between the degradation characteristics evaluated in vitro and those observed in actual clinical applications, thereby further increasing the risks and uncertainties associated with its clinical translation [57]. Therefore, long-term clinical trials are required to verify the in vivo degradation kinetics of silk fibroin. Additionally, studies have confirmed that silk fibroin scaffolds can promote the adhesion and contractile differentiation of small intestinal smooth muscle cells, colonic smooth muscle cells, and esophageal smooth muscle cells. However, such scaffolds still exhibit distinct limitations during the functional reconstruction of intestinal tissue, including insufficient innervation of regenerated tissue, weak peristaltic function, and a high tendency to induce local immune-inflammatory responses [34, 41, 58]. Therefore, how to effectively integrate and deliver the biosignaling molecules required for specific cellular activities to actively guide complex intestinal tissue regeneration also remains a critical challenge. Third, owing to the inherent characteristic of constant intestinal peristalsis, intestinal stents are required to possess flexibility and elastic modulus matching those of native intestinal tissue. Under ideal conditions, the stent should be able to withstand cyclic mechanical stress without fatigue or fracture. Multiple studies have shown that silk fibroin allows precise regulation of its tensile strength, flexibility, and durability through approaches such as blending, nano-reinforcement, and process optimization; however, achieving perfect mechanical compatibility with the dynamic physiological microenvironment still requires further in-depth research [59-62]. Fourth, the extraction of silk fibroin requires a lengthy process flow and costly specialized equipment, which results in the persistently high production cost of silk fibroin [63-65]. Manual operations, varying climatic conditions, and different production regions can compromise the batch stability of silk fibroin, which renders the standardization of raw materials and their processing procedures difficult. Therefore, regulating these aforementioned factors to control the stability of silk fibroin remains a considerable challenge. Finally, silk fibroin materials have achieved ideal tissue regeneration effects in in vitro experiments or small animal models such as mice, but lack sufficient clinical evidence to support their application. To date, only a small number of medical devices (such as sutures and dressings) have entered clinical practice, and the clinical translation of intestinal stents may require a considerable amount of time [66, 67]. In conclusion, to promote the development of silk fibroin-based intestinal stents, a great deal of research still urgently needs to be carried out.

Future development directions

Based on the aforementioned research gaps, the future research directions in this field can focus on the following aspects: First, focusing on the intrinsic structure and degradation mechanism of silk fibroin. Studies have demonstrated that macrophages are the primary cell type involved in silk fibroin degradation, which promotes the synergistic degradation of silk fibroin-based biomaterials by secreting various hydrolytic proteases, lysozymes, and oxidants [41, 68, 69]. In addition, the degradation process of silk fibroin is correlated with the content of the insoluble silk II structure (β-sheet) and the water-soluble silk I structure (α-helix); the higher the content of the silk II structure, the longer the degradation time [45, 70-72]. Therefore, researchers can construct intestinal stents with degradation cycles matching intestinal healing periods through strategies such as structural and molecular regulation of silk fibroin, as well as blending and crosslinking with other biomaterials. Second, focusing on the characteristics of the reactive groups of

silk fibroin to construct silk fibroin-polymer hybrid systems [73]. For instance, advanced technologies such as biomimetic peptide genetic modification, single-cell sequencing, and chip-based gene analysis systems can be employed to optimize the composition and structure of polymers, thereby achieving precise regulation of silk fibroin from the molecular level to multi-scale hierarchical stents. Alternatively, silk fibroin can be compounded with bioactive components, including growth factors and stem cells, to enhance the tissue regeneration-inducing ability of the stents [74-80]. In addition, by thoroughly exploring how silk fibroin affects cell behavior, immune response, and tissue regeneration processes, we are expected to develop silk fibroin-based intestinal stents with higher bioactivity and customizability. Third, optimizing the structural design and preparation process of stents based on the physiological characteristics of the large animal intestine, systematically conducting long-term biosafety evaluations, assessments of the metabolic regularity of degradation products, and evaluations of clinical efficacy, to accelerate the clinical translation process of silk fibroin-based degradable intestinal stents. Finally, four-dimensional (4D) printing technology has emerged as a novel and highly regarded research direction. This technology can overcome some limitations of 3D printing, such as constructing structures with complex dynamic characteristics of natural tissues [81-85] and optimizing the functional response of interactions between cells and stents [82]. Integrated with artificial intelligence technologies, the stent can achieve real-time monitoring of anastomotic parameters via built-in microsensors, dynamically adjusting its porosity, degradation rate and mechanical support, and thus advance toward the development of intelligent stents [86]. At present, patents for 4D printed intestinal stents have been filed. The core lies in providing an intestinal stent applicable to complex intestinal environments with anti-displacement properties. The integrated forming of 4D printing and the use of shape memory polymers ensure the deformation and stability of the stents. The preparation method is not limited by complex structures, enabling personalized customization, and has the advantages of rapid prototyping, low cost, and high practicality [81].

Conclusion

In summary, degradable intestinal stents are a new type of surgical implant following metal expandable stents. They have demonstrated broad application potential in clinical practice, capable of effectively alleviating symptoms of intestinal diseases and improving patients' postoperative quality of life. This review elaborates on the clinical indications, material selection of degradable intestinal stents, as well as the research status and challenges of silk fibroin-based stents, and fully demonstrates the great potential of silk fibroin as a candidate material for intestinal stents. Current research has achieved phased progress in aspects such as fabrication techniques (e.g., electrospinning, 3D printing, freeze-drying), degradation rate regulation, functional modification of materials, and in vitro and in vivo experiments of silk fibroin-based tissue engineering scaffolds. This has initially verified the feasibility of their application in scenarios including benign intestinal stenosis, prevention of anastomotic leakage, and palliative treatment of tumors, thereby providing highly valuable research ideas and technical support for solving the problems of scaffold materials in the clinical treatment of intestinal diseases. In the future, by overcoming key technical challenges such as precise matching of degradation rates, multi-active synergistic regulation, and clinical translation, researchers are expected to provide new and efficient biomaterial solutions for intestinal injury repair and tissue regeneration, thereby promoting technological innovation and clinical application breakthroughs in the field of intestinal tissue engineering.

Acknowledgements

We would like to express our sincere gratitude to Director Zhaojun Zhang and Director Xinpu Yuan for their invaluable contributions to their theoretical framework guidance and manuscript preparation for this review.

Disclosure of conflict of interest

None.

Address correspondence to: Drs. Chaojun Zhang and Xinpu Yuan, Department of Colorectal Surgery, Chinese People's Liberation Army General Hospital, No. 28 Fuxing Road, Haidian District,

Beijing 100853, China. Tel: +86-18716368749; E-mail: zcjdlyxzx@163.com (CJZ); Tel: +86-185-01342340; E-mail: yuanxin.pu@163.com (XPY)

References

[1] Chamseddine S, Azmi A and Saif MW. An overview of KRAS-targeting therapies for colorectal cancer in phase I and II development. Expert Opin Investig Drugs 2025; 34: 1011-1021.

[2] Lu J, Hu X, Yuan T, Cao J, Zhao Y, Xiong C, Li K, Ye X, Xu T and Zhao J. 3D-Printed Poly (P-Dioxanone) stent for endovascular application: in vitro evaluations. Polymers (Basel) 2022; 14: 1755.

[3] Spinelli A, Anania G, Arezzo A, Berti S, Bianco F, Bianchi PP, De Giuli M, De Nardi P, de Paolis P, Foppa C, Guerrieri M, Marini P, Persiani R, Piazza D, Poggioli G, Pucciarelli S, D'Ugo D, Renzi A, Selvaggi F, Silecchia G and Montorsi M. Italian multi-society modified Delphi consensus on the definition and management of anastomotic leakage in colorectal surgery. Updates Surg 2020; 72: 781-792.

[4] Matsubara N, Miyata H, Gotoh M, Tomita N, Baba H, Kimura W, Nakagoe T, Simada M, Kitagawa Y, Sugihara K and Mori M. Mortality after common rectal surgery in Japan: a study on low anterior resection from a newly established nationwide large-scale clinical database. Dis Colon Rectum 2014; 57: 1075-1081.

[5] Thomas MS and Margolin DA. Management of colorectal anastomotic leak. Clin Colon Rectal Surg 2016; 29: 138-144.

[6] Tsereteli Z, Sporn E, Geiger TM, Cleveland D, Frazier S, Rawlings A, Bachman SL, Miedema BW and Thaler K. Placement of a covered polyester stent prevents complications from a colorectal anastomotic leak and supports healing: randomized controlled trial in a large animal model. Surgery 2008; 144: 786-792.

[7] Pérez Roldán F, González Carro P, Villafáñez García MC, Aoufi Rabih S, Legaz Huidobro ML, Sánchez-Manjavacas Múñoz N, Roncero García-Escribano O, Ynfante Ferrús M, Bernardos Martín E and Ruiz Carrillo F. Usefulness of biodegradable polydioxanone stents in the treatment of postsurgical colorectal strictures and fistulas. Endoscopy 2012; 44: 297-300.

[8] Li G, Li Y, Lan P, He X and Hu H. Polydioxanone weft-knitted intestinal stents: fabrication and mechanics optimization. Textile Research Journal 2013; 83: 2129-2141.

[9] Wang Y, Cai X, Cai H, Liang Y, Huang D and Liang X. Experimental study of colonic anastomosis with a degradable stent in a porcine model. Am J Surg 2010; 199: 833-839.

[10] Jain D, Mahmood E and Singhal S. Biodegradable stents: an evolution in management of benign intestinal strictures. J Clin Gastroenterol 2017; 51: 295-299.

[11] Wu J, Zhao D, Lee B, Roy A, Yao R, Chen S, Dong Z, Heineman WR and Kumta PN. Effect of lithium and aluminum on the mechanical properties, in vivo and in vitro degradation, and toxicity of multiphase ultrahigh ductility Mg-Li-Al-Zn quaternary alloys for vascular stent application. ACS Biomater Sci Eng 2020; 6: 1950-1964.

[12] Wang C, Fang H, Hang C, Sun Y, Peng Z, Wei W and Wang Y. Fabrication and characterization of silk fibroin coating on APTES pretreated Mg-Zn-Ca alloy. Mater Sci Eng C Mater Biol Appl 2020; 110: 110742.

[13] Staiger MP, Pietak AM, Huadmai J and Dias G. Magnesium and its alloys as orthopedic biomaterials: a review. Biomaterials 2006; 27: 1728-1734.

[14] Zhang E, Yin D, Xu L, Yang L and Yang K. Microstructure, mechanical and corrosion properties and biocompatibility of Mg-Zn-Mn alloys for biomedical application. Materials Science and Engineering: C 2009; 29: 987-993.

[15] Wang Z, Sun Z, Han B, Zheng Q, Liu S, Zhang B and Duan T. Biological behavior exploration of a paclitaxel-eluting poly-l-lactide-coated Mg-Zn-Y-Nd alloy intestinal stent in vivo. RSC Adv 2020; 10: 15079-15090.

[16] Sun Z, Wang Z, Guan S, Zhu S, Duan T, Zheng Q and Liu S. Degradation of Mg-Zn-Y-Nd alloy intestinal stent and its effect on the growth of intestinal endothelial tissue in rabbit model. Journal of Magnesium and Alloys 2022; 10: 2208-2219.

[17] Lin WJ, Zhang DY, Zhang G, Sun HT, Qi HP, Chen LP, Liu ZQ, Gao RL and Zheng W. Design and characterization of a novel biocorrodible iron-based drug-eluting coronary scaffold. Materials & Design 2016; 91: 72-79.

[18] Ye H, You T, Nawaz H and Xu F. A comprehensive review on polylactic acid/lignin composites - structure, synthesis, performance, compatibilization, and applications. Int J Biol Macromol 2024; 280: 135886.

[19] Nakka K, Nagarajan SD, Sundaravadivel B, Shankaravel S and Vimalson C. An overview of the design, development and applications of biodegradable stents. Drug Delivery Letters 2020; 10: 2-13.

[20] Rui J, Zhu S, Xu X, Wang Y, Liu Z, Cheng G, Long D, Cheng L and Dai F. High-performance silk/polylactic acid composite scaffold material with immunomodulation and osteogenesis function. Mater Today Bio 2024; 29: 101316.

[21] Srivastava A, Ahuja R, Bhati P, Singh S, Chauhan P, Vashisth P, Kumar A and Bhatnagar N. Fabrication and characterization of PLLA/Mg composite tube as the potential bioresorb-

able/biodegradable stent(BRS). Materialia 2020; 10.
[22] Son SR, Franco RA, Bae SH, Min YK and Lee BT. Electrospun PLGA/gelatin fibrous tubes for the application of biodegradable intestinal stent in rat model. J Biomed Mater Res B Appl Biomater 2013; 101: 1095-1105.
[23] Fathi P, Capron G, Tripathi I, Misra S, Ostadhossein F, Selmic L, Rowitz B and Pan D. Computed tomography-guided additive manufacturing of Personalized Absorbable Gastrointestinal Stents for intestinal fistulae and perforations. Biomaterials 2020; 228: 119542.
[24] Ren Y, Li X, Wu L, Pan L, Ji Z, Shi C and Zhang X. Poly(trimethylene carbonate) flexible intestinal anastomosis scaffolds to reduce the probability of intestinal fistula and obstruction. J Mater Chem B 2021; 9: 5340-5351.
[25] Eisenach IA, Lapii GA, Uzyumova AK, Lushnikova EL, Ovchinnikov VS, Solovieva AO and Naprimerov VA. Application of hs-CRP in assessment of tissue inflammation following implantation of biodegradable polymer in experiment. Int J Mol Sci 2024; 25: 11183.
[26] Sadtler K, Wolf MT, Ganguly S, Moad CA, Chung L, Majumdar S, Housseau F, Pardoll DM and Elisseeff JH. Divergent immune responses to synthetic and biological scaffolds. Biomaterials 2019; 192: 405-415.
[27] Liu Z, Rütten S, Buhl EM, Zhang M, Liu J, Rojas-González DM and Mela P. Development of a silk fibroin-small intestinal submucosa small-diameter vascular graft with sequential VEGF and TGF-β1 inhibitor delivery for in situ tissue engineering. Macromol Biosci 2023; 23: e2300184.
[28] Clough A, Ball J, Smith GS and Leibman S. Porcine small intestine submucosa matrix (Surgisis) for esophageal perforation. Ann Thorac Surg 2011; 91: e15-16.
[29] Hoeppner J, Crnogorac V, Marjanovic G, Jüttner E, Keck T, Weiser HF and Hopt UT. Small intestinal submucosa for reinforcement of colonic anastomosis. Int J Colorectal Dis 2009; 24: 543-550.
[30] Huson H, Goodchild T, Sun L, Scarborough A, Novak T, Dubansky B, Morrison J and Hodgdon I. Use of polyvinyl alcohol-porcine small intestine submucosa stent in the prevention of anastomotic leaks in the porcine colon. J Surg Res 2022; 276: 354-361.
[31] Li G and Sun S. Silk fibroin-based biomaterials for tissue engineering applications. Molecules 2022; 27: 2757.
[32] Lujerdean C, Baci GM, Cucu AA and Dezmirean DS. The contribution of silk fibroin in biomedical engineering. Insects 2022; 13: 286.
[33] Sun W, Gregory DA, Tomeh MA and Zhao X. Silk fibroin as a functional biomaterial for tissue engineering. Int J Mol Sci 2021; 22: 1499.
[34] Franck D, Chung YG, Coburn J, Kaplan DL, Estrada CR Jr and Mauney JR. In vitro evaluation of bi-layer silk fibroin scaffolds for gastrointestinal tissue engineering. J Tissue Eng 2014; 5: 2041731414556849.
[35] Chen J, Yin Z, Tan G, Xing T, Kundu SC and Lu S. Research on silk fibroin composite materials for wet environment applications. J Mech Behav Biomed Mater 2024; 160: 106777.
[36] Rodriguez-Nogales A, Algieri F, De Matteis L, Lozano-Perez AA, Garrido-Mesa J, Vezza T, de la Fuente JM, Cenis JL, Gálvez J and Rodriguez-Cabezas ME. Intestinal anti-inflammatory effects of RGD-functionalized silk fibroin nanoparticles in trinitrobenzenesulfonic acid-induced experimental colitis in rats. Int J Nanomedicine 2016; 11: 5945-5958.
[37] Fuster MG, Carissimi G, Montalbán MG and Víllora G. Improving anticancer therapy with naringenin-loaded silk fibroin nanoparticles. Nanomaterials (Basel) 2020; 10: 718.
[38] Zhang B, Yan J, Jin Y, Yang Y and Zhao X. Curcumin-shellac nanoparticle-loaded GelMA/SilMA hydrogel for colorectal cancer therapy. Eur J Pharm Biopharm 2024; 202: 114409.
[39] DeStefano S, Hartigan DR, Josyula A, Faust M, Fertil D, Lokwani R, Ngo TB and Sadtler K. Conserved and tissue-specific immune responses to biologic scaffold implantation. Acta Biomater 2024; 184: 68-80.
[40] Pacheco KA and Thyssen JP. Contact dermatitis from biomedical devices, implants, and metals-trouble from within. J Allergy Clin Immunol Pract 2024; 12: 2280-2295.
[41] Zhu J, Du Y, Backman LJ, Chen J, Ouyang H and Zhang W. Cellular interactions and biological effects of silk fibroin: implications for tissue engineering and regenerative medicine. Small 2025; 21: e2409739.
[42] Yuan Y, Nasri M, Manayi A, Zhang J, Wu C, Jeon TJ and Kang L. Sericin coats of silk fibres, a degumming waste or future material? Mater Today Bio 2024; 29: 101306.
[43] Panilaitis B, Altman GH, Chen J, Jin HJ, Karageorgiou V and Kaplan DL. Macrophage responses to silk. Biomaterials 2003; 24: 3079-3085.
[44] Seo YK, Yoon HH, Park YS, Song KY, Lee WS and Park JK. Correlation between scaffold in vivo biocompatibility and in vitro cell compatibility using mesenchymal and mononuclear cell cultures. Cell Biol Toxicol 2009; 25: 513-522.
[45] Li X, Li N, Fan Q, Yan K, Zhang Q, Wang D and You R. Silk fibroin scaffolds with stable silk I crystal and tunable properties. Int J Biol Macromol 2023; 248: 125910.
[46] Lv J, Chen L, Zhu Y, Hou L and Liu Y. Promoting epithelium regeneration for esophageal tissue engineering through basement membrane re-

constitution. ACS Appl Mater Interfaces 2014; 6: 4954-4964.
[47] Hudita A, Radu IC, Galateanu B, Ginghina O, Herman H, Balta C, Rosu M, Zaharia C, Costache M, Tanasa E, Velonia K, Tsatsakis A and Hermenean A. Bioinspired silk fibroin nano-delivery systems protect against 5-FU induced gastrointestinal mucositis in a mouse model and display antitumor effects on HT-29 colorectal cancer cells in vitro. Nanotoxicology 2021; 15: 973-994.
[48] Xie X, Yu J, Zhao Z, Zheng Z, Xie M, Wang X, Han Z and Li G. Fabrication and drug release properties of curcumin-loaded silk fibroin nanofibrous membranes. Adsorption Science & Technology 2018; 37: 412-424.
[49] Feng Y, Han Z, Chen C, Wang X, Liu J, Khan Y, Xie M, Chen Y, Zhang Y and Li G. Psoralea corylifolia formula extract-loaded silk fibroin/polycaprolactone fibrous membrane for the treatment of colorectal cancer. Colloids Surf B Biointerfaces 2024; 233: 113635.
[50] Rahman M, Kabir M, Li K, Li Y, Chen S and Wu S. Electrospun zeolitic imidazole framework-8 loaded silk fibroin/polycaprolactone nanofibrous scaffolds for biomedical application. J Mech Behav Biomed Mater 2024; 160: 106769.
[51] Vaseghi A, Sadeghizadeh M, Herb M, Grumme D, Demidov Y, Remmler T and Maleki HH. 3D printing of biocompatible and antibacterial silica-silk-chitosan-based hybrid aerogel scaffolds loaded with propolis. ACS Appl Bio Mater 2024; 7: 7917-7935.
[52] Chen J, Zhang L, Han Z, Meng X, Sun X, Zhong Y, Zhi M, Huang D and Li G. Silk fibroin/chitosan-based anal fistula scaffolds loaded with curcumin and 5-aminosalicylic acid. Int J Biol Macromol 2024; 281: 135927.
[53] Pérez-Lloret M, Reidy E, Lozano-Pérez AA, Marchal JA, Lens PNL, Ryan AE and Erxleben A. Auranofin loaded silk fibroin nanoparticles for colorectal cancer treatment. Drug Deliv Transl Res 2025; 15: 1994-2008.
[54] Hu Y, Zhang Q, You R, Wang L and Li M. The relationship between secondary structure and biodegradation behavior of silk fibroin scaffolds. Advances in Materials Science and Engineering 2012; 2012: 1-5.
[55] Mariani E, Lisignoli G, Borzì RM and Pulsatelli L. Biomaterials: foreign bodies or tuners for the immune response? Int J Mol Sci 2019; 20: 636.
[56] Melke J, Midha S, Ghosh S, Ito K and Hofmann S. Silk fibroin as biomaterial for bone tissue engineering. Acta Biomater 2016; 31: 1-16.
[57] Chantarojanasiri T, Keeratihattayakorn S, Boonkruepan S, Jitpibull J and Ratanavaraporn J. Effect of silk-fibroin-coated polydioxanone biodegradable enteric stents on the degradation rate. ACS Omega 2025; 10: 28243-28251.
[58] Algarrahi K, Franck D, Ghezzi CE, Cristofaro V, Yang X, Sullivan MP, Chung YG, Affas S, Jennings R, Kaplan DL, Estrada CR Jr and Mauney JR. Acellular bi-layer silk fibroin scaffolds support functional tissue regeneration in a rat model of onlay esophagoplasty. Biomaterials 2015; 53: 149-159.
[59] Cho Y, Beak JW, Sagong M, Ahn S, Nam JS and Kim ID. Electrospinning and nanofiber technology: fundamentals, innovations, and applications. Adv Mater 2025; 37: e2500162.
[60] Sayin E, Rashid RH, Rodríguez-Cabello JC, Elsheikh A, Baran ET and Hasirci V. Human adipose derived stem cells are superior to human osteoblasts (HOB) in bone tissue engineering on a collagen-fibroin-ELR blend. Bioact Mater 2017; 2: 71-81.
[61] Bokhari N, Ali A, Nausheen S, Yasmeen A, Anjum MA and Sharif F. Biomimetic silk fibroin meshes for regenerative soft tissue repair: multiscale evaluation of a spatiotemporally active scaffold. Biomater Adv 2026; 178: 214435.
[62] Kambe Y, Kawano Y, Sasaki M, Koga M, Fujita N and Kameda T. Enhanced biodegradation of silk fibroin hydrogel for preventing postoperative adhesion. ACS Biomater Sci Eng 2024; 10: 7441-7450.
[63] Bucciarelli A and Motta A. Use of Bombyx mori silk fibroin in tissue engineering: from cocoons to medical devices, challenges, and future perspectives. Biomater Adv 2022; 139: 212982.
[64] Zhang T, Zhang R, Zhang Y, Kannan PR, Li Y, Lv Y, Zhao R and Kong X. Silk-based biomaterials for tissue engineering. Adv Colloid Interface Sci 2025; 338: 103413.
[65] Wang S, Wang J, Li M, Gao D, Yu X, Zhao P, Dou H, Guo C and Yuan S. Rapidly photocrosslinkable charged silk-based hydrogel for emergency hemostasis and multifunctional wound therapy. Bioact Mater 2026; 57: 694-709.
[66] Chandavaram BP, Kumbhar US and A PR. Effectiveness of silk fibroin dressing compared to saline dressing on wound healing in post-laparotomy patients with superficial surgical site infections: a single-blinded randomised control trial. Sultan Qaboos Univ Med J 2025; 25: 981-989.
[67] Ma L, Dong W, Lai E and Wang J. Silk fibroin-based scaffolds for tissue engineering. Front Bioeng Biotechnol 2024; 12: 1381838.
[68] Valentin JE, Stewart-Akers AM, Gilbert TW and Badylak SF. Macrophage participation in the degradation and remodeling of extracellular matrix scaffolds. Tissue Eng Part A 2009; 15: 1687-1694.

[69] Gao Y, Wang Y, Zhang J, Zhang M, Dai C, Zhang Y, Zhang L, Bian L, Yang Y, Zhang K and Zhao Y. Advancing neural regeneration via adaptable hydrogels: enriched with Mg(2+) and silk fibroin to facilitate endogenous cell infiltration and macrophage polarization. Bioact Mater 2024; 33: 100-113.
[70] Gaharwar AK, Singh I and Khademhosseini A. Engineered biomaterials for in situ tissue regeneration. Nature Reviews Materials 2020; 5: 686-705.
[71] Shang K, Rnjak-Kovacina J, Lin Y, Hayden RS, Tao H and Kaplan DL. Accelerated in vitro degradation of optically clear low β-sheet silk films by enzyme-mediated pretreatment. Transl Vis Sci Technol 2013; 2: 2.
[72] Zhao M, Qi Z, Tao X, Newkirk C, Hu X and Lu S. Chemical, thermal, time, and enzymatic stability of silk materials with silk I structure. Int J Mol Sci 2021; 22: 4136.
[73] Lu Q, Hu X, Wang X, Kluge JA, Lu S, Cebe P and Kaplan DL. Water-insoluble silk films with silk I structure. Acta Biomater 2010; 6: 1380-1387.
[74] Maia MV, Egito E, Sapin-Minet A, Viana DB, Kakkar A and Soares DCF. Fibroin-hybrid systems: current advances in biomedical applications. Molecules 2025; 30: 328.
[75] Manissorn J, Promsuk J, Wangkanont K and Thongnuek P. Biomimetic peptide conjugates as emerging strategies for controlled release from protein-based materials. Drug Deliv 2025; 32: 2449703.
[76] Yu Y, Chen K, Wang J, Zhang Z, Hu B, Liu X, Lin Z and Tan A. Custom-designed, mass silk production in genetically engineered silkworms. PNAS Nexus 2024; 3: pgae128.
[77] Du Y, Guo JL, Wang J, Mikos AG and Zhang S. Hierarchically designed bone scaffolds: from internal cues to external stimuli. Biomaterials 2019; 218: 119334.
[78] Mitchell AC, Briquez PS, Hubbell JA and Cochran JR. Engineering growth factors for regenerative medicine applications. Acta Biomater 2016; 30: 1-12.
[79] Luo Z, Jiang L, Xu Y, Li H, Xu W, Wu S, Wang Y, Tang Z, Lv Y and Yang L. Mechano growth factor (MGF) and transforming growth factor (TGF)-β3 functionalized silk scaffolds enhance articular hyaline cartilage regeneration in rabbit model. Biomaterials 2015; 52: 463-475.
[80] Sasaki A, Sakata H and Kinjo M. Single-cell quantitative analysis of DNA incorporation and protein expression in microwells. Curr Pharm Biotechnol 2010; 11: 117-121.
[81] Kirillova A, Maxson R, Stoychev G, Gomillion CT and Ionov L. 4D biofabrication using shape-morphing hydrogels. Adv Mater 2017; 29.
[82] Morouço P, Lattanzi W and Alves N. Four-dimensional bioprinting as a new era for tissue engineering and regenerative medicine. Front Bioeng Biotechnol 2017; 5: 61.
[83] Ding A, Tang F and Alsberg E. 4D printing: a comprehensive review of technologies, materials, stimuli, design, and emerging applications. Chem Rev 2025; 125: 3663-3771.
[84] Chen M, Hou Y, An R, Qi HJ and Zhou K. 4D printing of reprogrammable liquid crystal elastomers with synergistic photochromism and photoactuation. Adv Mater 2024; 36: e2303969.
[85] Xia Y, He Y, Zhang F, Liu Y and Leng J. A review of shape memory polymers and composites: mechanisms, materials, and applications. Adv Mater 2021; 33: e2000713.
[86] Sakakura Y, Kono K and Fujimoto T. Real time artificial intelligence assisted carotid artery stenting: a preliminary experience. J Neurointerv Surg 2025; 17: 410-414.
[87] Wang Y, Cai X, Mei J, Liu K and Cai X. Colonic anastomosis with a doxycycline-coated stent: an experimental study in a porcine model. Dig Surg 2014; 31: 87-94.
[88] Zhang B, Li X, Jiang C, Wang C, Que H, Zheng C, Ji Z, Tao X, Xu H and Shi C. Construction of PVA/OHA-Gs@PTMC/PHA double-layer nanofiber flexible scaffold with antibacterial function for tension free rectal in-situ reconstruction. Biomaterials 2025; 317: 123064.