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Advanced biomaterials for tendon repair: development and application

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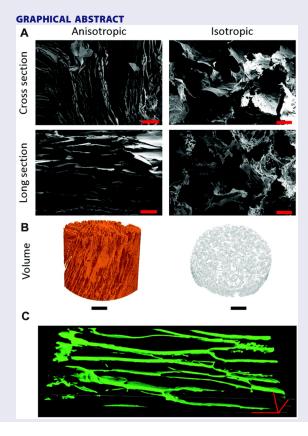
ABSTRACT

Professional sports such as tennis training require repetitive shoulder movements, which can result in tendon fatigue and injury due to overuse. This injury usually occurs when an incorrect force is applied or when the tendon is overused. Because the tendon lacks blood vessels, the repair process is slow and ineffective. The treatment of tendon injuries has always been a clinical challenge. In addition to conventional surgery and nonoperative conservative treatment, biomaterial-based scaffolds may be a solution. In this review, we described several of the most popular biomaterials for tendon repair and presented the latest research advances. These biomaterials include protein-based biomaterials, carbohydrates, glycosaminoglycans, and acellular matrices. They have shown improved tendon repair ability both *in vitro* and *in vivo*. However, no gold standard has been established, and further experiments are needed.

GRAPHICAL ABSTRACT

1. Introduction

In recent decades, competitive tennis has undergone rapid development worldwide. The level of sport skills noticeably improved, which also inevitably increased the injury frequency and severity in tennis athletes. This issue has been brought to the forefront, and solutions are needed. A noticeable characteristic of tennis is that the number of serves per
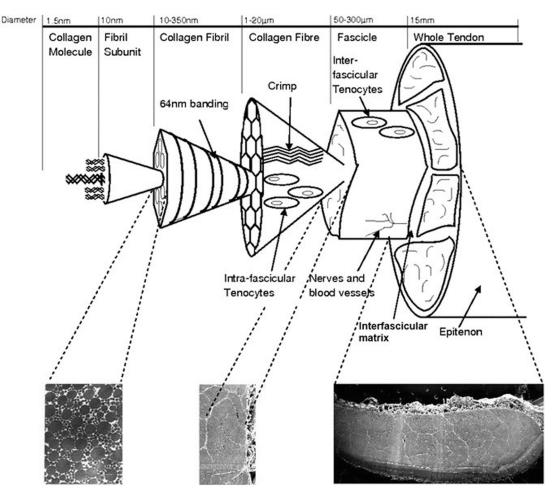
Figure 1. Multiple-scale hierarchical structure of the tendon. Collagen molecules consist of anisotropically aligned fibrils that then form larger tendon fibers. Adapted from reference[5].

game is greater than that of any other type of stroke[1]. Tennis stroke creates repeating, high-intensity, short-duration actions and pressures, especially in the serve. As a consequence, the glenohumeral ligaments, rotator cuff, biceps tendon, scapular region, and glenoid labrum are the shoulder structures most frequently injured, similar to baseball pitchers[2]. In another study in which US Open Tennis Championships were analyzed between 1994 and 2009, although the incidence of lower limb injuries was significantly greater than that of upper limb and trunk injuries, muscle or tendon injuries were still the most common type of acute injury[3]. The recovery of muscle tendon injury, which directly affects sport training and sport skills, has been an inevitable challenge for athletes as well as clinical practitioners for several decades. Because the integrity of the tendon sheath is damaged after injury, the synovial fluid system is not balanced, and the blood supply is reduced. The healing process relies mainly on direct peritendon tissue ingrowth; in contrast, the growth of tendon tissue itself is limited, leading to a longer healing period and even greater difficulty in achieving rehabilitation. In addition, massive scar tissues (fibrosis) frequently form during the healing process, so adhesion between the tendon and surrounding soft tissues is a common prognosis that significantly affects the rehabilitation effect[4]. Over the years, many clinical and experimental studies have been carried out on tendon anatomy, physiology, pathology and healing processes. Tendons are dense connective tissues composed of anisotropic substructures at the nano- and microscales (Figure 1). The structural and functional integrity of the tendon-bone system is the premise of effective force transmission and the basis of normal life activities[6].

Tendon injuries are also very common in daily life due to trauma, overuse and degenerative changes. Tendon disease is responsible for approximately 30% of all general clinical consultations for musculoskeletal discomfort[7]. Because tendinopathy is a fairly frequent soft tissue pain, determining its exact prevalence in the general population is challenging. Acute tendon injuries are another prevalent occurrence. Nearly two million people sought a doctor for rotator cuff disorders in 2008, according to the American Academy of Orthopedic Surgeons[8]. In the United States, more than 300,000 patients receive surgery for tendon and ligament repair annually[6]. Tendon injuries may affect people of all ages and can limit activities in the workplace or in sports for both young and elderly individuals. In summary, tendon disorders and injuries are frequent, have a large impact on quality of life and are an enormous financial burden on healthcare systems.

At present, the treatment of tendon tears involves conservative treatment via local injection to relieve inflammation

Table 1. Advanced biomaterials and their applications in tendon repair.

Biomaterial category	Examples	Applications
Protein-based biomaterials	Silk fibrin films	Used for tendon repair with properties mimicking healthy rat tendons, investigated for effects on rat tendon stem/progenitor cells.
Carbohydrate biomaterials	Cellulose nanocrystals	Developed as reinforcing nanofillers in aligned electrospun scaffolds for tendon tissue engineering.
Carbohydrate biomaterials	Alginate nonwoven scaffolds, alginate nonwoven-sponge composite scaffolds	Used in rotator cuff injury models and tendon injury repair; promotes tendon recovery, helps in well-organized collagen fiber and fibrocartilage formation at tendon-to-bone interface.
Glycosaminoglycans	Chitosan-collagen hydrogel	Used for tendon regeneration; coated scaffolds showed less protein adsorption, good tenocyte adherence and dispersion.
Acellular matrix grafts	Decellularized tendon scaffolds	Ideal for sophisticated tissue engineering applications, providing a blank canvas for cell growth while preserving natural architecture.

and pain. Surgical and minimally invasive techniques are important for treating tendon rupture and reconstructing tendon function, but there is a certain recurrence rate. The regeneration ability and healing ability of adult tendon cells are extremely poor. Neither conservative nor surgical treatment can restore the original biomechanical strength of the injured tendon. Therefore, patients often suffer pain, functional decline and even tendon rupture after treatment, which seriously affects their quality of life.

In recent years, the application of tissue engineering for promoting tendon regeneration has attracted increasing amounts of attention from researchers at home and abroad. This approach is expected to become a promising solution for repairing slight pathological changes in tendons. Ideal materials should have mechanical properties similar to those of physiological materials and good biocompatibility. To date, natural biomaterials (biological derivatives) have been recognized as one of the best choices for repairing materials. These materials can be classified according to their properties as protein-based biomaterials (e.g., collagen, gelatin, silk and fibrin), carbohydrate biomaterials (cellulose, chitin/chitosan, and alginate), glycosaminoglycans (hyaluronic acid, chondroitin sulfate) and acellular matrix grafts. In this paper, the types and preclinical applications of natural biomaterials in recent years were reviewed, and future clinical applications of natural biomaterials were proposed. A summary of these materials and their applications in tendon repair is presented in Table 1.

2. Protein-based biomaterials

Collagen is a classical component involved in tendon regeneration. Collagen is composed of a triple helix structure, which contributes to better mechanical properties than other natural biomaterials[9]. The function of the tendon is strongly related to this special collagen structure[10]. Collagen has been extensively studied because it is predominantly present in native tendon tissue. Self-assembly based aligned collagen scaffolds were first introduced in 1989[11]. The alignment of collagen is critical for matching the mechanical properties of native tendon tissue. In recent years, Kew et al. reported the construction of a unique multifiber collagen fascicle structure based on type-I collagen with a failure stress of 25–49 MPa, which closely resembles the strength and structure of natural tendon tissue. They described a microscopic manufacturing approach based on type I collagen fiber self-assembly that can be used to construct a controllable fascicle-like structure with varying numbers of fibers per fascicle. The resultant postfabrication type-I collagen structure preserved the fundamental phase behavior, alignment, and spectral features of the aligned natural type-I collagen[12]. An electrochemical method can also produce highly oriented and densely packed collagen bundles with mechanical strength approaching that of tendons and without causing biotoxicity. Tendon-derived fibroblasts and bone marrow stromal cells both displayed better proliferation and migration in response to electrochemically aligned collagen, although the advantages of these materials over randomly oriented collagen have not been further examined[13]. In addition, collagen is an outstanding backbone material that can be modified or functionalized into hybrids. Hortensius et al. developed amniotic membrane (AM)-integrated 3D collagen bioscaffolds for tendon repair in two ways: as a membrane wrap encapsulating a collagen–glycosaminoglycan scaffold to construct a core–shell composite or as a bulk scaffold to generate a porous collagen–AM scaffold. While MSCs respond to media challenge, the expression patterns of the immunomodulatory genes IL-6 and IL-8 revealed that MSCs within AM-functionalized collagen scaffolds respond differently in the early stages following inflammatory stress[14]. Another study utilized electrospun aligned poly(l-lactic acid) nanofibers with a chitosan-collagen hydrogel to mimic aligned collagen fibers and sheath ECM for tendon regeneration[15]. Similarly, poly(l-lactide-co-ε-caprolactone) [P(LLA-CL)] and natural collagen I electrospun complexes were fabricated[16]. The tenocytes showed good attachment and expansion on the above two collagen-functionalized nanofibres.

Gelatin is another well-known biodegradable and biocompatible material. Generally, gelatin is a derivative of collagen irreversibly hydrolyzed by heat or enzymes, during which the triple helix structure is lost[17]. Nevertheless, gelatin is an effective substitute for collagen because it is a very similar component to collagen. The most significant advantage of using gelatin is that it is more adaptable under different temperature and pH conditions, which provides convenience and possibility in composite synthesis. The other attractions of gelatin include rich sources and more affordable prices. The critical disadvantage of gelatin is its limited mechanical properties, which strongly limits its application[18]. Since tendons are tissues with high mechanical strength, gelatin usually undergoes modification, crosslinking, or hybridization with other biomaterials to enhance its mechanical properties.
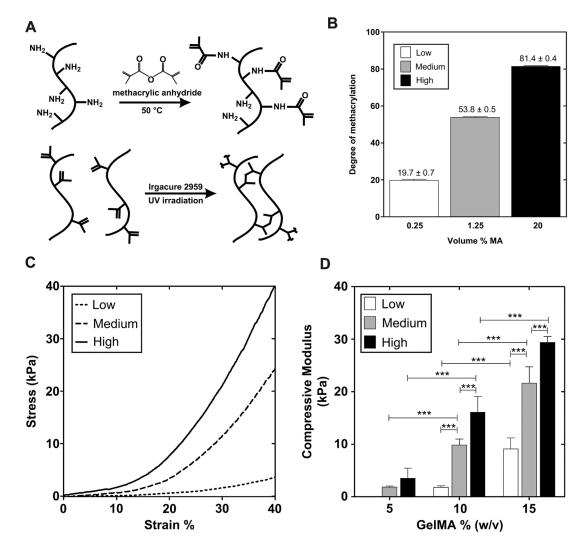
Figure 2. Typical GelMA synthesis process and adjustable mechanical properties. (A) The amide groups of gelatin were substituted by methacrylate pendant groups of methacrylic anhydride (MA). hydrogel crosslinking was initiated under UV irradiation in the presence of a photoinitiator. (B) The degree of methacrylation ranged from approximately 20% ('low') to 80% ('high') depending on the MA volume added. (C,D) The mechanical properties of GelMA could be easily controlled by the GelMA concentration and degree of methacrylation. Adapted from reference[19].

Among them, gelatin methacryloyl (GelMA) has been a popular and promising choice in recent decades. GelMA is a methacrylated gelatin that can be crosslinked by 405 nm wavelength light in the presence of a photoinitiator[19]. GelMA has the advantages of a simple synthesis process and adjustable mechanical properties because of the need to control the GelMA concentration, degree of methacrylation, etc. (Figure 2). The GelMA scaffold has been reported to be useful in rotator cuff tendon repair. The combination of GelMA and stem cells improved cartilage regeneration at the tendon-to-bone interface 8 and 12 weeks after repair and increased tendon maturation scores and ultimate load to failure of the repaired tendon[20]. Another study reported that tissue-engineered tendons consisting of 3D-printed GelMA and chemically empowered tendon stem/progenitor cells promoted the expression of tendon-related genes and proteins and enhanced mechanical properties in a mouse patellar tendon defect model after 4 weeks[21]. Despite the need to construct solid scaffolds, injectable adipose-derived stem cell (AMSC)-laden GelMA has been evaluated for use in chronic tendon injury repair[22] or mixed with

nanoparticles to form an injectable hybrid hydrogel system[23]. Overall, GelMA is the most widely investigated gelatin-based material for tendon repair.

Silk proteins are found in the glands of silk-producing arthropods (such as silkworms, spiders, scorpions, mites, and bees) and are spun into threads during metamorphosis. Silk fibrin has a distinct advantage over other natural biopolymers in terms of its mechanical properties. Good biocompatibility, water-based processing, biodegradability, and the presence of easily accessible chemical groups for functional changes are all major advantages[24,25]. Based on these promising characteristics, researchers have developed silk fibrin-based biomaterials for tendon repair. Lu et al.[26] prepared silk fibrin films with different bionic microstructures and mechanical properties mimicking healthy rat tendons and subsequently investigated their biological effects on rat tendon stem/progenitor cells. The results showed that the silk fibrin films they developed promoted early cell adhesion and proper cell biological behavior, as did the most significant upregulations of the expression of the COL1A1, TNC, TNMD and SCX genes. Considering the gradual mechanical stress transfer between tendons/
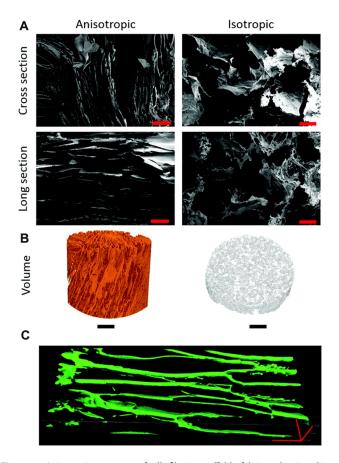
Figure 3. Anisotropic structure of silk fibroin scaffolds fabricated using directional freezing. (A) FESEM micrographs and (B) μCT volume reconstructions of aligned and nonaligned silk fibroin scaffolds; scale bar = 200 μm (FESEM) and 500 μm (μCT); (C) Confocal imaging of anisotropic scaffolds showing lamellar alignment; scale bars = 200 μm. FESEM, field-emission scanning electron microscopy; μCT, microcomputed tomography. Adapted from reference[27].

ligaments and bone, several researchers have fabricated biphasic silk fibrin scaffolds that mimic the structural features of the native interface (Figure 3). These authors showed that this type of silk fibrin scaffold was more promising for tendon/ligament-to-bone tissue engineering given its smooth transition zone, better mechanical behavior, and interesting effects on the gene expression of AMSCs[27]. Due to the similar structure of electrospun fibers to native fibers, electrospun poly(3-hydroxybutyrate) (P3HB) or polycaprolactone (PCL) nanofibers were made on twisted silk fibroin. The hybrid fiber demonstrated slightly improved mechanical properties due to the interaction between the nano- and microcomponents and showed no cytotoxicity or good cytocompatibility, making it a suitable candidate for tendon and ligament tissue engineering[28]. Compared to collagen and gelatin, fibrous biomaterials are easier to fabricate into anisotropic structures that well mimic the native structure of tendons and ligaments.

3. Carbohydrate biomaterials

Cellulose is an excellent choice in tendon tissue engineering because of its adjustable chemical, physical, and mechanical characteristics. Cellulose has abundant sources in nature and is simple to manufacture. Cellulose-based materials provide a low-cost tissue engineering platform[29]. However, cellulose alone is unable to fulfill the tensile properties of native tendons. To address this issue, cellulose is commonly fabricated into hybrids. Domingues et al.[30] developed cellulose nanocrystals (CNCs) as reinforcing nanofillers in aligned electrospun scaffolds based on a natural/synthetic polymer blend matrix, poly-ε-caprolactone/chitosan (PCL/CHT). A small amount of CNCs (up to 3 wt%) incorporated into tendon mimetic nanofiber bundles had a significant biomaterial-toughening effect (85%±5%, $p < 0.0002$) and elevated the scaffold's mechanical characteristics to tendon/ligament relevant ranges (=39.3 ± 1.9 MPa and E = 540.5 ± 83.7 MPa, $p < 0.0001$). Aligned PCL/CHT/CNC nanocomposite fiber scaffolds not only fulfill the mechanical criteria for tendon tissue engineering applications but also provide tendon mimetic extracellular matrix (ECM) topographic cues, which are important factors for tendon cell proliferation and function. Mathew et al.[31] fabricated fibrous cellulose nanocomposite scaffolds composed of a matrix phase and a reinforcing phase. After sterilizing with gamma rays, the mechanical characteristics of the composites under simulated body circumstances (37 °C and 95% RH) were equivalent to those of natural ligaments and tendons. In vitro biocompatibility studies also showed that both human ligaments and endothelial cells exhibited good adhesion, proliferation and differentiation. In addition, cellulose-collagen hydrolysate films[32] and collagen-cellulose nanocomposites generated by pH-induced fibrillation crosslinked by genipin[33] or glutaraldehyde[34] have been reported. The crosslinkers enhanced the mechanical strength of the composites and had little adverse effect on cell growth or differentiation.
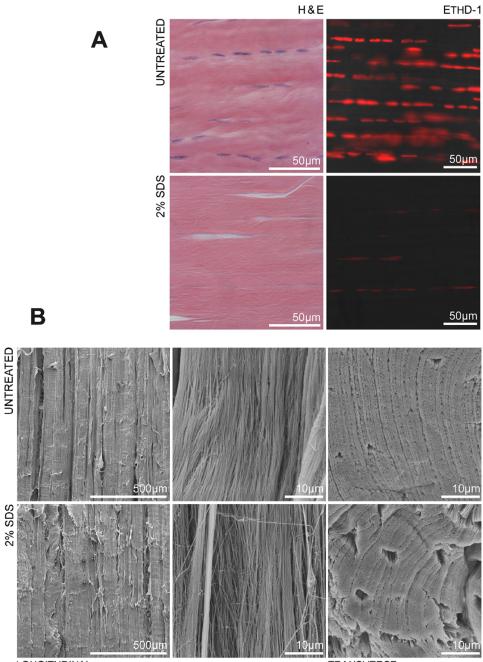
Chitin is the second most abundant natural polymer after cellulose. It is mostly found in the exoskeletons of arthropods and crustaceans, as well as in the cell walls of fungi[35]. Chitin and chitosan are essentially the same macromolecular entity, with the percentage of acetylated repeating units differing very slightly. Chitosan is produced primarily by the deacetylation of chitin[36]. However, it should be noted that such a distinction is arbitrary and created solely for comparison reasons. Chitin and chitosan are two points on a continuum of materials that have the same fundamental structure and differ only in the degree of acetylation. Currently, chitin and chitosan are usually processed into fibers by electrospinning. In one study, three different kinds of 3D circular braided scaffolds were fabricated. In comparison to scaffolds with smaller filament yarn, larger filament yarn scaffolds had significantly greater ultimate stress values. In terms of mechanical properties, the scaffolds could be compared to human supraspinatus tendons by adjusting the processing parameters. On the chitosan scaffold, human stem cells demonstrated up to six-fold growth over 28 days[37]. A model of polyion complex fibers prepared from alginate and chitosan was reported. This type of fiber has a tensile strength of more than 200 MPa. Additionally, morphologic analyses revealed dense fibers of type I collagen generated by rabbit tendon fibroblasts[38]. A study investigated nano-HA-doped PCL/chitosan hybrid nanofibres. The nanohydroxyapatite dopant enhanced the mechanical properties of the composite, for which the load and modulus were 250.1 N and 215.5 MPa, respectively, which are close to those of

native human tendons. In vitro experiments have shown that, compared to nanofibrous scaffolds lacking HAp nanoparticles, HAp-distributed PCL/chitosan nanofibrous scaffolds stimulate greater adhesion and proliferation of human osteoblasts[15,39]. Using electrospun aligned poly (l-lactic acid) (PLLA) nanofibres, Deepthi et al. developed a tendon construct to simulate aligned collagen fiber bundles and overlay PLLA fibers with chitosan-collagen hydrogel to replicate sheath ECM glycosaminoglycans (GAGs) for tendon regeneration. Protein adsorption experiments revealed that the coated scaffolds adsorbed less protein than the untreated scaffolds. The tenocytes adhered well to the scaffolds and dispersed widely.

Alginates have traditionally been used primarily for their gel-forming capabilities. Mechanical augmentation using absorbable alginate may promote tendon recovery following rotator cuff surgery, according to recent *in vivo* research based on a rat model[40]. In addition, more researchers have tended to functionalize or enhance alginate by adding small molecules or biomaterials. For instance, researchers developed alginate nonwoven scaffolds and alginate nonwoven-sponge composite scaffolds by adding an alginate sponge layer. Transforming growth factor-beta 1 (TGF-β1) was combined with the scaffold and gradually released into a rabbit rotator cuff injury model. The results showed that well-organized collagen fibers and fibrocartilage were present at the tendon-to-bone interface[41]. By combining PCL, alginate, and melatonin, electrospun composites could effectively promote tendon injury repair *in vivo* and *in vitro* via the controlled release of melatonin[42]. Choi et al.[43] reported hydrogels with a high aspect ratio of alginate–polyacrylamide double-network alginate–polyacrylamide to generate multiscale structures made of an anisotropically aligned polymer network embedded with aligned microparticles. Mesoporous silica microparticles are stretched and fixed by subsequent drying and ionic crosslinking. The degree of stretching, the amounts and functional groups of inorganic microparticles, and the kinds of crosslinking cations may all influence the mechanical characteristics of hydrogels. The degree of stretching, the amounts and functional groups of inorganic microparticles, and the kinds of crosslinking cations may all influence the mechanical characteristics of hydrogels. Other alginate-based composites reported include alginate-chitin scaffolds[44] and poly(lactic-co-glycolic acid)/alginate knitted scaffolds[45]. The versatility of alginate has been proven by its ability to hybridize with other natural and artificial materials in tendon engineering.

4. Glycosaminoglycans (GAGs)

Hyaluronic acid (HA) is a GAG that can be found in practically all tissues. HA regulates cell proliferation and migration and shields cells from harm. Water retention in the epidermis, lubrication in the intra-articular region, and permeability modulation in the vasculature are only a few of the physiological functions of HA. HA can bind to the CD-44 fibroblast receptor under normal physiological circumstances, causing cell aggregation. HA is a substance with strong water retention, good moisturizing capacity, and a great swelling ratio of up to 1,000 times its original weight in terms of material attributes[46]. According to the literature, in damaged tendons injected with hyaluronic acid solution containing tenocytes, there was a substantial difference in the healing state compared to that in the other groups. In the hyaluronic acid with tenocyte transplantation group, the stiffness and mobility of the Achilles tendons were enhanced in the rats with healed Achilles tendons. Hyaluronic acid combined with tenocyte injections accelerated the inflammatory phase in rats, which may be the main explanation for the greater percentage of functional results[46]. Platelet-rich plasma (PRP) was used as an autologous scaffold for cell development, with hyaluronic acid serving as a temporary dermal replacement. This process assists in the healing of open sores on the foot and ankle, both acutely and chronically[47]. A similar study combined plasma and HA, which improved the biological characteristics of HA by stimulating tendon cell migration and synovial fibroblast migration[48]. Apart from using HA directly to facilitate tendon regeneration, many authors have recognized that HA helps to prevent adhesions by reducing the creation of scars and granulation tissue after tendon repair[49–51]. Overall, HA acts as an enhancer instead of the backbone of a composite in tendon engineering.

Chondroitin sulfate (CS) is located mostly in tendon terminal locations that are subjected to compressional force. CS is a major ECM component and GAG with demonstrated anti-inflammatory properties and the ability to inhibit inflammatory cell attachment. On this basis, a research group used CS to reduce adhesion after animal surgery. In rabbit forepaws following surgical repair, polyhydroxyethyl methacrylate membranes coated on one side with CS were utilized to physically inhibit adhesion and minimize friction between recovering flexor tendons and the surrounding tissue[52]. In addition to its anti-inflammatory activity, CS more frequently acts as a candidate composite. Several authors have used a coaxial stable jet electrospinning technique to create highly aligned PLLA fibers with surfaces adorned with two important tendon ECM components, type 1 collagen (COL1) and CS. *In vitro* tenogenic differentiation of human mesenchymal stem cells (hMSCs) was examined using biomimetic COL1-CS (shell)/PLLA (core) fibers. When comparing the aligned COL1-CS/PLLA fibers to the plain PLLA fibers, the aligned COL1-CS/PLLA fibers showed higher rates of cell spreading and proliferation. The expression of tendon-associated genes was upregulated, suggesting that these genes could be used as an efficient scaffolding system for functional tendon regeneration[53]. The Silva group modified CS with methacrylate (MA), which endowed MA-CS with the ability to photocrosslink. The incorporation of iron-based magnetic nanoparticles further provided magnetic responsiveness. Within the hydrogel, osteogenically differentiated adipose-derived stem cells and/or tendon-derived cells proliferate and express bone- and tendon-related markers[54]. CSs also appeared in the form of patches. A CS-based knitted patch made of COL1/CS and poly(lactide)s (PLA) was found to have good tissue integration in rats subcutaneously 12 weeks after implantation[55].

Figure 4. Decellularization and microstructure of the equine tendon. (A) Brightfield images of H&E-stained sections (5 μm thick) and fluorescence micrographs of scaffolds imaged with EthD-1 (400 μm thick). SDS treatment (2%) significantly decellularized the tendon. Fewer nuclei (red) were observed. (B) SEM images showing that 2% SDS-induced decellularization did not alter the collagen ultrastructure. Adapted from reference[58].

Table 2. Clinical use of decellularized and acellular biomaterials in tendon surgery (from reference [59]).

Product/company	Tissue/ECM source	Applications
GraftJacket® (Wright Medical Inc., USA)	Human dermis	Augmentation of massive rotator cuff tears, arthroscopic rotator cuff and Achilles tendon repairs, lateral ankle stabilization, and posterior tibial tendon reinforcement
Conexa™ (Tornier, Inc., The Netherlands)	Porcine dermis	Reinforcement of rotator cuff, patellar, Achilles tendon, biceps, quadriceps, or other tendons
CuffPatch™ (Organogenesis, USA)	Porcine SIS	Rotator cuff and slap tear repair
TissueMend® (Stryker Orthopedics, USA)	Fetal bovine dermis	Reinforcement of the rotator cuff, Achilles tendon, biceps, quadriceps, or other tendons in both open and arthroscopic applications
Allopatch® (Conmed, USA)	Human dermis	Treating massive rotator cuff tears and revisions and tendon augmentation

5. Acellular matrix grafts

The extracellular matrix (ECM) is biosynthesised and secreted to benefit cells by providing mechanical support and a unique microenvironment that has a significant impact on inhabited cells. As a result, cellular components such as the nucleus are typically eliminated to create more biologically compatible biomaterials for medical applications[56]. The tendon acellular matrix is the tendon tissue that underwent decellularization, and the major components and native structure were preserved. Theoretically, the acellular matrix contains the most comprehensive biomolecules and has the closest mechanical properties as fresh tendon tissue. Woods et al.[57] compared three different methods for decellularization of porcine bone–anterior cruciate ligament–bone grafts and demonstrated that the grafts retained sufficient mechanical and biological characteristics after decellularization. Similarly, another study used equine flexor digitorum superficialis tendons to examine changes in scaffold composition and ultrastructure in response to various mechanical, detergent, and enzymatic decellularization protocols, employing microscopic techniques and a panel of biochemical assays to assess total protein, collagen, glycosaminoglycan, and deoxyribonucleic acid content. After decellularization, the collagen ultrastructure was well preserved (Figure 4). These decellularized tendon scaffolds are ideal for sophisticated tissue engineering applications because they provide a blank canvas for cell growth while preserving the natural three-dimensional architecture[58]. An *in vivo* rat Achilles tendon model study showed that tenocyte-seeded decellularized tendon matrix can enhance the histological and biomechanical features of tendon healing tissue without triggering immune responses[59]. A research group created a functional decellularized fibrocartilaginous matrix for rotator cuff enthesis regeneration. Recombinant SDF-1 (C-SDF-1) is capable of binding collagen and chemotaxis and was subsequently tethered to the collagen fibers of a book-shaped decellularized fibrocartilage matrix (BDFM). C-SDF-1/BDFM had no cytotoxicity or immunogenicity, permitted SMSC attachment or proliferation, and improved rotator cuff repair in a rat model. Promisingly, several commercial acellular matrices have been applied in clinical practice (Table 2)[60], which demonstrates the great potential of acellular matrix grafts in tendon engineering.

6. Conclusion

Tendon injury is still a challenge for both athletes and clinical practitioners. Successful recovery from tendon injury is critical for maintaining high-level skills throughout tennis players' careers. To improve rehabilitation after injury and reduce adhesion and fibrosis, researchers have studied a wide range of biomaterials based on proteins, carbohydrates, GAGs, and acellular matrix. These biomaterials are usually not used individually but are instead fabricated into composites to enhance their mechanical properties or biological activities. Many of these approaches have shown promising results both in vitro and in vivo. However, the best biomaterial and strategy are still elusive, and clinical trial data are limited. Overall, the development of biomaterials for tendon engineering is at the exploratory stage. However, further experiments are needed to determine the most suitable biomaterials for tendon repair.

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