Tampere University

Teemu Moilanen

COLLAGEN-CONTAINING SUTURES FOR WOUND CLOSURE

Faculty of Medicine and Health technology
Bachelor's Thesis
Maiju Juusela
May, 2025

ABSTRACT

Teemu Moilanen : Collagen-containing Sutures for Wound Closure
Bachelor's Thesis
Tampere University
Biotechnology and Biomedical Engineering
May, 2025

This thesis investigates the properties and biomedical applications of collagen-containing surgical sutures, with a focus on their potential to enhance wound healing. Collagen, an abundant natural biopolymer in the extracellular matrix, is known for its biocompatibility, biodegradability, and low immunogenicity. It is also known for its contribution in each phase of tissue repair: haemostasis, inflammation, proliferation, and remodelling. Rapid degradation and limited mechanical strength limit the use of pure collagen, which calls for the use of composite materials.

Sutures are materials used for wound closure, categorized by absorbability (absorbable or non-absorbable) and material origin (natural or synthetic). While absorbable sutures degrade over time and non-absorbable sutures require removal or remain in the body, both have limitations.
To overcome these limitations, sutures can be modified by incorporating bioactive agents such as collagen, either onto the surface as a coating or integrated within the fibre. Fabrication methods for modified sutures include dipping/coating, melt-spinning, and electrospinning. Incorporating collagen, particularly using a synthetic base with better mechanical properties, aims to combine structural support with biological activity.

The study explores the incorporation of collagen into/onto absorbable suture materials to improve tissue regeneration and reduce inflammatory responses. A comparative analysis was conducted between traditional synthetic sutures and collagen-enhanced variants, examining parameters such as tensile strength, degradation rate, and biological compatibility. In vitro studies showed that denatured collagen-coated PE/PEE sutures significantly enhanced adhesion and proliferation of human osteoblasts and tenocytes compared to uncoated sutures, especially when knotted and subjected to abrasion. Denatured collagen coating also promoted alkaline phosphatase activity, a marker for bone mineralization. In vivo studies using rat and mouse models demonstrated beneficial outcomes. A study on rat Achilles tendon repair found that atelocollagen-coated Vicryl resulted in improved load to failure at 6 weeks post-operation compared to standard Vicryl and DOPA-coated Vicryl, along with lower modified Bonar scores (indicating more normal histology) at both 1 and 6 weeks. The collagen coating also appeared to influence early collagen synthesis and organization, resulting in larger fibril diameters at week 1. Another study in a mouse acute incision wound healing model showed that electrospun PCL@COL sutures degraded slower than Vicryl or PCL and significantly accelerated wound closure efficacy. PCL@COL sutures demonstrated the highest mean collagen deposition density and increased formation of new blood vessels. While the findings indicate that collagen-containing sutures demonstrate favourable mechanical properties and enhanced biological activity, the study was limited by a relatively small number of experimental samples, which may affect the generalizability of the results.

However, the research supports the potential of collagen-based sutures as promising alternatives in surgical practice, particularly for wounds that are prone to infections, and for cosmetic scars.

Keywords

Collagen; Sutures; Suture modification; Medical devices

USE OF ARTIFICIAL INTELLIGENCE IN THESIS

Artificial intelligence (AI) has been used in my thesis:

☐ No
☒ Yes

The AI tools used in my thesis and the purpose of their use has been described below:

AI applications and their versions:

Scopus AI.

Purpose of use of AI

Scopus AI was used to find articles.

Parts in which AI was used

Chapter 4.

I am aware that I am totally responsible for the entire content of the thesis, including the parts generated by AI, and accept the responsibility for any violations of the ethical standards of publications.

CONTENTS

1. INTRODUCTION

Wound healing is a multifaceted process that involves multiple distinct phases [1]. Collagen plays an important role in these phases [2]. As the most abundant protein in the human body, it is a natural choice for this purpose. With the tensile strength approaching steel per weight basis, it is crucial in extracellular matrix formation [1]. It plays a vital role in tissue structure, cellular signalling, and wound healing. Collagen's inherent biocompatibility, biodegradability, and low immunogenicity make it an attractive material for biomedical applications, especially in the design of advanced wound closure devices [3]. In recent years, research has focused on developing collagen-containing sutures that can bridge the gap between traditional suturing techniques and modern tissue engineering strategies. This raises the question how using additional collagen in the wound site would affect the healing and scarring process.

Sutures are strands of material used for wound closure. Ideally not only holding tissues together but interacting favourably with the biological environment. Sutures have already evolved for 4000 years, but the procedure, which uses a needle and thread is still present. Sutures are made from multiple materials and commonly classified based on their absorbability, number of strands, and material origin into absorbable and nonabsorbable, mono- and multifilament, and synthetic and natural sutures. [4]

The purpose of this study was to determine whether collagen plays a significant role when included onto/into sutures by coating, or by other methods. Primary goal of this research is to investigate collagen-containing sutures, and their properties compared to same suture material without the collagen. Other goals include researching on modification techniques for sutures, and to find out whether it is sensible or not to modify the suture with collagen, and by which methods. Pure collagen sutures also exist, with both benefits and drawbacks in their properties.

Current problems in this technological field include the manufacturing of the collagen-containing sutures, since completed studies have had their own approaches that differ between each other [3], [5], [6]. There already exists a federally registered trademark on collagen-coated suture that is manufactured by Arthrex®. They offer a collagen-coated option for a FiberWire® suture that is constructed of ultra-high molecular weight polyethylene (UHMWPE) core that is coated with polyester and UHMWPE. They were the first

to commercially offer a collagen coated option, but they are not available for Eastern and Southern Hemisphere countries.

2. COLLAGEN – THE SUPPORTER OF TISSUES

The extracellular matrix is a space formed of a variety of molecules and proteins, such as collagens, elastin and fibrin. Its purpose is to grant mechanical and biochemical properties to tissues. This includes providing structural support with the fibrillar backbone of the extracellular matrix. [7], [8]

2.1 Collagen

Collagen is the most common protein in the human body. It has a variety of purposes from scar formation to being a biomaterial [7], [8], [9]. In total there are 28 different collagen types ranging from collagen type I to XXVIII [7], [10]. Different types can be distributed into fibrillar or non-fibrillar subfamilies. Collagen is the most common fibril-forming protein in the skin. About 90% of the total collagen in the human body is represented by the fibril-forming types I, II, III, V, XI. [10], [11]
Glycine, proline and hydroxyproline compose 57% of the amino acid content in collagen types I-VII [7]. Glycine is at every third position of the peptide sequence forming a $(Gly\text{-}X\text{-}Y)_n$ repeat structure. Proline is often observed at the X position and hydroxyproline at the Y position, but any other amino acid can also replace them, thus forming different variations of α-chains [7], [11]. In total, 25 different α-chain combinations have been discovered [7]. These α-chains then assemble into triple-helixes that can be formed of three identical α-chains (homotrimer) or two to three different α-chains (heterotrimer). [7]
Most prevalent collagen types in the adult dermal extracellular matrix (ECM) are collagen type I, III and V, with type I being the most abundant ranging approximately between 80-90%. The following, type III ranging between 8-11%, and type V ranking as third with about 2%. [8], [9], [10]

2.2 Collagen in cutaneous wound healing and scar formation

The objective of wound healing is to restore the original composition and function of the designated tissue [8], [12]. Regular cutaneous wound healing mainly consists of four integrated stages: haemostasis, inflammation, proliferation and remodelling [12], [13]. Different types of collagens, such as native, fibrillar or soluble fragments, are present in the wound healing process by regulating the stages.

Fibroblasts, including other cells, synthesize collagen in the dermal wound [1], [12], [13]. First collagen type to be synthesized is type III. As the healing proceeds, this type is gradually replaced by the main skin collagen type I. Foetal wounds can heal without a scar [1]. This is due to the higher ratio of collagen type III compared to type I. This ratio decreases as the foetus develops, which then leads to wound scarring. [1], [8], [12], [13]

In haemostasis, constriction of blood vessels occurs immediately after injury to prevent the loss of blood. Collagen is the activating factor of platelets. The role of platelets is to adhere and aggregate at the injury site, resulting in the accumulation of fibrin, thus forming a fibrin clot. [12], [13]

The inflammation stage involves the migration of fibroblasts, epithelial and endothelial cells to the injury site from surrounding tissues. Soluble fragments from collagen degradation recruit macrophages and other immune cells to remove microbes and weakened tissue [12]. Collagen degradation is regulated by extra- and intracellular routes. The intracellular degradation involves both membrane-bound and secreted proteolytic enzymes, whereas the intracellular degradation is regulated by the internalization of complete collagen fibrils and the fragmented collagen is broken down through enzymatic activity. Fibrosis may occur if these regulations are malfunctioning [8]. Macrophages maintain the proinflammatory environment, and may also command fibroblasts to begin the generation of the fibrous capsule [2].

During the proliferation stage, the fibrin clot is replaced by a new matrix of collagen fibres, proteoglycans and fibronectin [13]. Other important events include angiogenesis, the growth of new capillaries, and the development of granulation tissue and epithelialization. While fibroblasts synthesize new collagen molecules, the degradation of mature collagen releases fragments that furthermore promote fibroblasts to proliferate and synthesize other growth factors. These growth factors lead to the formation of new blood vessels and re-epithelialization. [12]

Final stage of wound healing is the remodelling of the tissue [1], [12], [13]. Remodelling is a process where the final scar forms. It can take years for remodelling to terminate. Myofibroblasts in the granulation tissue mature, consequently decreasing the collagen

III found in myofibroblasts and replacing it with collagen type I [1], [13]. The final scar tissue never fully gains the original mechanical properties (tensile strength ranging between 50-80%), and the functionality can be deficient. Other differences between scars and unwounded skin include collagen fibre thickness and orientation, but also the density of collagen [8]. [12], [13]

3. COLLAGEN-CONTAINING SUTURES AND SUTURE MODIFICATION

Sutures are strands of any material used for wound closure [4]. They can close blood vessels or approximate tissues. Sutures can be manufactured with one strand (monofilament) or multiple strands (multifilament). Monofilaments have a more simplified structure, which results in easier tissue passage and less organism harbouring. Multifilaments have a structure that is formed by twisting or braiding several strands together. Multiple filaments grant better tensile strength, pliability and flexibility, but they can drag the tissue more [4]. There is a myriad of materials for sutural applications, commonly categorized into absorbable and non-absorbable types. Main difference between these types is that absorbable sutures do not need removal whereas non-absorbable do. Sutures can furthermore be, sorted into natural and synthetic materials [4], [14]. The material choice depends on the purpose of the suture.

Absorbable sutures are classified as sutures that lose their tensile strength within 60 days [4]. Degradation of the material can be achieved by enzymatic degradation or hydrolysis [4], [14]. Hydrolysis is degradation caused by water, and enzymatic degradation is hydrolysis that is catalysed by enzymes. Absorbable sutures consist of, for example polyglactin (copolymer of glycolic and lactic acid) or polyglycolic acid (homopolymer of glycolic acid) [4] [15]. The degradation products depend on the used polymer. Aliphatic polyester-based sutures erode by random ester bond scission caused by water [16]. For instance, lactic acid from polylactic acid degradation is metabolized to carbon dioxide and water through the Krebs' cycle [17].

Non-absorbable sutures are sutures that are not degraded by hydrolyzation or body enzymes. Materials, such as polyamide polymer (PA) or polyethylene terephthalate (PET) can be used as non-absorbable suture applications. The need of suture removal can determine the choice of suture between absorbable and non-absorbable, since interior sutures are harder to remove compared to exterior sutures. Other factors, such as the tendency to form keloidal scars, should also be considered. [4]

Suture materials can be, for instance, modified by using different coatings on the base material [15]. This is usually done to lubricate the suture for less tissue drag, that could damage the tissue during suture implantation. Other purposes of coating include filling void space and antimicrobial agent carrying. Filling void space decreases capillarity, that

limits bacteria to spread from an infection [16]. If the material is familiar to the tissues, like collagen, the coating could also accelerate the healing process.

Collagen-based absorbable sutures are called surgical gut sutures [4]. Surgical gut is made of the intestines of bovine or ovine origin by processing highly purified collagen. Due to their natural origin, there may be inconsistencies within the performance of the strands [4], [15]. Gut sutures are separated into plain or chromic gut. The mechanical properties, such as tensile strength and absorption rate, can be altered by the collagen contents. Higher collagen content increases the stimulation of tissue reactivity, which then accelerates the absorption and tensile strength degradation [4], [14]. Collagen can also be modified in other ways, but it can also be used as a coating for other suture materials.

3.1 Plain and chromic gut

Plain gut sutures are non-modified collagen strands. They are swiftly absorbed, which limits their use for tissues that heal slowly and require high mechanical support. Acceptable tensile strength is retained for only 7 to 10 days [4]. Chromic gut is a surgical gut suture that is treated with a chromium salt solution. It increases the tensile strength and prolongs absorption (over 90 days) by decreasing tissue reactivity [4], [15]. Chromium(III) cations from chromium(III) acetate create a three-dimensional network with carboxylate groups, at least with poly(acrylamide-co-acrylic acid) [18]. Collagen also contains carboxyl and ammonium groups, that are able to form hydrogen bonding and ionic interaction [3], [19]. The inflammatory response with chromic gut is greater than the response of plain gut [20]. Chromic gut causes necrosis and granulation tissue formation in the suture environment. This is why the use of plain or chromic gut must be assessed for every occasion to achieve the best possible outcome.

3.2 Manufacturing modified sutures

There are multiple ways to manufacture sutures that have been modified with additional bioactive agents, such as antimicrobial agents, proteins and drugs [21]. Manufacturing techniques include for instance coating, melt-spinning and electrospinning. Both mono- and multifilament sutures can be coated to prevent wound infection. Coating is usually not the leading method in modified suture manufacturing, since usual surgical sutures do not have appropriate surface functional groups for the biological agents to bind into without surface modification [21]. Coating can be achieved by dipping sutures into solution that includes the wanted substance. Dipping method is the easiest since it does not need any equipment in addition to the suture and dipping solutions, but the coating surface may not become uniform [5]. Automated coating machines also exist which makes the dipping method controlled [22]. Although the dipping is automated, every strand would have to be placed one by one on the machine, which complicates the application of this method for industrial production. Coating sutures is also possible by spraying wanted agents with a pressurized gas stream [23]. The gas flow temperature can range from 20 to 1000 degrees Celsius. The gas picks up tiny powder particles of the wanted agent and then sprays the mixture on the wanted suture [23].

Melt-spinning is a manufacturing process, that uses high temperature to melt ingredients into solutions and blend them together before spinning them into a fibre. It is a common method, and applicable for industrial production. Solvent spinning requires toxic solvents to form a uniform solution, while melt-spinning does not. This makes melt-spinning more cost- and time-effective, since the recovery time from the heat is much faster than from toxins. Melt-spinning also produces fibres that include more void-free surface area than solution-spinning, which decreases capillarity [16], [24]. The produced monofilament polymer can be coated or uncoated, but multifilament fibres are also possible to manufacture by braiding or twisting the monofilament with another material. One drawback of melt-spinning is the heat, since bioactive agents may lose their activity due to the high heat. Heat resistant proteins, such as keratin, can be used with melt-spinning as a filler [25]. It can be added to thermoplastic polymers, such as polycaprolactone (PCL) to increase biocompatibility [25]. [24]

Electrospinning is also a spinning method to manufacture fibres that contain one or multiple substances. The main principle of electrospinning is a high-voltage power field that pushes the solvent from a nozzle, when the voltage is greater than the surface tension of the solution. When sprayed from the nozzle, the solution evaporates, and only solid

substances are left that form a fibre. Electrospinning produces tiny fibrous structures that greatly increase the surface-to-area ratio, which then allows more biological agents to bind [6]. Together these tiny fibres that are within the micrometre range, form a bigger fibre that can be used as a suture [26]. It is even possible to manufacture three-layer fibres, where one material forms the inner layer and another forms the outer layer, with a third material in between to separate them when the inner and outer materials are incompatible due to their functional groups. Disadvantage for electrospinning is that some of the fibres may be randomly oriented, which may decrease mechanical strength and increase abrasion [6]. [27]

The modification method depends on the used suture and desire of the modification. While the complexity increases from coating to melt-spinning to electrospinning, the affordability decreases. Simple dip coating can be achieved without machines, but other methods require some sort of professional equipment. Coating only changes the surface of the suture but melt-spinning forms the entire fibre. On the other hand, electrospinning can create totally new fibres but also produce coatings. [5], [23], [24]

3.3 Collagen incorporation into/onto sutures

As stated earlier, pure collagen has both fast absorption rate, and short tensile strength retention in tissues. On the other hand, synthetic nonabsorbable sutures do not possess biologically active properties. These limitations can be overcome by using synthetic nonabsorbable material, with greater mechanical properties, as a base, and using incorporated collagen for cell stimulation [5]. Collagen can also be, for example, electrochemically aligned to produce a collagen core material that can be then coated with growth factors, such as platelet derived growth factor-BB [28]. However, the purpose of this application is drug delivery, and not suture based reinforcement.

There are multiple ways of incorporating collagen into/onto sutures, such as weaving collagen into a base material or adsorbing native or denatured collagen onto suture. Weaving can be done for multifilament sutures, where one or several of the filaments are collagen fibres. Native collagen has the triple-helix form, while denaturation opens the structure into individual α-helixes. Both native and denatured collagen can be woven onto sutures; however, while denatured collagen enhances biological activity, it does so at the price of better mechanical strength. Denaturation can be achieved by, for example

heat treatment [5]. Collagen can also be incorporated into the suture by electrospinning fibres from solutions that contain multiple polymers, such as a mixture of collagen and PCL [6]. This process produces a fibre that has a uniform structure and fibre alignment [6].

4. COLLAGEN-CONTAINING MATERIAL COMPARISON

Suture properties, such as load to failure, wound healing efficacy, and tensile strength are compared in this chapter. Both in vivo, and in vitro studies were considered. In vitro study ‘’Tendon and bone responses to a collagen-coated suture material’’ by Mazzocca et al. was performed on human osteoblast (HOB) and tenocyte cells in a cell culture [5]. A rat experimental model was used for the in vivo study ‘’Fabrication of atelocollagen-coated bioabsorbable suture and the evaluation of its regenerative efficacy in Achilles tendon healing using a rat experimental model’’ by Y.H. Yeo et al [3]. Third study, “Highly Aligned Electrospun Collagen/Polycaprolactone Surgical Sutures with Sustained Release of Growth Factors for Wound Regeneration” conducted by J. Hu et al. [6] studied electrospun collagen-containing suture by mechanical evaluation, and in vivo using a mouse model.

4.1 Study design in the compared articles

The aim of the in vitro study by Mazzocca et al. was to evaluate whether weaving collagen onto polyester/polyethylene (PE/PEE) or coating PE/PEE sutures with type I collagen would enhance suture properties [5]. Evaluated properties include cell adhesion and proliferation, and furthermore the quantification of mechanical strength, durability and time. Alkaline phosphatase activity was also evaluated. Both native and denatured collagen were tested in the coating process, both on knotted and unknotted sutures. The manufacturer had already treated the native collagen with pepsin to remove telopeptides and other feasible protein impurities. Shelf-life (fresh vs. 6 weeks) and sterilization tests were also assessed. HOB and tenocyte responses were evaluated by culturing them on both coated and uncoated sutures. The HOBs and tenocytes were gathered from human bone and tendon samples. Comparison of the study design can be seen in **Table 1.** [5]

Table 1. Study design comparison

Study	*Study type*	*Test subject*	*Experimental groups / materials*	*Key procedure / approach*
Mazzocca et al.[5]	In vitro	Human osteoblasts and tenocytes	Coated and uncoated PE/PEE sutures with native and denatured collagen, both knotted and unknotted. Shelf-life (fresh vs. 6 weeks) and sterilization variations	Culturing HOBs and tenocytes on sutures. Evaluating their adhesion and proliferation, but also studying alkaline phosphatase activity
Y.H Yeo et al. [3]	In vivo	Sprague-Dawley rats (adult male, n=42, divided into three groups of 14)	Regular Vicryl (VC), pDOPA-coated VC, pDOPA- and atelocollagen-coated VC	Surgical rupture and repair of Achilles tendon. Healing evaluation at 1 and 6 weeks post-op.
J. Hu et al. [6]	In vivo	C57BL/6 mice (male, n=24, divided into four groups of six)	Regular PCL, COL@PCL (incorporated collagen), and bFGF-COL@PCL (excluded from further comparisons)	Surgical procedure: dorsal line incisions. Healing evaluation on days 0, 3, 5, 7, 10, and 13

The in vivo study by Y.H Yeo et al. investigated the coating of a copolymer of glycolic acid and lactic acid, thus forming poly(lactic-co-glycolic) acid (PLGA) [3]. Vicryl, which is a PLGA trademark, was further modified using a hydrophilic biomimetic polymer called 3,4-dihydroxy-L-phenylalanine (pDOPA) to modify the hydrophobic nature of the PLGA surface. pDOPA forms hydrogen bonds with both PLGA and collagen, which strengthens the molecular connections. This aimed to create a base for type I atelocollagen to bond into. Coating success evaluation was then performed. Terminal telopeptides of the collagen were removed by proteolytic enzymes to form atelocollagen. Atelocollagen has low immunogenicity and antigenicity, which makes it suitable for use in injuries. The key

procedure was surgical rupture and repair of the Achilles tendon. Three adult male rat groups of Sprague-Dawley strain from a total of 42 were formed (14 each), which were then operated and assigned with different suture materials. First group was regular Vicryl (VC), the second DOPA-polymer-coated VC/pDOPA, and the last one pDOPA and atelocollagen-coated VC/pDOPA/Col. Healing evaluation was performed at 1 and 6 weeks post operation. [3]

The aim of the study by J. Hu et al. was to fabricate and characterize collagen and basic fibroblast growth factor (bFGF) onto PCL, thus forming bFG-COL@PCL. Other aim was to evaluate whether suture modification had enhancing properties on wound healing. Experimental animal model that was used was C57BL/6 mouse. 24 male mice were operated surgically by making two 1 cm long incisions on both sides of each individuals' dorsal line. Then the mice were randomly distributed into four groups of six, each assigned with a different suture material. In total there were 48 incisions. 12 for PCL, COL@PCL, bFGF-COL@PCL and Vicryl each. Healing evaluation occurred on days 0, 3, 5, 7, 10, and 13. The bFGF brings an additional variable in addition to collagen, which is why it will not be present in further analyses. [6]

4.2 Suture fabrication methods

Different methods were used to fabricate sutures, primarily by adding collagen or other modifications to enhance properties. Differences in the collagen adhesion between PE/PEE/COL and VC/pDOPA/Col may have significance, since Vicryl was modified to decrease the hydrophobic nature, and PE/PEE was not. There were also differences in collagen coating techniques between both studies. The study by Mazzocca et al. explored weaving collagen onto high strength nonabsorbable PE/PEE sutures. However, due to the impracticality of manufacturing, this method was dismissed, despite showing favourable results compared to other commercial suture materials. Another method used was adsorbing collagen onto the PE/PEE suture by dipping it into a collagen solution. Denatured collagen solution that was used had a concentration of 0.5 mg/mL (0.05%). The dip-coating was achieved by dipping the sutures five times for 1 second only. These sutures were then air-dried under a laminar flow hood. Differences in suture fabrication methods can be seen in **Table 2.** [5]

Table 2. Suture fabrication methods

Feature	*PE/PEE/Col [5]*	*VC/pDOPA/Col [3]*	*PCL@COL [6]*
Base suture material	High strength nonabsorbable polyester/polyethylene (PE/PEE)	Vicryl (PLGA)	Polycaprolactone (PCL)
Collagen application method	Weaving (dismissed due to impracticality) and adsorption by dipping	Adsorption by dipping onto DOPA-coated PLGA	Dissolved in HFIP with PCL, then electrospun
Coating period	Dipped five times for 1 second each	Immersed for 10, 30, or 60 minutes	N/A
Post-coating	Air-dried under laminar flow hood. Washing not stated	Washed with deionized water after coating. Dried in a vacuum at 25 °C for 12 hours	Not detailed
Impracticalities mentioned	Weaving collagen onto PE/PEE was impractical for manufacturing	None mentioned	None mentioned

Vicryl (PLGA) sutures were modified to decrease their hydrophobic nature in the study by Y.H. Yeo et al. It involved dipping DOPA-coated Vicryl into a 0.5% collagen solution to achieve collagen coating. Three samples were produced by immersing the base material in the solution for 10, 30, or 60 minutes at room temperature. These samples were then washed with deionized water. After washing, they were dried in a vacuum at 25 °C

for 12 hours to prevent collagen deterioration. Weighing occurred after the sutures were dried. [3]

For collagen-containing polycaprolactone, the study by J. Hu et al. prepared solutions by dissolving collagen in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP). PCL was then added to this solution, and the mixture was stirred until thoroughly mixed. This mixture was then electrospun to create the PCL@COL monofilaments. Scanning electron microscopy (SEM) images showed that the electrospinning technique resulted in "well-aligned nanofibre bundles with very smooth nanosized fibre surfaces".

Every study had a distinct approach. Two studies used collagen as a coating on existing sutures (PE/PEE and Vicryl), while the third integrates collagen within PCL during the electrospinning process. This difference in integration might influence the interactions with tissues. Coating methods also varied. PE/PEE was dipped very briefly multiple times, while Vicryl was dipped for much longer durations after being pre-treated with DOPA. The pre-treatment of Vicryl may have significance, since Vicryl was modified to decrease the hydrophobic nature, and PE/PEE was not. VC/pDOPA/Col samples were also washed with deionized water after coating, which might, for example, detach collagen strands, that are not fully attached.

4.3 Suture properties

Suture properties were evaluated through both in vitro cell studies and in vivo animal models. Key properties that were examined include cell interaction, mechanical performance, degradation, and tissue healing response. These studies differed in their focus; in vitro studies concentrated on cell response, while in vivo studies examined the effects of collagen on tissue repair processes. [3], [5], [6]

4.3.1 Mechanical properties

Mechanical tests were conducted on both the modified sutures and the operated tissues (tendons or wounds). When examining denatured collagen-coated PE/PEE sutures alongside uncoated PE/PEE sutures, no significant differences were found in their peak load or load to failure values [5]. In a separate study evaluating Vicryl, VC/pDOPA, and

VC/pDOPA/Col sutures, the VC/pDOPA/Col suture demonstrated a significantly increased load to failure when compared to both the VC/pDOPA and standard Vicryl sutures [3]. When examining the mechanical strength of operated tendons in the rat model, there were no notable changes in load to failure among the groups at week 1. However, by 6 weeks post-operation, the most prominent difference in load to failure was observed between VC/pDOPA and VC/pDOPA/COL, with the VC/pDOPA/COL group exhibiting the highest values. The load to failure for the native tendon at 6 weeks was approximately the same as that for the Vicryl group. For electrospun PCL and PCL@COL materials, tensile tests indicated that PCL@COL achieved slightly higher tensile strength and elastic modulus values compared to PCL, although the difference in maximum tensile strength and elastic modulus was not that significant [6].

4.3.2 In vitro results

Results from the study conducted by Mazzocca et al. showed varying values for the collagen-modified PE/PEE sutures. Regular uncoated PE/PEE, native collagen-coated PE/PEE (NC), and denatured collagen-coated PE/PEE (DC) were compared. Scanning electron microscopy showed that the collagen fibres were aligned with the fibres of PE/PEE when using denatured collagen. Results of the adhesion and proliferation assays for HOBs can be seen in **Table 3.** The cell adhesions were observed at 24 hours, while proliferations were observed at 48 hours. Every knotted suture was tested after forming abrasion to simulate real wear. Commercially available sutures include MaxBraid, Herculine, Orthocord, FiberWire and Ethibond. [5]

Table 3. Comparison of HOB adhesion and proliferation [5].

Assay type	*Suture type*	*Comparison suture group*	*Results*
Adhesion	Collagen woven	Commercially available sutures	No significant difference
Proliferation	Collagen woven	Commercially available sutures	250% increase
Adhesion	NC-coated	DC-coated and uncoated	No significant difference
Proliferation	DC-coated	NC-coated and uncoated	90% increase over NC and 170% increase over uncoated
Adhesion	DC-coated with additional 5 dips in collagen	Uncoated	150% increase
Proliferation	DC-coated with additional 5 dips in collagen	Uncoated	120% increase
Proliferation	DC-coated knotted	Uncoated knotted	240% increase
Adhesion	DC-coated after 6 weeks	DC-coated freshly prepared	No significant difference
Proliferation	DC-coated after 6 weeks	DC-coated freshly prepared	No significant difference
Adhesion	DC-coated UV sterilized	DC-coated ethylene oxide sterilized	No significant difference
Proliferation	DC-coated UV sterilized	DC-coated ethylene oxide sterilized	No significant difference

Results from adhesion and proliferation assays for tenocytes can be seen in **Table 4**. All the assays performed on HOBs, such as sterilization tests, were not performed on tenocytes.

Table 4. Comparison of tenocyte adhesion and proliferation [5].

Assay type	*Suture type*	*Comparison suture group*	*Results*
Adhesion	Collagen woven	Commercially available sutures	No significant difference, more tenocytes adhered than HOBs
Proliferation	Collagen woven	Commercially available sutures	690% increase
Adhesion	NC-coated	DC-coated and uncoated	No significant difference
Proliferation	DC-coated	NC-coated and uncoated	80% increase over NC and 270% increase over uncoated
Adhesion	NC and DC-coated knotted	Uncoated knotted	110% increase
Proliferation	DC-coated knotted	Uncoated knotted	80% increase

A 24-hour cell adhesion assay demonstrated a significant increase in adhesion of both HOBs and tenocytes on collagen-coated PE/PEE sutures compared to uncoated PE/PEE. When comparing native and denatured collagen coatings on PE/PEE, no significant difference in cell adhesion was observed. However, knotted, denatured collagen-coated PE/PEE sutures subjected to abrasion (to simulate wear) showed the most fa-

vourable adhesion and proliferation of both HOBs and tenocytes, outperforming uncoated, unknotted PE/PEE. Insignificant differences were seen for HOBs and tenocytes in both adhesion and proliferation assays when comparing wet and dry sutures. [5]

Overall, both native and denatured collagen-coated PE/PEE sutures exhibited significantly improved HOB and tenocyte adhesion compared to uncoated PE/PEE, regardless of knotting. Sterilization methods did not significantly affect adhesion nor proliferation outcomes. Regarding proliferation, promising results were observed for both woven collagen and denatured collagen-coated sutures, whether knotted or not. [5]

Alkaline phosphatase activity, a marker of bone mineralization, was also assessed. Denatured collagen-coated sutures, both knotted and unknotted, demonstrated the highest alkaline phosphatase activity. In contrast, native collagen-coated sutures (knotted and unknotted) showed no significant improvement compared to the corresponding uncoated PE/PEE controls. [5]

4.3.3 In vivo results

The compared studies describe two primary in vivo investigations: one focusing on rat Achilles tendon repair using Vicryl, VC/pDOPA, and VC/pDOPA/Col sutures, and another evaluating mouse acute incision wound healing with PCL, PCL@COL, and Vicryl sutures [3], [6]. Both studies employed collagen-modified sutures and compared their performance to standard materials, allowing for direct evaluation of the impact of the modifications in a biological environment. Results from the study by Y.H Yeo et al. can be seen in **Table 5** [3]. Properties compared include Load to Failure (LtF), Modified Bonar Score (MBS), Mean Collagen Fibril Diameter (MCFD), Cross-Sectional Area (CSA), and stress. Load to failure, Suture value for native tendon was not applicable (NA), since the value was only for suture materials before operation. Specific stress value at week 6 for VC/pDOPA was not available, but it was comparable to the Vicryl value above.

Table 5. Comparison of properties across multiple materials [3].

Material	*LtF, Suture (N)*	*LtF, Tendon (N)*	*MBS at Week 1*	*MBS at Week 6*	*MCFD (nm)*	*CSA at Week 1 (mm^2)*	*Stress at Week 6 (N/mm^2)*
Native Tendon	NA	31.4 ± 10.6	0	0	154.9 ± 31.9	5.5 ± 1.9	6.5 ± 3.6
Vicryl	22.9 ± 4.1	31.6 ± 5.7	13.7 ± 0.6	9.0 ± 1.0	66.3 ± 20.2	25.8 ± 3.3	1.4 ± 0.3
VC/pDOPA	21.0 ± 2.1	25.3 ± 6.9	11.0 ± 2.0	8.3 ± 1.5	76.7 ± 21.2	14.5 ± 3.6	NA
VC/pDOPA/Col	27.6 ± 3.8	46.2 ± 4.7	9.7 ± 2.1	6.3 ± 0.6	171.0 ± 62.6	23.1 ± 4.8	2.5 ± 0.6

Histological assessment using a modified Bonar score evaluated tissue healing characteristics, with lower scores indicating more normal histology. The largest modified Bonar score at week 1 was for the Vicryl group, indicating less favourable initial healing characteristics compared to the modified sutures. Both VC/pDOPA and VC/pDOPA/Col showed lower scores at week 1, with VC/pDOPA/Col having the lowest score, suggesting better early healing histology. All modified Bonar scores decreased from week 1 to week 6 across all groups, indicating improvement in histology over time, and the rate of decrease was similar for all. By week 6, the lowest modified Bonar score was observed for the VC/pDOPA/Col group, implying the most favourable healing outcome based on this histological assessment among the operated groups. Comparing to the native tendon (which was not operated) may not be a fair comparison for the Bonar score, since Bonar score is 0 for healthy tissues. [3]

Measurements of the tendon's cross-sectional area showed that at week 1, areas were similar between Vicryl and VC/pDOPA/Col, while the VC/pDOPA group was lower. All operated groups had significantly larger cross-sectional areas compared to the native tendon at week 1. By week 6, the areas between the Vicryl, VC/pDOPA, and VC/pDOPA/Col groups were rather similar, but still considerably larger than the native

tendon. Stress values at week 6 showed differences, with VC/pDOPA/Col having the highest value compared to Vicryl. [3]

Analysis of collagen fibril diameters using transmission electron microscopy at week 1 showed that mean diameters were similar between the Vicryl and VC/pDOPA groups. However, the VC/pDOPA/Col group had much larger fibril diameters at this early stage. For reference, the mean fibril diameter in the native tendon was roughly double that of VC/pDOPA and slightly smaller than VC/pDOPA/Col. This suggests the collagen coating might influence early collagen synthesis and organization. Western blot analysis provided further insight into protein expression. The source compared the band intensities of collagen types I and III (COL1, COL3) and vascular endothelial growth factor (VEGF) relative to b-actin. While a table of these specific comparisons is not provided, the narrative implies that the VC/pDOPA/Col group showed potentially favourable trends in these markers related to tissue regeneration and vascularization compared to the other groups at different time points, though challenges in the Western blot procedure are noted. Overall, the study concluded that the VC/pDOPA/Col group was superior in all the comparisons performed among the tested suture materials in this tendon repair model. [3]

In the mouse acute incision wound healing model, PCL, PCL@COL, and Vicryl sutures were compared. Suture degradation time was evaluated. Vicryl sutures disappeared completely by day 3, and PCL began to disintegrate on day 5. The degradation of PCL@COL sutures was significantly slower, with approximately 70% degradation observed on day 5. Dermoscopic images over 13 days indicated that the efficacy of wound healing increased notably with the PCL@COL group, suggesting that the integration of collagen accelerated wound closure. Results from the study conducted by J. Hu et al. can be seen in **Table 6.** The comparison includes the materials PCL, PCL@COL and Vicryl. Maximum tensile strength (MTS), elastic modulus (EM), mean collagen deposition density (MCDD), quantified unhealed epithelium (QUE), quantified epithelium thickness (QET), expression density of Ki67 (Ki67), and formation of vessels per field (FoV). Maximum tensile strengths and elastic moduli were measured at different strain values. The strain was 63% for PCL and 68% for PCL@COL. [6]

Table 6. Comparison of properties across multiple materials [6].

Material	*MTS (kPA)*	*EM (kPA)*	*MCDD (day 5)*	*MCDD (day 13)*	*QUE, day 5 (mm)*	*QET, day 5 (μm)*	*Ki67, day 5 (%)*	*FoV (per field)*
PCL	2.43 ± 0.34	11.62 ± 0.26	5.5	6.6	2.9	117.18 ± 33.39	68.12 ± 5.27	4.00 ± 1.73
PCL@COL	2.83 ± 0.34	16.20 ± 0.67	6.7	8.6	0.22	98.09 ± 21.06	79.55 ± 1.63	5.00 ± 1.00
Vicryl	NA	NA	7.1	7.9	1.5	173.27 ± 38.97	74.80 ± 2.31	1.76 ± 0.58

Histological comparisons using hematoxylin-eosin staining showed no significant difference in healing observed at day 5 among the groups. By day 13, PCL showed the thinnest skin, while PCL@COL and Vicryl were quite similar in thickness. Collagen deposition density, assessed by Masson trichrome staining, increased over time for all groups. PCL@COL consistently showed the highest value for mean collagen deposition density on both day 5 and day 13. While PCL@COL and Vicryl values were similar, PCL@COL remained the largest at day 13, indicating that collagen promoted healing properties on PCL. [6]

Re-epithelization, evaluated by immunohistological staining of cytokeratin, suggested faster re-epithelization for the COL@PCL group compared to PCL or Vicryl, with greater keratinocyte production. Quantified unhealed epithelium on day 5 revealed that PCL@COL had a significantly lower value compared to both Vicryl and PCL, with Vicryl's value being half that of PCL. However, paradoxically, quantified epithelium thickness on day 5 showed that Vicryl had the highest thickness, followed by PCL, and then PCL@COL, suggesting that based on thickness, re-epithelization might have been slowest for PCL@COL at this early stage. [6]

Immunofluorescent staining of Ki67-labeled cells was used to quantify cell proliferation at mitosis. Higher density of Ki67 expression indicates higher amount of proliferation. Statistical analysis showed that the expression density for PCL was the lowest, but between Vicryl and PCL@COL there was no significant difference. The formation of new

blood vessels was evaluated by vascular endothelial cells marker (CD 31). Higher expression of CD 31 indicates greater formation of vessels. The quantitatively evaluated values of formation of vessels per field were highest for PCL@COL. The value was rather similar to regular PCL, but significantly larger compared to Vicryl. [6]

Both studies showcased beneficial properties for the modified sutures [3], [6]. Mechanical properties, such as maximum tensile strength in PCL@COL and load to failure in VC/pDOPA/Col, increased compared to their unmodified counterparts. Histological properties, such as Ki67 expression in PCL@COL and modified Bonar score in VC/pDOPA/Col also increased compared to unmodified sutures. Thus, it can be said that incorporating collagen onto/into sutures enhanced both mechanical and histological properties in these applications. It is important to note that these in vivo results were obtained in rodent models. Collagen fibre patterns in normal human skin differ from those in rodent skin, forming a crosslinking basketweave-like structure in humans versus a reticular structure in rodents [8]. Therefore, it cannot be assumed that these materials would behave identically in human skin.

5. CONCLUSIONS

Collagen, the most abundant protein in the human body, is a crucial component of the extracellular matrix, providing essential mechanical and biochemical properties to tissues, including structural support. With 28 different types ranging from I to XXVIII, collagen plays diverse roles, from forming the structural backbone of skin as the most common fibril-forming protein to being involved in scar formation and acting as a biomaterial. The prevalent types in the adult dermal extracellular matrix are collagen types I, III, and V, with type I being the most abundant. Collagen's structure is characterized by a triple-helix formed by alpha-chains, with a high content of glycine, proline, and hydroxyproline forming $(Gly\text{-}X\text{-}Y)_n$ repeats.

The objective of wound healing is the restoration of the original tissue composition and function. This process involves integrated stages including haemostasis, inflammation, proliferation, and remodelling. Collagen plays a significant role throughout wound healing, activating platelets for clot formation during haemostasis and its degradation products recruiting immune cells like macrophages during inflammation. Fibroblasts synthesize collagen in the wound, initially producing type III, which is gradually replaced by type I as healing progresses. This transition is the most important, as a higher ratio of collagen type III to type I is observed in foetal wounds that heal without scarring, whereas this ratio decreases with development, leading to scarring in adult wounds. During proliferation, a new matrix of collagen fibres replaces the fibrin clot, and collagen fragments promote fibroblast activity and the synthesis of growth factors. The final remodelling stage involves myofibroblasts replacing collagen III with collagen type I, forming the final scar tissue. Notably, scar tissue does not fully regain the original mechanical properties and functional capacity of unwounded skin.

Sutures are materials used for wound closure, available in monofilament or multifilament forms, and categorized as absorbable or non-absorbable, and natural or synthetic. While absorbable sutures degrade within 60 days through hydrolysis or enzymatic activity, non-absorbable sutures are not degraded by body enzymes or hydrolyzation and require removal when healed. Collagen-based absorbable sutures, known as surgical gut sutures, are made from highly purified collagen from bovine or ovine intestines. These can be plain gut, which is swiftly absorbed and has limited tensile strength retention (7-10 days), or chromic gut, treated with chromium salt to prolong absorption (over 90 days) and increase tensile strength by decreasing tissue reactivity. However, plain gut is less reactive

than chromic gut, which causes greater inflammatory response, necrosis, and granulation tissue formation.

Given the natural limitations of pure collagen sutures, such as fast absorption and short tensile strength retention, and the lack of biological activity in synthetic nonabsorbable sutures, incorporating collagen into or onto synthetic sutures presents a promising approach. This strategy influences the superior mechanical properties of synthetic materials with adding the cell-stimulating properties of collagen. Various methods exist for manufacturing modified sutures with added bioactive agents, including coating, spraying, melt-spinning, and electrospinning. Coating involves applying substances to the suture surface, potentially accelerating healing if the material, like collagen, is familiar to tissues. Spraying utilizes a powdered material that gets sprayed onto suture with gas. Melt-spinning uses high temperatures to form solutions for spinning, while electrospinning utilizes a high-voltage field to produce fine fibres with a large surface area for biological agent binding. Collagen can be incorporated by weaving collagen fibres into multifilament sutures or by electrospinning fibres from collagen mixtures. Both native and denatured collagen can be woven, although denaturation enhances biological activity at the cost of mechanical strength. Collagen-coating is also an option.

Since collagen is abundantly present in wound healing, collagen-containing sutures also improve multiple aspects of wound closure, such as mechanical properties and cell proliferation in the target area. Even though the core material was different between the inspected studies, it can be said that the application of collagen was beneficial for each study and holds significance. It was also beneficial despite the different approaches in coating technique. In vitro studies are unable to fully replicate the wound site environment, which affects the reliability of the results. Multiple additional large scale animal experiments, including human experiments, should be completed to acquire trustworthy knowledge of the effects of collagen-containing sutures. This also applies to the in vivo studies already conducted, since the animal sample size was quite small across all studies. Studies should also be conducted on several coating/incorporating techniques to see the most prominent approach for each application. It can be said that collagen-modifications are sensible, but some methods are more notable for mass production, such as coating and melt-spinning (though not for collagen) while others, such as electrospinning are better for applications of high specificity. However, these are not the only alterations that can be done to sutures, which allows the research of suture modification to continue further with a variety of different materials and methods.

In summary, combining the mechanical strength of synthetic sutures with the biological benefits of collagen holds potential for enhancing wound healing outcomes. By utilizing

techniques like weaving, adsorption, or electrospinning, sutures can be designed to support tissue closure effectively while simultaneously promoting the body's natural healing processes through collagen's inherent properties. The choice of material modification method depends on the desired outcome and the specific suture material, with complexity increasing from coating to melt-spinning to electrospinning. Further research and development in this area could lead to improved surgical materials that not only physically close wounds, but also actively contribute to optimal tissue repair and regeneration. Due to the differences in study focus, the observed benefits are study-specific and insufficient for comparison across studies.

REFERENCES

[1] G. S. Schultz, G. A. Chin, L. Moldawer, and R. F. Diegelmann, 'Principles of Wound Healing', in *Mechanisms of Vascular Disease: A Reference Book for Vascular Specialists*, R. Fitridge and M. Thompson, Eds., Adelaide (AU): University of Adelaide Press, 2011. Accessed: Feb. 04, 2025. [Online]. Available: http://www.ncbi.nlm.nih.gov/books/NBK534261/

[2] R. A. Bank, J. Zandstra, H. Room, A. H. Petersen, and S. M. Van Putten, 'Biomaterial Encapsulation Is Enhanced in the Early Stages of the Foreign Body Reaction During Conditional Macrophage Depletion in Transgenic Macrophage Fas-Induced Apoptosis Mice <sup/>', *Tissue Eng. Part A*, vol. 23, no. 19–20, pp. 1078–1087, Oct. 2017, doi: 10.1089/ten.tea.2016.0499.

[3] Y. H. Yeo *et al.*, 'Fabrication of atelocollagen-coated bioabsorbable suture and the evaluation of its regenerative efficacy in Achilles tendon healing using a rat experimental model', *Int. J. Biol. Macromol.*, vol. 271, p. 132564, Jun. 2024, doi: 10.1016/j.ijbiomac.2024.132564.

[4] D. L. Dunn, 'Wound Closure Manual'. Jan. 01, 2007. [Online]. Available: https://anwresidency.com/simulation/guide/resources/Ethicon_Wound_Closure_manual.pdf

[5] A. D. Mazzocca *et al.*, 'Tendon and bone responses to a collagen-coated suture material', *J. Shoulder Elbow Surg.*, vol. 16, no. 5, pp. S222–S230, Sep. 2007, doi: 10.1016/j.jse.2007.02.113.

[6] J. Hu *et al.*, 'Highly Aligned Electrospun Collagen/Polycaprolactone Surgical Sutures with Sustained Release of Growth Factors for Wound Regeneration', *ACS Appl. Bio Mater.*, vol. 3, no. 2, pp. 965–976, Feb. 2020, doi: 10.1021/acsabm.9b01000.

[7] L. E. Tracy, R. A. Minasian, and E. J. Caterson, 'Extracellular Matrix and Dermal Fibroblast Function in the Healing Wound', *Adv. Wound Care*, Feb. 2016, doi: 10.1089/wound.2014.0561.

[8] L. Gardeazabal and A. Izeta, 'Elastin and collagen fibres in cutaneous wound healing', *Exp. Dermatol.*, vol. 33, no. 3, p. e15052, Mar. 2024, doi: 10.1111/exd.15052.

[9] Y.-D. Nien, Y.-P. Han, B. Tawil, L. S. Chan, T.-L. Tuan, and W. L. Garner, 'Fibrinogen inhibits fibroblast-mediated contraction of collagen', *Wound Repair Regen.*, vol. 11, no. 5, pp. 380–385, 2003, doi: 10.1046/j.1524-475X.2003.11511.x.

[10] P. Li and G. Wu, 'Roles of dietary glycine, proline, and hydroxyproline in collagen synthesis and animal growth', *Amino Acids*, vol. 50, no. 1, pp. 29–38, Jan. 2018, doi: 10.1007/s00726-017-2490-6.

[11] E. Davison-Kotler, W. S. Marshall, and E. García-Gareta, 'Sources of Collagen for Biomaterials in Skin Wound Healing', *Bioengineering*, vol. 6, no. 3, p. 56, Jun. 2019, doi: 10.3390/bioengineering6030056.

[12] K. Gelse, 'Collagens—structure, function, and biosynthesis', *Adv. Drug Deliv. Rev.*, vol. 55, no. 12, pp. 1531–1546, Nov. 2003, doi: 10.1016/j.addr.2003.08.002.

[13] S. S. Mathew-Steiner, S. Roy, and C. K. Sen, 'Collagen in Wound Healing', *Bioengineering*, vol. 8, no. 5, p. 63, May 2021, doi: 10.3390/bioengineering8050063.

[14] M. Crumplin, 'Some Everyday Surgical Instruments: Part 13 - Surgical suture material', *Br. J. Surg.*, vol. 110, no. 12, pp. 1685–1687, Nov. 2023, doi: 10.1093/bjs/znad257.

[15] B. D. Ratner, *Biomaterials science: an introduction to materials in medicine*, 3rd ed. Amsterdam Boston: Elsevier/Academic Press, 2013.

[16] J. N. Im, J. K. Kim, H.-K. Kim, C. H. In, K. Y. Lee, and W. H. Park, 'In vitro and in vivo degradation behaviors of synthetic absorbable bicomponent monofilament suture prepared with poly(p-dioxanone) and its copolymer', *Polym. Degrad. Stab.*, vol. 92, no. 4, pp. 667–674, Apr. 2007, doi: 10.1016/j.polymdegradstab.2006.12.011.

[17] G. J. Jaffe, P. Ashton, and P. A. Pearson, *Intraocular Drug Delivery*. Hoboken: Taylor and Francis, 2013.
[18] L. P. Krul *et al.*, 'Interaction of carboxylated polyacrylamide with chromium(III) acetate: 13C NMR study of mechanism', *Russ. J. Gen. Chem.*, vol. 83, no. 11, pp. 2027–2031, Nov. 2013, doi: 10.1134/S1070363213110091.
[19] A. Sorushanova *et al.*, 'The Collagen Suprafamily: From Biosynthesis to Advanced Biomaterial Development', *Adv. Mater.*, vol. 31, no. 1, p. 1801651, Jan. 2019, doi: 10.1002/adma.201801651.
[20] M. G. S. Andrade, R. Weissman, and S. R. A. Reis, 'Tissue reaction and surface morphology of absorbable sutures after in vivo exposure', *J. Mater. Sci. Mater. Med.*, vol. 17, no. 10, pp. 949–961, Oct. 2006, doi: 10.1007/s10856-006-0185-8.
[21] H. Li, Z. Wang, J. A. Robledo-Lara, J. He, Y. Huang, and F. Cheng, 'Antimicrobial Surgical Sutures: Fabrication and Application of Infection Prevention and Wound Healing', *Fibers Polym.*, vol. 22, no. 9, pp. 2355–2367, Sep. 2021, doi: 10.1007/s12221-021-0026-x.
[22] K. Cetiner, B. Guclu, and S. Mihcin, 'Multifunctional automated angle-controlled multi-immersion coating machine for use in biomedical implant coatings', in *2019 Medical Technologies Congress (TIPTEKNO)*, Izmir, Turkey: IEEE, Oct. 2019, pp. 1–4. doi: 10.1109/TIPTEKNO47231.2019.8972040.
[23] T.-Y. Liao *et al.*, 'Multifunctional cold spray coatings for biological and biomedical applications: A review', *Prog. Surf. Sci.*, vol. 97, no. 2, p. 100654, May 2022, doi: 10.1016/j.progsurf.2022.100654.
[24] A. Lowe, W. Deng, D. W. Smith, and K. J. Balkus, 'Acrylonitrile-Based Nitric Oxide Releasing Melt-Spun Fibers for Enhanced Wound Healing', *Macromolecules*, vol. 45, no. 15, pp. 5894–5900, Aug. 2012, doi: 10.1021/ma300913w.
[25] A. Ghosh, A. Ali, and S. R. Collie, 'Effect of Wool Keratin on Mechanical and Morphological Characteristics of Polycaprolactone Suture Fibre', *J. Text. Eng.*, vol. 63, no. 1, pp. 1–4, 2017, doi: 10.4188/jte.63.1.
[26] J. Teno, M. Pardo-Figuerez, Z. Evtoski, C. Prieto, L. Cabedo, and J. M. Lagaron, 'Development of Ciprofloxacin-Loaded Electrospun Yarns of Application Interest as Antimicrobial Surgical Suture Materials', *Pharmaceutics*, vol. 16, no. 2, p. 220, Feb. 2024, doi: 10.3390/pharmaceutics16020220.
[27] L. Xu, Y. Liu, W. Zhou, and D. Yu, 'Electrospun Medical Sutures for Wound Healing: A Review', *Polymers*, vol. 14, no. 9, p. 1637, Apr. 2022, doi: 10.3390/polym14091637.
[28] M. Younesi, B. O. Donmez, A. Islam, and O. Akkus, 'Heparinized collagen sutures for sustained delivery of PDGF-BB: Delivery profile and effects on tendon-derived cells In-Vitro', *Acta Biomater.*, vol. 41, pp. 100–109, Sep. 2016, doi: 10.1016/j.actbio.2016.05.036.