REVIEW ARTICLE

Bioactive Sutures: A Review of Advances in Surgical Suture Functionalisation

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ABSTRACT

Sutures have been at the forefront of surgical medicine throughout time. With recent advances in suture technology, it has been possible to incorporate biologically active substances to enhance suture function and capability. Bioactive sutures represent a modality interest in controlled drug and cell delivery to traumatic sites. In this article, a comprehensive literature search of key bibliographic databases focusing on suture material fabrication and advanced modification was performed. The history, manufacturing process and cost-effectiveness of bioactive sutures are presented. Several novel modifications to enhance function in drug and growth factor delivery and cell therapy are also reviewed. Different antimicrobial drugs and anaesthetics have been shown to be effective in reducing inflammation and bacterial infection. Cellular therapy represents a unique modality augmenting the surgical repair of various soft tissue injuries. We propose a definition of bio-active sutures as *biomaterials that are engineered to have controlled*

tissue interaction to optimise wound/defect healing, in addition to their essential function in tissue approximation.

Keywords:

Surgery; Sutures; Wounds; Biomaterial; Bio-functionalization; Activation

1. INTRODUCTION

A suture is a strand of material used to approximate tissue or ligate blood vessels. Ligatures, often synonymous with sutures, are the same strands of material used to tie ends of structures to stop leakage, for example a blood vessels [1]. Sutures are generally categorized by a combination of their absorption, their fibre construct, or their origin as shown in **Table 1**. With ever-changing technology and a better understanding of cellular science, it is inevitable that suture technology will be enhanced to provide better quality and outcomes. Strength, different degrees of absorption, sterility, and high knot security, lack of allergic reaction together with ease of handling are among the important properties of an ideal suture material [1-3].

This article will give an in depth focus on the current trends in modifying suture materials to make them biologically active, and highlight novel studies that explore new possibilities.

Categorization	Types
Based on Absorption	• Absorbable. • Non Absorbable
Based on Fibre construct	• Monofilament • Multifilament/Twisted/Braided
Based on Origin	• Synthetic • Natural

Table 1. General categorizations of different suture thread materials.

2. BIOACTIVE SUTURES APPLICATION

Several applications of suture modifications have been reported. In the following section, a review of the different trials is discussed. Summary of reported trials is found in **Table 2.**

2.1. BIOACTIVE SUTURES IN DRUG DELIVERY

Commonly used biomaterials in sutures are recognised as foreign materials within the body, and often trigger a host of immune response. These processes can increase the chances of a surgical site infection (SSI) [4]. Additionally, the suture itself can be a vessel for bacterial colonisation that can result in an SSI [5].

The use of bioactive sutures coated with antimicrobial drugs and anaesthetics have been shown to be effective in reducing inflammation and bacterial infection in the wound site [6, 7]. The first commercially available antimicrobial suture was a polyglactin suture loaded with triclosan (Vicryl Plus®) in 2002 [8]. The initial method of drug delivery was to coat the suture with a second biodegradable layer but there was limited control over the rate of drug release, which is a critical factor for optimised wound healing [9]. Electro-spinning technique was implemented as an alternative pathway creating nano-fibrous hybrid poly(ε-caprolactone) (PCL) suture material with controllable drug release. Further assessment showed better drug release profile but with inferior mechanical properties of developed suture [10]. It is important to note that although favourable drug release fashion can be attained, it should not come at the expense of tensile strength contracting the sole purpose of using sutures for tissue approximation.

New methods have been developed to further aid controlled drug release while maintaining tensile strength. Hu *et al*. described coaxial spinning techniques in which cefotaxime sodium (CFX-Na) was mixed with poly(L-lactic acid) "PLLA" [11-13]. Traditional electro-spinning extrudes the CFX-Na/PLLA solution directly, while in co-axial fabrication,

each fibre has a core and sheath with varying concentrations of the drug that were extruded together [12, 13]. The concentration of CFX-Na was 33% in the core-shell co-axial method and 3% in the traditional blend-fibres. The higher concentration in the co-axial method was consistent with a release profile of 14.7% in the first 4 h, compared to 24% was released from the blend sutures within same period. Furthermore, 24-hours assessment of blend sutures showed that 40.9% of the total drug was released, whereas 20.4% from the core–sheath sutures. This was attributed to be a necessity to prevent the initial proliferation of bacteria directly after the suturing was complete. The porosity was also controlled using electrospinning as the pores have to be small enough so that pathogens are not able to penetrate the suture and compromise its mechanical integrity, while allowing for a high specific surface area to volume ratio to aid bio-absorbability and effective drug release [14]. Hu *et al.* also reported that the co-axial nano-fibre surfaces were smoother with fewer defects when compared to the blend fibres. The co-axial fibres also had a better mechanical performance with a breaking force of 7.74 ± 1.66 N, and tensile strength of 80.52 ± 9.31 MPa for core–sheath sutures than blend sutures having 7.14 ± 1.35 N breaking force and a tensile strength of 78.64 ± 8.53 MPa [11].

Kim *et al.* also described the blend electrospinning of cefotaxime with a poly(lactide-co-glycolide) (PLGA) suture which eluted 60% of CFX-Na within the first 24 hours, which represents a high rate of release compared to the CFX-Na/PLLA blend which released 41% of the drug in the same time frame [11, 15]. The difference can at least partially be attributed to the slower hydrolytic degradation of PLLA due to its semi-crystalline condensed structure [16].

Additional reports have investigated the use of synthetic polymer blends with anti-inflammatory and anaesthesia drugs. Further approaches to control the rate of drug release were also investigated, like the incorporation of magnesium and aluminium hydroxycarbonates (HT) compounds into suture material. These HT compounds consist of a layer of inorganic

clays that self-arranges to form a bi-layer and becomes a nano- or micro-vessel for immobilising anionic drugs with more sustainable drug release [10, 17].

A melt-spun suture containing poly(ε-caprolactone) (PCL) and diclofenac (Dic), as an antiinflammatory drug, created by forcing a polymer melt through a small spinneret capillary to obtain strong fibres (11). *In-vivo* assessment showed a reduction in the inflammatory profile.

Catanzano *et al.* also conducted an *in-vitro* release study of PCL/HT-Dic in Phosphate buffered saline (PBS) at pH 7.4 and 37^{o}C. The PCL/HT-Dic conjugate showed controlled release over 55 days suggesting that the release profile can be finely tuned. There was a significant reduction in tensile strength as the breaking stress was 400 MPa for the PCL control, but approximately 190 MPa for the PCL/HT-Dic [10]. Knotting did not have a significant effect on tensile strength.

Another example of a controlled release system was presented by Weldon *et al*. Sutures were fabricated using poly-(lactic co-glycolic acid) (PLGA) mixed with bupivacaine HCl and extruded to form a blend fibre. It was noted that the suture exhibited a controlled and consistent release profile at the expense of tensile strength. The hybrid fibres showed a three-fold decrease with respect to pure PCL fibres in terms of breaking stress. The tensile breaking stress force was < 1.5 N for 6-0, 4-0 and 2-0 sizes (specific American Pharmacopoeia Standards [18]) Poly(lactic-co-glycolic acid) (PLGA, 90:10 glycolide:L-lactide) sutures loaded with bupivacaine at more than 15 wt.% of the suture material demonstrated a 88% reduction in tensile strength compared to control [18].

2.2. BIOACTIVE SUTURE IN GROWTH FACTOR DELIVERY

Different bio-active molecules including peptides and hormones influence cell division, growth, differentiation and protein synthesis. Growth factors were being used to aid healing in tissues with variable level of success [19]. The progress on incorporation of the different growth factors with bio-active suture fabrication aiming to alter the healing

properties of approximated tissue is summarised as follows.

Kopf *et al.* reported the use of vascular endothelial growth factor (VEGF)-poly(D,L–Lactide) (PDLLA) blend coated on non-absorbable polyethylene terephthalate polyester (PET) sutures (Ethibond) to treat meniscal lesions. This was later concluded in that; it did not improve meniscal healing or increase angiogenesis in sheep meniscal model [20]. However, Bigalke *et al* developed an effective VEGF/ poly(L-lactide) (PLLA) blend coated polydioxanone (PDS) suture with improved mechanical properties compared to uncoated ones and a greater concentration (2 µg/100 mm PDS suture) than did Kopf reported (0.1 µg/100 mm PET suture). Bigalke *et al. showed increased* biological activity and cellular viability *using human umbilical vein endothelial cells.* Further *in-vivo* assessment using rat hind limb model showed significant histologically enhanced vascularisation in the wound site sutured with PLLA/1.0 µg VEGF-coated suture material [21]. The disparity in results in terms of disruption of the coating layer during suture entry through tissue may be explained by the concentration of growth factor, coating process, and polymer structure.

Recombinant human platelet-derived growth factor BB (rhPDGF-BB) [22, 23] and growth factor 5 (GDF5) were also investigated [19, 24, 25]. Cummings *et al.* used rhPDGF-BB coated Vicryl® (Ethicon, Somerville, NJ) a multifilament absorbable sutures made of poly (lactide-co-glycolide) fibres to repair transacted Achilles tendon in mice model and showed a marked increase in tendon tensile strength [22]. Dines *et al.* showed through *in-vivo* assessment showed that GDF5 was beneficial for up to three weeks after the sutures were administered, resulting in higher tensile load and stiffness compared to the control group in the initial healing period ($p=<0.05$) [26]. Henn *et al*. also presented similar results through an *in-vivo* trial using gelatin/GDF5 coated Vicryl® polyglactin 910 sutures on zone II flexor tendon repair [25].

The use of growth factors in bioactive sutures has shown a largely dose dependent

relationship between the active substances and biological activity as shown, however it is not known whether this is due to the inherent nature of the growth factors or due to the absence of an appropriate controlled release system.

2.3. BIOACTIVE SUTURES IN CELL DELIVERY AND TRANSFER

Cell therapy represents a unique modality augmenting the surgical repair of various soft tissue injuries. The application of such process associated with certain challenges in cell hosting and delivery [27, 28]. Bioactive sutures played a major role as a vehicle (scaffold) to host and deliver various cell lines. In this section, a critical review of the currently known trials implementing the use of bioactive sutures is presented.

Casado *et al*. investigated a range of clinically used sutures with different surface coatings as a carrier of mesenchymal stem cells (MSCs). They showed that Vicryl ® (copolymer of 90% glycolide and 10% L-lactide, PLGA) was superior in its cell attachment properties than Dexon-II ® (braided absorbable suture made of polyglycolic acid (PGA) and coated with copolymer of poly(ε-caprolactone/glycolide), Assufil® (braided multifilament absorbable suture made of PGA and coated with a mixture of polycaprolactone and calcium stearate), Safil Quick® (braided absorbable suture made of PGA and coated with magnesium stearate), Safil® (braided absorbable suture made of PGA and coated with hydrolytic degradable glyconate) and Ticron® (non-absorbable suture made of polyethylene terephthalate coated with silicone). Vicryl was then coated with porcine-derived gelatin, poly-L-lysine hydrobromide, or treated with NaOH. Porcine and murine bone marrow-derived mesenchymal stem cells (BMSCs) were used in their assessment. NaOH treatment and poly-L-Lysine coating associated with statistically significant highest level of cell attachment. In terms of cell adhesion tendency, poly-L-Lysine coated sutures were highest in their adhered cells (P=0.053). Mechanical assessment however, showed reduction of the tensile strength with NaOH treatment with no significant difference in the in-vitro degradation rate [29]. The results presented

reflect the importance of how the modification of material structure and properties of sutures can increase the surface area with an altered porosity and more hydrophilic interference. However, a trade-off of reduction of mechanical compliance/strength could make such treatment of less clinical importance.

Vicryl was also coated differently using fibronectin, poly-L-lysine or albumin in order to increase its cell attachment. The coating was applied through freeze-drying technique. *In-vitro* and *in-vivo* assessments performed by using both human bone marrow stromal cells (BMSCs) and rat mesenchymal stem cells (MSCs). Albumin coating was associated with significantly higher human BMSCs attachment with higher proliferation rate compared to other coated sutures and uncoated controls. The sutures were then fixed to rat's triceps surae muscle where viable cells were seen up to 5 week's post-implantation [30]. In a follow-up study, the authors further investigated the potential mechanical effects after incubating such absorbable sutures. They concluded that a non-significant difference exists in breaking force between 48hrs incubated and control sutures. A significant reduction however was found in the breaking force by 16 to 19% after incubating the sutures for a longer period (168 hours) [31].

Tendon injuries represent a challenging obstacle in which suturing repair is the gold standard treatment. This however is associated with certain limitation in which histological assessment of repaired tendon showed a distinct acellular zone surrounding the repairing sutures with a negative effect on the healing tendon [32]. Augmentation of the repair process with cell-loaded sutures was tried.

FiberWire ®, sutures are made with a core of non-absorbable polyethylene and coated with a braided polyester for lower friction and cell adhesion. This suture material is characterized by high mechanical properties as a promising choice in tendon repair. The maximum load to failure reaches up to 620 ± 29 N, stiffness up to 62 ± 18 N/mm, and a strain of 23 ± 7% [33]. Fiberwire ® suture was coated with fibronectin, poly-L-lysine, or phosphate-buffered saline (PBS). *In-vitro* assessment using mouse

C3H10T1/2 pluripotent embryonic stem cells (ESCs) showed a significant adherence with both types of coating compared to PBS controls. Poly-L-lysine was however superior in its attachment properties [34]. This study showed the possibility to activate Fiberwire sutures by increasing its surface attachment properties; however it lacked further detailed assessment of cellular activity and adherence properties at *in-vivo* environment. In a subsequent study, the authors have utilized the same coating technique using only poly-L-lysine in an *in-vitro* assessment of ESCs survivability. Decellularised rabbit Achilles tendons were used as a model in which cell-seeded coated sutures were passed through adjacent tendon segments. They showed successful delivery of cells with preserved activity and proliferation properties after 48 and 96 hours of incubation ($P<0.001$) even after tissue passing effect [35].

Yao *et al*. investigated the use of Ethibond Excel ® suture in cell delivery [36]. Ethibond Excel ® made from braided polyester (PET) with polybutyrate coating that is not absorbable. The mechanical properties of these sutures were shown to reach up to 247 ± 10 N as a maximum load. Stiffness reached up to 25 ± 2 N/mm, and strain up to 18 ± 2 % [33]. Coating the sutures with poly-L-lysin and intercellular cell adhesion molecule 1 (ICAM-1) was done. Fluorescent-labelled rat MSCs were used for suture seeding. *In-vivo* assessment with rat's Achilles tendon repair was investigated and showed a significantly increased load to failure level in repaired tendon with cell-seeded sutures compared to controls at both 7 and 10 days. Additional improvement in the mechanical properties tested up to 28 days post repair was not statistically significant [36].

Collagen was also used as a coating molecule to increase cell attachment properties. Type I bovine collagen was used to coat sutures made of a non-absorbable polyethylene/polyester (Arthrex, Naples, FL). The coating was applied by overnight incubation of either native or denatured (heat treated) collagen at a concentration of 0.5 mg/ml followed by air-drying. Human osteoblasts (HoBs) and

tenocytes were both used in the *in-vitro* adhesion assessment. Adhesion assay of HoBs and tenocytes showed no significant difference between collagen-coated and uncoated sutures. Proliferation assay however showed 1.9 and 1.8 fold increases in proliferation of HoBs and tenocytes, respectively when denatured collagen coating is used compared to native collagen. The effect of the knot tying process, sterilization technique, shelf life availability, and mechanical properties were also tested. It was shown that HoBs adhesion had a 1.9 fold increased amount when denatured collagen knotted suture is used compared to uncoated control. Tenocytes showed a 2.1 fold increased adhesion when denatured, or native collagen knotted suture is used compared to control. No significant difference revealed when freshly applied coating compared to 6-week post-coating indicating the possible availability of a shelf product. No significant difference was also found in terms of cell adhesion or proliferation between Ultraviolet or ethylene oxide sterilization of denatured collagen-coated sutures [37].

Different protocols utilizing other activation molecules like RGD (Arginine-glycine-aspartic acid) peptides were also tried. RGD is an amino acid sequence presents in different extracellular matrix proteins with various effects that involve cell attachment and activation. RGD was attached to silk suture. The attachment process was obtained through covalent coupling by activating the carboxyl group of GRGDS peptides (glycine-arginine-glycine–aspartic acid-serine). Human derived tenocytes were used in the *in-vitro* assessment model. They showed significantly more human tenocytes attachment at 4 hours of seeding on RGD-silk surface. By six weeks of culture, the cells assumed the best morphologic features on silk-RGD coated surfaces compared to silk alone and tissue culture plastic control. Growth and proliferation were also significantly higher in silk-RGD sutures than other groups [38]. Additional report investigated RGD with the use of high-strength non-absorbable polyester/polyethylene (PE/PEE) using acid hydrolysis. They showed significantly higher cell attachment together with a possibility of a

shelf product. The modified suture was also shown to withstand sterilization with both ultraviolet light and ethanol immersion with no significant effect on load to failure strength [39].

Pascual *et al*. have investigated the potential of direct attachment of fluorescent-labelled adipose-derived stem cells (ADSCs) to Vicryl ® sutures. The attachment process obtained through direct incubation of the cells with sutures in ultra-low attachment culture plates. *In-vivo* assessments using rat's colonic anastomosis repair showed that a significant difference in the adhesion index with Vicryl-ADSCs sutures compared to cell free sutures [40]. In another report, the authors investigated these sutures with icodextrix 4% intra-peritoneal injection to decrease adhesion formation in syngeneic BDIX rats and showed increased anastomosis resistance with a similar adhesion index to conventional sutures [41]. Vicryl-ADSCs sutures were also investigated in modulating the inflammatory response in rat's tracheal resection repair [42]. Histological assessment showed abundant macrophages with low neutrophil count with viable ADSCs at day 1 and 4 post tracheal tissue in approximation with cell-loaded sutures. The authors mentioned another preliminary assessment of the sutures in which cell density reduced after being passed twice in muscle tissue with no detailed description of the cell adhesion tendency.

2.4. GENERAL SUTURE FABRICATION TECHNIQUES IMPLEMENTING ACTIVE MOLECULE INCORPORATION

Modification of commonly available suture materials with the addition of different substances aiming to alter certain mechanical and surface properties or more importantly, with the addition of an active molecules altering certain physiologic phenomena were investigated and summarised in the following section.

Bioglass® was one of the material used to modify sutures. . 45S5 Bioglass® is a bioactive material that contains 45% SiO_2, 24.5% Na_2O, 24.5% CaO, and 6% P_2O_5. This material was

implemented for its osteo-conductive and osteo-productive behaviour due to a layer of hydroxyapatite formation upon contact with biologic fluids. This material was used to coat Vicryl® sutures in order to alter its extent of degradation using layer pressing technique. An initial reduction in the tensile strength of treated sutures (404 MPa Vs. 463 MPa in control) was found and was attributed to the manufacturing technique implemented [43]. In order to avoid the harmful pressing effect upon incorporation of Bioglass® to the sutures, the authors reported a slurry-dipping technique. It was shown that homogeneous coating with higher chemical properties represented by hydroxyapatite formation was obtained. However, mechanical assessment showed also a lower tensile strength of modified sutures compared to the native one (385 MPa vs. 467 MPa). Concerning the tensile strength assessed after 28 days of SBF incubation, the coated suture showed 83 MPa compared to 88 MPa for uncoated ones [44].

Silver ion ($Ag^{+)}$ is known for its antimicrobial properties. Blaker *et al.* investigated the use of Ag^{+} containing bioglass as a coating molecule of suture material. Vicryl® and Mersilk® were used in the assessment process. Mersilk® is a braided non-absorbable suture that is made of silk and beeswax coating. A sol-gel derived silver-doped bioactive glass (AgBG) powder was used. They showed that with the use of powder with < 38 μm particle size and an immersion time of 2 minutes for Vicryl and 5 minutes for Mersilk suture, a uniform, stable coating was obtained. Knot tying or passing through eyes of surgical needle had no effect on coating process. The authors showed that the addition of Ag^{+} did not affect the biologic behaviour of bioactive glass by hydroxyapatite formation. However, the incorporation of Ag^{+} was not clearly assessed [45].

Subsequent reports investigated the antibacterial properties using silver coating. Mersilk sutures coated with AgBG in a similar fashion described earlier. Incubation of AgBG coated suture, Bioglass 45S5 coated sutures and uncoated mersilk sutures with Staphylococcus epidermis at both batch and flow cell techniques was made. AgBG coating associated

with a statistically significant lower colony forming units (CFUs) with limited cell attachment in comparison to other groups [46]. However, assessment of silver ion release assays together with silver ion quantification, period and interval length of release were lacking.

De Simone *et al.* investigated the use of in-situ photo-reduction of silver solution containing the suture material using ultraviolet (UV) light. The solution was made containing 0.5 wt/v% silver nitrate mixed with 5 v/v% methanol in which the later was added as a reducing factor. Photo-reduction resulted in the deposition of silver clusters on silk sutures used. The use of this modality was associated with uniform distribution of silver particles on the surface of the sutures as evident by electron microscopic assessment. No significant reduction in the tensile strength of the treated sutures was found. Anti-bacterial assessments using E.coli and Staphylococcus aureus incubation showed reduced growth tendency with reported percentage of antibacterial efficacy to be 78% against E.coli and 81% against Staph. Aureus. Silver treatment sutures. Cell cytotoxic analysis of fibroblasts incubation with treated sutures resulted in 82% cell viability compared to 92% with untreated sutures [47]. Although the reported findings are of interest, detailed statistical analysis needs further elaboration.

An additional report investigated the use of silver nanoparticles to coat Vicryl® sutures. In this study, the silver coating was obtained through layer-by-layer deposition. The silver solution was prepared by mixing silver nitrate with poly-methacrylic acid under ultraviolet light to yield silver nano-particles (AgNPs) after photo-reduction. Analysis of modified sutures showed denser deposition of silver particles depending on the cycles of immobilization. *In-vitro* antibacterial activity against E.coli showed a significant growth inhibition area around the silver-coated and antibacterial (Vicryl Plus) sutures compared to control. Extended inhibition (9 days) was significantly higher in silver-coated sutures compared to other groups. *In-vivo* assessment with the use of mouse intestinal anastomosis

repair showed reduction in the inflammatory response with less early neutrophil and macrophage infiltrates compared to controls. Additionally anastomosis sites treated with silver coated sutures showed more collagen content [48].

Other substances like butyric acid (BA) have been incorporated into suture materials. BA is a naturally formed fatty acid with a potential effect on angiogenesis. Several reports had investigated its incorporation in tendon and ligament suture repair. Soaking Ticron® sutures (ultra-high- molecular weight polyethylene) with BA at a concentration of 6.2 µg/cm in meniscal repair resulted in significant mechanically superior repair strength in comparison to uncoated controls [49]. Additional effort reported the use of same sutures in tendon repair with significantly increased tensile strength and young's modulus. The attributed results linked to higher angiogenesis and cell proliferation [50, 51].

Doxycycline was also used in such assessment. Doxycycline was linked with modulation of the inflammatory process through inhibiting matrix metalloproteinase (MMPs) and improving tendon suture repair. The coating process was applied using plasma treatment of sterile polybutester monofilament sutures (Novafil, Switzerland). Incubation with fibrinogen assumed cross liking to the suture surface. This was followed by doxycycline introduction. The authors showed improved suture holding capacity and force of failure of repaired animal Achilles tendon [52].

Application	Bio-active Suture Type	Remarks
Drug Delivery	Cefotaxime loaded PLLA suture. **Hu, Huang, & Liu, 2010)**	Showed that blend braided fibres retain more rigidity and strengt compared to non-braided sutures.
	PLGA with bupivacaine. **(Weldon e al., 2012)**	Electrospun drug-eluting sutures for local anaesthesia. Suture offered very low tensile strength
	Triclosan-coated polyglactin 910. **Okada et al., 2014)**	Anti-microbial coated suture to reduce incidence of SSIs Incidence of SSI reduced from 14.5% to 4.5%
	PCL suture with diclofenac and ydrotalcite. **(Catanzano et al., 2014)**	Sutures containing nanohybrids for local delivery of anti-inflammatory drugs
Growth Factor Delivery	PDLLA-VEGF. **(Kopf et al., 2010)**	Intended in the treatment of meniscal lesions using VEGF but lacked a control release system.

	PLLA-VEGF. **(Bigalke et al., 2014)**	Intended to promote angiogenesis in sutured gastrocnemius muscle tissue using VEGF
	Vicryl ®-rhGDF-5. **(Dines et al., n.d., 2011)**	Intended in tendon repair using rhGDF-5 in which entry trauma considered and factored into GF release calculations
	5-0 polyglactin 910 sutures-rhGDF- **(Henn et al., 2010)**	Intended in tendon repair using rhGDF-5 with significant increas in maximum load.
	Vicryl® - rhPDGF-BB **(Cummings e l., 2012)**	Intended in rotator cuff healing using rhPDGF-BB with improvement in healing results 4 weeks post repair.
	FiberWire ®-rhPDGF-BB **(Uggen et al., 2010)**	Gelatin suture coating with intended application in Achilles tendon healing using rhPDGF-BB
Biologically active molecu ncorporation	Vicryl-Mersilk®/silver-doped ioglass coating. **(Blaker et al., 2004)**	Intended in the delivery of silver ion for antibacterial properties.
	Silk - Silver coating. **(De Simone et al 2014)**	Intended in the delivery of silver ion for antibacterial properties demonstrated against E.coli and staph. S. aureus.
	Vicryl - nano-silver coating. **(Zhang l., 2014)**	Intended in the delivery of silver ion for antibacterial properties.
	Ticron butyric acid soaking. **(Acton e l., 2004, Leek et al., 2012, Tracy et al., 2011)**	Intended in the delivery of active molecule to promote angiogenesis.
	Polybutester monofilament sutures / ibrinogen / Doxycycline coating. **(Pasternak et al., 2007)**	Intended in the delivery of Doxycycline modulating Matrix metalloproteinase (MMPs)
Cell Delivery and Transfe	Vicryl® treatment with NaOH / elatin / poly-L-lysin. **(Casado et al., 2014)**	Intended for MSC cell delivery.
	Vicryl® coating with Albumin/Fibronectin / Poly-L-lysine. **(Horvathy et al., 2013a)**	Intended for MSC cell delivery.
	Vicryl® coating with albumin/ ibronectin / Poly-L-lysine .**(Horvathy e l., 2013b)**	Intended for MSC cell delivery.
	FiberWire® coating with poly-L- ysine / Fibronectin / PBS. **(Yao et al., 2008)**	Intended for ESC cell delivery.
	FiberWire® coating with poly-L- ysine/ PBS. **(Yao et al., 2011)**	Intended for ESC cell delivery.
	Ethibond® coating with poly-L-lysi ICAM-1. **(Yao et al., 2012)**	Intended for MSC cell delivery.
	Polyethylene/polyester coating with native type I collagen / denatured type collagen. **(Mazzocca et al., 2007)**	Intended for human osteoblasts and Tenocytes delivery.
	Silk suture with RGD coating. **(Kardestuncer et al., 2006)**	Intended for tenocytes delivery.

Table 2. Summarised literature implicating the use of different biologically active suture materials.

3. CONCLUSION.

As summarised in this article, the scope of sutures and their materials have vastly evolved since the use of horsehairs and ant heads for tissue approximation. With the advent of antibiotics, integration of suture material and antimicrobial agents have been tried and tested. The effect of having bioactive sutures

extends to conserving costs on follow-ups and potential further treatment post surgical procedure. A well devised human experiment using triclosan-coated sutures showed a savings of at least $4000 per surgical site infection prevented for the hospital. In addition to cost savings the sutures also conveyed an improvement in surgical site infection rates [53]. This model can be used to infer the potential cost benefits for bioactive sutures. As technology takes us to new advancements in sutures, the authors propose a definition for bioactive sutures that will hold true for future prospects. Bioactive sutures are "*biomaterials that are engineered to have controlled tissue interaction to optimise wound/defect healing, in addition to their essential function in tissue approximation and ligation*".

4. CONFLICT OF INTEREST

The authors confirmed that the contents of this article have no conflict of interest.

5. ACKNOWLEDGEMENTS

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