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Advancements in Biomaterials for Functionalized Biomedical Sutures: A review

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Abstract. This paper reviewed recent advancements in surgical suture technologies, focusing on coating based antibacterial sutures, therapeutic delivery systems, and biosensors. Silver nanoparticles and Triclosan were two antibacterial coatings that combat infections effectively. Additionally, innovative therapeutic delivery systems for suture coatings enable localized delivery of drugs using the strategies of nanoparticle coating, drug or bioactive mixture adhesion and hydrogel coating, which enhances wound healing. The review also covers smart suture sensors designed for monitoring infection, tensile strength, and pH conditions of suture or suture sites, which would improve post-surgical outcomes. These innovations signify a leap forward in surgical care, enhancing both patient recovery and surgical precision.

Keywords: Suture, Biomaterial, Wound Healing, Antibacterial, Coating, Therapeutic Delivery, Biosensor.

1. Introduction

As the most widely used material in surgeries, sutures are familiar to almost all doctors and medical employees. Sutures could provide structural support in order to stitch and close wounds, which will promote wound healing, and support tissue repair and reconstruction. Due to the huge application of sutures and spurred by the growing demand for more advanced, safer wound closure materials, sutures have quickly emerged as a promising frontier and have gained more and more attention. The recent past development of surgical sutures including suture techniques [1, 2], and physical properties such as tensile strength and biodegradation [3-6], and biocompatibility [7, 8] of the suture material were heavily investigated. Besides the enhanced developments in the physical properties of suture materials, a lot of innovation and novel techs have been made on sutures in past decades, several different functions have also been integrated into sutures, including but not limited to, antibacterial coating, therapeutic delivery system and biosensors.

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2. Antibacterial coating

Even though suture materials are widely used in surgeries, there is a huge problem in that they are very susceptible to microbial colonization and may lead to infections. Post-operative infections are almost unavoidable and very troublesome for every surgery that uses normal sutures because these sutures could transport bacteria into wounds and cause surgical site infections (SSI), which have been demonstrated to have a strong association with high mortality and morbidity.

To solve such problems, antibiotic-coated sutures were designed and produced, which are sutures with coatings that are demonstrated to have a strong antibacterial efficacy. In the following paragraphs, this article will be going to discuss two mainstream materials that are used as antibacterial coating of sutures, AgNP and Triclosan.

2.1. AgNP (silver nanoparticle)

Since ancient times, silver has been used widely in medical fields because of its antibacterial properties, where silver compounds are commonly used to treat burns, and infections and to prevent eye diseases in newborns [9]. About a decade ago, silver nanoparticles were developed and quickly stood out because of their high surface-to-volume ratio and unique properties. Nowadays, AgNPs have more than 200 different kinds of medical products, which makes it become one of the most commonly used nanoparticles.

2.1.1. AgNP's Sterilization Mechanism

AgNP is effective against various bacteria, fungi and viruses. Although the antibacterial mechanism of silver ions has been studied for a long time, scientists still cannot fully understand the mechanism of AgNP action on bacteria.

Silver ions are able to interact with nitrogen bases in DNA[10] and thus affect DNA's replication capacities. Moreover, AgNP could release silver ions into wounds, which is the key process in its antimicrobial activity. Electron microscopy has shown that those silver ions could easily penetrate the cell wall and membrane[11, 12] and change the potential difference in and out of the cell, which will interfere with the permeability of the cell membrane. Moreover, silver ions also play a role in the inhibition of cell respiration. In addition, silver ions are proven that they are able to bind to sulfhydryl groups of bacterial proteins, interfering with their activity and causing apoptosis [11]. The specific effects of AgNP on DNA and its potential oxidative damage mechanism have not been discussed in detail. Studies have pointed out that AgNP and silver ions can inhibit respiratory enzymes and hinder the formation of reactive oxygen species [13, 14], which may lead to oxidative damage of DNA, and oxidative stress may be an important mechanism leading to DNA damage [15, 16].

2.1.2. The production of AgNP

In recent years, with the development of science and technology, we have incremental methods for preparing nano silver ions. Reduction using chemicals or light, irradiation with gamma rays, lasers, electron beams or microwaves, and biosynthesis are all currently mainstream methods.

(1) Chemical reduction methods

The chemical reduction method is currently the most widely used and highly efficient AgNP preparation method. The process mainly uses two kinds of materials, reducing agent and silver-containing salt [17]. Using a reducing agent (such as hydrogen, sodium citrate, etc.), the ions in silver-containing compounds (mainly silver nitrate or silver acetate) are replaced and reduced into atoms, nucleated and then grow into particles.

(2) Photochemical synthesis

Photochemical synthesis is also a novel AgNP synthesis method, which mainly uses light as a reducing agent to reduce metal precursors, and then through nucleation and aggregation. Its advantage is that it can form nanoparticles in a variety of different media, such as cells, polymerfilms and even glassware [13]. At the same time, the selection of reducing agents in this method is also very broad, although ultraviolet light is the most common choice -- ultraviolet light, laser light, sunlight, etc., can

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be used as reducing agents. The reduction efficiency of silver ions can be controlled by simply adjusting the laser intensity and the wavelength of the light source

(3) Green synthesis

Although the chemical methods mentioned above have extremely high efficiency and great scale, AgNP will inevitably attach some chemicals to the surface during its formation, such as sodium citrate, ethylene and so on, which is highly toxic and hazardous to humans. As the carriers of those chemicals, those NPs will affect our health negatively. Because of the hazards of those chemical methods, green synthesis of AgNP quickly got into view and became widely used.

The principal of ecological synthesis is still the reducing model, but the reducing agent is no longer chemicals like sodium citrate, but some plant extracts, for example, Eucalyptus extract and myrtle extract [14].

2.1.3. Antibacterial efficacy of AgNP-coated sutures

According to the assessment by ASTM E2149, AgNP-coated sutures have strong bacteriostatic effects on several Gram-negative bacteria (Eg. Escherichia coli, Acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella pneumoniae) of bacteria, which more than 3 log (99.9%) of reduction in cell growth has been observed within 3-12 hours [18]. That is because these bacteria' cell walls are relatively thin to human cells, so that AgNPs could easily go through the cell wall and thus have an efficacy bactericidal effect.

2.2. Triclosan

In addition to silver ions, there are many antibacterial agents used in suture coating, Triclosan is one of the most widely used. As a broad-spectrum antibacterial agent, Triclosan is widely used in toothpaste, soaps and body washes. Triclosan-coated products, meanwhile, were approved by the Food and Drug Administration in 2002. Mainstream products currently on the market include triclosan-coated polyglactin 910 antimicrobial suture, triclosan-coated poliglecaprone, antimicrobial suture and triclosan-coated polydioxanone antimicrobial suture.

Triclosan has a strong pharmacological effect on cells, especially a broad-spectrum antimicrobial activity on prokaryotes. Triclosan could inhibit the synthesis of lipids like phospholipids by inhibiting the enzyme enoylacyl carrier protein reductase. In eukaryotes, Triclosan mainly plays a role on the membranes, it could mimic the natural substrate of enoyl-ACP in Gram-negative and Gram-positive bacteria as well as in the mycobacteria, acts as a site-specific inhibitor [19].

2.2.1. Safety

As a chlorinated aromatic compound, triclosan will contain some residual by-products during its industrial synthesis process, which may be toxic to people. These by-products include polychlorinated dibenzo-dioxins polychlorinated dibenzofurans and a lot of other materials. Even though these toxic residues may not threaten human health because of their low doses and mature purification methods, as a product that will have direct contact with the human body, the safety of Triclosan-coated sutures is still gaining extensive attention and research.

According to the research of the U.S. Environmental Protection Agency, 58-kg adults will be exposed to these by-products at about 119pg/day, and as the worst type of Triclosan-coated sutures, coated polyglactin 910 suture only contribute about 0.00016% [20]. Moreover, with a lot of safety clinical applications, Triclosan-coated polyglactin 910 sutures are seen as one of the most well-tolerated biomaterials available for implantation.

2.2.2. Efficacy

Triclosan-coated sutures have been proved by many studies and clinical trials to have the ability to reduce the infection rate on surgical sites and wounds. For example, a study has shown that Triclosan-coated 910 PLA antibacterial suture can reduce the infection rate of pediatric appendectomy from

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10.94 %to 5.94% [19, 21] In another study, The shunt infection rate of cesarean section was reduced from 1080 to only 4 by using the antibacterial suture coated with prolactin 910 with triclosan [21].

3. Therapeutic delivery system on suture coating

Recently, there has been a surge in new strategies aiming at functionalizing the suture to further improve wound closure via coating the suture with functional layers. The coated layers enable the suture to deliver drugs, proteins, and stem cells to the wound site to improve wound healing. In recent decades, coating techniques for drugs or bioactive compound delivery include the following three main areas:

1. nanoparticle capture and release,
2. degradation of drug or bioactive mixture on coating,
3. hydrogel layers with loaded drug and cell.

3.1. Nanoparticle capture and release

One of the often-used coating technology is nanoparticle attachment and their gradual release in wound site. Polydopamine-modified suture enables the capture of nanoparticles to which the genes are attached. A suture carrying nanoparticle/growth factors complexes are obtained by the incubation of suture in the nanoparticle/plasmid complex [22], without sacrificing the mechanical strength of the material. This coating can deliver genes into local cells effectively and increase the expression of growth factors to promote healing, where the gene-carried-nanoparticles are unloaded through biodegradation of the coat, which makes protein releasing process gradual and sustained [22].

When it comes to the means to deliver silver nanoparticles (AgNP), scientists had come up with multiple solutions. The group of López-Saucedo et al. used N-vinyl imidazole (NVI) as a load of AgNP that is grafted on polypropylene suture, which obtained promising antimicrobial activity against Escherichia coli and Staphylococcus aureus with reasonable toxicity [23]. A study delivers the AgNP through different coating by immersing the silk suture in a silver nitrate- Eucalyptus ca-maldulensis aqueous leaf extract solution to prepare AgNP-coated suture, that achieved 99% reduction in pathogen growth [24]. Similarly, AgNPs are coated on the silk via incubation of cell-free supernatant and AgNO3 mixture solution. The release of AgNP achieved a steadier rate with great growth inhibition of three pathogenic microorganisms, while controlling the dose under the level of reaching toxicity of human cells [25].

3.2. Degradation of drug or bioactives mixture on coating

When delivering drug materials, one of the most popular coating strategies is mixing the drug with degradable material that can adhere to suture materials. Liu et al. investigated the drug release of Tea Polypheno (TP) [26] and ciprofloxacin (CPFX) [27] with polycaprolactone (PCL)/ polyglycolide (PGA) carrier to achieve controllable drug delivery. The PLA suture is coated through dip-padding of emulsified drug-PCL/PGA solution. The control of the proportion of PCL to PGA physically adhered to the PLA suture can manage the strength of the suture and degradation kinetics. As the release of drugs depends on the sustained degradation of the material, increasing the PGA proportion of PCL/PGA coating can, in turn, increase the drug release rate. By adjusting the polymer composite simply when preparing dip-padding solution coated to the suture, the drug release can be more precisely modified with specific surgical needs.

Moreover, mineral growth on suture is also a recently used technique. Lee et al. provided a solution to controllable protein delivery kinetics using calcium phosphate CaP coatings. Nano-porous hydroxyapatite mineral is grown on the suture through biomimetic modified simulated body fluid incubation. By altering the composition of fluid, specifically, carbonate substitution, protein release can be controlled. Moreover, decreasing pH conditions during the course of incubation could trigger an improved coating dissolution kinetics, ie faster protein delivery. In this solution, the coating enables the binding of both acidic and basic proteins, retaining 90.7% bioactivity after the protein release without sacrificing the mechanical strength of the suture. The coating remains attached after times passing through tissues, showing feasible applications in a clinical environment [28].

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3.3. Hydrogel layers with loaded drug and cell

Hydrogel coatings are generally believed to be more biocompatible and can better mimic the natural extracellular matrix [29]. The team of Lee et al. developed a hydrogel coating is a promising method for suture functionalization with improved physical properties. The poly(ethylene glycol) diacrylate and alginate fabricate with double-network hydrogel were coated on a suture that was made from pig tissue fiber which was decellularized with less than 1% DNA content. Alginate was combined to N-hydroxysuccinimide (NHS) to make it amines reactive [30], whereby the amine group on the fiber and the carboxylic group of the hydrogel polymer bonded tightly [30]. This ensures the stability of the adhesion of layers when penetrating body tissue, as well as maintaining the physical properties of the suture itself. The hydrogel layer can encapsulate drugs and stem cells, which can deliver them locally. The hydrogel layer itself can be used as a drug carrier for hydrophilic drugs, with the potential for Microparticles to be fabricated with functional molecules; stem cells stay 90% viable after fabrication and can secrete VEGF growth factor to facilitate vascularization and improve tissue recovery [30].

4. Suture sensing

Previous developments in the materials and fabrication techniques for smart sutures have significantly advanced the field. Include thermally drawn polymer designs, which allow for the creation of complex structures with high precision and consistency. Tubular microfluidics, enabling the integration of micro-scale channels within the sutures to facilitate many therapeutic agents directly to the wound site.

There were challenges for the suture sensing field.

First, the sensor must eliminate the structural mismatch with the target tissue or organ.

Second, to develop a wireless readout.

Third, no additional process is required during the surgery when applying it.

Currently, there are three main types of biosensors on sutures with different purchase and usage.

1. Monitoring infection in deep surgical wounds [30-32].
2. Targeting tensile strength on inner injuries [33, 34].
3. pH sensing for monitoring inflammation [35].

4.1. Monitoring infection in deep surgical wounds and preventing infection

In the case of deep surgical sutures, Kalidasan et al. developed a correspondent sensor, the sensor and the suture comprise two parts: the suture and the sensor circuit.

The suture, coated with conductive polymer PEDOT: PSS and treated with dimethyl sulfoxide, responds to radio-frequency fields. It is then insulated with a thin layer of parylene-C. The wireless sensing circuit is a battery-free electronic pledget containing a nonlinear circuit and capacitive sensor.

To achieve wireless connectivity, a transmitter is set in the body, and a receiver is placed above the skin for real-time monitoring. A custom radiofrequency system (1–2 GHz) functions as a radio-frequency identification (RFID) to connect the sensor and the readout [31].

Moreover, the team of Lee et al. shared an inflammation sensing technique used on deep gut sutures: using a polystyrene microsphere modified with MMP-1-degradable peptide that is able to upregulate under inflammatory conditions. Under inflammation conditions, the MMP-1-degradable peptide cleaves and releases the peptide attached with tetramethyl rhodamine (TAMRA) dye. This release can be detected in urine, which provides an inflammation indication for the wound healing process [30].

A research group introduced a remote temperature monitoring technique via suture functionalization. Polycaprolactone (PCL) is used as a carrier of Functionalized nanodiamond (FND) and reduced graphene oxide (rGO) to coat the FND to the suture. FNDs have a nitrogen-vacancy that has fluorescence change under varied temperatures, and the response to temperature changes is measured by subjecting them to scanning microwave (MW) frequency. The shift of 75 ± 10 kHz/°C in the ODMR spectra indicates temperature variation in the sutured site, in turn, signaling protentional infection or inflammation at the wounded site [32].

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4.2. Targeting and monitoring tensile strength on inner injuries

The strain sensor structure had two elastic fibers coated with polydimethylsiloxane for insulation, arranged in a double helical structure with a hollow core. Tensile strength was estimated by the length per turn of the two coils using a formula. The stretchability of the sensor was in direct proportion to the length of the diameter of the hollow core, the wider the hollow, the longer it stretches.

However, the sensitivity was relatively low. To increase that, we could replace the elastic conductive fibers with rigid conductive wires to reach high sensitivity, but it irreversibly resulted in the structure after the first stretch.

There are plenty of advantages to this linear-formed sensor, which is more applicable to various tissues and no soldering is required. It solved the third problem and simplified the surgery process by being able to directly suture onto the organ [33, 34].

Another biosensor is built by Meyers&Ong. The sensor structure is built to monitor the strain of the suture utilizing the deformation of poly-lactic acid and passive inductor-capacitor. The altered capacity can be detected through a two-turn planar inductor coil outside of the body. This allows the real-time detection of suture strain, which is capable of detecting tensile force ranging 2-12 N, to provide evidence for therapies such as tendon rehabilitation which relies much on suture strength [34]. This biosensor can be improved by building the structure using biodegradable materials to avoid additional damage from removal.

4.3. pH-sensing for long-term monitoring of inflammation

A group of scholars [35] researched another advanced smart suture, this pH-sensing suture comprises two fiber electrodes helically wound around a supporting suture core, each Au-based fiber was respectively AgCl-coated reference electrode, and Polyaniline-coated (PANI) working electrode. And encapsulated in an elastomeric coating as a whole, the reason for doing that was to maintain a low surface friction of the suture to prevent unwanted tissue damage during the suturing process. This pH-sensing suture was tested on a piece of porcine meat, it exhibited a raging force of 14.55N m-1, which is comparable to the force of common nylon-based medical sutures of 13.36 N m-1, and even lower than some other silk and vicryl-based suture.

PANI is a pH-responsive material, the sensor could depict inflammation by measuring the open circuit potential (OCP) between the two electrodes. It has shown long-term high chemical and thermal stability. An improvement to be made was the elimination of the hysteresis between the input and output results [35].

4.4. Section Summary

In summary, the field of suture sensing has made many improvements in addressing structural compatibility, wireless readout, and integration into surgical processes. Key developments include infection monitoring sensors for deep wounds, tensile strength sensors for inner injuries, and pH-sensing sutures for long-term inflammation monitoring. Overall, the continuous innovation in suture sensing technology promises improved patient outcomes and more efficient post-surgical monitoring.

5. Conclusion

In this paper, we have concluded multiple advanced surgical suture-based advancements, including antibacterial coating, therapeutic delivery systems and biosensors.

The usage of antibacterial coatings on sutures represents a significant role in the reduction of post-surgical infections, which was once a huge challenge in medical fields. This article highlights two prominent materials used for such coatings: silver nanoparticles (AgNPs) and triclosan.

AgNPs gained attention due to their extraordinary antibacterial properties. The synthesis of AgNPs evolved through several different methods, which include but not limited to chemical reduction, photochemical synthesis, and green synthesis. On the other hand, as a broad spectrum antimicrobial, triclosan, has also been used extensively. Its mechanism involves inhibiting lipid synthesis in bacteria and thus preventing their growth.

Both AgNP and triclosan coatings offer valuable solutions for reducing surgical infections. However, the choice between these materials should consider factors such as antimicrobial efficacy, safety profiles, and potential environmental impacts. Future research and innovation in coating technologies will be crucial in optimizing these factors and ultimately improving patient outcomes in surgical care.

The major therapeutic delivery systems on suture coating were discussed in the paper. Recent advancements in suture coatings have enabled the delivery of bioactive or drugs directly to wound sites, significantly enhancing healing in surgical conditions. The sutures are functionalized with promising coating materials and coating strategies. Key strategies include nanoparticle capture for controlled bioactive delivery, drug delivery techniques for precise kinetics, and hydrogel layers coating which all enabled therapeutic applications. In suture sensors, we discuss three different aimed smart sensors, including infection monitoring sensors for deep wounds, tensile strength sensors for inner injuries, and pH-sensing sutures for long-term inflammation monitoring. These technologies enhanced surgical outcome by providing real-time data, improving precision, and reducing procedural complexity.

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