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Surgical site infection and development of antimicrobial sutures: a review

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Abstract. – Sutures are used to facilitate wound healing and play an important role in ensuring the success of surgical interventions in healthcare facilities. Suture-associated surgical site infection (SSI) may develop when bacterial pathogens colonize the suture surface and establish biofilms that are highly resistant to antibiotic treatment. The outcome of SSI affects postoperative care, leading to high rates of morbidity and mortality, prolonged hospitalization, and increased financial burden. Antimicrobial sutures coated with antiseptics such as triclosan and chlorhexidine have been used to minimize the occurrence of SSI. However, as the efficacy of antiseptic-based sutures may be affected due to the emergence of resistant bacterial strains, new approaches for the development of alternative antimicrobial sutures are necessary. This review provides an update and outlook of various approaches in the design and development of antimicrobial sutures. Attaining a zero SSI rate will be possible with the advancement in suturing technology and implementation of good infection control practice in clinical settings.

Key Words:
Antimicrobial sutures, Biofilm, Review, Suture, Surgical site infection.

Introduction

Surgical site infections (SSIs) are surgery-related infections that occur within 30 days after a surgical intervention, or within one year after the introduction of a medical implant[1-3]. Depending on the anatomic sites where the infections take place, SSIs can present as either (i) superficial infection that affects the skin and subcutaneous tissues; (ii) deep incisional infection that affects deeper tissues, for instance, fascial and muscle; (iii) organ and/or space infection that affects any site of the body, other than the surgical site[1]. Patients with SSIs often have a higher risk of hospital re-admittance, longer ICU stay, and postoperative complications[3]. Not surprisingly, SSIs also end up with financial and emotional burdens due to the high medical cost and poor healthcare quality[3,4]. Penel et al[5] reported an additional length of hospital stay (16 days) and increased direct medical costs (17000 Euros) due to SSI after head and neck cancer surgery. MRSA SSI was reported to prolong hospital stay by 19.3 days and increased medical expenditure by $7015 after colorectal surgery[6]. Tuon et al[7] reported a mortality rate of 5.4% due to SSIs related to orthopedic trauma.

The incidences of SSI ranged from 1.2 to 5.2% in developed countries[8]. Ling et al[9] described a reduction in the incidence of SSI, with the cumulative rates ranging from 0.9% in the United States of America (USA) to 2.6% and 2.8% in Italy and Australia, respectively[9]. The reduced incidence of SSIs may be attributed to the recent progress in medical practice; in particular, the introduction of minimally invasive surgery with smaller incision size and faster mobilization, better safeguarding of patient's immunity, and reduced utilization of central venous catheters for parenteral nutrition[10]. However, SSI is still amongst the most common type of hospital-acquired infection (HAI) in Europe and the USA[11].

While data on the incidence of SSI in developed countries is comprehensive, such data is lacking in Asia and low middle-income countries (LMIC). In Asia, the incidence of SSI ranged between 2.0% and 9.7% in Korea[12], while in Japan, the cumulative incidence of SSI was 15.0%

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(6691/44 751 procedures) and 17.8% (3230/18 187 procedures) for colon and rectal surgery, respectively[13]. The overall incidences of SSI were 7.8% in South East Asia (SEA)[9] and 6.1% in LMIC[11]. SSI was reported as the most common HAI in LMICs, with significantly higher risk than in developed countries[8,14].

Risk Factors of SSI

Multiple procedure- and patient-related risk factors are known to cause the initiation and progress of SSI[9,15,16]. The procedure-related risk factors are associated with the nature of the surgical intervention such as the surgical site, conditions of wound contamination, and quality of pre- and postoperative care[17]. For instance, colon, gastrointestinal and urinary tract surgeries are associated with a high risk of SSI due to a heavier bacterial load at the surgical site; hence, a higher chance of developing intraoperative contaminations[18]. A correlation between wound category and incidence of SSI had been reported whereby the risk of SSIs increased from clean to dirty/infected wound[19].

Additionally, the type of surgery (elective/emergency), duration of surgery, the complexity of surgical procedures and length of pre-operative hospital stays are also correlated with SSIs. A surveillance study[20] in Europe (2010-2011) showed that the highest cumulative incidence of SSI in patients is colon surgery (9.5% episodes per 100 operations), followed by coronary artery bypass graft (3.5%), and caesarean section (2.9%). Other procedure-related risk factors include degree of wound contamination and patients' clinical condition[21,22].

The age, sex, lifestyle, body mass index, pre-existing infection, diabetes, comorbidities, and surgical history are among the patient-related risk factors contributing to SSI[2,3]. Aga et al[23] reported that 22.1% of patients undergoing abdominal surgery developed SSIs up to 30 days post-surgery. Orthopedic SSIs require a multifaceted approach as patients experience a substantial loss of physical function and an overall poorer quality of life[24,25]. Li et al[26] observed that diabetes mellitus, smoking, operations for >3 hours, absence of antibiotic prophylaxis, and a history of previous surgery had each contributed to a significant increase in the risk of SSIs. Additional factors that have been reported include movement and number of hospital staff, structural features of operating theatre[21,27], high body mass index, and severe scores based on US National Nosocomial Infections Surveillance (NNIS) risk index[28,29].

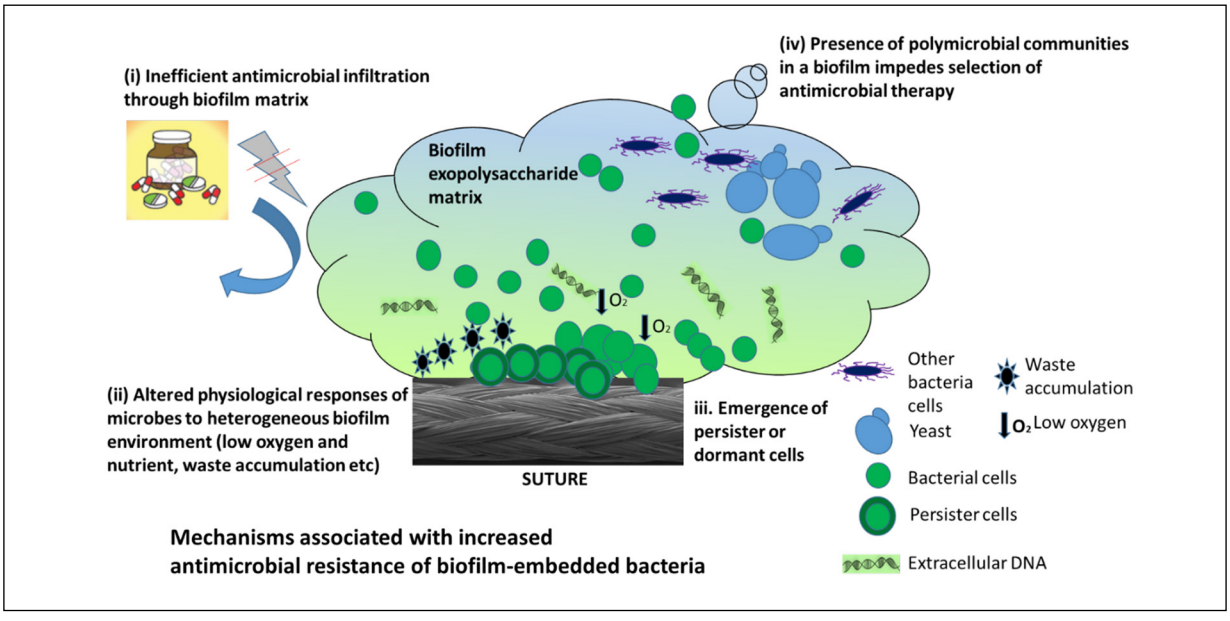

Figure 1. Several mechanisms have been associated with the increased antimicrobial resistance of biofilm-embedded bacteria: (i) inefficient antimicrobial infiltration through biofilm matrix, (ii) altered physiological responses of microbes to the heterogeneous environment of biofilm, (iii) emergence of persister or dormant cells, and (iv) presence of polymicrobial communities in the biofilm environment (i.e. co-infection of bacteria and fungi), which impede the selection of appropriate antimicrobial therapy for multidrug-resistant bacteria (Image courtesy of Amelia Low CY).

Sutures also provide a conducive surface for bacterial adherence, colonization, and biofilm formation[30-32] (Figure 1). The presence of foreign materials (suture or medical implants) in a wound incision provides an anchoring surface for biofilm formation and a reservoir for shielding exogenous bacteria from the host-defense mechanism. The surface conformation of the multifilament suture is known to harbor a higher density of bacterial cells than monofilament suture[31], while the interstices on suture knots provide a large surface area for bacterial propagation and colonization[33]. A study[34] comparing absorbable and non-absorbable sutures during dento-alveolar surgery showed that non-absorbable sutures were more prone to biofilm formation. Since sutures under different host/environments can initiate SSI, the use of appropriate sutures for surgical procedures plays an important role in preventing SSI[31].

Common Microorganisms Associated with SSI

Wound contamination and insufficient disinfection prior to surgical closure are the main reasons for SSI. Local microflora or environmental contaminants are frequently associated with the initiation of SSIs. *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli, Pseudomonas aeruginosa*, *Acinetobacter* species and *Enterococcus* species are common organisms isolated from patients with SSI[35,36]. *S. aureus*, which is present on the skin or anterior nares of almost 80% healthy individuals, represents the most predominant organism in causing SSIs during surgical intervention[35-37].

The microbiological profiles of SSI vary with the type and site of surgical manipulations. *S. aureus* is more likely to be implicated among patients undergoing cardiac, neurosurgery, breast, and orthopedic surgeries, as well as patients receiving grafts, prostheses, or implants, while infections caused by Gram-negative bacilli are more frequently associated with patients receiving appendectomy, colorectal, urologic, obstetric and gynecologic procedures[2]. Strict compliances to infection control measures including decolonization of *S. aureus* prior to surgery, good hygienic practice of healthcare professionals and patients, as well as the usage of proper antiseptics for disinfection are recommended to reduce the rate of SSIs effectively[38-40].

Antimicrobial Resistance and SSIs

The injudicious use of antibiotics has been identified as a cause for the emergence of antibiotic-resistant bacteria in healthcare facilities worldwide. The World Health Organization (WHO) warned that antibiotic-resistant bacteria may pose severe threats to human health if the situation is left uncontrolled[41]. Bacteria acquire antibiotic resistance traits through intrinsic, acquired, and adaptive mechanisms[42,43]. Intrinsic antibiotic resistance refers to the natural characteristics of bacteria in conferring resistance towards certain classes of antibiotics[43,44]. For instance, Gram-negative bacteria are relatively less sensitive to β-lactam antibiotics as compared to Gram-positive bacteria. The lipopolysaccharide cell wall, present only in Gram-negative bacteria, acts as a physical barrier to prevent the entry of hydrophilic β-lactam antibiotics, thus conferring intrinsic resistance towards antibiotics[44]. Acquired antibiotic resistance, on the other hand, occurs when microbes attain resistance to antibiotics previously susceptible due to mutations in the drug targets, changes of cellular physiology or adoption of foreign genes encoding antibiotic resistance via horizontal gene transfer[43]. Bacteria exhibit adaptive antibiotic resistance in a reversible, temporal manner in response to the alteration of environmental stress in the presence of antibiotics[45], and as a result of metabolic alterations and changes on gene/protein expression profiles[44,46].

The antibiotics used for the treatment of staphylococcal SSI depend on the location and depth of the infection site, adequate removal of damaged tissue or foreign object from surgical wound, and the occurrence of MRSA SSI[47]. Commonly employed antimicrobial treatment for methicillin-sensitive *S. aureus* (MSSA) SSI are first-generation cephalosporins and antistaphylococcal penicillins[47,48], while for MRSA SSI, the conventional antibiotic employed is vancomycin[47,49]. Although vancomycin-containing antibiotic prophylaxis has resulted in decreased SSI rates[50], the use of vancomycin alone has been associated with a higher risk of MSSA in MRSA-negative patients[51]. Hence, routine administration of vancomycin antibiotic prophylaxis in MRSA-negative patients is not recommended[52]. According to published guidelines, supportive data are still required for local and topical antibiotic therapy including antibiotic irrigations, antimicrobial-impregnated dressings, and wound sealants, in reducing SSI risk[52,53].

Since the emergence of MRSA, the proportion of SSIs due to the superbug has increased from 9.2% to 63.5%[54], depending on postoperative

antibiotic policy and surveillance programs at various clinical settings. Limited choices of drug are available for the treatment of MRSA infections. Multidrug-resistant (MDR) strains of *E. coli* and *P. aeruginosa* are also frequently reported in SSI[2,55,56]. About 68.6% of bacteria isolated from orthopedic-related SSIs were resistant to cefuroxime a major teaching hospital in China[26]. A systematic review of 41 studies published between 1994 and 2016 on multi-drug resistant HAI among ICU patients in South East Asia revealed the predominance of MRSA (23 studies)[56], vancomycin-resistant enterococci (VRE), extended-spectrum β-lactamase (ESBL)–producing organisms, MDR *A. baumannii*, MDR *P. aeruginosa*, and MDR *Klebsiella pneumoniae*[57,58].

SSIs caused by MDR bacteria often result in longer hospital stays, higher rates of readmissions and mortality, increased financial cost and treatment complexity[53,57,59]. Due to the use of more extensive drug regimens and aggressive treatment strategies, it has been estimated that an additional hospitalization cost of between USD 10,000 and USD 40,000 would be required for treating MDR bacterial infections[60-62]. High incidences of SSIs caused by MDR bacteria have been reported to pose a serious threat to patients and the healthcare system[63].

Biofilm-Associated Infections

Biofilm is a multi-layered structure of microbial communities embedded in extracellular polymeric matrixes which are composed of polysaccharides, extracellular DNA, protein, lipid, and other biopolymers[64-66]. The microbial communities in the biofilm show higher resistance (up to 1000-fold) to antimicrobial therapy in comparison to the planktonic counterparts[67]. Several mechanisms have been associated with the increased antimicrobial resistance of biofilm-embedded bacteria, as shown in Figure 1. These include (i) inefficient antimicrobial infiltration through biofilm matrix, (ii) altered physiological responses of microbes to heterogeneous environment of biofilm, (iii) emergence of persister or dormant cells, and (iv) the presence of polymicrobial communities in a biofilm (i.e., co-infection of bacteria and fungi), which impede the selection of appropriate antimicrobial therapy for MDR bacteria[68]. Additionally, as biofilms can host different species of bacteria in close contact with each other, this may facilitate the dissemination of genes encoding drug resistance or plasmid exchange in the microbial communities[68].

Biofilms on implanted medical devices (e.g., catheters, implants and surgical sutures) are difficult to be eradicated with the administration of systemic antibiotics[69]. Surgical intervention is essential for the management of infected tissues and implanted medical devices[70-72]. As biofilm-associated infections are one of the main factors behind the onset of recurrent and chronic infections, special care and appropriate strategies should be instituted for the prevention and eradication of the infections[70,73].

Staphylococcus aureus displays a high capacity to colonize new surfaces and is recognized as a major cause of biofilm-associated infections in medical devices[32,74]. Begun et al[75] showed that *S. aureus* strains producing excessive biofilm killed *Caenorhabditis elegans* worms quicker than the strains with less biofilm production, suggesting that staphylococcal biofilm is an important virulence factor. Biofilm formation, a process involving bacterial adherence, accumulation, maturation, and dispersion, is determined by quorum sensing and various genetic factors. The density of biofilm is determined by bacterial species, availability of nutrients, and surface charges of the cells[76]. The emergence of antibiotic resistance in clinical settings worldwide has led to limited options for the treatment of *S. aureus* biofilm-associated infections. As conventional approaches target bacterial viability, selection for resistant subpopulations frequently occurs in clinical settings. On the other hand, suppression of *S. aureus* virulence presumably exerts less selective pressure for antibiotic resistance[74], and thus, may serve as a promising approach for combating *S. aureus* biofilm-associated infection[77-79].

Antimicrobial Sutures

Several organizations have recommended the use of antimicrobial-coated sutures as a preventive measure against SSI[80-82]. The Centers for Disease Control and Prevention (CDC) and WHO guidelines on reducing the risk of SSI provide recommendations on the use of triclosan-coated sutures, regardless of the type of the surgery[11,53]. The National Institute for Health and Care Excellence (NICE) stated that the overall evidence favored triclosan-coated sutures over standard sutures; and a clear benefit has been shown by the triclosan-coated sutures in pediatric surgery[83]. The triclosan-coated suture is also recommended by the American College of Surgeons & Surgical Infection Society (ACS/SIS) for wound closure in clean and clean-contaminated abdominal cases[52].

A series of clinical studies and meta-analyses[80-82,84] indicated the superior efficacy of triclosan-coated sutures to prevent SSI in comparison to non-antimicrobial sutures. However, there have been conflicting opinions on the use of triclosan-coated sutures to reduce SSI risk and more evidence on the benefits of using triclosan-coated suture for the dressings of different wounds are required to draw a firm conclusion[85]. As the impact of antiseptic-impregnated sutures on the development of resistance to antiseptics is not clear, the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) guidelines do not recommend antiseptic-impregnated sutures for routine use as a strategy to prevent SSI[86]. Meanwhile, the Asia Pacific Society of Infection Control (APSIC) recommends the use of antimicrobial-coated sutures in settings with high SSI rates in clean surgeries[9].

Table I shows antimicrobial sutures that have been marketed for medical and veterinary use. Braided polyglactin 910 coated with triclosan (Vicryl Plus) was the first antimicrobial suture to receive approval for clinical use by the US Food and Drug Administration (US FDA). To date, other triclosan-coated sutures, i.e., monofilament poliglecaprone (Monocryl Plus), monofilament polydioxanone (PDS Plus) and multifilament polyglactin 910 (Petcryl Plus) are commercially available. Several types of chlorhexidine-based sutures have also been marketed for veterinary use (Table I).

Antimicrobial Agents and Suturing Technology

The physical, biological, and handling characteristics of sutures are essential to facilitate wound healing[87]. There are two types of synthetic sutures based on the feature of absorption into the body. Absorbable sutures are made of polydioxanone, polyglycolic acid (PGA), monocryl polymer, and polylactic acid, while non-absorbable sutures are made of nylon, polyester, and polypropylene (PP) etc. Poly (lactic-co-glycolic acid) (PLGA)[88], polyvinyl alcohol (PVA) and poly-L-lactic acid (PLLA) are increasingly used in the manufacturing of modern sutures. Table II summarizes the characteristics (antimicrobial compounds, suture materials and technique) of antimicrobial sutures that have been reported from 1990-2020, besides triclosan-coated sutures.

The approaches used for incorporation of antimicrobial compounds on sutures (as illustrated in Figure 2) include (i) dip-coating, whereby sutures are dipped in a solution containing the antimicrobial agents and the polymeric coating agents (i.e., PLGA, PVA, and PLLA) for a predefined period for physical adsorption onto the sutures, (ii) surface modification and compound immobilization; whereby the suture surface is modified either by plasma treatment, radiation, or chemical grafting for introduction of a functional group to facilitate antimicrobial immobilization via formation of covalent bonding, and (iii) blending and compounding, whereby antimicrobial agents are blended with suture materials followed by synthesis of the antimicrobial suture. In this approach, electrospinning technique has been used to produce very thin fibers (micro or nano scales)[89]. Amongst these methods, dip-coating approach is the most common method for incorporation of bioactive molecules onto suture as it is less expensive and technically less demanding compared to other drug-elution/fabrication methods and does not affect the mechanical properties of sutures[89,90].

Table I. Antimicrobial sutures that have been commercialized.

Suture type	Brand name	Properties	Manufacturer
Medical use			
Triclosan-based suture	VICRYL Plus	Multifilament, absorbable polyglactin 910	Ethicon Inc.
	MONOCRYL Plus	Monofilament, absorbable poliglecaprone	
	PDS Plus	Monofilament, absorbable polydioxanone	
	Petcryl Plus	Multifilament, absorbable polyglactin 910	Futura Surgicare Pvt Ltd
Chlorhexidine-based suture	Trisorb Plus	Multifilament, absorbable poly(glycolic acid)	SamYang Biopharmaceuticals Corp
	Neosorb Plus	Multifilament, absorbable poly(glycolic co-lactic acid) (90:10)	
	Monosorb Plus	Monofilament, absorbable polydioxanone	
Veterinary use			
Chlorhexidine-based suture	Mono-Dox Plus	Monofilament, absorbable polydioxanone	CP Medical Inc.
	Visorb Plus	Multifilament, absorbable poly(glycolic acid)	
	Monoswift Plus	Monofilament, absorbable poly(glycolide-co-caprolactone) 25	

Table II. A summary of the studies conducted on the development of antimicrobial sutures (1990-2020).

Antimicrobial sutures	Main suturing technology	Type of suture investigated	Ref.
Antiseptics-based sutures			
Chlorhexidine and octenidine	Dip-coating	Braided, absorbable PGA acid suture (Gunze PGA)	73
Iodine	Dip-coating	Nylon fibers (Modipon (India) Ltd., Modinagar-India)	109
2,5-dimethoxy-2,5-dihydro-furan (DMDF)–-iodine	Cross-linking	Raw silk from Bombyx mori (Safia Silk Industries, Kolkata)	110
Octenidine hydrochloride, chlorhexidine dipalmitate, chlorhexidine dilaurate	Dip-coating	Synthetic absorbable PGA suture (PGA Resorba)	111
Octenidine	Dip-coating	PGA suture (PGA Resorba, USP 1.0), Vicryl and Vicryl Plus (Ethicon)	112
Povidone-iodine, chlorhexidine	Dip-coating	Braided nylon, non-braided nylon, silk, and Vicryl (Ethicon, USP 3-0) sutures	114
Chlorhexidine-functionalized polyelectrolyte films	Dip-coating	Silk, polyester, and copolymer of glycolide and L-lactide sutures	120
Chlorhexidine and poly (hexamethylene biguanide) (PHMB)	Dip-coating	Monofilament sutures of polyglycolide-b-poly(glycolide-co-trimethylene carbonate-co-ε-caprolactone)-b-polyglycolide suture (Monosyn)	121
Chlorhexidine	Blending	PCL monofilament	122
K21	Dip-coating	Chromic gut, polyester suture, silk, and nylon suture	128
Natural product-based sutures			
Chitosan	Dip-coating	*B. mori* silk filaments	90
Aloe vera gel and silver (Ag)	Plasma functionalisation	Poly (ethylene terephthalate) (PET, Reliance Industries Ltd. India)	91
Grapefruit seed extract	Dip-coating	PLGA synthetic absorbable braided suture (Meta Biomed Co., Ltd.)	129
Aloe vera gel	Dip-coating	Braided, nonabsorbable silk sutures (1.5 metric, size 4-0)	130
Aloe vera ethanolic extract and ciprofloxacin	Dip-coating	Silk sutures (USP 3-0)	131
Chitosan	Dip-coating	Cotton yarn	133
Chlorinated high molecular weight chitosan (N-halamine)	Coating by layer-by-layer assembly	PGA suture (Jinhuan Medical Products, China)	134
Hydrolyzed chitosan, turmeric, and clove oil	Dip-coating	Multifilament polyethylene terephthalate (PET; linear densities 540) and polyamide (nylon 6) (1260 denier) threads	135
Totarol	Spray coating	Monofilament suture (Resonlon®, 75 cm USP 3/0) and the multifilament sutures (Ethibond Excel, 75 cm, USP 3-0)	136
Eugenol	Dip-coating	Cotton-sutures (Techno 3-0/30 mm, São Paulo, Brazil)	137
Chitosan and ethanolic extracts of *C. dactylon*	Dip-coating	Silk filament (20 denier, Sarvodhya Sangam, Coimbatore)	138
Trans-resveratrol and rifampicin	Dip-coating	Braided, non-absorbable, nylon sutures (USP 0)	139

Continued

Table II *(Continued)*. A summary of the studies conducted on the development of antimicrobial sutures (1990-2020).

Antimicrobial sutures	Main suturing technology	Type of suture investigated	Ref.
Nanoparticle-based sutures			
Sodium alginate-Ag nanoparticles	Dip-coating	Supramid polyamide sutures (ref SD208000, Serag-Wiessner)	140
Sodium alginate-Ag nanoparticles	Dip-coating	Surgical gut plain suture (Ethicon Inc.)	141
Ag nanoparticles encapsulated in hyperbranched polylysine	Dip-coating	Multifilament PGA sutures (Aesculap AG)	142
Ag nanoparticles (synthesized using hot water extract of *H. inuloides*)	Dip-coating	Catgut suture (Atramat, USP 3-0)	143
Bio-silver nanoparticles (AgNP)	Dip-coating	Nonabsorbable silk sutures) (Dogsan, Turkey, USP 3-0	144
Bio-silver nanoparticles (AgNP)-propolis	Dip-coating	Nonabsorbable silk sutures (Doğsan, Istanbul, Turkey, USP 4-0)	145
Zinc oxide nanoparticles	Dip-coating	Degummed silk fibers	146
Curcumin PEGylated gold nanoparticles	Dip-coating	TRUGLYDE FAST absorbable PGA suture	147
Silver nanoparticles conjugated with trans-cinnamic acid and povidone–iodine	Dip-coating	Multifilament, braided and absorbable PGA sutures (DAMACRYL, USP 3-0)	148
Antibiotic-based sutures			
Gentamicin and silver (Ag)	Blending	PCL suture	149
Sulfamethoxazole	Dip-coating	Silk suture (Jiangsu Medical Supplies Co., Ltd.)	150
Ciprofloxacin-PCL/PGA	Dip-padding	PLA suture (Zhejiang Gaoxin Company, Jiaxing, China)	151
Levofloxacin	Electrospinning	PCL suture	152
Kanamycin, gentamicin, monomycin, and doxycycline	Graft polymerization	PCA and PP twisted suture	153
Tetracycline hydrochloride	Radiation grafting	PP suture	154
Tetracycline hydrochloride, chitosan, and silver nanoparticles,	Plasma functionalization	PP suture	155
Vancomycin	Covalent immobilization	PP monofilament suture	156
Other antimicrobial-based sutures			
Spider silk protein linked with human neutrophil defensin-1(HNP1)	Dip-coating	Non-absorbable, multifilament silk sutures (USP 3-0; Perma-Hand, Ethicon, USA)	157
Poly[(aminoethyl methacrylate)-co-(butyl methacrylate)] (PAMBM)	Dip-coating	Vicryl Plus sutures (VCP259, Ethicon Inc)	158
Poly(N-methylvinylimidazolium) iodide	Surface functionalization	PP monofilaments (Atramat suture threads)	159
Poly(2-methacryloyloxyethyl phosphorylcholine (MPC)-co-n-butyl methacrylate) (PMB)	Dip-coating	Absorbable polyglactin sutures (KRAYON Plus, KEISEI Medical Industrial Ltd., Tokyo, Japan)	160

Silver (Ag), nanoparticle (NP), polycaprolactone (PCL), polyglycolic acid (PGA), polypropylene (PP), poly-L-lactic acid (PLLA), polycaproamide (PCA).

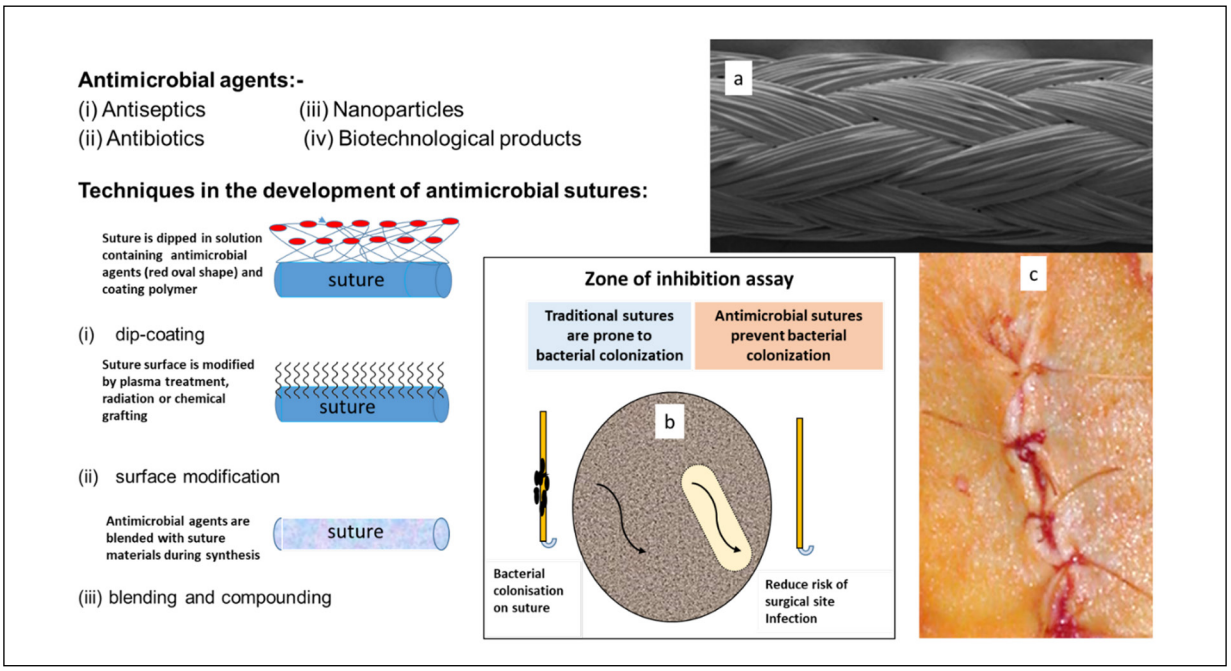

Figure 2. A variety of novel sutures have been developed with antiseptics, nanoparticles, antibiotics, and biotechnological products using techniques including (i) dip-coating, (ii) surface modification and (iii) blending and compounding, to provide antimicrobial effects and improve the wound healing properties of sutures. **a**, A multifilament suture (scanning electron microscopy, ×250 magnification). **b**, The antimicrobial effect of a suture can be determined by a zone of inhibition assay. The clear zone surrounding suture on an agar plate lawn with bacterial culture indicates growth inhibition by an antimicrobial suture. **c**, Use of antimicrobial sutures and good suturing techniques can minimize the risk of surgical site infection.

Although the delivery of many bioactive molecules via sutures can be facilitated using melt spinning, electrospinning, and radiation, the mechanical properties of sutures may be affected during fabrication. Currently, plasma functionalization of the suture and subsequent conjugation with bioactive molecules are recognized as an effective strategy as both the mechanical and infection prevention features are not likely to be affected during the fabrication process[91].

A variety of antimicrobial compounds including antiseptics, natural products, antibiotics, nanoparticles, and biotechnological products have been applied for the development of antimicrobial sutures (Table II). The evaluation of antimicrobial activities of sutures is often performed using zone of inhibition (ZOI) assays against both Gram-positive and Gram-negative bacteria (Figure 2). Antimicrobial activities are confirmed when inhibition zones are observed surrounding sutures on agar plates lawn with SSI organisms. Additionally, bacterial adherence assays are performed to determine the effectiveness of antimicrobial suture in resisting bacterial adherence and colonization. A review of the development of antimicrobial sutures over the last 30 years (1990-2020) is provided in Table II.

Antiseptic-Based Sutures

Triclosan (5-chloro-2-(2,4-dichlorophenoxy) phenol) is one of the antiseptics used in the early stage of antimicrobial suture development. It is a broad-spectrum, non-cationic, lipid-soluble chlorinated phenoxyphenol compound used in the formulation of personal care products including hand soap, toothpaste, antiperspirants shower gel, dishwashing liquid and toothpaste[92-95]. It is also used as a topical decontamination agent for hospital patients colonized with MRSA[96]. Triclosan exhibits antibacterial activity against various Gram-positive and Gram-negative bacteria, as well as some antifungal, anti-mycobacterial and antiparasitic activities[95,97]. It interferes with bacterial fatty acid formation through direct binding to the FabI protein (enoyl-acyl carrier protein reductase) and displays bacteriostatic activity at low concentrations (0.025 to 1.000 μg/ml), and bactericidal at high concentrations (7.5 to 8.0 μg/ml)[95,98-101]. Several studies[102-104] have reported the development of triclosan resistance in bacteria because of the high usage of triclosan in personal and healthcare products. Triclosan resistance is frequently reported in *S. aureus*[100]. Bacterial strains with triclosan minimum inhibitory con-

centrations (MICs) between 0.025 and 1 μg/ml have been found resistant to multiple antibiotics[105,106]. *Pseudomonas aeruginosa* is inherently resistant to triclosan due to the presence of the *FabV* gene (encoding an isozyme of FabI protein)[99,107]. Hence, triclosan-coated surgical sutures are not suitable for surgical procedures associated with *P. aeruginosa* infections.

Iodine and povidone-iodine (PVP-I) are broad-spectrum antiseptics that act by oxidation of the reactive moieties on bacterial membranes and inactivation of bacterial enzymes in the respiratory electron transport system[108]. Iodine has been incorporated either alone or with other antiseptics onto sutures to produce promising antimicrobial results[109]. In a study by Francis et al[110], radio-opaque antimicrobial sutures were developed by stepwise 2,5-dimethoxy-2,5-dihydro-furan (DMDF)–iodine cross-linking reaction for fabrication of silk fibers. The sutures inhibited *S. aureus* and *E. coli* and were non-cytotoxic against 3T3-fibroblast cells.

Chlorhexidine is an oral antiseptic with proven safety and efficacy that has been used for the development of antimicrobial sutures[73,111,112]. Chlorhexidine exhibits broad-spectrum bactericidal activity against *S. epidermidis*, MRSA, methicillin-resistant *S. epidermidis* (MRSE) and *E. coli*[113-118] through interaction with the phosphate moieties of bacterial membrane[119]. Walker et al[114] demonstrated antimicrobial activities of nylon, silk and polyglactin (Vicryl) sutures coated with chlorhexidine against *S. aureus*, MRSA and *S. epidermidis*. Sutures functionalized with chlorhexidine, poly(ethyleneimine), poly(sodium-4-styrene sulfonate), poly(allylamine hydrochloride), poly(L-glutamic acid), and poly(L-lysine) were demonstrated to inhibit *E. coli* up to 7 days[120]. The inhibition against *S. epidermidis* and *E. coli* has been shown by monofilament sutures coated with a combination of chlorhexidine, lactide, trimethylene, carbonate, and polyhexamethylene biguanide (PHMB)[121]. Scaffaro et al[122] explored a novel coating method by incorporating chlorhexidine diacetate (CHX) onto polycaprolactone (PCL) monofilament suture via a single-step approach during melt processing. Antimicrobial activities against *E. coli*, *Micrococcus luteus* and *Bacillus subtilis* strains were observed at a low CHX concentration without affecting the tensile properties of the sutures.

Octenidine is an antiseptic that has been identified as a replacement compound for triclosan[123,124]. The compound interacts with membrane cardiolipin, causes interference on the bilayer structure, and cytoplasmic leakage[123]. The cationic surfactant has a broad-spectrum activity against MDR bacteria[125]. A study by Obermeier et al[112] reported high biocompatibility, slow drug release and antimicrobial effect for up to 9 days of octenidine (11, 22 and 33 μg/cm) coatings on sutures using palmitic acid.

A series of antimicrobial sutures coated either with chlorhexidine or octenidine on PGA sutures using laurate or palmitate as drug carriers exhibited excellent antimicrobial activities[111]. Obermeier et al[73] reported higher inhibition (1.7 log reduction) of *S. aureus* adherence on sutures coated with chlorhexidine/laurate, in comparison to Vicryl Plus sutures[112]. Recently, K21, a new class of quaternary ammonium silane (SiQAS) disinfectant[126,127] has been introduced as a coating agent for different sutures. K21-coated sutures demonstrated dose-dependent inhibitory activity against oral microorganisms (*Porphyromonas gingivalis* and *Enterococcus faecalis*)[128].

Natural Product-Based Sutures

Natural products including plant extracts have been recognized as a potential source of antimicrobial coatings on sutures. Various natural products including grapefruit seed extract, aloe vera, chitosan, turmeric, clove oil, and eugenol have been explored for coating on sutures (Table II). Lee et al[129] showed the feasibility of incorporating grapefruit seed extracts on sutures for wound healing applications. Ghafoor et al[130] investigated the efficacy of aloe vera-based antimicrobial suture against bacteria (*E. coli* and *P. aeruginosa*) and filamentous fungi (*Aspergillus flavus* and *Aspergillus tubingensis*). In their study, aloe vera gel was incorporated with PVA using a dip-coating approach. Silk sutures coated with 5% aloe vera/PVA demonstrated the best inhibition against target organisms and reduced bacterial colony counts at the incision sites of Balb/c mice.

In another approach undertaken by Ravishankar et al[131], silk suture was dipped in an ethanolic extract of aloe vera, dried, and challenged with *E. coli* (ATCC 25922) using ZOI assays. The suture demonstrated inhibitory activity to *E. coli* but did not outperform suture pre-treated with ciprofloxacin. A new approach of antimicrobial polyethylene terephthalate (PET) suture development using plasma functionalization followed by immobilization of aloe vera and silver (Ag) has been recently described by Anjum et al[91]. The antimicrobial sutures demonstrated superior

bacteriostatic and bactericidal activities against *E. coli* and *S. aureus* and improved the wound healing process of Swiss albino mice.

Chitosan is a natural antimicrobial agent well recognized for its low toxicity, biodegradability, and biocompatibility. It binds to bacterial teichoic acids, and disrupts cell morphology and division[132]. Chitosan-coated surgical sutures have been reported to exhibit good antimicrobial activity and prevent bacterial adherence[90,133]. The amino group of chitosan can be functionalized with other antimicrobial agents to enhance its antimicrobial property. Umair et al[134] developed novel N-halamine-based antibacterial sutures by coating PGA suture with chitosan-poly-sodium-p-styrenesulfonate (PSS) via a layer-by-layer assembly technique to attain a linear relationship between the number of layers and chlorine (released by N-halamine for its antimicrobial activity) loadings. Nine layers of chlorinated high molecular weight chitosan were found to give the most potent antibacterial effects, killing *E. coli* and *S. aureus* within 15 minutes of contact.

In a study by Masood et al[135], multifilament nonabsorbable PET and polyamide (Nylon 6) sutures coated with varying ratios of hydrolyzed chitosan, clove oil and turmeric, and corn starch showed inhibition against *S. aureus* and improved tensile and knot strength. Reinbold et al[136] incorporated totarol ((4bS,8aS)-4b,8,8-trimethyl-1-propan-2-yl-5,6,7,8a,9,10-hexahydrophenanthren-2-ol), a plant-derived diterpenoid and PLGA onto non-absorbable monofilament and multifilament sutures. The totarol/PLGA-coated sutures showed inhibition against *S. aureus* for over 15 days without causing cytotoxicity to L929 murine fibroblast cells. Cotton sutures coated with eugenol (4-allyl-2-methoxyphenol), an aromatic constituent of clove, have been demonstrated to prevent *Streptococcus mutans* adherence[137]. Additionally, silk suture coated with chitosan and *Cynodon dactylon*, a herbal drug, also demonstrated inhibition against *S. aureus* and *E. coli*[138]. Recently, a polymerized β-cyclodextrin-based coating of trans-resveratrol (a plant antimicrobial) and rifampicin has been reported to show 24-day long antimicrobial effects towards *S. aureus* and 14-day long anti-inflammatory effects[139].

Nanoparticle-Based Sutures

The potential application of nanoparticles against infectious agents is well recognized in the medical field. Dubas et al[140] were amongst the first to use a layer-by-layer approach for coating Ag nanoparticles onto polyamide sutures. Taking the advantage of the negative charges of Ag nanoparticle binding to the cationic PDADMAC, Ag nanoparticles were rapidly adsorbed to pre-coated PDADMAC layer on sutures. The resulting suture showed a 76.82% reduction in *S. aureus* colony counts. In a study conducted by Augustine and Rajarathinam et al[141], surgical gut plain suture coated with Ag nanoparticles and sodium alginate demonstrated inhibition against *S. aureus* and *E. coli* for up to 72 hours. A hyperbranched-polylysine-based PGA suture was developed by Ho et al[142] to ensure long-term release of Ag nanoparticles. The coating agent was made up of a hydrophilic core (polylysine) and a hydrophobic shell (stearoyl/palmitoyl chloride or glycidyl hexadecyl ether) and encapsulated with at least 10 μg/cm of Ag nanoparticles. The suture reduced more than 99.5 % of bacterial adherence in comparison to the uncoated control and exhibited a stable release of Ag ions for up to 30 days.

Biogenic Ag nanoparticles have attracted considerable attention as antimicrobial agents, largely due to their safety and high biocompatibility, as compared to synthetic nanoparticles. Biogenic Ag nanoparticles are made from plant extracts or biological materials, thus bypassing the need for reducing agents such as hydrazine, dimethylformamide, and sodium borohydride. Guadarrama Reyes et al[143] reported the use of a medicinal plant (*Heterotheca inuloides*) extract to circumvent the harmful effect of chemical-based reducing agents. After immersion in the nanoparticle solution, Ag nanoparticle-based catgut suture threads showed inhibitory activities against *S. aureus* and *E. coli*. Using a similar approach, Baygar et al[144] reported the synthesis of Ag nanoparticles using *Streptomyces sp.* AU2 cell-free extract as a reducing agent. The resulting silk sutures demonstrated inhibitory activities against *Candida albicans, E. coli* and *S. aureus* with minimal cytotoxicity towards 3T3 fibroblasts.

Antimicrobial sutures have been developed by coating propolis extract with Ag nanoparticles on silk sutures[145]. Besides Ag nanoparticles, zinc oxide (ZnO) nanoparticles have also been explored for coating on silk suture[146]. The nanoparticles, synthesized using honey as a bio-reductant, were incubated with silk sutures for adsorption. The sutures demonstrated inhibition against *S. aureus* (MTCC 6908) for up to 6 days. By conjugating curcumin with PEGylated-gold nanoparticles, the solubility and metabolic stability of curcumin for coating on PGA sutures have been improved[147]. A

recent publication[148] showed the use of hybrid materials (based on synergistic antimicrobial action of biosynthesized silver nanoparticles, natural compounds, and antiseptic) as promising materials for the development of nanoparticle-based antimicrobial sutures.

Antibiotic-Based Sutures

Bacterial colonization is less likely to occur on suture in the presence of antibiotics (Table II). The development of antibiotic-based sutures is dependent on the biocompatibility, retention of antibiotic activity, and the target organisms. Sustained co-delivery of gentamicin and silver on PCL sutures using blending approach has been described[149]. Pre-treatment of braided-silk sutures with 0.1N sodium hydroxide solution, followed by coating of sulfamethoxazole trimethoprim using PCL produced a longer duration (5 days) of antimicrobial activities against *S. aureus* and *E. coli,* in comparison to the untreated suture (4 days)[150]. Liu et al[151] reported synergistic effects generated by PGA and PCL after incorporation with ciprofloxacin. Using a rat model of bacterial keratitis, Parikh et al[152] reported the development of nanofiber-based sutures loaded with a variety of drugs, including levofloxacin for the prevention of rat ocular infection.

A method to introduce ion-exchange properties to polycaproamide (PCA) and PP fibers has been described for the development of antimicrobial sutures[153]. Methacrylic acid-grafted PCA and sulfonated styrene-grafted PP sutures facilitated the adsorption of antibiotics including kanamycin, gentamicin, monomycin, and doxycycline, resulting in long-term *in vivo* antimicrobial efficacy (45 and 78 days on gentamicin-immobilized PCA and PP sutures, respectively) and good shelf-life for storage (more than 3 years). A radiation grafting approach described by Gupta et al[154] was used to immobilize tetracycline hydrochloride onto PP suture. The suture surface was first activated using radiation followed by grafting of acrylonitrile to introduce extra carboxyl groups for immobilization of tetracycline. The resulting sutures demonstrated antimicrobial activity against *E. coli* and *S. aureus* with drug release duration of 4 to 5 days, and anti-infective activity in albino rats. Additionally, graft polymerization of acrylic acid via plasma-induction followed by chitosan binding for immobilization of tetracycline hydrochloride and Ag nanoparticles showed promising *in vitro* and *in vivo* antimicrobial and drug release properties[155]. A new approach has been recently described by García-Vargas et al[156] using grafting followed by covalent immobilization of vancomycin on polypropylene (PP) monofilament sutures pre-irradiated using a (^{60})Co γ-source. The resulting suture showed a reduced number of *S. aureus* colonizing the suture.

Other Antimicrobial-Based Sutures

Biotechnological products such as synthetic peptides and recombinant proteins have been explored for the development of antimicrobial sutures. The coating of silk suture with a chimeric recombinant protein consisting of spider silk protein and alpha-defensin using dip-coating approach was reported by Franco et al[157]. The antimicrobial suture showed a reduction in the viability, adherence, and biofilm formation of MRSA and *E. coli*, and high bio- and hemocompatibility.

Amphiphilic polymers have been investigated for development of antimicrobial suture. Poly [(aminoethyl methacrylate)-co-(butylmethacrylate)] (PAMBM)-coated suture demonstrated a higher reduction in bacterial viability as compared to the triclosan-coated (Vicryl Plus) sutures[158]. Technological-wise, a novel method for grafting of bacteriostatic polymer, polyvinylimidazole (PNVIm), onto PP suture has been described by López-Saucedo et al[159]. In that study, suture exposed to gamma-ray treatment followed by acrylic monomers formed 2-hydroxyethyl methacrylate (HEMA) or N-isopropylacrylamide (NIPAAm) brushes for grafting of methyl iodide and methylimidazolium iodide which were inhibitory to *S. aureus* and *E. coli*. In a recent study[160], polyglactin sutures coated with poly (2-methacryloyloxyethyl phosphorylcholine (MPC)-co-n-butyl methacrylate) (PMB) were reported to exhibit significant inhibition against adhesion and biofilm formation of MRSA and MSSA.

Conclusions and Future Perspectives

In line with the current advances in human and veterinary medicine, there has been an increasing demand for surgical sutures for various procedures and wound management. This review presents a summary of a variety of novel antimicrobial sutures that have been developed over the last three decades. The enthusiasm of scientific research and innovation has led to the discovery of novel antimicrobial compounds, new formulations, and improvements in suturing technology.

Achieving a zero SSI rate is the goal for all healthcare providers. An ideal surgical suture should be non-toxic, does not cause host inflam-

matory response, and at the same time, is able to minimize the risk of SSIs. Together with good aseptic technique and compliance to infection control practice in the healthcare facilities, antimicrobial sutures would be able to deliver the best possible effects for wound care. Since the beginning of COVID-19 pandemic, cessation of non-urgent surgical procedures has been recommended to minimize healthcare provider-to-patient contact. Hence, the use of absorbable sutures with antimicrobial property may be an option to reduce unnecessary patients' visits to healthcare facilities. As there is no "one size fits all" suture, future development of antimicrobial suture should be tailored to the needs and assessment of SSI risk factors in each individual patient. Concomitantly, urgent actions are required to find the best effective solution to tackle antibiotic resistance.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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References

1) Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC Definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol 1992; 13: 606-608.
2) Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Infect Control Hosp Epidemiol 1999; 20: 247-280.
3) Owens CD, Stoessel K. Surgical site infections: epidemiology, microbiology and prevention. J Hosp Infect 2008; 70: 3-10.
4) Badia JM, Casey AL, Petrosillo N, Hudson PM, Mitchell SA, Crosby C. Impact of surgical site infection on healthcare costs and patient outcomes: a systematic review in six European countries. J Hosp Infect 2017; 96: 1-15.
5) Penel N, Lefebvre JL, Cazin JL, Clisant S, Neu JC, Dervaux B, Yazdanpanah Y. Additional direct medical costs associated with nosocomial infections after head and neck cancer surgery: a hospital-perspective analysis. Int J Oral Maxillofac Surg 2008; 37: 135-139.
6) Kashimura N, Kusachi S, Konishi T, Shimizu J, Kusunoki M, Oka M, Wakatsuki T, Sumiyama Y. Impact of surgical site infection after colorectal surgery on hospital stay and medical expenditure in Japan. Surg Today 2012; 42: 639-645.
7) Tuon FF, Cieslinski J, Ono AFM, Goto FL, Machinski JM, Mantovani LK, Kosop LR, Namba MS, Rocha JL. Microbiological profile and susceptibility pattern of surgical site infections related to orthopaedic trauma. Int Orthop 2019; 43: 1309-1313.
8) WHO. Report on the burden of endemic health care-associated infection worldwide. Geneva: World Health Organization, 2011. 9241501502.
9) Ling ML, Apisarnthanarak A, Abbas A, Morikane K, Lee KY, Warrier A, Yamada K. APSIC guidelines for the prevention of surgical site infections. Antimicrob Resist Infect Control 2019; 8: 174.
10) Tae BS, Park JH, Kim JK, Ku JH, Kwak C, Kim HH, Jeong CW. Comparison of intraoperative handling and wound healing between (NEOSORB plus) and coated polyglactin 910 suture (NEOSORB): a prospective, single-blind, randomized controlled trial. BMC Surg 2018; 18: 45.
11) World Health Organization. Global guidelines for the prevention of surgical site infection. World Health Organization; 2018.
12) Lee KY, Coleman K, Paech D, Norris S, Tan JT. The epidemiology and cost of surgical site infections in Korea: a systematic review. J Korean Surg Soc 2011; 81: 295-307.
13) Morikane K, Honda H, Yamagishi T, Suzuki S, Aminaka M. Factors associated with surgical site infection in colorectal surgery: the Japan nosocomial Infections surveillance. Infect Control Hosp Epidemiol 2014; 35: 660-666.
14) Allegranzi B, Nejad SB, Combescure C, Graafmans W, Attar H, Donaldson L, Pittet D. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. Lancet 2011; 377: 228-241.
15) Alfonso-Sanchez JL, Martinez IM, Martín-Moreno JM, González RS, Botía F. Analyzing the risk factors influencing surgical site infections: the site of environmental factors. Can J Surg 2017; 60: 155-161.
16) Sartelli M, Pagani L, Iannazzo S, Moro ML, Viale P, Pan A, Ansaloni L, Coccolini F, D'Errico MM, Agreiter I, Amadio Nespola G, Barchiesi F, Benigni V, Binazzi R, Cappanera S, Chiodera A, Cola V, Corsi D, Cortese F, Crapis M, Cristini F, D'Arpino A, De Simone B, Di Bella S, Di Marzo F, Donati A, Elisei D, Fantoni M, Ferrari A, Foghetti D, Francisci D, Gattuso G, Giacometti A, Gesuelli GC, Marmorale C, Martini E, Meledandri M, Murri R, Padrini D, Palmieri D, Pauri P, Rebagliati C, Ricchizzi E, Sambri V, Schimizzi AM, Siquini W, Scoccia L, Scoppettuolo G, Sganga G, Storti N, Tavio M, Toccafondi G, Tumietto F, Viaggi B, Vivarelli M, Tranà C, Raso M, Labricciosa FM, Dhingra S, Catena F. A proposal for a comprehensive approach to infections across the surgical pathway. World J Emerg Surg 2020; 15: 13.

17) Ansari S, Hassan M, Barry HD, Bhatti TA, Hussain SZM, Jabeen S, Fareed S. Risk factors associated with surgical site infections: a retrospective report from a developing country. Cureus 2019; 11: e4801-e4801.

18) Okasha H. Risk factors and key principles for prevention of surgical site infections. In: Surgical Infections-Some Facts. IntechOpen; 2019.

19) Reichman DE, Greenberg JA. Reducing surgical site infections: a review. Rev Obstet Gynecol 2009; 2: 212-221.

20) European Centre for Disease Prevention and Control. Surveillance of surgical site infections in Europe 2010–2011. Stockholm: European Centre for Disease Prevention and Control, 2013.

21) Spagnolo AM, Ottria G, Amicizia D, Perdelli F, Cristina ML. Operating theatre quality and prevention of surgical site infections. J Prev Med Hyg 2013; 54: 131-137.

22) Haque M, Sartelli M, McKimm J, Abu Bakar M. Health care-associated infections - an overview. Infect Drug Resist 2018; 11: 2321-2333.

23) Aga E, Keinan-Boker L, Eithan A, Mais T, Rabinovich A, Nassar F. Surgical site infections after abdominal surgery: incidence and risk factors. A prospective cohort study. Infect Dis (Lond) 2015; 47: 761-767.

24) Whitehouse JD, Friedman ND, Kirkland KB, Richardson WJ, Sexton DJ. The impact of surgical-site infections following orthopedic surgery at a community hospital and a university hospital adverse quality of life, excess length of stay, and extra cost. Infect Control Hosp Epidemiol 2002; 23: 183-189.

25) Prasad S, Zaveri G. Surgical management of surgical site infections in orthopaedics. J Clin Orthop 2019; 4: 17-25.

26) Li Gq, Guo Ff, Ou Y, Dong Gw, Zhou W. Epidemiology and outcomes of surgical site infections following orthopedic surgery. Am J Infect Control 2013; 41: 1268-1271.

27) Cristina ML, Sartini M, Schinca E, Ottria G, Spagnolo AM. Operating room environment and surgical site infections in arthroplasty procedures. J Prev Med Hyg 2016; 57: E142-E148.

28) Korol E, Johnston K, Waser N, Sifakis F, Jafri H, Lo M, Kyaw M. A systematic review of risk factors associated with surgical site infections among surgical patients. PLoS One 2013; 8: e83743-e83743.

29) Zhang Y, Zheng QJ, Wang S, Zeng SX, Zhang YP, Bai XJ, Hou TY. Diabetes mellitus is associated with increased risk of surgical site infections: a meta-analysis of prospective cohort studies. Am J Infect Control 2015; 43: 810-815.

30) Edmiston CE, Seabrook GR, Goheen MP, Krepel CJ, Johnson CP, Lewis BD, Brown KR, Towne JB. Bacterial adherence to surgical sutures: can antibacterial-coated sutures reduce the risk of microbial contamination? J Am Coll Surg 2006; 203: 481-489.

31) Edmiston CE, Krepel CJ, Marks RM, Rossi PJ, Sanger J, Goldblatt M, Graham MB, Rothenburger S, Collier J, Seabrook GR. Microbiology of explanted suture segments from infected and noninfected surgical patients. J Clin Microbiol 2013; 51: 417.

32) Kathju S, Nistico L, Tower I, Lasko LA, Stoodley P. Bacterial biofilms on implanted suture material are a cause of surgical site infection. Surg Infect (Larchmt) 2014; 15: 592-600.

33) Tummalapalli M, Anjum S, Kumari S, Gupta B. Antimicrobial surgical sutures: recent developments and strategies. Polym Rev (Phila Pa) 2016; 56: 607-630.

34) Banche G, Roana J, Mandras N, Amasio M, Gallesio C, Allizond V, Angeretti A, Tullio V, Cuffini AM. Microbial adherence on various intraoral suture materials in patients undergoing dental surgery. J Oral Maxillofac Surg 2007; 65: 1503-1507.

35) Alexiou K, Drikos I, Terzopoulou M, Sikalias N, Ioannidis A, Economou N. A prospective randomised trial of isolated pathogens of surgical site infections (SSI). Ann Med Surg 2017; 21: 25-29.

36) Birhanu Y, Endalamaw A. Surgical site infection and pathogens in Ethiopia: a systematic review and meta-analysis. Patient Saf Surg 2020; 14: 7.

37) David MZ, Daum RS. Community-associated methicillin-resistant Staphylococcus aureus: epidemiology and clinical consequences of an emerging epidemic. Clin Microbiol Rev 2010; 23: 616-687.

38) Bhattacharya S, Pal K, Jain S, Chatterjee SS, Konar J. Surgical site infection by methicillin resistant Staphylococcus aureus- on decline? J Clin Diagn Res 2016; 10: DC32-DC36.

39) Abbas M, Aghayev E, Troillet N, Eisenring MC, Kuster SP, Widmer AF, Harbarth S, Balmelli C, Eisenring MC, Harbarth S, Kuster SP, Marschall J, Spicher VM, Pittet D, Ruef C, Sax H, Schlegel M, Schweiger A, Troillet N, Widmer AF, Zanetti G. Temporal trends and epidemiology of Staphylococcus aureus surgical site infection in the Swiss surveillance network: a cohort study. J Hosp Infect 2018; 98: 118-126.

40) O'brien WJ, Gupta K, Itani KMF. A longitudinal study of S. aureus infection in a national cohort of surgical patients. Open Forum Infect Dis 2019; 6.

41) WHO. Antibiotic resistance: World Health Organization 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance.

42) Munita JM, Arias CA. Mechanisms of antibiotic resistance. Microbiol Spectr 2016; 4: 4-2.

43) Reygaert WC. An overview of the antimicrobial resistance mechanisms of bacteria. AIMS Microbiol 2018; 4: 482-501.

44) Arzanlou M, Chai Wern C, Venter H. Intrinsic, adaptive and acquired antimicrobial resistance in Gram-negative bacteria. Essays Biochem 2017; 61: 49-59.

45) Sandoval-Motta S, Aldana M. Adaptive resistance to antibiotics in bacteria: a systems biology perspective. Wiley Interdiscip Rev Syst Biol Med 2016; 8: 253-267.

46) Sun E, Gill EE, Falsafi R, Yeung A, Liu S, Hancock REW. Broad-spectrum adaptive antibiotic resistance associated with mucin-dependent surfing motility. Antimicrob Agents Chemother 2018; 62: e00848-00818.

47) Anderson DJ, Kaye KS. Staphylococcal Surgical Site Infections. Infect Dis Clin North Am 2009; 23: 53-72.

48) Lewis RT. Soft tissue infections. World J Surg 1998; 22: 146-151.

49) Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJC, Gorbach SL, Hirschmann JV, Kaplan EL, Montoya JG, Wade JC. Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections. Clin Infect Dis 2005; 41: 1373-1406.

50) Schweizer ML, Chiang H-Y, Septimus E, Moody J, Braun B, Hafner J, Ward MA, Hickok J, Perencevich EN, Diekema DJ, Richards CL, Cavanaugh JE, Perlin JB, Herwaldt LA. Association of a Bundled Intervention With Surgical Site Infections Among Patients Undergoing Cardiac, Hip, or Knee Surgery. JAMA 2015; 313: 2162-2171.

51) Bull AL, Worth LJ, Richards MJ. Impact of vancomycin surgical antibiotic prophylaxis on the development of methicillin-sensitive staphylococcus aureus surgical site infections: report from Australian Surveillance Data (VICNISS). Ann Surg 2012; 256: 1089-1092.

52) Ban KA, Minei JP, Laronga C, Harbrecht BG, Jensen EH, Fry DE, Itani KMF, Dellinger EP, Ko CY, Duane TM. American College of Surgeons and Surgical Infection Society: surgical site infection guidelines, 2016 update. J Am Coll Surg 2017; 224: 59-74.

53) Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, Reinke CE, Morgan S, Solomkin JS, Mazuski JE, Dellinger EP, Itani KMF, Berbari EF, Segreti J, Parvizi J, Blanchard J, Allen G, Kluytmans JAJW, Donlan R, Schecter WP, Committee HICPA. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. JAMA Surg 2017; 152: 784-791.

54) Iyamba JML, Wambale JM, Lukukula CM, Takaisi-Kikuni NzB. High prevalence of methicillin resistant Staphylococci strains isolated from surgical site infections in Kinshasa. Pan Afr Med J 2014; 18: 322-322.

55) Călina D, Docea AO, Rosu L, Zlatian O, Rosu AF, Anghelina F, Rogoveanu O, Arsene AL, Nicolae AC, Drăgoi CM, Tsiaoussis J, Tsatsakis AM, Spandidos DA, Drakoulis N, Gofita E. Antimicrobial resistance development following surgical site infections. Mol Med Rep 2017; 15: 681-688.

56) Manyahi J, Matee MI, Majigo M, Moyo S, Mshana SE, Lyamuya EF. Predominance of multi-drug resistant bacterial pathogens causing surgical site infections in Muhimbili national hospital, Tanzania. BMC Res Notes 2014; 7: 5002014; 7: 500.

57) Teerawattanapong N, Panich P, Kulpokin D, Na Ranong S, Kongpakwattana K, Saksinanon A, Goh BH, Lee LH, Apisarnthanarak A, Chaiyakunapruk N. A systematic review of the burden of multidrug-resistant healthcare-associated infections among intensive care unit patients in Southeast Asia: the rise of multidrug-resistant Acinetobacter baumannii. Infect Control Hosp Epidemiol 2018; 39: 525-533.

58) Lim C, Takahashi E, Hongsuwan M, Wuthiekanun V, Thamlikitkul V, Hinjoy S, Day NPJ, Peacock SJ, Limmathurotsakul D. Epidemiology and burden of multidrug-resistant bacterial infection in a developing country. Elife 2016; 5: e18082.

59) Li B, Webster TJ. Bacteria antibiotic resistance: new challenges and opportunities for implant-associated orthopedic infections. J Orthop Res 2018; 36: 22-32.

60) Cecchini M, Langer J, Slawomirski L. Antimicrobial resistance in G7 countries and beyond: economic issues, policies and options for action. Paris: Organization for Economic Co-operation and Development, 2015.

61) Michalopoulos AS, Tsiodras S, Rellos K, Mentzelopoulos S, Falagas ME. Colistin treatment in patients with ICU-acquired infections caused by multiresistant Gram-negative bacteria: the renaissance of an old antibiotic. Clin Microbiol Infect 2005; 11: 115-121.

62) Friedman ND, Temkin E, Carmeli Y. The negative impact of antibiotic resistance. Clin Microbiol Infect 2016; 22: 416-422.

63) Teillant A, Gandra S, Barter D, Morgan DJ, Laxminarayan R. Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: a literature review and modelling study. Lancet Infect Dis 2015; 15: 1429-1437.

64) Boles BR, Horswill AR. Agr-mediated dispersal of Staphylococcus aureus biofilms. PLoS Pathog 2008; 4: e1000052.

65) Boles BR, Horswill AR. Staphylococcal biofilm disassembly. Trends Microbiol 2011; 19: 449-455.

66) Otto M. Staphylococcal biofilms. Microbiol Spectr 2018; 6: 6-4.

67) Vergidis P, Patel R. Novel approaches to the diagnosis, prevention, and treatment of medical device-associated infections. Infect Dis Clin North Am 2012; 26: 173-186.

68) Francolini I, Donelli G. Prevention and control of biofilm-based medical-device-related infections. FEMS Immunol Med Microbiol 2010; 59: 227-238.

69) Halawani EM. Nanomedicine opened new horizons for metal nanoparticles to treat multi-drug resistant organisms. Int J Curr Microbiol Appl Sci 2016; 5: 397-414.

70) Kathju S, Nistico L, Hall-Stoodley L, Post JC, Ehrlich GD, Stoodley P. Chronic surgical site infection due to suture-associated polymicrobial biofilm. Surg Infect (Larchmt) 2009; 10: 457-461.

71) Henry-Stanley MJ, Hess DJ, Barnes AM, Dunny GM, Wells CL. Bacterial contamination of surgical suture resembles a biofilm. Surg Infect (Larchmt) 2010; 11: 433-439.

72) Edmiston CE, McBain AJ, Roberts C, Leaper D. Clinical and microbiological aspects of biofilm-associated surgical site infections. Springer International Publishing; 2015.

73) Obermeier A, Schneider J, Harrasser N, Tubel J, Muhlhofer H, Pforringer D, Deimling CV, Foehr P, Kiefel B, Kramer C, Stemberger A, Schieker M, Burgkart R, von Eisenhart-Rothe R. Viable adhered Staphylococcus aureus highly reduced on novel antimicrobial sutures using chlorhexidine and octenidine to avoid surgical site infection (SSI). PLoS One 2018; 13: e0190912.

74) Gordon CP, Williams P, Chan WC. Attenuating Staphylococcus aureus virulence gene regulation: a medicinal chemistry perspective. J Med Chem 2013; 56: 1389-1404.

75) Begun J, Gaiani JM, Rohde H, Mack D, Calderwood SB, Ausubel FM, Sifri CD. Staphylococcal biofilm exopolysaccharide protects against Caenorhabditis elegans immune defenses. PLoS Pathog 2007; 3: e57.

76) Di Ciccio P, Vergara A, Festino AR, Paludi D, Zanardi E, Ghidini S, Ianieri A. Biofilm formation by Staphylococcus aureus on food contact surfaces: relationship with temperature and cell surface hydrophobicity. Food Control 2015; 50: 930-936.

77) Gao P, Ho PL, Yan B, Sze KH, Davies J, Kao RYT. Suppression of Staphylococcus aureus virulence by a small-molecule compound. Proc Natl Acad Sci U S A 2018; 115: 8003.

78) Cegelski L, Marshall GR, Eldridge GR, Hultgren SJ. The biology and future prospects of antivirulence therapies. Nat Rev Microbiol 2008; 6: 17-27.

79) Escaich S. Antivirulence as a new antibacterial approach for chemotherapy. Curr Opin Chem Biol 2008; 12: 400-408.

80) Guo J, Pan LH, Li YX, Yang XD, Li LQ, Zhang CY, Zhong JH. Efficacy of triclosan-coated sutures for reducing risk of surgical site infection in adults: a meta-analysis of randomized clinical trials. J Surg Res 2016; 201: 105-117.

81) Sandini M, Mattavelli I, Nespoli L, Uggeri F, Gianotti L. Systematic review and meta-analysis of sutures coated with triclosan for the prevention of surgical site infection after elective colorectal surgery according to the PRISMA statement. Medicine (Baltimore) 2016; 95: e4057.

82) Onesti MG, Carella S, Scuderi N. Effectiveness of antimicrobial-coated sutures for the prevention of surgical site infection: a review of the literature. Eur Rev Med Pharmacol Sci 2018; 22: 5729-5739.

83) Kim JM, Park ES, Jeong JS, Kim KM, Kim JM, Oh HS, Yoon SW, Chang HS, Chang KH, Lee SI, Lee MS, Song JH, Kang MW, Park SC, Choe KW, Pai CH. Multicenter surveillance study for nosocomial infections in major hospitals in Korea. Am J Infect Control 2000; 28: 454-458.

84) Henriksen NA, Deerenberg EB, Venclauskas L, Fortelny RH, Garcia-Alamino JM, Miserez M, Muysoms FE. Triclosan-coated sutures and surgical site infection in abdominal surgery: the TRISTAN review, meta-analysis and trial sequential analysis. Hernia 2017; 21: 833-841.

85) Wu X, Kubilay NZ, Ren J, Allegranzi B, Bischoff P, Zayed B, Pittet D, Li J. Antimicrobial-coated sutures to decrease surgical site infections: a systematic review and meta-analysis. Eur J Clin Microbiol Infect Dis 2017; 36: 19-32.

86) Anderson DJ, Podgorny K, Berríos-Torres SI, Bratzler DW, Dellinger EP, Greene L, Nyquist AC, Saiman L, Yokoe DS, Maragakis LL, Kaye KS. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol 2014; 35: 605-627.

87) Rothenburger S, Spangler D, Bhende S, Burkley D. In vitro antimicrobial evaluation of Coated VICRYL* Plus Antibacterial Suture (coated polyglactin 910 with triclosan) using zone of inhibition assays. Surg Infect (Larchmt) 2002; 3: S79-87.

88) Lim TY, Poh CK, Wang W. Poly (lactic-co-glycolic acid) as a controlled release delivery device. J Mater Sci Mater Med 2009; 20: 1669-1675.

89) Champeau M, Thomassin JM, Tassaing T, Jérôme C. Current manufacturing processes of drug-eluting sutures. Expert Opin Drug Deliv 2017; 14: 1293-1303.

90) Viju S, Thilagavathi G. Effect of chitosan coating on the characteristics of silk-braided sutures. J Ind Text 2012; 42: 256-268.

91) Anjum S, Gupta A, Kumari S, Gupta B. Preparation and biological characterization of plasma functionalized poly(ethylene terephthalate) antimicrobial sutures. Int J Polymer Mater Po 2020; 69: 1034-1042.

92) Bhargava HN, Leonard PA. Triclosan: applications and safety. Am J Infect Control 1996; 24: 209-218.

93) Schweizer HP. Triclosan: a widely used biocide and its link to antibiotics. FEMS Microbiol Lett 2001; 202: 1-7.

94) Aranami K, Readman JW. Photolytic degradation of triclosan in freshwater and seawater. Chemosphere 2007; 66: 1052-1056.

95) Cakmak A, Cirpanli Y, Bilensoy E, Yorganci K, Calis S, Saribas Z, Kaynaroglu V. Antibacterial activity of triclosan chitosan coated graft on hernia graft infection model. Int J Pharm 2009; 381: 214-219.

96) Z AD, Morrison D, Philpott-Howard J. Small colony variants and triclosan resistance in five international clones of methicillin resistant Staphylococcus aureus. J Mol Biol Res 2017; 7: 112.

97) Saleh S, Haddadin RN, Baillie S, Collier PJ. Triclosan - an update. Lett Appl Microbiol 2011; 52: 87-95.

98) McMurry LM, Oethinger M, Levy SB. Triclosan targets lipid synthesis. Nature 1998; 394: 531-532.

99) Russell AD. Whither triclosan? J Antimicrob Chemother 2004; 53: 693-695.

100) Suller MTE, Russell AD. Triclosan and antibiotic resistance in Staphylococcus aureus. J Antimicrob Chemother 2000; 46: 11-18.

101) Suller MT, Russell AD. Antibiotic and biocide resistance in methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococcus. J Hosp Infect 1999; 43: 281-291.

102) Kampf G. Biocidal agents used for disinfection can enhance antibiotic resistance in Gram-negative species. Antibiotics (Basel) 2018; 7: 110.

103) Westfall C, Flores-Mireles AL, Robinson JI, Lynch AJL, Hultgren S, Henderson JP, Levin PA. The widely used antimicrobial triclosan induces high levels of antibiotic tolerance in vitro and reduces antibiotic efficacy up to 100-fold in vivo. Antimicrob Agents Chemother 2019; 63: e02312-e02318.

104) Bischofberger AM, Baumgartner M, Pfrunder-Cardozo KR, Allen RC, Hall AR. Associations between sensitivity to antibiotics, disinfectants and heavy metals in natural, clinical and laboratory isolates of Escherichia coli. Environ Microbiol 2020; 22: 2664-2679.

105) Yazdankhah SP, Scheie AA, Høiby EA, Lunestad B-T, Heir E, Fotland TØ, Naterstad K, Kruse H. Triclosan and antimicrobial resistance in bacteria: an overview. Microb Drug Resist 2006; 12: 83-90.

106) Copitch JL, Whitehead RN, Webber MA. Prevalence of decreased susceptibility to triclosan in Salmonella enterica isolates from animals and humans and association with multiple drug resistance. Int J Antimicrob Agents 2010; 36: 247-251.

107) Chuanchuen R, Karkhoff-Schweizer RR, Schweizer HP. High-level triclosan resistance in Pseudomonas aeruginosa is solely a result of efflux. Am J Infect Control 2003; 31: 124-127.

108) Kanagalingam J, Feliciano R, Hah JH, Labib H, Le TA, Lin JC. Practical use of povidone-iodine antiseptic in the maintenance of oral health and in the prevention and treatment of common oropharyngeal infections. Int J Clin Pract 2015; 69: 1247-1256.

109) Singhal JP, Singh J, Ray AR, Singh H, Rattan A. Antibacterial multifilament nylon sutures. Biomater Artif Cells Immobilization Biotechnol 1991; 19: 631-648.

110) Francis NK, Pawar HS, Ghosh P, Dhara S. In situ iodination cross-linking of silk for radio-opaque antimicrobial surgical sutures. ACS Biomater Sci Eng 2016; 2: 188-196.

111) Matl FD, Zlotnyk J, Obermeier A, Friess W, Vogt S, Büchner H, Schnabelrauch H, Stemberger A, Kühn KD. New anti-infective coatings of surgical sutures based on a combination of antiseptics and fatty acids. J Biomater Sci Polym Ed 2009; 20: 1439-1449.

112) Obermeier A, Schneider J, Föhr P, Wehner S, Kühn KD, Stemberger A, Schieker M, Burgkart R. In vitro evaluation of novel antimicrobial coatings for surgical sutures using octenidine. BMC Microbiol 2015; 15: 186.

113) Hennessey TD. Some antibacterial properties of chlorhexidine. J Periodontal Res 1973; 8: 61-67.

114) Walker G, Rude M, Cirillo SLG, Cirillo JD. Efficacy of using sutures treated with povidone-iodine or chlorhexidine for preventing growth of Staphylococcus and Escherichia coli. Plast Reconstr Surg 2009; 124: 191e-193e.

115) Koburger T, Hübner NO, Braun M, Siebert J, Kramer A. Standardized comparison of antiseptic efficacy of triclosan, PVP–iodine, octenidine dihydrochloride, polyhexanide and chlorhexidine digluconate. J Antimicrob Chemother 2010; 65: 1712-1719.

116) Schlett CD, Millar EV, Crawford KB, Cui T, Lanier JB, Tribble DR, Ellis MW. Prevalence of chlorhexidine-resistant methicillin-resistant Staphylococcus aureus following prolonged exposure. Antimicrob Agents Chemother 2014; 58: 4404.

117) Russell AD, Path FRC. Chlorhexidine: antibacterial action and bacterial resistance. Infection 1986; 14: 212-215.

118) Hiom SJ, Furr JR, Russell AD, Dickinson JR. Effects of chlorhexidine diacetate on Candida albicans, C. glabrata and Saccharomyces cerevisiae. J Appl Bacteriol 1992; 72: 335-340.

119) Cheung HY, Wong MMK, Cheung SH, Liang LY, Lam YW, Chiu SK. Differential actions of chlorhexidine on the cell wall of Bacillus subtilis and Escherichia coli. PLoS One 2012; 7: e36659-e36659.

120) Harnet JC, Le Guen E, Ball V, Tenenbaum H, Ogier J, Haikel Y, Vodouhê C. Antibacterial protection of suture material by chlorhexidine-functionalized polyelectrolyte multilayer films. J Mater Sci Mater Med 2009; 20: 185-193.

121) Márquez Y, Cabral T, Lorenzetti A, Franco L, Turon P, del Valle LJ, Puiggalí J. Incorporation of biguanide compounds into poly(GL)-b-poly(GL-co-TMC-co-CL)-b-poly(GL) monofilament surgical sutures. Mater Sci Eng C Mater Biol Appl 2017; 71: 629-640.

122) Scaffaro R, Botta L, Sanfilippo M, Gallo G, Palazzolo G, Puglia AM. Combining in the melt physical and biological properties of poly(caprolactone) and chlorhexidine to obtain antimicrobial surgical monofilaments. Appl Microbiol Biotechnol 2013; 97: 99-109.

123) Hübner NO, Siebert J, Kramer A. Octenidine dihydrochloride, a modern antiseptic for skin, mucous membranes and wounds. Skin Pharmacol Physiol 2010; 23: 244-258.

124) Leaper D, McBain AJ, Kramer A, Assadian O, Sanchez JLA, Lumio J, Kiernan M. Healthcare associated infection: novel strategies and antimicrobial implants to prevent surgical site infection. Ann R Coll Surg Engl 2010; 92: 453-458.

125) Greener M. Octenidine: antimicrobial activity and clinical efficacy. Wounds UK 2011; 7: 74-78.

126) Daood U, Parolia A, Elkezza A, Yiu CK, Abbott P, Matinlinna JP, Fawzy AS. An in vitro study of a novel quaternary ammonium silane endodontic irrigant. Dent Mater 2019; 35: 1264-1278.

127) Daood U, Burrow MF, Yiu CKY. Effect of a novel quaternary ammonium silane cavity disinfectant on cariogenic biofilm formation. Clin Oral Investig 2020; 24: 649-661.

128) Meghil MM, Rueggeberg F, El-Awady A, Miles B, Tay F, Pashley D, Cutler CW. Novel coating of surgical suture confers antimicrobial activity against Porphyromonas gingivalis and Enterococcus faecalis. J Periodontol 2015; 86: 788-794.

129) Lee HS, Park SH, Lee JH, Jeong BY, Ahn SK, Choi YM, Choi DJ, Chang JH. Antimicrobial and biodegradable PLGA medical sutures with natural grapefruit seed extracts. Mater Lett 2013; 95: 40-43.

130) Ghafoor B, Ali MN, Ansari U, Bhatti MF, Mir M, Akhtar H, Darakhshan F. New biofunctional loading of natural antimicrobial agent in biodegradable polymeric films for biomedical applications. Int J Biomater 2016; 2016: 6964938.

131) Ravishankar PL, Vijayan V, Rao SK, Vadivelu SA, Narayanaswamy D, Teja S. In vitro antibacterial efficacy of sutures coated With Aloe vera and ciprofloxacin: a comparative evaluation. J Pharm Bioallied Sci 2019; 11: S164-S168.

132) Raafat D, von Bargen K, Haas A, Sahl H-G. Insights into the Mode of Action of Chitosan as an Antibacterial Compound. Appl Environ Microbiol 2008; 74: 3764-3773.

133) Shanmugasundaram O, Dev V, Neelakandan R, Madhusoothanan M, Rajkumar GS. Drug release and antimicrobial studies on chitosan-coated cotton yarns. Indian J Fibre Text Res 2006; 31: 543-547.

134) Umair MM, Jiang Z, Ullah N, Safdar W, Xie Z, Ren X. Development and characterisation of antibacterial suture functionalised with N-halamines. J Ind Text 2015; 46: 59-74.

135) Masood R, Hussain T, Umar M, Azeemullah, Areeb T, Riaz S. In situ development and application of natural coatings on non-absorbable sutures to reduce incision site infections. J Wound Care 2017; 26: 115-120.

136) Reinbold J, Uhde AK, Muller I, Weindl T, Geis-Gerstorfer J, Schlensak C, Wendel HP, Krajewski S. Preventing surgical site infections using a natural, biodegradable, antibacterial coating on surgical sutures. Molecules 2017; 22: 1570.

137) Carneiro VA, de Fatima Furtado E, Silva ML, Silva RL, Fidelis QC, Junior FEAC. Inhibition of Streptococcus mutans (ATCC 25175) biofilm formation on eugenol-impregnated surgical sutures. Afr J Microbiol Res 2019; 13: 168-175.

138) Sudha D, Dhurai B, Ponthangam T. Development of herbal drug loaded antimicrobial silk suture. Indian J Fibre Text Res 2017; 42: 286-290.

139) Haley RM, Qian VR, Learn GD, von Recum HA. Use of affinity allows anti-inflammatory and anti-microbial dual release that matches suture wound resolution. J Biomed Mater Res A 2019; 107: 1434-1442.

140) Dubas ST, Wacharanad S, Potiyaraj P. Tunning of the antimicrobial activity of surgical sutures coated with silver nanoparticles. Colloids Surf A Physicochem Eng Asp 2011; 380: 25-28.

141) Augustine R, Rajarathinam K. Synthesis and characterization of silver nanoparticles and its immobilization on alginate coated sutures for the prevention of surgical wound infections and the in vitro release studies. Int J Nanodimens 2012; 2: 205-212.

142) Ho CH, Odermatt EK, Berndt I, Tiller JC. Long-term active antimicrobial coatings for surgical sutures based on silver nanoparticles and hyperbranched polylysine. J Biomater Sci Polym Ed 2013; 24: 1589-1600.

143) Guadarrama Reyes SC, Morales Luckie RA, Sánchez Mendieta V, González Pedroza MG, Lara Carrillo E, Velazquez-Enriquez U, Scougall Vilchis RJ. Green synthesis of silver nanoparticles using Heterotheca inuloides and its antimicrobial activity in catgut suture threads. In: Engineered Nanomaterials-Health and Safety. IntechOpen; 2019.

144) Baygar T, Sarac N, Ugur A, Karaca IR. Antimicrobial characteristics and biocompatibility of the surgical sutures coated with biosynthesized silver nanoparticles. Bioorg Chem 2019; 86: 254-258.

145) Baygar T. Characterization of silk sutures coated with propolis and biogenic silver nanoparticles (AgNPs); an eco-friendly solution with wound healing potential against surgical site infections (SSIs). Turk J Med Sci 2020; 50: 258-266.

146) Shubha P, Gowda ML, Namratha K, Shyamsunder S, Manjunatha HB, Byrappa K. Ex-situ fabrication of ZnO nanoparticles coated silk fiber for surgical applications. Mater Chem Phys 2019; 231: 21-26.

147) Sunitha S, Adinarayana K, Sravanthi R, Sonia G, Nagarjun R, Pankaj T, Veerabhadra S, Sujatha D. Fabrication of surgical sutures coated with curcumin loaded gold nanoparticles. Pharm Anal Acta 2017; 8: 1-12.

148) Edis Z, Haj Bloukh S, Ibrahim MR, Abu Sara H. "Smart" antimicrobial nanocomplexes with potential to decrease surgical site infections (SSI). Pharmaceutics 2020; 12.

149) Chen S, Ge L, Mueller A, Carlson MA, Teusink MJ, Shuler FD, Xie J. Twisting electrospun nanofiber fine strips into functional sutures for sustained co-delivery of gentamicin and silver. Nanomedicine 2017; 13: 1435-1445.

150) Pethile S, Sizo N, Lloyd N. A study of the antimicrobial efficancy of silk suture. Ethiop J Text Appar 2019; 1.

151) Liu S, Yu J, Li H, Wang K, Wu G, Wang B, Liu M, Zhang Y, Wang P, Zhang J, Wu J, Jing Y, Li F, Zhang M. Controllable drug release behavior of polylactic acid (PLA) surgical suture coating with ciprofloxacin (CPFX)—polycaprolactone (PCL)/polyglycolide (PGA). Polymers (Basel) 2020; 12.

152) Parikh KS, Omiadze R, Josyula A, Shi R, Anders NM, He P, Yazdi Y, McDonnell PJ, Ensign LM, Hanes J. Ultra-thin, high strength, antibiotic-eluting sutures for prevention of ophthalmic infection. Bioeng Transl Med 2020: e10204.

153) Zhukovskii VA, Khokhlova VA, Korovicheva SY. Surgical suture materials with antimicrobial properties. Fibre Chem 2007; 39: 136-143.

154) Gupta B, Jain R, Singh H. Preparation of antimicrobial sutures by preirradiation grafting onto polypropylene monofilament. Polym Adv Technol 2008; 19: 1698-1703.

155) Saxena S, Ray AR, Kapil A, Pavon-Djavid G, Letourneur D, Gupta B, Meddahi-Pelle A. Development of a new polypropylene-based suture: plasma grafting, surface treatment, characterization, and biocompatibility studies. Macromol Biosci 2011; 11: 373-382.

156) García-Vargas M, González-Chomón C, Magariños B, Concheiro A, Alvarez-Lorenzo C, Bucio E. Acrylic polymer-grafted polypropylene sutures for covalent immobilization or reversible adsorption of vancomycin. Int J Pharm 2014; 461: 286-295.

157) Franco AR, Fernandes EM, Rodrigues MT, Rodrigues FJ, Gomes ME, Leonor IB, Kaplan DL, Reis RL. Antimicrobial coating of spider silk to prevent bacterial attachment on silk surgical sutures. Acta Biomater 2019; 99: 236-246.

158) Li Y, Kumar KN, Dabkowski JM, Corrigan M, Scott RW, Nüsslein K, Tew GN. New bactericidal surgical suture coating. Langmuir 2012; 28: 12134-12139.

159) López-Saucedo F, Flores-Rojas GG, Bucio E, Alvarez-Lorenzo C, Concheiro A, González-Antonio O. Achieving antimicrobial activity through poly(N-methylvinylimidazolium) iodide brushes on binary-grafted polypropylene suture threads. MRS Commun 2017; 7: 938-946.

160) Kaneko T, Saito T, Shobuike T, Miyamoto H, Matsuda J, Fukazawa K, Ishihara K, Tanaka S, Moro T. 2-methacryloyloxyethyl phosphorylcholine polymer coating inhibits bacterial adhesion and biofilm formation on a suture: an in vitro and in vivo study. Biomed Res Int 2020; 2020: 5639651.