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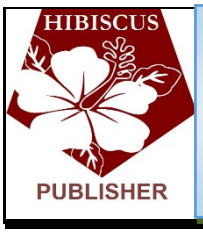

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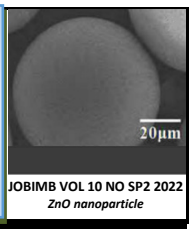

A Review on Polymer Based Antimicrobial Coating

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ABSTRACT

Antimicrobial coatings have become a key component of the worldwide microbial infection mitigation plan. A wide range of alternatives for designing surfaces with antimicrobial qualities is now accessible, attributed to the recent developments in materials science, biotechnology, and environmental microbiology. Antimicrobial coatings have a big role to control the spread of disease, preventing microbial colonisation on the substrate used in various applications. The antimicrobial coatings could be formed on the substrate by utilizing the polymer with antimicrobial properties or incorporating the antimicrobial agents into the polymer. By manipulating the use of polymers and surrounding conditions, the antimicrobial activity of the coating could be tailored accordingly. Due to the difference in physicochemical properties of both antimicrobial polymers and agents, the antimicrobial mechanism could be demonstrated by antimicrobial agent release, antimicrobial agent retention, contact-killing, and anti-adhesion. This paper provides information on antimicrobial coatings, in terms of the synthesis methods, antimicrobial mechanism, influencing factors, and applications in various industries.

INTRODUCTION

Coating is the process of depositing single or multiple layers of material onto a substrate surface [1]. Attributing to the good chemical stability, good mechanical properties, production flexibility, and lower cost, polymeric materials have been widely used as coating materials. Not to mention, some polymers demonstrated antimicrobial properties intrinsically or after chemical alteration, making them a good candidate used for coatings on pre-existing components to primarily inhibit microbial activity. However, polymeric materials often lack the bulk properties required for use in structural engineering components and intrusive medical devices that require similar mechanical solicitations. In such cases, a monolithic or composite polymer is used as a coating to add antimicrobial properties to the surfaces of other materials [2].

The spread of diseases via viral and bacterial infection had caused significant losses to the personal and financial. This issue is getting more attention since the occurrence of COVID-19. Thus, antimicrobial coating has been extensively studied and applied in industries, such as food processing, medical and textile as to protect the consumer from getting infection. The antimicrobial property of coatings with directed nanotopography is being produced to prevent the adhesion of bacteria, which could be critical to both the active host colonization and the surroundings [3]. Over the years, the innovation in antimicrobial coating is focused on developing new skills in the areas of:

- Systematic, organised international studies on the impact of antimicrobial coatings in various industries [4]

- Awareness of various materials' availability and uses, (nano)coatings' modes of action, and the intended applications, processes, and goods [2]
- Details on the materials' potential negative effects on the environment [2]
- Performance comparison between laboratory-fabricated and conventional antimicrobial coatings obtained from various manufacturers [4]
- Evaluation of the effectiveness of antimicrobial coatings via field experiments; Determination of coating functionality in a wide range of conditions via regular performance test [4]
- Hospitals and healthcare authorities, facilities, or product manufacturers should communicate and/or publish best practices [4]
- Safe by design approaches is being developed during the innovation stage to detect any risks and ambiguities and to implement the new ideas into the innovation process [2]. Safe by design is referred to the incorporation of active antimicrobial ingredients into or eluted from a finished coating product to identify, control and eliminate the potential, unintentional, and unforeseen effects, if possible and necessary [4,5]. **Fig. 1** shows the effect of the active ingredients in the biocide.

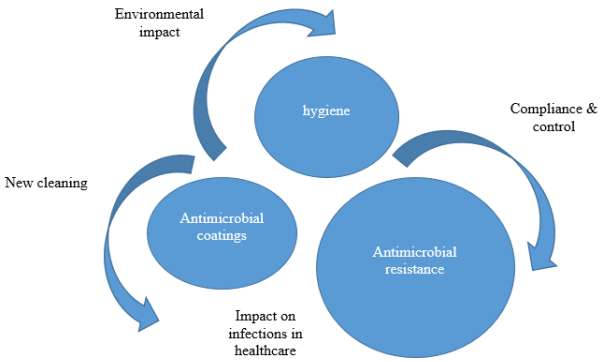

Fig. 1. Anti-microbial coating innovations (AMiCI) will contain information on the impact of innovative antimicrobial coatings on medical-associated pathogens, as well as the makeup of such coatings, fresh cleaning techniques, the effects on the environment, and the possibility for the development of antibiotic resistance [4].

When it comes to producing antimicrobial coatings, knowing where they will be used is important. Surface characteristics of materials (e.g., fabrics, gloves, paints, etc) must be taken into account as the antimicrobial property is easily affected by both internal and external factors, such as inadequate chemical binding and UV radiation [4]. It is crucial to understand the antimicrobial mechanisms as the mechanisms can be influenced by physical infrastructure, surface application, and manufacturing processes. The following section highlights the synthesis methods of various antimicrobial coatings, followed by the functional approaches of antimicrobial coating and the influencing factors of the antimicrobial activity. Afterwards, the application of the antimicrobial coating in various industries is discussed accordingly. The last part of this chapter will discuss the key challenges of antimicrobial coatings.

Synthesis of antimicrobial coatings

a) Antimicrobial Polymers

Natural polymers like chitosan and chitin (as shown in **Fig. 2**) have been widely studied in antibacterial research [6,7]. Depending on the sources, chitin has various structural forms (i.e., α, β and γ) which could be distinguished by the carbohydrate chain arrangement [8]. **Fig. 3** demonstrates the various structural form of chitin with varied in carbohydrate chain arrangement. For example, the carbohydrate chain in α form is arranged alternately antiparallel; the β form has all chains arranged in parallel; while the γ form has an alternate chain arrangement of two chains in one direction followed by an inverted chain [9]. The carbonyl and hydroxyl groups in α-chitin involved more hydrogen bonding between molecules, resulting in a structure with higher compactness and better stability in water [10]. On the other hand, β-chitin has fewer intermolecular hydrogen bonds, resulting in a more loosely organized structure [10].

Chitosan is a polysaccharide that could resist the growth of various microorganisms [11]. The intrinsically positive charge on chitosan could further disrupt the negatively charged residues on the bacteria. It interacts with the bacteria's membrane to change cell permeability [12]. Subsequently, the diffused hydrolysis products containing microbial DNA inhibit the synthesis of mRNA and protein [13].

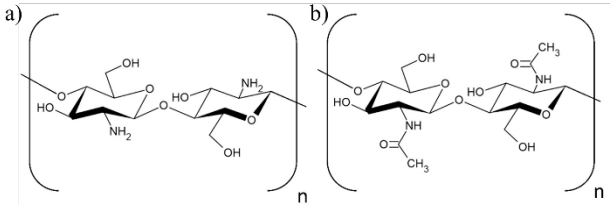

Fig. 2. (a) Structure of chitosan **(b)** Structure of chitin [7].

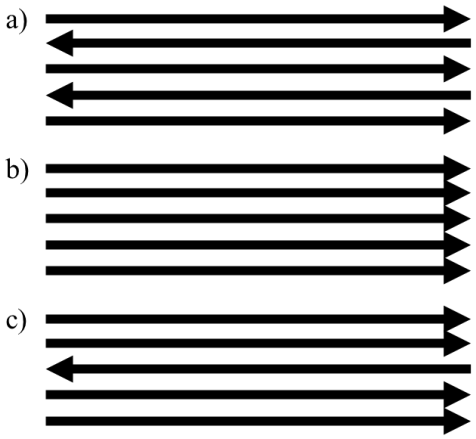

Fig. 3. Structural form of chitin with varied chain arrangement: **(a)** α-chitin, **(b)** β-chitin and **(c)** γ-chitin [8].

b) Antimicrobial Agents and non-Antimicrobial Polymers

Several researchers have demonstrated that combining nanomaterials (e.g., ZnO, TiO_2, and Ag) can improve membrane permeability, selectivity, structural resilience, antifouling, antibacterial, and photodegradation capabilities [14]. **Table 1** presents various hybrid polymer/metals antimicrobial coating with its associated coating methods and performance. Membrane characteristics (e.g., flux, rejection, and antimicrobial) of polyamide 6,6 nanocomposite membranes containing silver-graphene oxide nanoparticles (Ag-GO NPs). GO nanoplates as nanofillers in membrane research to stabilise nanoparticles. For example, Ag NPs might be painted onto GO nanoplates to increase dispersibility, reducing Ag NPs aggregation in the

membrane matrix and, as a result, increasing Ag antimicrobial efficacy. However, GO nanoplates offered superior anchor sites for NPs, keeping them from leaking out of the polymer matrix [15].

Metal NPs composites, particularly Ag-GO nanocomposites, are the most desired nanostructures nowadays because these nanostructures can govern the biological activity of Ag NPs. The GO nanoplates' large specific surface area makes the ideal for trapping Ag NPs. Once the Ag NPs are entrapped between the GO nanoplates, the ability to agglomerate is greatly reduced, and the ability to release and move freely is severely limited. When compared to either of the NPs alone, it is predicted that the combination of Ag NPs and GO nanoplates will have more desired biological effects. These NPs are immediately exposed to bacterial cells since they are positioned on the surface of GO nanoplates. The GO nanoplates platform inhibits the agglomeration and expansion of Ag NPs, increasing the composite's performance. However, the stability of Ag NPs on the GO nanoplates surface regulates their release into the environment [16].

Antimicrobial coating functional approach

The limitation of bulk materials as compared to functionalized surfaces has driven the development of biocompatible coatings [17]. Various antimicrobial approaches, such as antibacterial agent release, contact killing and anti-adhesion were employed in eliminating the adhesion of bacteria. For instance, in antibacterial agent release, the infection transmission is hindered to prevent bacterial colonisation of biomedical surfaces. Antibacterial agents could be released into the solution through hydrolysis of covalent bonds, degradation or diffusion [18]. As opposed to conventional antibiotic delivery methods, direct elution from the drug surface could deliver a higher concentration of antibacterial agent locally without violating the systemic toxicity limits [17]. However, since antibacterial agent reservoirs in coatings are inherently small, their action is only temporary. On the other hand, for contact killing, antimicrobial agents are covalently anchored onto the substrate surface through flexible and hydrophobic polymeric chains [19]. The attached agents approach the microbial envelope by the long tethering chains and kill the adhered bacteria by disrupting their cell membrane. Some common powerful antimicrobial agents used for contact-killing coatings include enzymes and cationic compounds (e.g., chitosan) which mainly depend on the interaction between bacteria membrane and antimicrobial agents, such as charge disruption and physical lysing. Lastly, anti-adhesion coatings follow non-cytotoxic mechanisms by avoiding the formation of biofilm at its earliest stage [20]. The adhesion of bacteria on the surfaces of biomaterial is a two-stage process [17]. Stage 1 is a fast and reversible process, involving non-specific physicochemical interactions, while Stage 2 is the ‘locking' stage, involving species-specific bacterial adhesion protein. Polyethylene glycol and zwitterion are commonly used as an anti-adhesion coating due to their excellent anti-adhesion property in vitro.

a) Passive Approach

Passive coatings do not involve the release of antibacterial agents [21]. It prevents the attachment of bacteria or kills the bacteria when the bacteria get closed to the coating surface. Examples of passive coatings are contact killing and anti-adhesion coating. One of the coating methods that work passively is plasma treatment. Despite plasma treatment being less well known in antibacterial surface alteration and coating approaches, it is an alternative method to the solvent-based processes grows, not to mention, it also shows high robustness and long-term stability in antimicrobial applications [17]. Plasma-deposited material is used as a bed for antimicrobial agents, which can be filled in situ or during the deposition process. Plasma processes could further impart multiple functional groups to the substrate, including hydroxyl, amino, and carboxyl groups. Plasma processes could also immobilise biomolecules with antimicrobial properties on the substrate. Furthermore, plasma processes are could be integrated with masking techniques, allowing for surface patterning, making them a viable choice for developing multi-release antibacterial coatings [17]. Apart from that, plasma polymerization is a promising process for depositing the top layer [17]. By depositing a thin layer of polymer on top of the antibacterial coating, it could serve as a barrier which extends the length of the sustainable release of the antibacterial agent. The thickness of the top layer, degree of crosslinking and surface hydrophobicity was found to be the most important factors affecting release kinetics.

b) Active Approach

Unlike passive coatings, active coatings involve the release of an antibacterial agent to damage or kill the bacteria in the medium [22]. One of the common active approaches is through the coating of stimuli-responsive antimicrobial materials. There is a lot of potential for bioactive coatings made from materials that react to physical exogenous stimuli, can be applied externally, have great signal regulation, and are not diffusion-limited. They might improve the usable lifetime of coatings and induce antibacterial properties on demand. The main difficulties that stimuli-triggered coatings encounter are minimising non-triggered background leaching from surfaces while achieving substantial dosage release over numerous cycles. A possible method for removing background leaching from a HEMA is to control swelling by co-polymerizing poly(2-hydroxyethyl methacrylate) (HEMA) with a hydrophobic monomer, hydroxypropyl methacrylate (HPMA), and applying a methylene-chain coating with controllable density and organisation [17]. The additional layer acted as a rate-limiting barrier, slowing both water entry and antibiotic release from the underlying hydrogel. Future applications should choose between tighter delivery control and greater given dosages. A nanoporous top membrane controls the passage of chemicals into and out of the agar middle layer, which acts as the home for *Penicillium chrysogenum*, giving the fungus nutrition enables it to produce penicillin [17].

Despite that the active approach via stimuli-responsive materials had a limited antibacterial ingredient and use, this method may be one of the few permanent antibacterial coatings accessible [17]. The utilisation of embedded metallic NPs as plasmon-resonators for light-trigger release is an important but mostly unexplored area in antibacterial coatings. Ag NPs, which are currently widely utilised in antibacterial coatings, have the potential to make coatings that include antibacterial agents disintegrate when exposed to near-infrared light. Nanocontainer-based smart coatings, an emerging subject with significant promise for controlled delivery, might provide a versatile solution for precise and scheduled active release of antibacterial agents, despite the increased difficulty of their manufacturing process [17].

c) Bacteria-Triggered Approach

The pinnacle of controlled release is achieved by antibacterial coatings that only release antibacterial agents when close to or in

contact with germs [23]. Acidic substances like lactic and acetic acid are produced during bacterial metabolism, which

Table 1. Summary of antimicrobial performance induced by various polymer/metal coating.

Formulation	Surface	Technique	Performance	Reference
Ag NPs/polypropylene-grafted polyethylene glycol (PP-g-PEG)	Titanium screws	Dip coating	Methicillin-resistant *Staphylococcus aureus* bacterial colony count reduced from 200 × 10^3 CFU/mL (unmodified) to 17.2 CFU/mL (modified)	[24]
Ag NPs/Poly (diallyldimethylammonium chloride) (PDADMAC)	Nylon and silk fiber	Mutlilayer dip coating	Reduction of bacteria by 80% (modified silk fiber) and 50% (modified nylon fibre)	[25]
Hybrid chitosan/ZnO	Cotton fabric	Sonochemical technique	Increase in antibacterial activity by 48% (*Staphylococcus aureus*) and 17% (*Escherichia coli*)	[26]
Composite Ag NPs/alginate	Cotton fabric	Physical deposition	Antibacterial activity up to 95% against *Staphylococcus aureus*	[27]
Chitosan/Ag/ZnO composite films	Glass slides	Sol cast method	Enhanced antimicrobial activities against *B. subtilis*, *E. coli*, *S. aureus*, *Penicillium*, *Aspergillus*, *Rhizopus* and *yeast*	[28]
Polytetrafluorethylene (PTFE)/polyamide (PA)/Ag composite	PTFE substrate	Physical vapor deposition	Modified surface prevents reversible attachment of *P. aeruginosa*	[29]
Ag NPs/chitosan and bioactive glass.	316 stainless steels	Electrophoretic deposition	Antimicrobial activity against *Staphyloccocus aureus* up to 10 days	[30]
Polyacrylic acid/Ag NPs	Polyethylene terephthalate (PET) meshes	Plasma polymerization	Reduction of bacteria concentration by at least 99 % against *Staphylococcus aureus* and *Escherichia coli* compared to unmodified mesh	[31]

lowers the pH of the local environment. By layer-by-layer assembling the positively charged medicines gentamicin, tobramycin, and polymyxin B with their polyanionic analogue, tannic acid, antibacterial polyelectrolyte multilayer were created [17].

In acidic environments, the coatings release bursts of antibiotics dependent on how much the pH is lowered [32]. It was believed that the motivation behind the release was the charge balance inside the polyelectrolyte multilayer films. Tannic acid builds up positive amino groups in the film when it is protonated at a lower pH, which leads to an imbalance and the release of cationic antibiotics to maintain electroneutrality . The molecular contacts' frequency was discovered to have the biggest impact on the coating's release kinetics. Using similar design concepts, gentamicin was combined with poly(methacrylic acid) (PMMA) and polyacrylic acid (PAA) to create hydrogel-like films with bacteria-triggered release capabilities [33]. A portion of the antibiotic was kept bound inside the coating by the formation of pH-independent gentamicin binding sites when the anionic clay platelets were applied to the hydrogel matrix. Activating bacterial-triggered reactions in coatings has also been accomplished using pH-mediated chemical bond cleavage [17].

Factors affecting the antimicrobial activity of coating

Molecular weight of the antimicrobial polymer

The molecular weight of polymers can be adjusted by carefully altering design parameters and performing structure-activity correlations [34]. Polymer with higher molecular weight has a greater amount of hydrophobic and cationic sites which could interact and disrupt the membrane of bacteria cells . However, lower molecular weight polymers were found to have better antimicrobial effectiveness against both Gram-positive and Gram-negative bacteria [34]. Not to mention, high molecular weight polymers have lower solubility and could easily form aggregates in the biological media making them hard to diffuse

Besides, high molecular weight polycations have a higher tendency to cause toxicity in human cells.

Presence of counterions

The presence of counter anions was found to influence the antimicrobial performance of polymers coating. The antimicrobial performance of polymers containing various anions was in the following order: hexafluorophosphate < tetrafluoride perchlorate < chloride [35]. This is because the presence of counterions affects the solubility and the formation of ion pairs. When an anion possesses a hydrophobic property, the ion will lower the polymer's solubility in the test media, affecting the amphiphilic balance [34]. Besides, the anion could also form a stronger ion-pair with the polymer cation, obstructing the cations in the polymer-biomembrane interaction. As a result, when performing the design of antimicrobial coating, the counterion parameter should be one of the important criteria [36].

Polymer architecture

The number of carbons in the polymer side chains could be adjusted to achieve the best combination of antimicrobial potency and low red blood cell toxicity [34]. Pyridinium and imidazolinium, as well as biodegradable poly(carbonates) with quaternary ammonium functional groups and hydrophobic alkyl chain lengths, have been extensively studied. The polymer with an alkyl chain length of four carbon tails showed a better selectivity among other polymers with different alkyl chain lengths, with a factor of >256 for *Escherichia coli* (*E. Coli*) and >1026 for *Staphylococcus aureus (S. Aureus)* [36]. Due to improved membrane insertion and permeabilization ability, amphiphilic polymers that demonstrated longer alkyl substituents could disrupt most of the vancomycin-and methicillin-resistant strains of *S. aureus* (MRSA) and *Candida albicans* (*C. Albicans*) [34]. Permit fine customization of the biological activity of antimicrobial macromolecules by using an additional design parameter to accurately modulate the average chain length with limited dispersion. Antimicrobial performance is influenced by the source of cations, the density of charge as well as the spatial arrangement of charges within the polymeric architecture [34].

By changing the alkyl groups in the quaternary ammonium salts polymers from methyl to butyl, the overall hydrophobicity of the macromolecules was increased, resulting in high bactericidal activity. Also, it was found that primary amine functionalized polymers had better effectiveness than the tertiary amine groups against the *E. coli* and *Bacillus subtilis* (*B. Subtilis*), attributing to the steric hindrance induced by the bulky groups, mitigating the cation-microbial cell interactions [37]. Furthermore, the synergistic effect between the electrostatic attraction forces and hydrogen bonding strengthened the interaction between the primary amine groups and the phospholipids of the bacteria. Moreover, copolymer sequence and architecture are also important design parameters that could affect the antibacterial activity of polymer coatings [34]. Copolymers with higher complexity structure and chain architecture may be one of the macromolecular approaches. For example, longer alkyl tails in phosphorus-based cationic copolymers showed better antibacterial effectiveness. With the addition of carbohydrate pendant units, cytotoxicity was reduced while antimicrobial activity was maintained.

Amphiphilic ratio

Peptides had been found to adopt worldwide amphiphilic helices when they came into contact with lipid membranes, even though no stable helix was formed [38]. The cationic amphiphilic peptides have a high amount (30-60%) of hydrophobic sites and positively charged amino acids at neutral pH. Although it is not visible in monomeric solution, the "facial amphiphilicity" is usually caused when binding to biomembranes [34].

The use of amphiphilic macromolecules to attain biocompatible antimicrobial properties is an appealing approach. To increase biocompatibility, primary amine functionalized polymethacrylates were converted into hydrophilic moieties. Indeed, when compared to their hydrophobic and cationic parents, hydrophilic and cationic polymers showed membrane active ability against bacteria and a decrease in hemolysis, resulting in significantly better selectivity [34].

Amphiphilic carbonate block copolymers have high selectivity for bacteria cells and primary amine groups [39]. Three different Gram-positive bacteria were tested, and the diblock copolymer and random copolymers showed strong biological activity. Self-assembling block copolymers form dynamic biodegradable micelles with excellent antibacterial nanomaterial potential. When compared to acyclic homologous copolymers, copolymers having cyclohexane subunits demonstrated higher antibacterial effectiveness with less hemolytic action. Differential activity between cyclic and acyclic polymers could be caused due to the difference in local backbone flexibility [40]. Thus, its copolymer sequence and architecture should be considered in design characteristics. Self-assembling block copolymers form dynamic biodegradable micelles with significant antibacterial nanomaterial potential. *E. coli* growth was entirely inhibited by amphiphilic copolymers containing primary or tertiary amines. Strong antibacterial activity (MIC < 10 µg/mL) against *Pseudomonas aeruginosa* (*P. aeruginosa*) and *S. aureus* for degrees of quaternization (DQ > 50%) and outstanding non-hemolytic activity (HC50 > 5000 g/mL), resulting in a high selectivity ratio [34]. To provide significant antibacterial action, efficient antimicrobial polymers aim for the lowest possible hydrophobicity.

pH

Attributing to the high content of amino groups in chitosan [8], it shows a polycationic property at pH 6 and could interact efficiently with negatively charged molecules (e.g., proteins, fatty acids, phospholipids, etc) [41]. At low pH (< pH 6), chitosan shows a better antimicrobial activity. This is because the amino groups in chitosan are ionised, inducing a greater positivity and thus had better adsorption on the bacterial cells [41]. On the other hand, by increasing the pH (> pH6), the chitosan would deprotonate by losing its charges. Subsequently, the chitosan will precipitate in the solution. Generally, the polycationic nature of chitosan is the dominant factor affecting its antibacterial activity against *Klebsiella pneumonia*. By controlling the degree of polymerization and the pH of the medium, the number of positive charges on chitosan could be varied, so as the antimicrobial activity. [42]. Studies found that low bacterial counts occurred at pH lower than 6.2, indicating a better biocides effect [42]. The number of positively charged amino groups was found to be around 75% at this pH, while an increase in pH to 7.4 reduced the positively charged groups to about 10%. The researcher further noted that a greater number of amine groups could lower the apparent pKa of the polymer because of the electrostatic repulsion between neighbouring charges, limiting the extent of amine group ionisation in comparison to monomeric counterparts [42].

Incorporation of antimicrobial agents

The incorporation of antimicrobial is another factor that could affect the antimicrobial activity of polymer coatings. For example, Ag incorporation could cause higher surface energy than similar surfaces without modification, increasing the reactivity of the modified coating [29]. Since silver is in its metallic state, it must be oxidised to release the antibacterial ion, silver ion to damage the surrounding bacteria. This reaction will be aided by a higher reactive surface.

Application of antimicrobial coating

Food Industry

Food packaging is essential for ensuring food products' microbiological protection without affecting their nutrition content and organoleptic properties [42]. Antimicrobial agents may be integrated into the packaging to build an atmosphere within the package that can slow or eliminate the microorganisms from growing on the food, subsequently, increasing its shelf life. Chitosan is a functional polysaccharide that has been well incorporated into food packaging, attributed to its intrinsic antimicrobial and antifungal properties and film-forming ability [43].

Medical And Healthcare Industry

Biofilm generation on medical equipment is a very expensive issue in the clinic. Such issues lengthen the treatment time and necessitate extra surgery to replace in-dwelling devices [44]. Consequently, new approaches to preventing the formation of biofilm or destroying biofilms are important. The effectiveness of antimicrobial coatings has been demonstrated in appropriate field trials [34]. In the war against healthcare-acquired infections, antimicrobial coatings on healthcare instruments are a relatively new technical approach [34]. Despite that, in a healthcare setting, antimicrobial coatings pose ethical and functional problems. This is because the intervention site (e.g., textiles, washing, etc) will possess a direct effect on the care environment's overall ecosystem.

For decades, the healthcare procedures for cleaning and hygiene have remained relatively consistent, except for the use of detergent and disinfectant technology. Chemical contamination threats and the proliferation of multidrug-resistant microbes have necessitated creativity. Various evidence suggests that cleaning near-patient surfaces is insufficient. The combination of mechanical cleaning and chemical interactions when applying liquid disinfection was found to reduce the efficiency of antimicrobial coatings to sub-inhibitory levels, resulting in resistance generation [4]. Thus, wise consideration is required when applying chemical disinfectant with an instrument coated with an antibacterial coating.

Textile Industry

Over the year, the outbreaks of antibiotic-resistant bacterial strains have increased the number of cross infections through the textile materials in medical institutions and hospitals [45]. Polyethylene terephthalate (PET) is commonly used to fabricate protective textile in hospitals attributed of its superior mechanical features, simple production and low cost [46]. However, PET is easily contaminated by microorganisms, becoming a source of infection transmission. For that reason, antibacterial agents and/or coatings were applied to the textile. For example, antibacterial NPs have recently been discovered for their uses in textiles, food packaging, wound dressings and cosmetic products . The ability of PET textures treated with antimicrobial chemicals to inhibit the development of harmful microbes has been studied extensively [46]. Antimicrobial varnishes made of antimicrobial compounds (Zn, Cu, and Ag) have been used on fabric materials. Owing to the high valence state demonstrated by the Ag NPs which induce significant electrostatic interaction between the ion and bacteria, Ag is well known as a potential antibacterial agent [47]. Besides, Ag_2O has been widely employed on cotton and synthetic fibres. Attributing to its broad spectrum killing as well as the fairly low danger of bacteria resistance development, the antibacterial properties of Ag_2O have been well acknowledged [48].

Key challenges of antimicrobial coatings

Antibacterial coatings should not be considered a panacea or a universally efficient technique [17]. Instead, they should be viewed as part of a systematic initiative to minimise identified nosocomial infection risk factors. Nonetheless, to enhance the effectiveness of release-based coatings in the battle against pathogens, many main obstacles must be addressed, including controlled release, multi-functionality as well as long-term stability.

Controlled Release

To ensure the optimum and controlled release of antimicrobial agents, carrier materials and deposition methods are of vital importance . Polymer coatings such as poly(lactic-co-glycolic acid), hydroxyapatite, polyurethane, hyaluronic acid, chitosan and polyelectrolyte multilayers (PEMs) are widely utilised carriers [49]. Among them, PEMs coating has better control in releasing the antibacterial agents [17]. PEMs are formed by the layer-by-layer assembly, consisting of alternating layers with opposite charges, which are nanostructured polymeric structures. Layer-by-layer assembly involves a simple process, is highly versatile in materials used and has low production, making it one of the alternative methods to incorporate antibacterial compounds into coatings [50]. Apart from that, ceramics, hydrogels and plasma-deposited polymers were investigated as antibacterial carrier coatings [17]. It is crucial to determine the chemical compatibility of the scaffold with the antibacterial agent, the necessary matrix functionalities and the release modality before selecting the proper coating material [17].

Due to the unique properties of each antibacterial agent/scaffold system, it is also important to take into consideration the specifications for targeted application when synthesis of the released-based antibacterial coatings [17]. Disruptors of bacterial signalling pathways, in addition to traditional biocide release, have been extensively studied as they could better restrict the adhesion of bacteria and the formation of biofilm . Besides, the *in vitro* antibacterial properties of quorum-sensing (QS)-inhibiting molecules could be embedded in release-based coatings for enhanced antibacterial performance . In Gram-positive bacteria, peptides have also shown promise as QS inhibitors. A study found that the released RNAIII-inhibiting peptide (RIP) from PMMA beads could prevent the formation of *S. aureus* biofilm *in vivo* [17].

Multi-Functionality

Coatings with multi-functionality are expected to perform better in biological systems due to their fundamentally complex and hierarchically organised properties [17]. Various categories of release-based antibacterial polymer coatings with multi-functionality were created, including multi-release, multi-approach, and multi-property [51]. First of all, multi-release coatings are known for their reduction in bacterial resistance induction as well as the synergistic antibacterial action [52]. Materials, such as antibiotics and metals could be incorporated with silver to resist bacteria, resulting in better synergistic results.

On the other hand, multi-approach coatings involve multiple antibacterial approaches toward pathogens rather than relying on the release of antibacterial agents [51]. For example, researchers mixed immobilised QACs with bilayers of PAH and PAA containing Ag and found that the Ag released from the coating has a strong antibacterial effect, while the QACs showed considerable contact-killing activity despite the depletion of Ag in the later stage [53]. There have also been records of coatings with both releases of antibacterial agents and anti-adhesion properties. This approach could be done by immobilising PEG chains on the surface of an antibacterial agent-release-based coating for imparting anti-biofouling properties. Lastly, the multi-property coatings are the most challenging aspect of designing such multifunctional coatings to ensure the functionalities do not interfere negatively with each other over the coating's useful life [51].

Long-Term Stability

The long-term stability of biofilm prevention is always a concern in the research of antibacterial coatings [54]. The cellular debris is formed by lysis which will then adhere to the substrate surface, inducing fouling and the formation of biofilm throughout time [17]. As a result, new approaches are required to tackle this problem.

Generally, the release of antibacterial agents in high dosage is desired for a short-term view [17]. It provides antibacterial protection and maintains good bacterial resistance during the early post-operative phase, also known as the critical phase for transmission of infection. The surfaces of the implanted devices have to retain their antibacterial properties to prevent the formation of bacteria colony integrates with the surrounding tissues. Thus, the long-term release of an antibacterial agent is crucial in the case of revision or second surgery to prevent the contamination of tissues surrounding the primary implant. [17].

One of the most important considerations in assessing the applicability of a coating surface in clinical applications is durability [55]. Durability is referred to the ability of a coating to preserve its properties over time. Several studies have shown that common antibacterial coatings, such as PEG-based and polyelectrolyte films are unstable after long periods of exposure time [54]. Problems, such as chain cleavage, weak physical and chemical strength, weak adhesion to substrate as well as surface conditioning, reduce the long-term stability of the antibacterial coating [17].

Conclusion and future perspective

Antimicrobial coating provides the much-needed potential to restrict pathogen colonisation on the surfaces of substrate by supplying antibacterial agents locally. Consequently, the restriction reduces the burden of biomaterial-associated infections and enhances the efficacy of conventional antibiotic therapies. This paper defines various features of antibacterial coatings to optimise their efficacy and extend their application area. Since the time and expense of evaluating potential antibacterial coating in regulated human trials is prohibitive, researchers across disciplines will need to collaborate to solve these important challenges, but there should be plenty of opportunities for innovation.

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