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Antimicrobial polymer nanostructures: Synthetic route, mechanism of action and perspective

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ABSTRACT

Protection against bacterial infections is an important research field in modern society. Antimicrobial polymers have received considerable attention as next-generation biocides because they represent an ecologically friendly approach that does not promote resistance. In the last decade, many authors have reported the development of nano-sized antimicrobial polymers with enhanced bactericidal performance by increasing the active-area of biocides. This review presents several suitable methods of synthesis of antimicrobial polymer nanomaterials with various shapes, including a nanosphere and fibrous and tubular structures. We also discuss the antimicrobial mechanisms of these polymers. In addition, antimicrobial polymer thin films, which can inhibit bacterial adhesion, are introduced briefly with examples. Our aim is to present synthetic routes and formation mechanisms of various antimicrobial polymer nanostructures.

Contents

1. Introduction

The advancement of science and technology has resulted in the fabrication of tiny materials with at least one dimension in the range 1–100 nm; defined as nanomaterials [1–3]. Thanks to the efforts of numerous research groups, nanostructures of metals [4–6], inorganic complexes [7–10] and polymers [11–14] of myriad shapes, such as spheres, cones, rods, fibers, tubes and sheets, have been realized. Interest in nanostructured materials has been growing steadily due to their fascinating properties and potential applications, both of which stem from their nanoscale dimensions [15–17]. From the early work on gold nanoparticles to the recent development of graphene nanosheets, myriad nanomaterials have been discovered and studied in diverse fields.

Despite the difficulty in controlling size and shape at the nanoscale, polymeric nanostructures have been drawing increased attention due to their tunable surface functionality, light weight and low cost of synthesis. Thanks to intensive research over the last few decades, various

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smart and facile synthetic methods for fabrication of polymeric nanomaterials have been developed. Nano-sized templates for surfactant, liquid crystal, anodic aluminum oxide and biomaterial have been used as directing materials for the formation of polymer nanostructures [18–23]. In addition, use of template-free techniques such as electrochemical synthesis, dispersion polymerization and aqueous/organic interfacial polymerization in the synthesis of polymer nanomaterials has been investigated extensively [24–26]. Precisely synthesized polymer nanostructures have been used in various applications, including energy storage [27,28], chemical/biological sensors [11,29,30], drug delivery systems [31,32], solar cells [33,34] and antibacterial fields [35–37]. In particular, antimicrobial polymeric nanomaterials have been intensively studied because of the excellent bactericidal performance originating from their dramatically increased surface area to volume ratio [35–37]. Until now, numerous polymeric antimicrobial nanostructures have been successfully developed via various synthetic routes to kill harmful bacteria as summarized in Table 1.

In this review, we focus on the synthesis of polymeric nanostructures for use as antimicrobial agents. First, current knowledge on the antimicrobial activity of polymeric biocidal agents and the necessity for nano-sized biocidal materials, are briefly reviewed. The main part of this manuscript is divided into three sections based on the morphology of synthesized polymers: 1) nanoparticles, 2) one-dimensional nanostructures and 3) thin films. In each section, several notable methods that enable fabrication of antimicrobial polymer nanostructures are introduced with examples from recent research. Strategies for controlling the shape and size of antimicrobial polymer nanomaterials are also highlighted. In the end, a short summary on perspective of antimicrobial polymer nanostructures is given.

2. Antimicrobial mechanisms of biocidal polymers and necessity for nano-sized biocides

Although human mortality from bacterial infections has decreased over the last century due to developments in medical science, these remain an important problem in public health. Globally, over 13 million people died per year by infectious diseases [38]. A large number of bacterial infections originate from viable bacteria that adhere to implants and medical devices [39,40]. When bacteria attach to a material surface and cell numbers increase, they start to form a biofilm. After developing on a surface, this biofilm is extremely difficult to remove and allows microbial cells to survive even under harsh conditions. In contrast to planktonic (free-floating) bacteria, the bacteria in biofilms are up to 1000 times more tolerant to antibiotics and other biocides [41,42]. Thus, inhibition of biofilm formation is considered to be the most important goal in antimicrobial research. To do this, it is necessary to inhibit the early stages of bacterial adhesion. In general, this can be achieved by either killing the planktonic bacteria prior to adhesion using biocides, or by modifying surface properties to inhibit bacterial adhesion. During the last decades, numerous effective bactericidal materials that inhibit bacterial growth have been developed. In particular the field of antimicrobial polymers has great advances in terms of efficacy enhancement, control of size and morphology and synthetic route development.

Polymeric antimicrobial materials can be divided into two categories based on their biocidal mechanism: biocide-releasing polymers and contact-active polymers. The first kills bacteria via the release of a low-molecular-weight biocide. *N*-halamine compounds, which contain releasable halogen atoms, are widely used as disinfecting agents. In 1996, Sun and Worley designed *N*-halamine groups containing polymers to achieve long-term storage of antimicrobial chlorine [43,44]. In *N*-halamine functioned polymers, halogen atoms are covalently bonded to the nitrogen atoms of the functional groups of polymer which provide stability and slowly release active halogens into the environment. The released halogen or hypochlorite interacts with the biological receptor (thiol or amino groups) of bacterial cells, leading to metabolic inhibition or cell death [43,44].

In addition, nitric oxide (NO)-containing polymers that kill bacteria via release of the biocidal NO have been developed [45]. NO, a diatomic free radical, known as 'reactive nitrogen species (RNS)' generate broad antimicrobial activity. Recently, Lowe et al. synthetized an acrylonitrile-co-1-vinylimidazole copolymer fibers that are capable of storage and delivery of NO. The acrylonitrile in the copolymer allows for the formation of the NO molecular donor group, a diazeniumdiolate, under high

Table 1
Synthetic route and applications of polymeric antimicrobial nanostructures.

Polymers	Preparation route	Morphology	Size[a]	Bacteria	Ref.
Poly[2-(tert-butylaminoethyl) methacrylate	Surface-initiated photopolymerization	Polymer-coated titania nanoparticle	~20 nm	*E. coli*, *S. aureus*	88
Poly[2-(tert-butylaminoethyl) methacrylate	Vapor deposition polymerization	Polymer-coated silica nanosphere	17–50 nm	*E. coli*, *S. aureus*	59
Poly[2-(tert-butylaminoethyl) methacrylate	Radical-mediated dispersion polymerization	Ag nanoparticles embedded nanofiber	~40 nm	*E. coli*, *S. aureus*	127
Poly(2-(dimethylamino) ethyl methacrylate)	Surface-initiated atom transfer radical polymerization	Polymer coated Fe_3O_4 nanosphere	50–150 nm	*E. coli*	82
Poly(2-(dimethylamino) ethyl methacrylate)	Electrospinning	Polymer fibrous structure	19–69 nm	*E. coli*, *S. aureus*	155
Poly(2-(dimethylamino) ethyl methacrylate)	Vapor deposition polymerization	Polymer-coated silica nanosphere	0.3–1.3 μm	*E. coli*, *S. aureus*	105
Poly(3-allyl-5,5-dimethylhydantoinco)	Radical polymerization	Polymer-coated magnetic silica nanosphere	~144 nm	*S. aureus*, *P. aeruginosa*	152
Poly(3-allyl-5,5-dimethylhydantoinco)	Seeded polymerization	Polymer-coated silica nanoparticle	11–26 nm	*E. coli*, *S. aureus*	37
Poly(dimethylamino methylstyrene)	Vapor crosslinking method	Polymer film	~800 nm	*B. subtillis*, *E. coli*	148
Polyrhodanine	Seeded polymerization	Polymer-coated silica nanosphere	15–56 nm	*E. coli*, *S. aureus*	60
Polyrhodanine	Chemical oxidation polymerization	Polymer-coated γ-Fe_2O_3 nanosphere	~10 nm	*E. coli*, *S. aureus*	94
Polyrhodanine	Chemical oxidation polymerization	Ag nanoparticles embedded nanofiber	~30 nm	*E. coli*, *S. aureus*, *C. albicans*	131
Polyrhodanine	Chemical oxidation polymerization	Ag nanoparticles embedded nanotube	~200 nm	*E. coli*, *S. aureus*	132
N-halamines introduced nylon 6	Electrospinning	Nanofiber membrane	100–500 nm	*E. coli*, *S. aureus*	153
Poly(ethylene terephthalate)/chitosan	Electrospinning	Nanofiber mat	300–500 nm	*S. aureus*, *K. pneumoniae*	104
Magainin-I grafted copolymer brush	Atom transfer radical polymerization	Polymeric brush film	~100 nm	*L. ivanovii*, *E. coli*	149
Poly(N-isopropyl acrylamide)	Sonochemically synthesize	Polymer-coated silica nanoparticle	~170 nm	*Bacillus* sp.	66
Chitosan-polycaprolactone	Electrospinning	Nanofibrous membranes	200–400 nm	*S. aureus*	118
Quaternized chitosan	Electrospinning	Nanofibrous mat	50–500 nm	*E. coli*, *S. aureus*	103
Carboxymethyl chitosan	Repetitive reaction between Michael addition and amidation	Dendrimer core–shell nanoparticle	~20 nm	*E. coli*, *S. aureus*	154

[a] Size means the diameter (nanoparticle, nanofiber and nanotube) or the thickness (film).