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An Overview for the Design of Antimicrobial Polymers: From Standard Antibiotic-Release Systems to Topographical and Smart Materials

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Abstract

Microorganisms attach on all kinds of surfaces, spreading pathogens that affect human health and alter the properties of products and of the surface itself. These issues motivated the design of a broad set of antimicrobial polymers that have great versatility to be chemically modified, processed, and mixed with other compounds. This review presents an overview of these different strategies, including antimicrobial-release systems and inherently antimicrobial polymers, alongside novel approaches such as smart materials and topographical effects. These polymers can be used in any application affected by microbes, from biomaterials and coatings to food packaging.

1. INTRODUCTION

Antimicrobial: a chemical compound that inhibits the development of pathogens such as bacteria, fungi, yeasts, and algae

Antibiotics: substances that inhibit or destroy particular bacteria or fungi in humans and animals and are mainly used as chemotherapeutic drugs

The presence of microorganisms can generate a very broad range of human, social, and economic issues. A material's surface, where most microorganisms stay, is a key player in most of these problems as it can act by providing the conditions for microbial growth (e.g., support for biofilm formation), spreading pathogens that affect human health (e.g., through biomedical implants and food), altering the properties of products in contact with that surface (e.g., in food spoilage), and affecting the surface itself (e.g., biofouling or biocorrosion). The survival of a microorganism on a surface highly depends on the chemical, physicochemical, and physical properties of the material/cell interface and the surface, alongside environmental conditions and type of microbe (1). In this context, a great scientific and technological effort has been devoted to designing, through a broad set of approaches, antimicrobial polymers that can prevent the survival of different microbes in the context of a specific problem. The topic is so vast that a review focusing on the big picture while avoiding highly focused details is needed to put into context the currently existing approaches in the field. To do that, this review is organized to answer four key questions for the design of antimicrobial polymers: why, when, how, and for what, highlighting the general concepts for future multidisciplinary strategies in the field.

2. WHY? RELEVANCE OF MICROORGANISMS AND THEIR NEGATIVE EFFECTS

Microbes and microbial communities, formed mainly by bacteria, fungi, yeasts, algae, protozoa, and viruses, are found in nearly every terrestrial environment and affect our health and most of our domestic and industrial activities (2). The relevance of microorganisms is shown by considering, for instance, that bacterial cells in our body are at least as numerous as human cells (3). These microorganisms are mostly observed forming complex structures on a surface. For instance, bacteria prefer to attach to and colonize a surface (sessile state) rather than to exist freely in bulk solution (planktonic state) as nutrients exist at higher concentrations in these interfaces as compared with the bulk fluid (4, 5). Under these conditions, a biofilm is formed that is characterized by a community of different microorganisms that are irreversibly attached to the surface, producing extracellular polymeric substances (EPSs) (4). It is generally accepted that biofilm development occurs in several sequential phases: (*a*) surface conditioning, (*b*) reversible attachment of bacterial cells to a surface, (*c*) irreversible attachment of bacterial cells due to cell-to-cell bridges cementing the cells to the surface through the production of EPSs, and (*d*) colonization from the attached bacteria to form microcolonies and the biofilm (4). Bacteria are the most studied microorganisms in this context, although fungi, yeasts, algae, protozoa, and viruses are also present in biofilms. Besides their structural role, biofilms constitute a protected growth mode in hostile environments, conferring reduced susceptibility to dehydration, phagocytosis, metal toxicity, acid exposure, antibiotics, and biocides (6). In general, the main issue from biofilm formation is its reduced susceptibility to antimicrobial agents as compared with planktonic cells (6).

The impact of microbes and biofilms is due to their presence in almost all kinds of surfaces, such as furniture, medical implants, wounds, teeth, indwelling medical devices, water systems, membranes, fishing gear, endoscopes, pipes, heat exchangers, food and food-contact surfaces, and textiles (4, 5). Microorganisms on those surfaces can generate infection, food and product spoilage, reduced production efficiency, corrosion, unpleasant odors (malodors), unsightliness, increased drag, pipe blockages, and equipment failure, among other negative effects (2, 7). The relevance of the microorganism–surface interaction is exemplified by the fact that contaminated surfaces play a critical role in spreading viral and bacterial infections. This contamination by indirect contact is one of the three routes of infection, alongside direct contact with infected individuals and airborne

transmission via droplets (8). For instance, it is estimated that 80% of microbial infectious diseases in humans are caused by biofilm formation, and microbial cells in biofilms exhibit 10–1,000 times greater resistance to antibiotics than planktonic cells (9). Indeed, biofilms may be involved in 65% of hospital-acquired (nosocomial) infections (6). This surface-related indirect contamination can occur not only in hospital medical devices (e.g., catheters, bed rails) but also in any frequently touched infected surfaces. Potentially infected surfaces include doorknobs, elevator buttons, personal protective equipment, light and fan switches, telephones, handrails, taps, benches, tables, sinks, and toilets (8, 10). Bacteria, viruses, and parasites, together with toxic chemical substances, are also responsible for unsafe food that causes more than 200 diseases, affecting 1 in 10 people in the world who fall ill after eating contaminated food (11). Altogether, microorganisms produce an estimated 420,000 deaths every year, with US $110 billion lost each year in productivity and medical expenses in low- and middle-income countries. Biofilms also have a significant negative economic impact on other industries and processes, such as aquaculture (5–10% of the industry cost), heat exchange (~7.5% of maintenance costs), oil and gas (20–30% of corrosion-related costs), maritime transport (35–50% increased fuel consumption), and water desalination (~30% of total operating expenses) (12).

Disinfection: the process of removing microorganisms from the surfaces of nonliving objects

-static: describes an agent that inhibits growth (e.g., bacteriostatic or fungistatic)

-cidal: describes an agent that kills a microorganism (e.g., virucidal or bactericidal)

3. WHEN? RATIONALE OF ANTIMICROBIAL MATERIALS

Surface sterilization through chemical disinfection, heat, or ionizing radiation is extensively used to eliminate microorganisms, although with short-term action due to recontamination from the steady presence of pathogens (13). Even in well-controlled places, while rigorous cleaning techniques with proper chemicals significantly reduce pathogen levels, they are not enough to avoid microbes entirely. For instance, after patient discharge in hospitals, room cleaning was effective on only 49% of the standardized surfaces, with fewer than 30% of toilet handholds, bedpan cleaners, room doorknobs, and bathroom light switches adequately cleaned (14). Moreover, cell attachment to surfaces can occur within a few minutes to hours, making frequent cleaning unfeasible as a means to prevent cell attachment (4). Disinfectants, besides contributing to the growth of resistant microbial strains, can also negatively affect both the environment and the user's health and safety, which has motivated some restrictive legislation (7). For these reasons, there is a growing interest in developing materials able to actively prevent the formation of biofilms to complement current disinfectant and hygienic actions (7).

Based on the mechanism of biofilm formation and the high resistance of mature biofilms to biocides, the main goal of antimicrobial materials is to prevent the initial attachment of microorganisms (5). Chemical composition, electrostatic charge, mechanical properties, and surface topography affect this initial attachment (15). Therefore, a broad range of antimicrobial polymers can affect the initial microbial attachment by, for instance, (*a*) reducing or inhibiting the growth of microorganisms (-static effect), (*b*) avoiding the attachment of microorganisms (antibiofouling effect), and/or (*c*) damaging the structure of microorganisms (-cidal effect). Out of all possible materials, we focus on polymers due to their extreme versatility from a chemical and physical point of view, allowing, for instance, a broad range of functionalities and mechanical behavior. Polymers can be designed to produce almost all kinds of commercial products using standard thermoplastics, coatings, and smart hydrogels. Moreover, other surfaces (e.g., metals) can easily be coated with polymers, extending the application of these materials beyond plastic- and polymer-based products. The use of antimicrobial polymers is further supported by their high activity against a broad range of microorganisms, such as bacteria. **Figure 1** shows examples of the bacterial survival found in representative antimicrobial polymers discussed in this review.

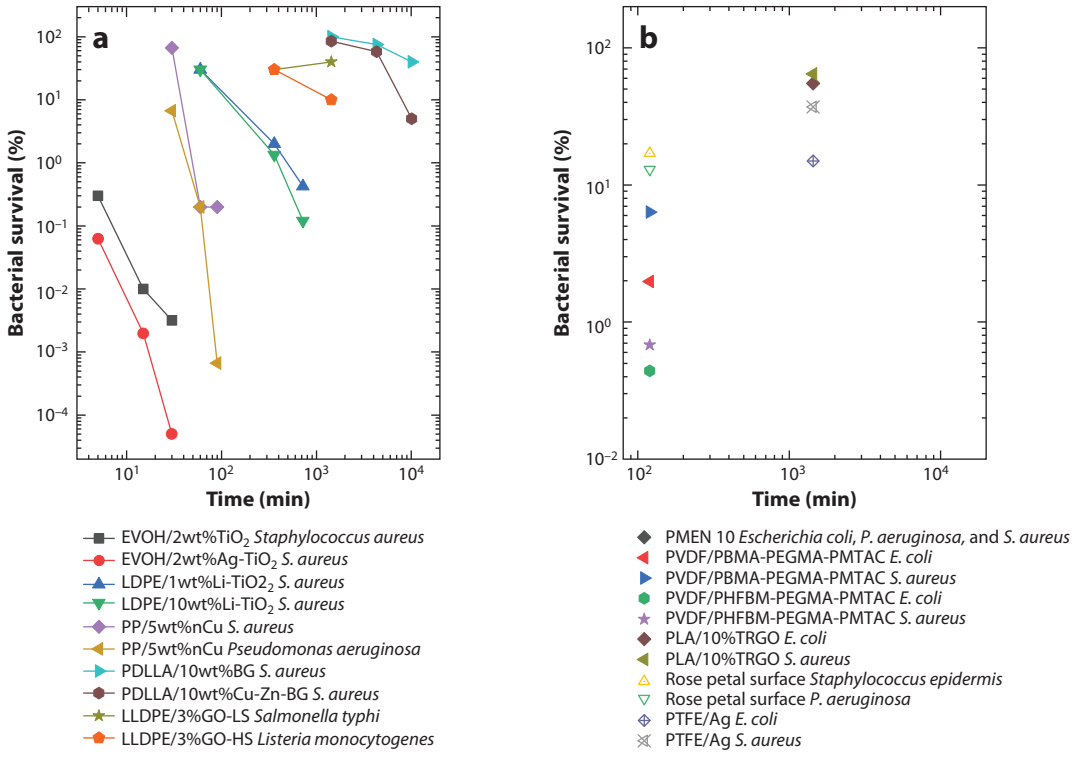

Figure 1

Percentage of bacterial survival (from 100% at time = 0) of some representative antimicrobial polymers at different time points (*left*) and at a single time (*right*). Abbreviations: Ag, silver; BG, bioglass; Cu, copper; EVOH, ethylene-vinyl alcohol copolymer; GO-HS, graphene oxide with high oxidation level sonicated after synthesis; GO-LS, graphene oxide with low oxidation level sonicated after synthesis; LDPE, low-density polyethylene; Li, lithium; LLDPE, lineal LDPE; nCu, copper nanoparticles; PBMA, polybutylmethacrylate; PDLLA, poly(D,L-lactic acid); PEGMA, poly(poly(ethylene glycol) methyl ether methacrylate); PHFBM, poly(hexafluorobutyl methacrylate); PLA, poly(lactic acid); PMEN 10, phosphorylcholine zwitterion polymer containing 10% p-nitrophenoxycarbonyloxyethyl active ester group side chains; PMTAC, poly[2-(methacryloyloxy)ethyl trimethylammonium chloride]; PP, polypropylene; PTFE, polytetrafluoroethylene; PVDF, polyvinylidene fluoride; TiO_2, titanium dioxide; TRGO, thermally reduced graphene oxide; Zn, zinc. Data obtained from References 16, 20, 27, 54, 65, 67, 72, 81, 82, and 89. These data were obtained from different antimicrobial tests and conditions, so direct comparison between samples is not possible, and they are displayed to show the effectiveness of different antibacterial materials.

4. HOW? KINDS OF ANTIMICROBIAL MATERIALS AND MECHANISMS

Discussion of antimicrobial polymers is complicated due to the large number of parameters involved, not only from the material point of view but also from the microorganism's point of view. For instance, the discussion could include the mechanism of the antimicrobial polymer, the material properties (coating, thermoplastic, hydrogel, nanomaterial, etc.), the microorganisms (bacteria, viruses, fungi, etc.), the antimicrobial effect (-static, -cidal, antibiofouling, etc.), the problem (food spoilage/contamination, biomaterial infection, etc.), and the adhesion mechanism and environment (i.e., airborne, foodborne, or waterborne pathogens). Other questions arising from the concept of an antimicrobial mechanism include: (*a*) What is the final active agent or structure affecting the cells?; (*b*) What are the roles and properties of the polymer in the antimicrobial effect?; and (*c*) What happens to the microorganism? For instance, for a polymer

composite containing biocidal copper (Cu) nanoparticles, the antimicrobial mechanisms are related to (*a*) the active agent (Cu ions rather than the nanoparticle itself) produced by oxidation or dissolution processes on the particle surface; (*b*) the release of the active agent from the inert matrix triggered by water absorption followed by diffusion out of metal ions; and (*c*) the Cu ions disrupting the microorganism membrane, generating reactive oxygen species (ROSs), and interacting with the DNA, which results in a biocidal effect. These different mechanisms are currently overlapped with the discussion of antimicrobial polymers.

This broad range of polymers and parameters, as well as other variables such as the antimicrobial test used (for instance, by measuring the inhibition halo, the microbial concentration in the media after material immersion, or the survival of bacteria on the material surface), further explains the variability of the efficacy of antimicrobial polymers. In this context, **Figure 1** allows not only the conclusion that antimicrobial polymers are effective in reducing bacterial survival but also that their activity can vary by several orders of magnitude depending on the polymer, active agent, time, stimulus, bacteria, antimicrobial test, and other factors.

To classify this broad range of antimicrobial polymers and their mechanisms, we use the material point of view to define three sets of polymers: (*a*) antimicrobial-release polymers (the polymer is just an inert matrix where the antimicrobial agent is added), (*b*) intrinsically antimicrobial polymers (IAMPs) (the polymer does not release any active agent and its chemical or topographical structure renders the antimicrobial effect), and (*c*) smart antimicrobial polymers (the polymer response under a specific stimulus triggers the antimicrobial effects). This classification focuses on the material–microorganism surface interaction without considering the polymer material's size or the kind of antimicrobial agent. For instance, although antibacterial nanoparticles are discussed in the context of their incorporation in the polymer matrix, antimicrobial polymeric nanoparticles are not described separately in this review. **Figure 2**, which presents a summary of the structure of this section, stresses the need to specify the material and the application to contextualize the research. Further, this focus on the different polymers and applications is needed to explain the large number of commercial technologies based on antimicrobial polymers; some examples are described in **Figure 2**.

Biocidal: a general term describing a chemical agent, usually having a broad spectrum, that kills or inactivates microorganisms

Antibacterial: a substance that stops only bacteria from developing

4.1. Antimicrobial-Release Polymers

The ability of polymeric materials to dissolve in some solvents, to be fluid above some transition temperature, or to be polymerized or crosslinked in a liquid state easily allows the physical incorporation of different kinds of particles, molecules, and even other polymers. Today, this strategy is so mature that almost every existing antimicrobial compound can be physically incorporated into a polymer that acts as a passive/inert matrix carrying the active agent to be released under some driving force. Under these conditions, the polymer acts like a drug-delivery device. From the material design point of view, when the antimicrobial is embedded in the polymer matrix, the effectiveness is dependent not only on the antimicrobial effect but also on mass transfer processes. A summary of the different processes that can be involved is displayed in **Figure 3*a–d***. The antimicrobial can also be impregnated on the polymer surface, simplifying not only the incorporation of the active agent but also the diffusion processes for release (**Figure 3*e***). However, issues related to the burst release and short-time effectiveness should be considered in this methodology. For antimicrobials embedded into a polymer, the interaction between the polymer matrix and the microbe media is relevant. For a noninteracting matrix (for instance, hydrophobic polymers), the antimicrobial release is diffusion-driven and triggered by the concentration gradient between the antimicrobial polymer and the media (Fickian regime), as displayed in **Figure 3*a*** (17). However, when the media and the polymer have similar polarities, the solvent (for instance,

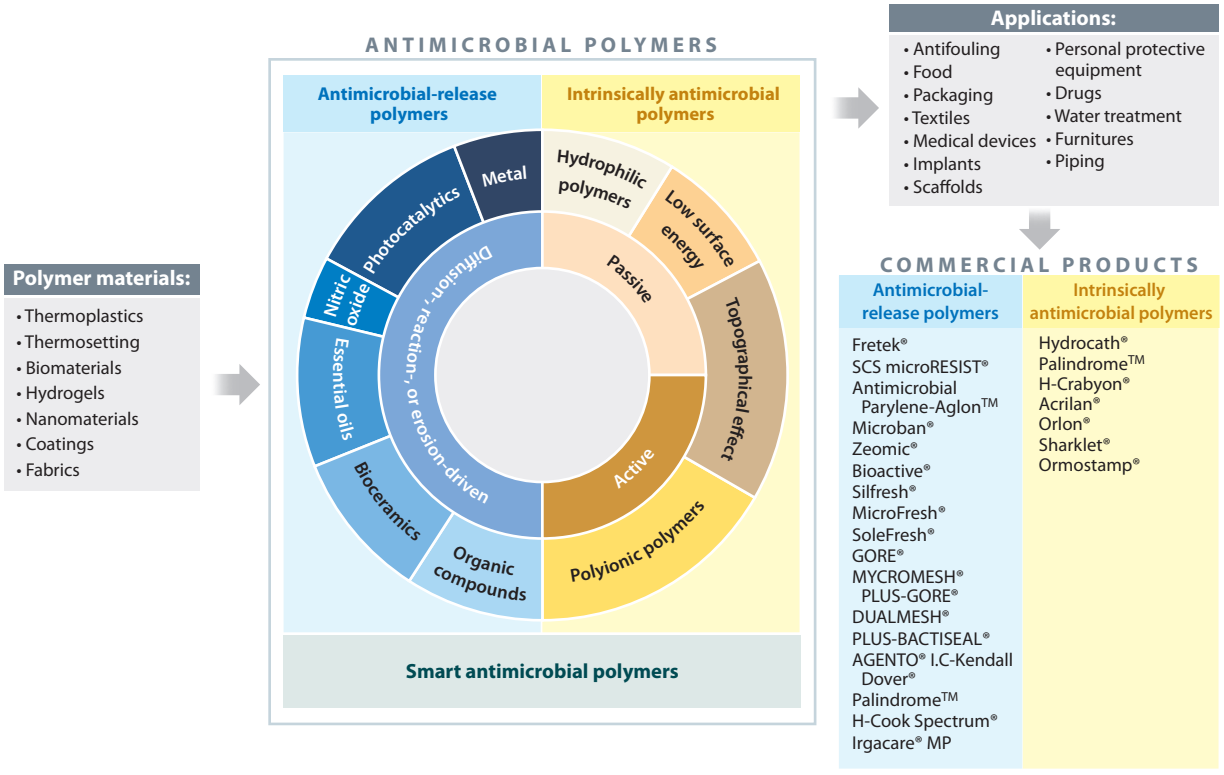

Figure 2

A general overview of antimicrobial polymers according to the role of the material (antimicrobial release polymers on the left, IAMPs on the right, and smart antimicrobial polymers on the bottom) and the main mechanisms involved (active, passive, and diffusion-, reaction-, or erosion-driven). It further highlights the different kinds of polymer materials that can be produced and a broad range of applications. In this classification, antimicrobial topographical surfaces are considered to be IAMPs. Smart polymers can be either antimicrobial-release systems or IAMPs, and they are presented separately in this review. Abbreviation: IAMPs, intrinsically antimicrobial polymers.

water) can diffuse into the material (**Figure 3*b***), affecting the structural polymer network and the diffusion processes (non-Fickian regime) (17) and generating a swelling-driven release. The degradation of the polymer may also be relevant, as encapsulated antimicrobials are exposed and released to the media after matrix erosion (**Figure 3*d***). The complexity can be even greater because the antimicrobial agent can interact with the polymer matrix, limiting the active agent's release (18). Indeed, in polymers containing nanoparticles, the interaction between both phases is relevant, as it can create voids in the polymer–particle interface, increasing the permeation of water (19).

It should be noted that the antimicrobial released from the polymer matrix can be different from the compound initially added into the polymer matrix. These reactive antimicrobial compounds need an external stimulus (e.g., radiation) or substances (such as water) to produce the final reaction-driven antimicrobial agent. For instance, in polymers containing photoactive particles (e.g., TiO_2), the antimicrobials released are ROSs generated on the particle surface (20).

Based on the above, any discussion about the antimicrobial behavior of a polymer should consider the mechanisms associated with: (*a*) diffusion out of the antimicrobial compound from the polymer matrix (**Figure 3*a–d***) and (*b*) diffusion of water or solvent molecules in through the

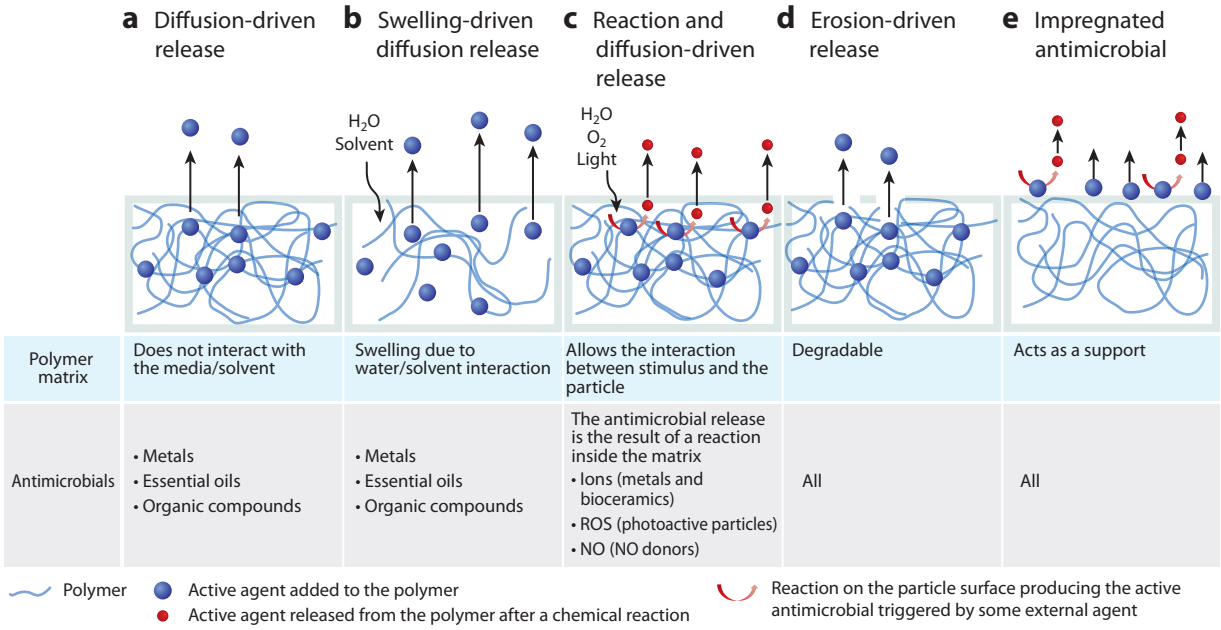

Figure 3

A summary of the different mechanisms involved in antimicrobial-release polymers based on the diffusion processes that occur when the antimicrobial is embedded in the matrix. Water or solvent can interact with the matrix, changing the mechanism from (*a*) a pure diffusion-driven process to (*b*) a swelling-driven diffusion process. (*c*) In other systems, the active agent released is not the original antimicrobial but rather a reaction product that diffuses out. (*d*) Polymer matrices can also suffer degradation that exposes the antimicrobial. (*e*) For impregnated antimicrobials, the diffusion mechanisms are simplified as they are a direct release of the active agent. Abbreviations: NO, nitric oxide; ROS, reactive oxygen species.

matrix, producing a polymer swelling or relaxation process (**Figure 3*b***). If the antimicrobial agent is produced by a chemical reaction inside the polymer matrix, the following should be further considered: (*a*) propagation of the stimulus that activates the antimicrobial compound (**Figure 3*c***), (*b*) generation of the antimicrobial through the specific reactions triggered by the stimulus, and (*c*) diffusion of the active antimicrobial agents out through the polymer matrix (**Figure 3*c***). The probability of polymer degradation or erosion on the timescale of the desired antimicrobial activity and under its specific conditions also should be considered (**Figure 3*d***).

Below, we briefly describe some of the most relevant compounds used in this field: metals, photocatalytic particles, nitric oxide (NO), essential oils (EOs), bioceramics, and organic compounds.

4.1.1. Metals. Metals have been recognized for centuries as effective antimicrobial materials, killing bacteria, viruses, and fungi, among other microbes, with silver (Ag), Cu, zinc (Zn), and magnesium being used to treat diseases long before the pharmaceutical antibiotic revolution (21, 22). The complexity of antimicrobial metals comes from the different metal-based materials and compounds that are active, from a simple salt to complex metal clusters. From the polymer point of view, we stress antimicrobial metal nanoparticles as they open up new opportunities arising from their superior antimicrobial activity, which occurs due to the double effect of the particle-based and metal-ion-based mechanisms (23). Antimicrobial metal nanoparticles can interact with both the negatively charged cell membrane and subcellular molecules (e.g., proteins, enzymes, and DNA), causing substantial damage and killing the microrganisms (21, 23, 24). However, metal

nanoparticles are antimicrobial primarily because they release metal ions. These ions can not only damage the membrane but also interact with subcellular structures, either by directly binding to the amino acids of these structures or by producing ROSs (21, 23). This ion release mechanism is common to most of the metal particles used in these antimicrobial polymers.

The mechanisms of metal-release antimicrobial polymers depend on the particle and polymer characteristics. For instance, in polymers with metal nanoparticles, hydrogels release the particles (**Figure 3*b***), but crystalline thermoplastic matrices release mainly metal ions (**Figure 3*c***) (25). In the latter matrices, the metal-ion release increases when polymers with high polarity and water uptake are used instead of nonpolar matrices (26). Particle size has an effect too; nanoparticles yield higher ion releases and antibacterial behavior than microparticles due to the higher surface area of the filler for the former (27). These results stress that the mechanism for the ion release is based on the water/oxygen diffusion in that it produces corrosion on the metal particle surface. Noteworthily, the antimicrobial behavior was correlated with the number of ions released (27). The polymer processing conditions can also affect the ion release and, therefore, the antimicrobial effect, as found for zeolite/Ag fillers (26, 28). Another relevant strategy in antimicrobial metal-release polymers is the surface impregnation of the metal structure on the polymer surface that simplifies the mass transfer issues and can be easily incorporated into different materials, such as wound dressings and fabrics (29, 30). In addition, hydrogels are extensively used as metal carriers for antimicrobial applications, allowing the addition and release of either metal ions or metal particles, including oxides, such as in alginate-based systems (31, 32). Polymers releasing metal ions or particles displayed antibacterial, antifungal, and antiviral behavior against a broad range of pathogens (24, 33), including influenza A viruses and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), for both Cu- and Zn-impregnated fabrics (34, 35).

4.1.2. Photocatalytic particles. A semiconductive photocatalytic particle can be stimulated by light irradiation equal to or larger than the bandgap exciting its electrons (e^-) from the valence band to the conduction band, which leaves a positive hole (h^+). These charge carriers migrate to the surface, producing a set of ROSs, as h^+ is a powerful oxidizing agent to produce hydroxyl radicals (·OH) from surface water. At the same time, e^- is a reducing agent able to generate a superoxide radical ($\cdot O^{-2}$) from adsorbed oxygen, among other ROSs (36, 37). The ROSs generated on the particle surface can quickly and nonselectively oxidize a wide spectrum of microorganisms, such as bacteria, fungi, algae, protozoa, and viruses (38). The disinfection mechanism includes the decomposition of the cell wall and the cytoplasmic membrane due to generation of ROSs (mainly ·OH and H_2O_2). Examples of nonhazardous photocatalysts able to inactivate microorganisms include TiO_2, g-C_3N_4, CuO, ZnO, and Ag_3PO_4, with different morphologies and structures (39). Although direct contact is relevant for antimicrobial behavior, some ROSs can act from a couple of micrometers away from the particle surface (38).

Based on the antimicrobial mechanism of photoactive particles, antimicrobial polymers containing semiconductor particles can be considered ROS-release systems, allowing them to overcome some of the limitations of pure nanoparticles needing a separation process after use. For instance, it is well recognized that for water treatment applications, photoactive particles should be immobilized in the membrane of the reactor (37, 40). Consider, as an example of a general mechanism, a low crystalline polyethylene matrix containing embedded TiO_2 nanoparticles. In this nonpolar/inert matrix, the diffusion of water and oxygen molecules through the amorphous regions of the matrix can reach the photoactive particle surface that, under light radiation, will produce ROSs able to diffuse out toward the cell membrane (20, 41). Indeed, under a proper polymer–nanoparticle interaction, an energy or charge transfer can occur between the phases, producing a synergic effect that allows visible light absorption and exceptional antimicrobial

effects (16). Polymers with photoactive nanoparticles under the proper light stimulus have been extensively studied to eliminate bacteria and yeasts (10, 16). However, issues related to the decrease of the accessible light and the particle contact area, as well as polymer degradation due to ROS, should be further considered in these polymer–semiconductor systems (37, 40).

Preservative: compound that prevents microbial spoilage of a product, reducing the risk to the consumer of acquiring an infection

4.1.3. Nitric oxide. NO is a free radical gas molecule that is endogenous to the human body and microorganisms, regulating several physiological processes (42). Exogenous NO can exert a promising antimicrobial action against bacteria, fungi, parasites, viruses, and yeasts, as it reacts with oxygen or reactive oxygen intermediates to form products with highly oxidizing activities, including peroxynitrite ($ONOO^-$) (43). This high activity motivated the immobilization of NO in polymers for antimicrobial NO-release systems (43, 44). The main strategy is the use of NO donors, such as *N*-diazeniumdiolates (NONOates), that can be covalently added into polymers, physically blended, or added into carriers (such as zeolite and silica) that act as filler in polymer matrices (44). NONOate-based polymers can release NO under physiological conditions (mainly in response to a pH or a proton source). *S*-nitrosothiols (RSNOs) are also extensively used to prepare NO-release polymers through a catalytic reaction involving UV light, heat, metal ions, ascorbic acid, or enzymes (43, 44). The first mechanism motivated the design of a broad set of photoresponsive NO-release polymers (43, 44). Besides being active against bacteria, fungi, and even parasites, NO-release polymers can also show antiviral activity, for instance, in topical hydrogels with NONOate-modified polysiloxane (43–45).

4.1.4. Essential oils. EOs are mixtures of highly concentrated oily, aromatic, and volatile hydrophobic liquids that contain a huge number of secondary plant metabolites, including molecules such as terpenes, terpenoids, and phenylpropenes. They can be obtained from roots, fruits, wood, herbs, bark, twigs, leaves, seeds, buds, rhizomes, peels, flowers, and even the entire plant of distinct botanic species (46, 47). EOs act as protective agents for plants and therefore are antibacterial, antiparasitic, insecticidal, antiviral, and antifungal (46). The lipophilic nature of essential oils facilitates their penetration through bacterial cell membranes such that they primarily destabilize the cellular architecture, leading to the breakdown of membrane integrity and increasing membrane permeability (48). The chemical components of EOs are volatile and susceptible to easy degradation. Therefore, mixing with a polymer matrix to create EO-release systems (for instance, through encapsulation) enables EOs to overcome these issues, allowing the controlled release of the active agents (48). A broad range of polymers have been tested as antibacterial and fungicidal agents, mainly through a casting process to avoid high temperatures (49). The release mechanism is diffusion-driven with polymer–EO interaction (particularly with terpenes) limiting the release, especially in biopolymers (18). The primary motivation for EO-release polymers is the growing tendency to replace synthetic preservatives and antimicrobials with natural ones, mainly in applications related to the food industry.

4.1.5. Bioceramics. Bioceramics are inorganic materials that can be implanted into the body without causing a foreign body reaction. They include bioactive glasses, glass ceramics, calcium silicates, hydroxyapatite, calcium phosphates, and cement and sealers for dentistry applications (50). Some of these bioceramics exhibit antimicrobial behaviors, mainly against bacteria, allowing the design of multifunctional biomaterials for tissue engineering, especially for hard tissues, aimed at reducing material infections. Bioglasses, in particular, present both high bioactivity and antibacterial behavior arising from their chemical composition, which is based mainly on SiO_2, with other compounds such as CaO and P_2O_5. This composition allows the exchange of network-modifier ions (e.g., Na^+, K^+, Ca^{2+}) with H^+ or H_3O^+ ions from surrounding bodily fluids

(51, 52). The different ions released can increase the pH and the osmolarity of the medium, killing bacteria and further reacting with phosphate and ester groups from the lipid membranes through electrostatic and hydrophobic interactions (51, 52). Noteworthily, the addition of antimicrobial ions, such as Cu, lithium (Li), Zn, and Ag, can improve the antibacterial effect of these bioceramics (52–54). Bioglasses are active against the most relevant bacteria for biomaterial infections and dental issues, including aerobic, anaerobic, multidrug-resistant, and even biofilm bacteria. Different biopolymers have been mixed with these bioceramics in order to improve not only their bioactivity but also their antibacterial characteristics. For tissue engineering, 3D porous structures (scaffolds) are used to facilitate cell interactions and diffusion of nutrients through the material. Most of these systems are bioabsorbable, and therefore, when antimicrobial bioceramics are incorporated into these porous matrices, they are easily exposed, facilitating the antibacterial behavior (**Figure 3*d***). From the material point of view, this process is the primary mechanism, besides the diffusion out of cations (53–55). Bioceramic particles also have been tested in dental polymers with high antibacterial efficacy (56).

4.1.6. Organic compounds. The ability of polymers to be mixed with almost all kinds of compounds motivated the development of an extraordinary number of materials able to release organic antimicrobials, including low-molecular-weight compounds [such as ciprofloxacin (57), penicillin, ampicillin (58), and triclosan (59)], high-molecular-weight compounds [such as pediocin, nisin peptides, and ethanolic propolis extracts (60)], and even polymers [such as chitosan (61) and polyvinylpyrrolidone–iodine (62)]. Like previous antimicrobial-release polymers, the efficacy (mainly antibacterial) of these compounds or blends depends on the interaction of both the polymer matrix and the organic antimicrobial with the water molecules that allow the active-agent dissolution, especially in high-molecular-weight antimicrobials. This family of organic compounds is so vast that the antimicrobial mechanisms cannot be summarized here, and it is mentioned only for a broad perspective about the possibilities of antimicrobial-release polymers.

4.2. Intrinsically Antimicrobial Polymers

IAMPs present inherent pathogen growth inhibition or elimination without releasing any antimicrobial agent. IAMPs can therefore avoid burst effects and the leaching of potentially toxic agents. The mechanism of action of IAMPs is based on the direct polymer–microbe interaction, for instance, (*a*) electrostatic, (*b*) hydrophobic/hydrophilic, (*c*) topographic, or (*d*) internalization. IAMPs can act passively, meaning that the polymer inhibits the microbe attachment (antiadhesive effects), or actively, meaning that the polymer interacts directly with the microbe to affect its viability (biocidal consequences) (63).

Topographically intrinsic antimicrobial polymers (TIAMPs) are based on physical or topographical biocide strategies, and they are starting to be used to reduce the prevalence of microorganisms on a surface. This new approach can overcome issues related to microbes' adaptative survival mechanisms to hazardous conditions such as antibiotic resistance and reduced susceptibility to antimicrobials when an EPS spreads over a surface (**Figure 4*a***). The topography of a surface (i.e., the arrangement of its physical features) can hinder the survival of microorganisms by impeding their initial adhesion (passive) or rupturing their external structure (active) through physical mechanisms that do not expel chemical antimicrobial substances (**Figure 4*b–d***). These physical features can exist as protrusions or cavities over the surface, with shapes such as pillars (circular or square), cones, riblets, and lines, along with some inspired by nature, such as the rose petal (64, 65). The efficiency of this kind of antimicrobial surface depends on its topological geometry (65) and the roughness, a parameter commonly used to define the surface characteristic

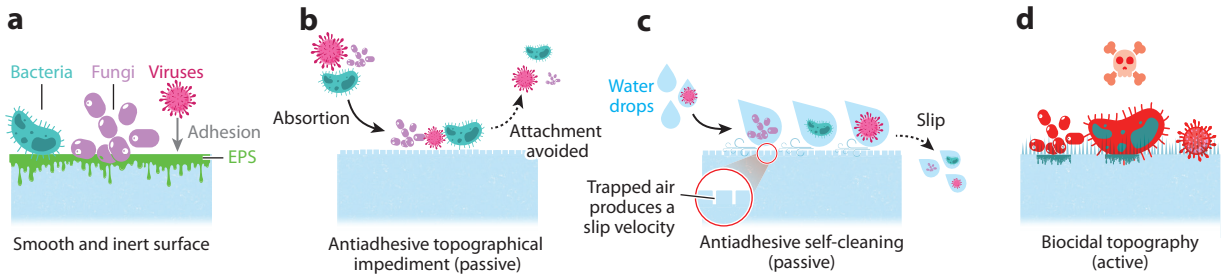

Figure 4

Scheme showing the impact of the surface topography for the attachment of microorganisms in topographically intrinsic antimicrobial polymers. (*a*) On a smooth and inert surface, the initial attachment of microorganisms promotes the production of extracellular polymeric substances (EPSs) and a biofilm. (*b*) On a surface presenting a topographical impediment, the adhesion of microorganisms is hindered, decreasing the contact area via geometrical features. (*c*) On a self-cleaning surface, the adhesion of water drops is hindered by the existence of a slip velocity due to the presence of air pockets at the interface (Cassie-Baxter state), and the water drops in this process carry microorganisms attached on the surface (the same mechanism avoids the adhesion of microorganisms already present in the water drops). (*d*) On nanosized geometrical features, the cell membranes of bacteria and fungi and the capsids of viruses are ruptured.

(66). The versatility and intrinsic properties of polymer materials, along with their propensity to standardization at different length scales, make them an excellent option for fabricating surfaces with antimicrobial topography (15).

4.2.1. Antiadhesive approach. IAMPs and TIAMPs can be designed to present antimicrobial action by avoiding the attachment of microbes due to either the specific characteristics of the polymer itself (IAMPs) or the specific topography of the polymer surface (TIAMPs).

4.2.1.1. Passive IAMPs. The primary action of passive IAMPs is based on either a fouling-resistant mechanism, with electrostatic or hydrophilic/hydrophobic polymer–microbe interactions preventing the cell attachment (**Figure 5*a*, subpanel *i***), or a fouling-release mechanism employing polymers with low surface energy through a cell attachment/detachment process (**Figure 5*a*, subpanel *ii***) (67). The membrane, wall, or envelope outer layers of microbes are composed of organic structures conferring a negatively charged (e.g., carboxylate and phosphate groups) and/or hydrophobic character (i.e., lipids) to the microbe surface (68–70). Hydrophilic polymers can therefore be used as passive IAMPs to prevent bacterial adhesion and proliferation because of their repulsion by the hydrophobic compounds of the microbe surface. The hydrophilic character of this kind of IAMP creates a superficial water layer that acts as an energetic barrier producing thermodynamically unfavorable interactions with approaching microbes (71). Among the various passive IAMPs based on hydrophilic and hydrophobic interactions, polyethylene glycol (PEG) is a highly hydrophilic polymer that has been extensively used as a coating to prevent biofouling. Indeed, PEG is an important component in synthesizing polymer structures through grafting or block copolymerization (67). Other hydrophilic fouling-resistant IAMPs include poly(glycerol), poly(2-methyl-2-oxazoline), and zwitterion-containing polymers (71). This strategy has demonstrated robust antifouling action against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* attachment (72, 73). Polymeric hydrogels can also avoid microbe attachment, especially when used as a coating, due to their high water uptake (73). Alternatively, low surface energy polymers such as fluoropolymers [e.g., polytetrafluoroethylene (PTFE)] and silicones [e.g., polydimethylsiloxane (PDMS)] exhibit a fouling-release action by weakly binding with the foulants (71, 73).

Fouling-resistant: antifouling mechanism frequently employed to elevate material surfaces' hydrophilicity through the introduction of hydrophilic materials

Fouling-release: antifouling mechanism where the attached and adhering foulants are more easily removed from the depositing surfaces at low hydrodynamic shear forces

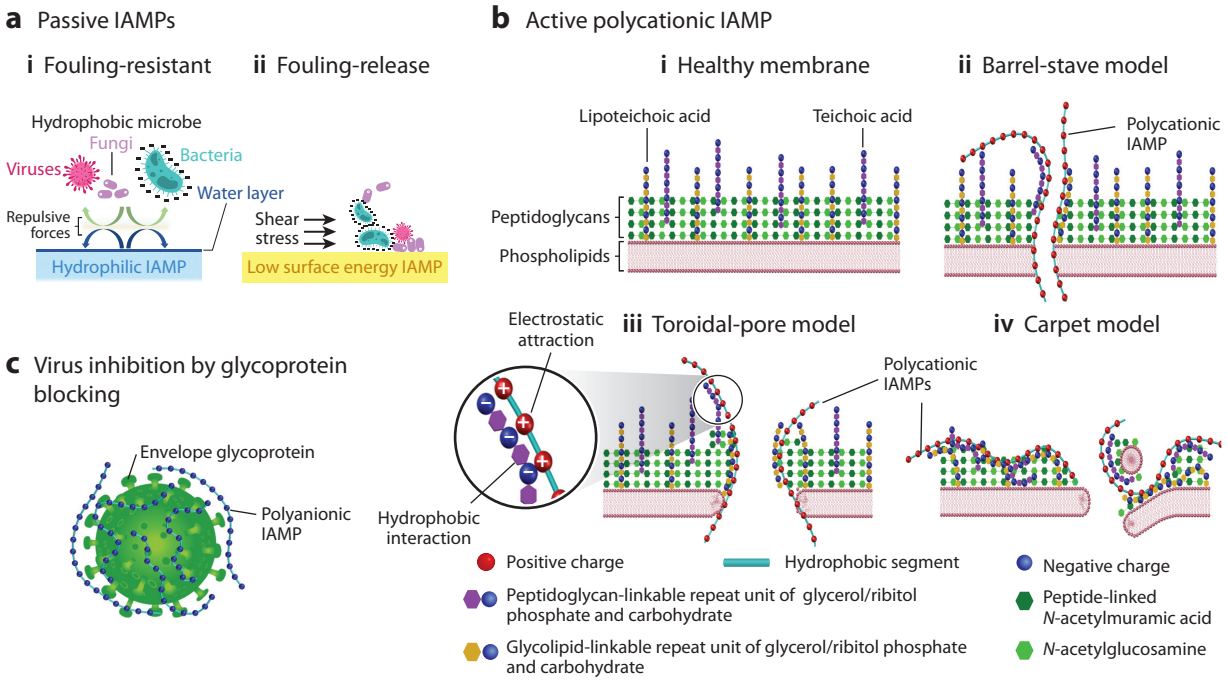

Figure 5

Principal mechanisms of intrinsically antimicrobial polymers (IAMPs). (*a*) Mechanism of passive IAMPs based on (*i*) fouling-resistant hydrophilic polymers and (*ii*) fouling-release low surface energy polymers. (*b*) Membrane disruption of Gram-positive bacteria with an active polycationic IAMP. The three typical mechanisms of pore formation in the (*i*) healthy membrane are (*ii*) barrel-stave, (*iii*) toroidal-pore, and (*iv*) carpet models. (*c*) Inhibition of a coronavirus-type virus by an active polyanionic IAMP. Negative charges of the polymer can interact with the positively charged regions of the envelope glycoproteins.

4.2.1.2. Passive TIAMPs. Two topographical strategies have been used to avoid microbial adhesion in passive TIAMPs: topographical impediment and self-cleaning surfaces. Topographical impediment means that the surface's physical features (geometric structure) do not allow microorganisms to settle over the material freely. Rough surfaces can hinder the attachment of microorganisms by providing less surface area for adhesion and creating gaps at the material–microbe interface (**Figure 4*b***) (74, 75). Therefore, bacteria attach more to smooth surfaces compared to micropatterned ones (76), although depending on the geometric design, bacteria can accumulate at the bottom of the physical features (valleys) (77). For a topographical arrangement not to entrap microorganisms, the pitch of the surface must be smaller than the size of the microbe (15, 66). As viruses infectious to humans have sizes between 20 and 300 nm (78), much smaller than bacteria and fungi (which are measured in micrometers), antimicrobial topological surfaces should have nanometric structures so that they do not act as fomites (i.e., surfaces that carry infectious viruses). Topographical impediment can also hinder bacterial attachment and biofilm formation by delaying direct contact between cells (65).

PDMS has been widely used to manufacture antimicrobial topographies due to its innocuity, elasticity, and workability (79). This polymer allows the design of various physical topographical features—such as lines, holes, pillars, cross hatch, Sharklet® (a surface that mimics the shark-skin topography), wrinkles, and cones (64)—mostly through mold replication. Of interest in this context is the rose petal surface with hierarchical physical features consisting of micropapillae

(~20 μm diameter) and nanosized folds (~700 nm length) and showing significantly less attachment of bacteria than a flat surface (65). A PDMS surface with a biomimicked hierarchical structure consisting of micrometric papillae (around 10 μm diameter and 8.7 μm peak to valley roughness) with nanometric features on top of them reduced the attachment of bacteria by 82% as compared to flat samples (80). Thermoplastics containing graphene-derivative nanoparticles, such as polycaprolactone, low-density polyethylene, and polylactic acid, can also exhibit a surface roughness able to inhibit bacteria attachment, which can be a much simpler route for producing topographically antimicrobial surfaces (81, 82).

Surface topography also affects the near-surface hydrodynamic environment (83), allowing the self-cleaning phenomenon, often called the lotus effect. This effect is found in nature on the surfaces of plants, insects, and vertebrates (84) to avoid fouling (accumulation of unwanted contaminants) through the presence of hierarchical physical features that repel water (**Figure 4*c***). Microorganism attachment develops mostly under specific water-flow conditions (2, 66), so the wettability of a surface plays a crucial role in adhesion, as wet surfaces can provide the ideal conditions for biofilm formation (74, 85). Hydrophobic self-cleaning surfaces may therefore protect plants against harmful microorganisms, whose growth is inhibited by dry plant surfaces, and further ensure efficient gas exchange through a thin film of air clinging to the surface when the leaves are submerged (84).

Superhydrophobicity is a type of wettability that can provide a slip velocity at the interface between the solid material and a drop of water (86), allowing the fluid to roll over the surface and not attach to it due to the existence of air pockets (Cassie state). This phenomenon means that microorganisms and EPSs slip over these kinds of materials, hindering the first attachment of microbes (**Figure 4*c***). Moreover, the small number that attach to the surface can be self-cleaned (87). In the case of viruses transported via respiratory droplets, superhydrophobic surfaces inhibit their attachment and decrease the possibility of infection (88). For instance, a multilayer superhydrophobic antibacterial film of polydopamine (PDA) with Ag nanoparticles and modified with perfluorodecanethiol exhibited 0% bacterial covering compared to an uncoated control surface (30% covering) and PDA+Ag samples without modification (9% covering). These results showed that superhydrophobic topography could increase the antibacterial properties of Ag nanoparticles (89). Bacteria-repellent superhydrophobic polyurethane sponges were developed using a coating based on 1H,1H,2H,2H-perfluorooctyltriethoxysilane-modified hydrophobic ZnO and Cu nanoparticles that show a significant reduction in the adhesion of bacteria (*S. aureus*) by up to 99.9% (90). TiO_2 nanoparticles chemically crosslinked with a PDMS matrix can also produce superhydrophobic films. These films show photocatalytic activity and can be used as self-cleaning blood-repelling dressings with antibacterial properties (91).

4.2.2. Biocidal approach. The flexibility of these inherent antimicrobial polymers allows for the design of IAMPs and TIAMPs than can further kill microorganisms with biocidal mechanisms that will depend on the characteristics of each surface.

4.2.2.1. Active IAMPs. Nature provides some outstanding examples for the design of active IAMPs. For instance, the immune systems of different organisms employ a series of peptide oligomers (10–60 amino acids) that can act as intrinsic and specific antimicrobial agents (92). Most antimicrobial peptide oligomers (AMPOs) are composed of a cationic segment and a hydrophobic segment, which could interact with and disrupt the cell membranes of microbes (93). The amphiphilic chemical structure of AMPOs is the basis for the design of synthetic active IAMPs, such as polycations (e.g., quaternized nitrogen polymers and polyphosphonium polymers), amphiphilic copolymers (e.g., PEG-b-PDMS-b-PEG), and chemically modified polymers (e.g., quaternized

Quaternary ammonium: derivative of ammonium compounds in which all four of the hydrogens bonded to nitrogen have been replaced with hydrocarbyl groups

chitosan and antibiotic-grafted polymers). Nowadays, the aim is to obtain rationally synthesized IAMPs by mimicking the architecture of AMPOs based on amphipathic structures having active functional groups with biocidal ability (e.g., amino, imino, nitrilo, quaternary ammonium, imidazolium, guanidine, sulfonium, and phosphonium groups) and a hydrophobic segment (i.e., apolar groups or a polymer block). The biocidal groups are commonly incorporated into synthetic IAMPs as either a main-chain or side-chain architecture feature (63, 67, 94–99). Another strategy for active IAMPs is mixing them with inert nonantimicrobial polymers, such as in food packaging, extending their field of applications (100).

In addition to AMPOs, nature also produces active bio-IAMPs such as chitosan [a polysaccharide consisting of β-(1→4)-linked D-glucosamine and *N*-acetyl-D-glucosamine] and poly-ε-lysine (a homopolypeptide). These polymers present a polycation structure in which the amino groups of the repetitive units are protonated (at a pH below the pK_a) (101). These positive charges attract the negative charges of the outer layer of the microbe's membrane and induce its disruption. In contrast, negatively charged natural polymers (polyanions), such as glycosaminoglycans and λ-carrageenans, have also shown antimicrobial activity. In particular, these natural polyanions exhibit high antiviral capacity against viruses such as the human immunodeficiency virus (HIV), influenza viruses, the herpes simplex virus (HSV), and coronaviruses (102–104). Synthetic polyanions such as sialic acid–containing polymers, poly(aurintricarboxylic acid), and polyacrylic acid also exhibit antimicrobial activity, for instance, against viruses (104). A direct relationship between the type of negative charges (e.g., carboxylate, sulfonate, or phosphate/phosphonate groups), hydrophobic polymer backbone, and antiviral activity has been reported in reversible addition–fragmentation chain-transfer (RAFT)-synthesized IAMPs with antiviral activity against Zika, Ebola, Lassa, lyssa, rabies, Marburg, and influenza viruses, as well as the severe acute respiratory syndrome (SARS) coronavirus, HSV, and HIV (70).

Chemical modification of natural or synthetic polymers with biocidal agents such as drugs and cationic nitrogen–containing molecules offers a versatile approach for obtaining IAMPs for microbe-specific applications. For instance, several polymers covalently linked with antimicrobial agents have been reported (94, 97, 104–108). These antimicrobial agents can bind through amidation, esterification, epoxy ring opening, and click chemistry reactions. Among natural polymers, chitosan is one of the most widely used for attaching antibiotics, antivirals, AMPOs, and antifungal agents (109, 110). The advantage of this approach is the synergic effect in the antimicrobial action of these agents bonded to the intrinsic antimicrobial chitosan chains. Recently, chitosan functionalized with cationic groups by reacting the amino groups with glycidyltrimethylammonium chloride presented an inhibitory effect against SARS-CoV-2 (110).

Regarding the mechanisms of biocidal action, the primary pathway is based on a membrane-targeting activity through the formation of pores by three main models, as summarized in **Figure 5*b*** for Gram-positive bacteria (92, 93). The amphipathic properties of active IAMPs allow them to interact with the negatively charged and/or lipophilic components of the microbe's membrane, wall, or envelope. This interaction can induce the formation of pores in the membrane through the barrel-stave shape (**Figure 5*b***, **subpanel *ii***), toroidal-pore (**Figure 5*b***, **subpanel *iii***), and carpet model mechanisms (**Figure 5*b***, **subpanel *iv***). Disruption of microbial membranes affects cell proliferation (for bacteria and fungi) and may also result in cytoplasmic leakage, leading to the death of the microbe (**Figure 5*b***). In antiviral IAMPs, the mechanism of action, besides membrane disruption, is usually the inhibition of virus adhesion to host cells by mimicking cellular receptors that bind to virus envelope proteins to avoid cell infection (**Figure 5*c***) (70). Other antimicrobial mechanisms inhibit biochemical processes such as protein biosynthesis, DNA replication, and metabolic activity through the internalization of IAMPs (93).

4.2.2.2. Active TIAMPs. Biocidal topographies inactivate microorganisms by mechanically rupturing their outer structure, either the cell membrane (in the case of bacteria and fungi) or protein capsid (in the case of viruses) (**Figure 4*d***) (76, 78). This rupture can be via stretching (mechanical stress) of the cell's outer layer or via puncture. For instance, superhydrophilic micronanotextured plasma-treated poly(methyl methacrylate) surfaces with microhills around 1 μm and nanofilaments presented a 100% bactericidal efficacy (111). Natural surfaces have also been an inspiration for the development of biocidal surfaces. A gecko skin biomimetic acrylic resin surface having nanometric spinules with an aspect ratio of 2.5 and a pitch of 500 nm presented bacteria-killing capabilities similar to the gecko skin: 66% and 88% survival reduction of *Streptococcus mutans* and *Porphyromonas gingivalis*, respectively (112). The surfaces of dragonfly and cicada wings have nanopillars of different heights that are able to rupture bacteria by adhering to them and causing a mechanical strain when the microbes try to move over the surface, rupturing their membrane and causing cytoplasmic leakage (74, 113). A theoretical model of this mechanical process concluded that the antibacterial surfaces depended on the geometric structure (114). Using this principle as inspiration, a nanostructured Ormostamp® (a commercial polymer based on an acrylate-modified polysiloxane, as described by the company) surface with 80-nm-diameter nanopillars with an average pillar density of 40 pillars/μm^2 (surface roughness of 39.1 nm) has a bactericidal efficiency against *S. aureus* of ∼100% (115). However, high-density structures with ∼70 pillars/μm^2 and low-density structures with <20 pillars/μm^2 reduce the bactericidal efficiency to almost the level of flat samples. The biocidal mechanism observed corresponds to a rupture of the outer membrane of the Gram-positive bacteria via stretching.

Zwitterionic polymer: ampholytic polymer containing ionic groups of opposite signs, commonly on the same pendant groups

4.3. Smart Antimicrobial Polymers

Smart antimicrobial polymers (SAMPs) exhibit antimicrobial properties when exposed to a stimulus, such as light, electrical fields, pH changes, or heat. Among SAMPs, light-responsive IAMPs are attractive for controlled and localized biocidal action. The antimicrobial mechanism is usually based on the oxidative stress of the microbe produced by light-activated singlet oxygen and ROS generated by photosensitizers in the polymer structure (98, 116). A photothermally activated polymeric nanofiber mat was developed by adding reduced graphene oxide, presenting an on-demand release of antibiotics, previously added by immersion, upon irradiation in the near-infrared (117). The physiological temperature has also been used as a stimulus in thermoresponsive hydrogels for the controlled release of antibiotics (118). Smart IAMPs can be developed with susceptibility to pH changes, which trigger their antimicrobial action through charge variation on polymer chains because of a protonation–deprotonation process (119). For instance, a pH-sensitive zwitterionic polymer showed on-demand antibacterial behavior under acidic conditions (such as on an infection site), changing from neutral to cationic characteristics (120). Another approach is to encapsulate high antimicrobially reactive compounds, such as ClO_2, ZnCl, and AgI, using polymers that, in addition to the standard diffusion-driven release, present an increased antimicrobial release after being touched or after being pressed by droplets containing the microorganisms at the sites of contamination (121–123). A simple approach for the on-demand release of antimicrobial Fe^{3+} ions was also developed using a hyaluronic acid hydrogel crosslinked with a Fe complex that locally degrades as surrounding bacteria excrete hyaluronidase (124).

Another family of SAMPs corresponds with electrically active polymers showing antimicrobial behavior under an electrical field or current (125). The electrical field can kill microbes, especially bacteria, and even increases the effectiveness of some traditional antimicrobial agents. Membranes made of intrinsically conductive polypyrrole coated with graphene derivatives present enhanced electric conductivity and improved biofouling suppression because of higher

electrostatic repulsions between the conductive surface and the bacteria (126). A more recent approach is based on percolated electrically conductive thermoplastic composites having graphene derivatives (82, 127). A strong antibacterial effect was observed in these percolated polymers under direct current, eradicating 100% of the bacteria from the surface. Piezoelectricity generated either by the polymer itself or by mixing a polymer matrix with piezoelectric nanoparticles is another new approach to prepare antimicrobial polymers stimulated by deformation (128, 129). The mechanisms are based on both electricidal and piezocatalytic effects (130).

5. FOR WHAT? APPLICATIONS AND RELEVANCE

The widespread use of polymers and the prevalence of microbes and biofilms on almost any surface, which triggers a set of negative effects, explain the large number of potential applications of antimicrobial polymers. One of the first relevant commercial applications was antibiofouling coatings for the marine industry, where Cu, tributyltin, and tin were originally used in antimicrobial-release polymers (131). Environmental concerns motivated the use of novel strategies based on IAMPs and TIAMPs, such as polymer brush coatings, PEGylated materials, hydrogels, polyzwitterions, fluoropolymers, silicones, and topographical surfaces (131). The food packaging industry is also currently using antimicrobial-release polymers, mainly through commercial additives (132). The goal is to prevent microbial growth on the surface of foods, where a large portion of spoilage and contamination occurs, thus reducing the need to add larger quantities of antimicrobials to the bulk of the food itself (132). Examples of antimicrobial compounds added into the polymers are zeolite-containing Ag triclosan, although new strategies such as those based on EOs and enzymes are emerging. IAMPs have also been studied for food packaging (100). Antimicrobial textiles (most of them polymer-based) are another example of commercial applications; consumer demand for hygienic clothing and activewear created a large market for such textiles (133). Sportswear, socks, shoe linings, and underwear accounted for 85% of the production of antimicrobial textiles. For synthetic fibers, the antimicrobial agent can be incorporated into the polymer matrix before fiber formation. For natural fibers, conventional exhaust dyeing and pad-dry-cure processes have been used for antimicrobial finishing (133).

Biomaterial-associated infections, especially in medical devices, have attracted considerable attention for applications of antimicrobial polymers. For instance, it is estimated that urinary catheters and central venous catheters present infection rates of 10–30% and 3–8%, respectively (71). Antimicrobial polymers in this area have been studied for cardiovascular, aural, orthopedic, nephrological/urological, and neural implants, as well as ocular, dental, and oral nondental devices (134). Surgical meshes and pouches, prosthetic heart valves, intravascular stents, cerebrospinal shunts, contact lenses, endotracheal tubes, urinary catheters, and sutures are some specific applications in which antimicrobial polymers have been tested. Other applications of antimicrobial polymers, for instance IAMPs, include nonwoven fiber for the manufacture of fabrics for personal protective equipment (63, 94), scaffolds for tissue engineering (135), and drug development (102, 103, 107, 108). Recently, Moakes et al. (102) developed a nasal prophylactic formulation against SARS-CoV-2 infection. In another example, Zhang et al. (89) reported the antiadhesion capabilities of Ag-PTFE nanocomposite coating on urinary catheters. The coated catheter decreased the first attachment of bacteria by 60% and reduced biofilm formation by 97% for the bacteria *E. coli* and *S. aureus* due to the increased roughness of the surface (69.3 $\pm$ 7.3 nm) compared to a flat, uncoated catheter (17.8 $\pm$ 2.3 nm), complementing the antimicrobial action of Ag^+ cations.

Another potential application of antimicrobial polymers is as a membrane for water treatment (67, 106), in particular for filtration systems (136). The attachment of microorganisms, and the biofouling produced, is considered to be one of the main hindrances to membrane performance,

POLYMERS FACING A PANDEMIC: A WELL-KNOWN DILEMMA

The coronavirus disease 2019 (COVID-19) pandemic magnified the dilemma of our society regarding polymers. There is no doubt about the positive effect of polymeric personal protective equipment (PPE) to avoid virus transmission. However, the massive use of disposable face masks is the most remarkable example of a polymer PPE product that, due to their outstanding properties and benefits, our society overconsumes worldwide. Antimicrobial polymers emerge as a strategy complementing not only the performance of PPE but also other protocols against COVID-19. This scenario stresses the concern about the negative effect of deficient waste management of these materials due to the presence of plastics in almost all kinds of terrestrial and aquatic environments. In this context, there is an opportunity to improve our current situation by applying strategies from eco-design and circular economy for developing more sustainable PPE and antimicrobial polymers.

reducing system productivity and increasing energy consumption. Initial efforts used hydrophilic membranes, although today antimicrobial-release systems are emerging as a possible solution to avoid biofouling in these membranes (136).

Relevant to the context of the applications of antimicrobial polymers are the results of studies of plastic waiting room chairs with embedded metal Cu nanoparticles and metal hospital IV poles coated with an organic paint with nanostructured zeolite/Cu particles, which were produced at industrial scale and tested in a hospital environment (137). These prototypes were sampled once weekly for 10 weeks, and the chairs with Cu reduced the total viable microorganisms present by around 73%, showing activity regardless of the microorganism tested. In operating rooms, IV poles with the antimicrobial coating installed presented fewer total viable microorganisms than uncoated samples despite rigorous hygiene protocols (137).

Successes in the design of different polymers with high antimicrobial activity (see **Figure 1** for some representative examples) and the above-mentioned potential applications have fostered a growing antimicrobial plastics market. **Figure 2** shows some examples of the different commercial antimicrobial polymers and technologies that can be found today. By taking advantage of the developments and technologies described in the present review, this market could grow from US $36.9 billion in 2020 to US $59.8 billion by 2025 (138), triggered by the increasing need from various sectors, mainly healthcare and medical, for antimicrobial plastics.

The growing production of antimicrobial polymers should motivate further studies regarding the effect of the additives or chemical modifications presented in this review on the recycling processes of plastics. This is even more relevant considering the high demand for antimicrobial products due to the appearance of pandemic-related issues. For instance, see the sidebar titled Polymers Facing a Pandemic: A Well-Known Dilemma.

6. SUMMARY

Antimicrobial polymers are a versatile approach to reduce or avoid the initial attachment of microorganisms on a surface, eliminating the formation of biofilms. The ability of polymers to be modified chemically and mixed with other compounds explains how today almost all kinds of antimicrobials can be used for the design of antimicrobial polymers. The high processing capacity of polymers also provides novel designs for antimicrobial topographies, in addition to the development of smart systems for on-demand activity. The challenge today is to validate in situ the antimicrobial performance of these materials and to expand the range of applications where these polymers can add value by solving relevant health, industrial, and domestic issues.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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