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Review

Nanomedicines for antimicrobial interventions

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SUMMARY

The development of new antimicrobial therapeutic tools addresses the emergence of multidrug-resistant micro-organisms or clones and the need for more effective antimicrobial strategies. Overcoming the hurdles in providing early diagnosis and intervention on hard-to-reach and/or resting bacteria (i.e. biofilm-embedded cells) represents a challenging task. In this review, we identify a set of organic, inorganic, and hybrid materials that might be used for prevention and control of healthcare-associated infections. We report the current knowledge on nano- and microparticle-based antimicrobial agents and describe the possible mode of their action.

Introduction

Micro/nanomedicine is nowadays a well-established branch of science that deals with design of micro/nanodevices, i.e. micro/nanoparticles, possessing unique therapeutic and diagnostic properties. A schematic illustration of nano/microsystems currently used for the delivery of therapeutic agents is shown in Figure 1. The biological and therapeutic properties of micro/nanoparticles (MPs, NPs) are correlated to their structural and functional characteristics. A large number of studies aimed at understanding the interactions between MPs/NPs and cells as a function of their size, shape, and surface chemistry have been published. Indeed particle surface and bulk properties (size, charge, shape, elasticity, and functional groups) have a significant impact on their cellular association and internalization. For instance, a significant diminution of particle association with cells was observed when the particles had a negative surface charge versus particles showing a positive surface charge.[1] Rigidity and elastic modulus of MPs/NPs have also been found to greatly affect cellular internalization, trafficking, in-vivo circulation lifetime, and biodistribution.[2] Plasticity and versatility of nanomaterials are such that almost any platform can be adapted for a specific use: in this way, when a specific particle or material is deemed suitable for its antimicrobial properties, it can then be structured for either prophylactic or therapeutic purposes.

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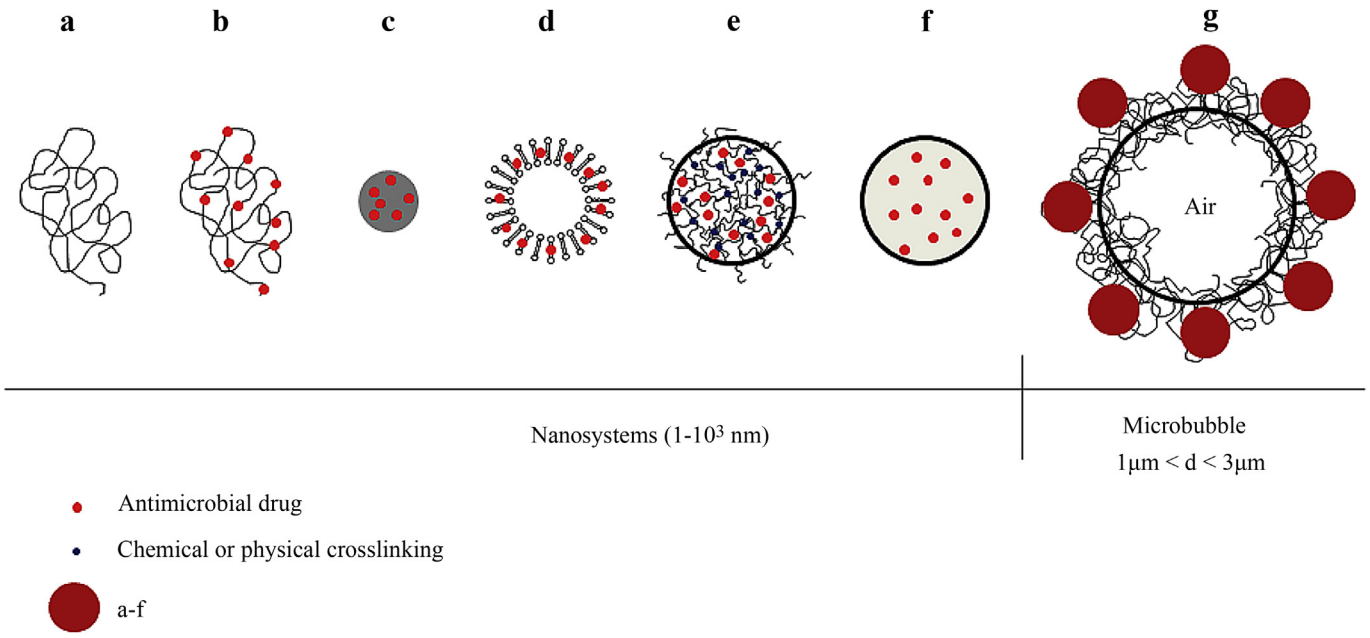

Figure 1. Schematic illustration of nano/microsystems: (a) antimicrobial polymers; (b) polymer chains, (c) inorganic nanoparticles, (d) liposomes, (e) polymeric nanoparticles, (f) solid lipid nanoparticles loaded with antimicrobial drug; (g) microbubbles loaded with nanoparticles.

This review assesses current knowledge on nano- and microparticle-based antimicrobial agents. In addition, the possible modes of their action are described. Understanding of structure–function relationship in nano- and microparticle-based antimicrobial agents is crucial for the design of new devices.

Micro/nanosystems

Among antimicrobial micro/nanosystems, a set of organic, inorganic, and hybrid materials can be identified. The antimicrobial activity exhibited by these systems depends on their different physical, chemical, and functional properties.

Metal-based nanoparticles

Nanoparticles based on metals that express antimicrobial ability are among the most studied. Compared to the ionic form of a metal, NPs exhibit an equivalent or superior antimicrobial activity.[3–5]

Size, shape, and surface properties (ζ-potential) are crucial features determining the antimicrobial efficacy of NPs. In particular, the huge increase in the surface area determines a higher interaction of NPs with the surrounding materials. In this context, the real added value of the nanotechnology is the capability to tune the particle properties by selecting different methods of synthesis for NPs. Physical methods used to produce metallic NPs include sputtering, evaporation, laser ablation, ion ejection, photolithography and electron-beam lithography. Chemical approaches to obtain NPs require the reduction of the metallic ions to form a well-dispersed colloidal solution. In particular, chemical reduction of metallic ions is widely performed with citrate, ascorbate, and sodium borohydride as reducing agents.[6–8] The toxicity of the reagents and the agglomeration and precipitation of NPs are disadvantages of these methods. In order to prevent NPs coalescing during synthesis, NPs can be trapped inside a carbon matrix or stabilized by water-soluble polymers such as polyvinyl sulphonate or polysaccharides.[9–14] When the stabilizer possesses antimicrobial activity, i.e. chitosan, the hybrid system chitosan–NPs may exhibit a synergistic effect.[13,15,16]

Nanocomposites are produced by using metallic NPs supported by polymer matrices to form hybrid sponges, electrospun nanofibres, membranes, and nanowires. These nanocomposite materials are used to coat medical devices and for production of antimicrobial cotton textiles that have been demonstrated to reduce postoperative infections.[12,17–19]

Inorganic NPs can also be produced by environmentally friendly technology (bionanotechnology) that uses plants and micro-organisms (bacteria, yeasts, fungi, and actinomycetes) as nanofactories for fabrication of inorganic NPs.[20] Micro-organisms possess significant ability to reduce a wide range of metal oxides, the synthesis of which can occur intra- and/or extracellularly. In the intracellular pathway, ions are transported into the microbial cell where the synthesis of NPs is mediated by enzymes. In the extracellular process, ions are trapped on the cells' surface and reduced in the presence of enzymes.[21] Unfortunately, micro-organism-mediated NP preparations may yield metallic NP suspensions that are not well dispersed. Moreover, when the bacterial biomass method is used, the biological hazard should be taken into account.

Synthetic antimicrobial polymers

Synthetic antimicrobial polymers represent a huge class of molecules with great potential for effective antimicrobial therapy. Compared to low molecular weight antimicrobial agents, synthetic polymers possess an improved and prolonged antimicrobial activity due to the capability to destroy the