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Review

Bioinorganic antimicrobial strategies in the resistance era

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ABSTRACT

The emergence of Multi-Drug-Resistant (MDR) organisms has become a major worldwide clinical problem. The extensive and routine use of the first-line antibiotics to control infections imposed the development of multiple mechanisms of microbial resistance. Despite the fact that numerous advanced technologies enable the molecular design of new antibiotics, the MDR-associated infections remain a great challenge to modern medicine. Consequently, there is an urgent need to find other methods for reducing the antimicrobial resistance problem. Innovative bioinorganic antimicrobial platforms offer an interesting alternative for combating the microbial resistance. Herein, we describe the bioinorganic strategies with multiple mechanisms of action based on *i)* small metal complexes, *ii)* metal modified macromolecules, *iii)* metal and metal oxides nanoparticles, *iv)* light-activated bioinorganic platforms, to overcome the pathogen's resistance.

Abbreviations: aBL, antimicrobial blue light; AgNPs, silver nanoparticles; AlPcCl, chloroaluminium phthalocyanine; AMP, ampicillin; AMPs, natural antimicrobial peptides; ATP, adenosine triphosphate; AgNPs, silver nanoparticles; AuNPs, gold nanoparticles; Au@Ag, coreshell gold and silver nanoparticles; bLf, bovine lactoferrin; BODIPY, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene; BSA, bovine serum albumin; BSA-CuNPs, copper NPs modified with bovine serum albumin; bpy, 2,2′-bipyridine; CAP, cationic antimicrobial peptides; CAT, catalase; CFU, colony-forming unit; ClGaTCPP, chloro[5,10,15,20-tetra-(4-carboxyphenyl)porphyrinato]gallium(III); CMC, carboxymethyl cellulose; COL, colistin; CS-Lys-NPs, chitosan nanoparticles with lysozyme; CS-NPs, chitosan nanoparticles; CuNPs, copper NPs; Cys-AgNPs, cysteine protected AgNPs; dmp, 2,9-dimethyl-1,10-phenanthroline; EPL-g-butyl@AgNPs, ε-polylysine/silver nanoparticles; EPS, extracellular polymeric substance; ESBL, expanded spectrum β-lactamase; GSNO, S-nitrosoglutathione; GRAS, Generally Recognized As Safe; HIV, human immunodeficiency virus; holoLf, holo-lactoferrin; HPIX, hematoporphyrin; HPV, human papilloma virus; HSPs, heat shock proteins; IC, internal conversion; ICG, indocyanine green; ImMPP, imidazolium-substituted porphyrin; ISC, intersystem crossing; Lf, lactoferrin; LPS, lipopolysaccharide; MB, Methylene Blue; MDR, Multi-Drug-Resistant; MDRAB, multidrug-resistant *A. baumannii*; MEP, microbial efflux pump; Mn-bLf, manganese bovine lactoferrin; MNPs, magnetic iron oxide nanoparticles; MNP@Au, core-shell magnetic iron oxide nanoparticles coated with gold; MRSA, methicillin-resistant *Staphylococcus aureus*; MRSE, methicillin-resistant *Staphylococcus epidermis*; NO-NPs, nitric oxide-releasing nanoparticles; NPs, nanoparticles; PAH, polyallylamine hydrochloride; PB, Prussian Blue; PBP, penicillin-binding protein; Pc, phthalocyanine; Pc4, silicon phthalocyanin; PDI, photodynamic inactivation; Ph, phosphorescence; phen, 1,10-phenanthroline; PK, pharmacokinetic; PLA, poly(lactid acid); PS, tetrapyrrolic nanoparticles; pSiNPs, porous silicon nanoparticles; PtNPs, platinum nanoparticles; PTT, photothermal therapy; PVA, polyvinyl alcohol; PVP/PB NPs, poly(vinylpyrrolidone)-coated Prussian Blue nanoparticles; PVP-AgNPs, polyvinylpyrrolidone protected AgNPs; RNS, reactive nitrogen species; ROS, reactive oxygen species; SDS, sodium dodecyl sulfate; SEM, scanning electron microscope; SNO, S-nitrosothiol; SOD, superoxide dismutase; SPIONS, superparamagnetic iron oxide nanoparticles; TGSP, TiO_2–graphene nanosheets; THPTS, tetramethylpyridinium bacteriochlorin; TMPyP, 5,10,15,20-tetrakis(1-methyl-4-pyridinio)porphyrin; TPA, tris(2-pyridylmethyl)amine; tRNA, transfer RNA; UCNPs, upconverting nanoparticles; UV, ultraviolet; UVA, ultraviolet light of wavelength 320–400 nm; UVB, ultraviolet light of wavelength 290–320 nm; UVC, ultraviolet light of wavelength 100–290 nm; VAN, vancomycin; VRE, vancomycin-resistant *Enterococcus*; XRD, X-ray diffraction; ZnDPA, zinc(II)-dipicolylamine; ZnF_2PMet, *meso*-tetrakis(2,6-difluoro-5-*N*-methylsulfamylophenyl)porphyrinate zinc(II); ZnPcs, zinc phthalocyanines; ZnTPP, zinc tetraphenylporphyrin.

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1. Introduction

The major challenges in modern medicine encompass drug-resistance associated with advanced stage diseases that cannot be completely cured. Resistance has increasingly become a worldwide problem because the pace at which we are discovering novel drugs has slowed down dramatically while their use is constantly increasing. Antimicrobial drugs discovery and development is locked in co-evolutionary battle with natural resistance mechanisms. The discovery of the first antibiotics changes dramatically the quality of our life. For the first time it was possible to effectively control infection diseases. Unfortunately the use of large quantities of antibiotics to control infections in human and animal diseases has created exceptional conditions for mobilization of resistance elements in microorganism populations and their capture by previously antibiotic sensitive pathogens [1–5].