DEVELOPMENT OF HYBRID ANTIMICROBIAL PLATFORMS VIA COORDINATION CHEMISTRY

DOI: 10.66951/BRWX2380; https://doi.org/10.66951/BRWX2380

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Abstract

Antimicrobial resistance is driving the search for materials that deliver bactericidal agents with spatial and temporal control. Coordination chemistry offers a versatile approach, because bonds between metal centers and nitrogen-donor linkers combine structural tunability with stimuli-dependent stability. Two hybrid antimicrobial platforms are presented: zeolitic imidazolate framework-8 (ZIF-8) loaded in situ with essential oil components eucalyptol or thymol, and a silver coordination polymer (Ag-CP) grown on chitosan-coated surgical steel. In ZIF-8, the host-to-guest stoichiometry determined morphology, colloidal behavior and release, while in the Ag-CP coating the metal-to-ligand ratio determined surface architecture and silver ion release. Eucalyptol-loaded ZIF-8 inhibited *Staphylococcus epidermidis* and *Escherichia coli* more effectively than thymol-loaded samples, which suffered from pore blocking and aggregation. The equimolar Ag-CP coating remained cytocompatibility at physiological pH and turned bactericidal under mildly acidic conditions. These results support coordination chemistry as a unifying strategy linking porous carriers with functional antimicrobial surfaces.

1 Introduction

Bacterial infections that no longer respond to antibiotics represent one of the pressing challenges in modern medicine, and mortality projections related to antibiotic resistance in the coming decades further highlight the urgency of implementing alternative antibacterial strategies [1,2]. Traditional antibiotic therapy is increasingly being supplemented by approaches based on materials in which the antibacterial effect is incorporated into a solid carrier or surface, rather than being administered as a free active ingredient [3,4]. Such approaches allow the active species to be localized, protected, and ideally released only when and where it is required.

Coordination chemistry provides a particularly flexible basis for this purpose. Materials composed of metal ions and organic linking units, including metal-organic frameworks (MOFs) and coordination polymers, combine high structural order with porosity and surface chemistry that can be tuned during synthesis [5–7]. Two features make them interesting for antibacterial use. First, several of the metal centers commonly used, among them Zn^{2+}, Ag^{+} and Cu^{2+}, are themselves bactericidal, so the framework can act at once as a structural host and a source of active ions [7,8]. Second, the bonds between metal centers and nitrogen-donor linkers such as 2-methylimidazole are sensitive to

protonation, so the assembly remains stable at physiological pH but dissociates in acidic environments [9,10]. Because bacterial colonization and biofilm formation lower the local pH through the secretion of organic acids, this acid sensitivity can be exploited as a trigger that induces release to the presence of infection [11–13].

In this context, two material archetypes are particularly important. Porous frameworks such as ZIF-8 offer a large pore volume in which guest molecules can be stored and from which they are released upon framework breakdown, which makes them suitable nanocarriers for antibacterial agents [5,9,14]. Among the potential substances, the components of essential oils have gained attention because they come from natural sources and affect bacterial membranes, although their volatility and low water solubility complicate their direct use [15,16]. Encapsulation in a porous matrix can mitigate these disadvantages by restricting the movement of the volatile molecule and slowing its release [14,17]. The second archetype relates to coordination polymers grown on a metal surface, which is important for preventing implant-associated infections. Stainless steel is widely used for load-bearing implants, but it is not resistant to localized corrosion or bacterial colonization *in vivo* [18,19]. Silver is a proven broad-spectrum antibacterial agent with a low tendency to induce resistance, but coatings based on physically adsorbed silver often release it in uncontrolled doses that are short-lived and locally toxic [20,21]. Trapping silver in such a coordination polymer, anchored via a chitosan interlayer that both promotes adhesion and chelates metal ions, offers a path to more controlled behavior [22–24].

The aim of this paper is to provide a comprehensive overview of the development of these two hybrid antimicrobial platforms and to identify the design principles they have in common. Here, we summarize the synthetic rationale, relevant literature, and results that demonstrate how coordination chemistry can be used to achieve controlled antibacterial activity.

2 Platform development and antibacterial evaluation

2.1 Porous frameworks as carriers for essential oil components

ZIF-8, built from Zn^{2+} nodes linked with 2-methylimidazolate, offers well-defined microporosity and high chemical stability, making it a suitable nanocarrier for volatile antibacterial molecules [5]. Two essential oil components with contrasting properties were selected as guests: (i) eucalyptol, a cyclic ether with moderate antibacterial activity, and (ii) thymol, a phenolic monoterpenoid with stronger intrinsic potency [15,16]. The resulting composites are denoted ZIF-8-EUC and ZIF-8-THY according to the encapsulated guest.

Powder X-ray diffraction confirmed retention of the sodalite ZIF-8 topology in both composites, with no evidence of guest coordination to zinc by Fourier-transform infrared spectroscopy. Nitrogen sorption and colloidal characterization revealed that ZIF-8-THY blocked the pore network more extensively and showed poorer colloidal stability than ZIF-8-EUC, consistent with the aggregation behavior observed in suspension.

The most important differences appeared in antibacterial performance (**Figure 1.**), assessed against *Escherichia coli* (*E. coli*) and *Staphylococcus epidermidis* (*S. epidermidis*) by the drop method. Pristine ZIF-8 was only weakly active against the Gram-positive strain but inhibited *E. coli* more effectively. Loading with eucalyptol (ZIF-8-EUC) improved performance against both strains in a concentration-dependent manner. This contrast follows from colloidal and textural behavior, because the pore blocking and aggregation caused by thymol restrict its release and keep the extracellular concentration below the level needed to disrupt bacterial membranes [25].

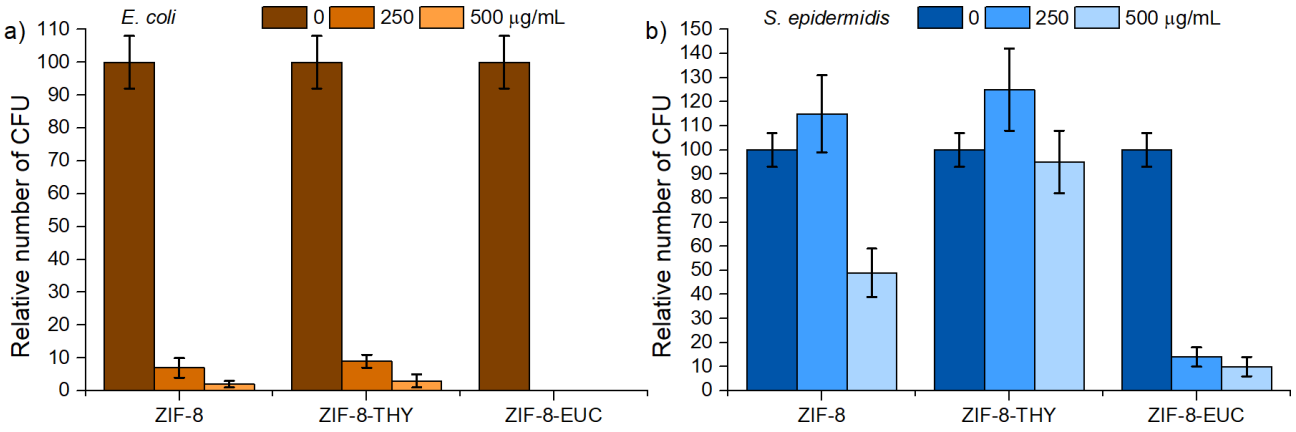


Figure 1. Relative number of CFU for pristine ZIF-8, ZIF-8-THY and ZIF-8-EUC against (a) E. coli and (b) S. epidermidis at different concentrations of samples.

2.2 Silver coordination polymer coatings on chitosan-coated surgical steel

The second platform applies the same principles of coordination chemistry to a functional surface. Surgical steel substrates were first coated with chitosan, a cationic polysaccharide whose amine and hydroxyl groups improve adhesion and sequester metal ions [22,23]. A silver coordination polymer (Ag-CP), formed from silver nitrate and 2-methylimidazole, was then grown *in situ* on this interlayer. The silver-to-ligand ratio was tuned to control the architecture of the deposited phase, and an equimolar formulation producing discrete clusters on the chitosan interlayer was identified as the most favorable [10,24]. Infrared spectroscopy confirmed Ag-CP formation through the band assigned to the Ag-N coordination bond.

The antibacterial and cytotoxic responses depended strongly on this architecture, and the equimolar Ag-CP coating proved the most useful (**Figure 2.**). At physiological pH it was only moderately inhibitory, yet under the mildly acidic conditions associated with infection the same coating eradicated both strains completely (**Figure 2a**). This on-demand switch arises from two cooperative events. Protonation and swelling of the chitosan interlayer, combined with acid-induced dissociation of the silver-imidazole coordination bonds, together release silver ions only where they are needed [9,11]. The equimolar Ag-CP coating also remained cytocompatibility toward fibroblasts at physiological pH (**Figure 2b**). As with the porous carriers, structural stability rather than sheer silver content determined whether the material behaved in a controlled manner [21,26].

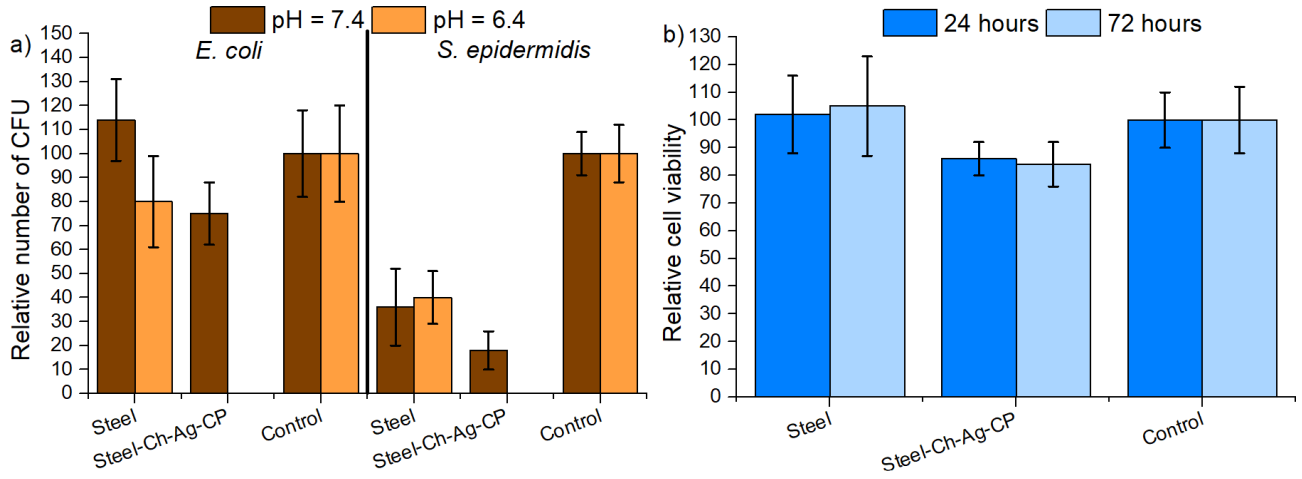


Figure 2. (a) Antibacterial activity against *E. coli* and *S. epidermidis* at physiological pH = 7.4 and at pH = 6.4, (b) cell viability after 24 and 72 hours.

3 Conclusions

Two hybrid antimicrobial platforms were developed on a shared coordination-chemistry foundation: (i) ZIF-8 nanocarriers loaded with essential oil components, and (ii) a silver coordination polymer grown on chitosan-coated surgical steel. In ZIF-8, the host-to-guest stoichiometry controlled the structure, colloidal stability and release of the encapsulated compounds, while in the Ag-CP coating the metal-to-ligand ratio determined the surface architecture and the pattern of silver ion release. Eucalyptol proved more effective than thymol as a ZIF-8 guest because it was released more readily, and the equimolar Ag-CP coating combined cytocompatibility at physiological pH with potent, infection-triggered bactericidal activity. Taken together, these results indicate that controlled antibacterial behavior depends less on the intrinsic potency of the active agent than on the stability and release characteristics imparted by the coordination environment. Future work will focus on extended concentration ranges, additional sample variants, and systematic release quantification to further optimize both platforms.

4 Acknowledgement

This work has been funded by a grant from the Programme Johannes Amos Comenius under the Ministry of Education, Youth and Sports of the Czech Republic CZ.02.01.01/00/22_008/0004558 Advanced MUltiscaLe materials for key Enabling Technologies.

5 References

[1] Kariuki S. Global burden of antimicrobial resistance and forecasts to 2050. The Lancet 2024;404:1172–3. https://doi.org/10.1016/S0140-6736(24)01885-3.

[2] Okeke IN, De Kraker MEA, Van Boeckel TP, et al. The scope of the antimicrobial resistance challenge. The Lancet 2024;403:2426–38. https://doi.org/10.1016/S0140-6736(24)00876-6.

[3] Arshadi Edlo A, Akhbari K, Henry DJ. Beyond antibiotics: novel solutions to address antibacterial resistance. Mater Adv 2025;6:7662–84. https://doi.org/10.1039/D5MA00552C.

[4] Wang C, Wei X, Zhong L, et al. Metal-Based Approaches for the Fight against Antimicrobial Resistance: Mechanisms, Opportunities, and Challenges. J Am Chem Soc 2025;147:12361–80. https://doi.org/10.1021/jacs.4c16035.

[5] Park KS, Ni Z, Côté AP, et al. Exceptional chemical and thermal stability of zeolitic imidazolate frameworks. Proc Natl Acad Sci USA 2006;103:10186–91. https://doi.org/10.1073/pnas.0602439103.

[6] Wu M, Yang Y. Metal–Organic Framework (MOF)-Based Drug/Cargo Delivery and Cancer Therapy. Advanced Materials 2017;29:1606134. https://doi.org/10.1002/adma.201606134.

[7] Tian Y, Wang B, Zhang Z, et al. Recent advances in metal–organic frameworks for antibacterial applications: mechanisms and emerging strategies. RSC Adv 2025;15:26710–27. https://doi.org/10.1039/D5RA02955D.

[8] Yan D, Yang M, Cheng F, et al. Novel antimicrobial agents prepared on the basis of metal- organic frameworks (MOFs) and their applications in the food field. Trends in Food Science & Technology 2025;161:105070. https://doi.org/10.1016/j.tifs.2025.105070.

[9] Sun C-Y, Qin C, Wang X-L, et al. Zeolitic imidazolate framework-8 as efficient pH-sensitive drug delivery vehicle. Dalton Trans 2012;41:6906. https://doi.org/10.1039/c2dt30357d.

[10] Seyedpour SF, Arabi Shamsabadi A, Khoshhal Salestan S, et al. Tailoring the Biocidal Activity of Novel Silver-Based Metal Azolate Frameworks. ACS Sustainable Chem Eng 2020;8:7588–99. https://doi.org/10.1021/acssuschemeng.0c00201.

[11] Radovic-Moreno AF, Lu TK, Puscasu VA, et al. Surface Charge-Switching Polymeric Nanoparticles for Bacterial Cell Wall-Targeted Delivery of Antibiotics. ACS Nano 2012;6:4279–87. https://doi.org/10.1021/nn3008383.

[12] Zhang T, Liu Q, Meng F, et al. Recent advances in stimuli-responsive antibacterial coatings: Bacteria-killing and releasing mechanism, design strategies, and potential applications. Progress in Organic Coatings 2024;186:107923. https://doi.org/10.1016/j.porgcoat.2023.107923.

[13] Wang X, Shan M, Zhang S, et al. Stimuli-Responsive Antibacterial Materials: Molecular Structures, Design Principles, and Biomedical Applications. Advanced Science 2022;9:2104843. https://doi.org/10.1002/advs.202104843.

[14] Angeli GK, Kotzabasaki MI, Maraveas C. Metal Organic Frameworks for Smart Storage and Delivery of Aromatic Volatiles and Essential Oils in Agrifood. Applied Sciences 2025;15:5479. https://doi.org/10.3390/app15105479.

[15] Yao B, He B, Peng J, et al. The comprehensive review of eucalyptol: synthesis, metabolism, and therapeutic applications in disease treatment. Mol Biol Rep 2025;52:346. https://doi.org/10.1007/s11033-025-10461-y.

[16] Modareskia M, Fattahi M, Mirjalili MH. Thymol screening, phenolic contents, antioxidant and antibacterial activities of Iranian populations of Trachyspermum ammi (L.) Sprague (Apiaceae). Sci Rep 2022;12:15645. https://doi.org/10.1038/s41598-022-19594-7.

[17] Hernández-López R, Cuellar-Sánchez JÁ, López-Malo A, et al. Synthesis, characterization and evaluation of ZIF-8/CMC composites loaded with eugenol for sustained antimicrobial activity. Cellulose 2025;32:8371–93. https://doi.org/10.1007/s10570-025-06718-1.

[18] Sultana N, Nishina Y, Nizami MZI. Surface Modifications of Medical Grade Stainless Steel. Coatings 2024;14:248. https://doi.org/10.3390/coatings14030248.

[19] Chew K-K, Zein SHS, Ahmad AL. The corrosion scenario in human body: Stainless steel 316L orthopaedic implants. NS 2012;04:184–8. https://doi.org/10.4236/ns.2012.43027.

[20] Stensberg MC, Wei Q, McLamore ES, et al. Toxicological Studies on Silver Nanoparticles: Challenges and Opportunities in Assessment, Monitoring and Imaging. Nanomedicine 2011;6:879–98. https://doi.org/10.2217/nnm.11.78.

[21] Feng QL, Wu J, Chen GQ, et al. A mechanistic study of the antibacterial effect of silver ions onEscherichia coli andStaphylococcus aureus. J Biomed Mater Res 2000;52:662–8. https://doi.org/10.1002/1097-4636(20001215)52:4%3C662::AID-JBM10%3E3.0.CO;2-3.

[22] Marsico M, Azari R, Curcio M, et al. Enhancing the Antibacterial Properties of Chitosan Coatings: Ag@Chitosan and Chitosan from Insects. Coatings 2024;14:925. https://doi.org/10.3390/coatings14080925.

[23] Qin Y, Zhu C, Chen J, et al. The absorption and release of silver and zinc ions by chitosan fibers. J of Applied Polymer Sci 2006;101:766–71. https://doi.org/10.1002/app.23985.

[24] Gordon O, Vig Slenters T, Brunetto PS, et al. Silver Coordination Polymers for Prevention of Implant Infection: Thiol Interaction, Impact on Respiratory Chain Enzymes, and Hydroxyl Radical Induction. Antimicrob Agents Chemother 2010;54:4208–18. https://doi.org/10.1128/AAC.01830-09.

[25] Muthalagu S, Natarajan S. Deciphering the Antimicrobial and Antibiofilm Efficiency of Thyme Essential Oil

Encapsulated Zeolitic Imidazole Framework-8 Against Foodborne Pathogens. Curr Microbiol 2025;82:49. https://doi.org/10.1007/s00284-024-04025-9.

[26] Slavin YN, Asnis J, Häfeli UO, et al. Metal nanoparticles: understanding the mechanisms behind antibacterial activity. J Nanobiotechnol 2017;15:65. https://doi.org/10.1186/s12951-017- 0308-z.