Liposomal Formulations of Gold(III) Complexes against Multidrug Resistant *Staphyloccocus* spp. strains

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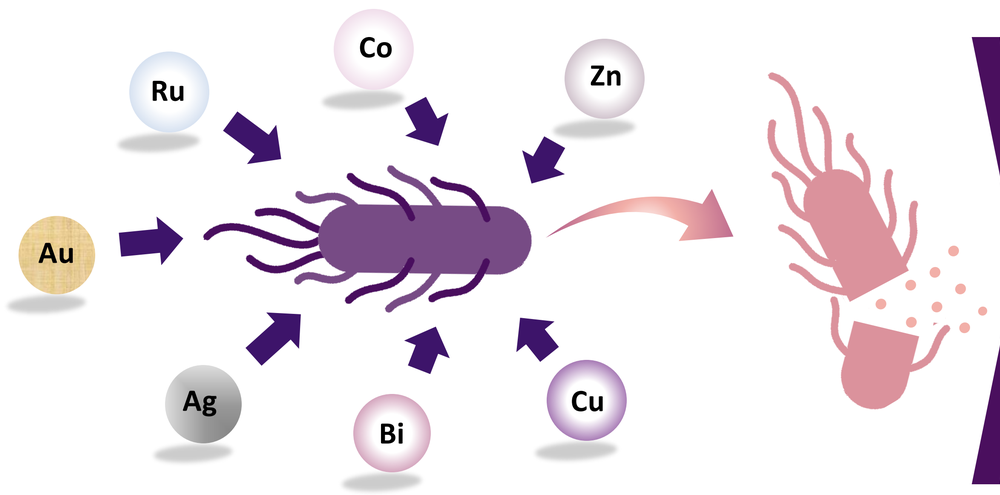
Metals to Combat Antimicrobial Resistance



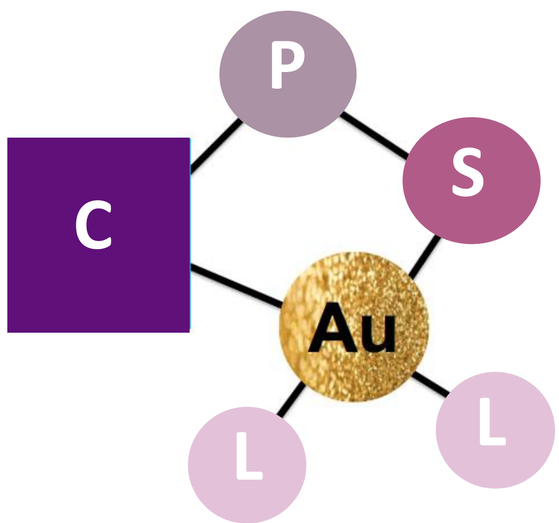
- ✓ Vast diversity of types of oxidation states, coordinating ligands, and geometries
- ✓ Highly underexplored chemical space
- ✓ Fewer steps when compared to organic compounds
- ✓ Unique modes of action: abolish enzyme activities, disrupt membrane, damage DNA.

Cationic Au(III) complexes

✓
- Active against Gram+ and Gram- Multi and Pan-Resistant bacterial strains
- Active at lower concentrations than clinical antibiotics

quinolones (ciprofloxacin, levofloxacin)
aminoglycosides (tobramicin, gentamicin)
glycopeptides (vancomycin)
β-lactames (imipenem)

- Low cost and easy access
- Synergy with aminoglycoside antibiotics
- Patent WO 2019211222



- ➢ Novel chemical family
- ➢ No cross-resistance
- ➢ Novel mode of action
- ➢ Active against critical priority bacterial strains

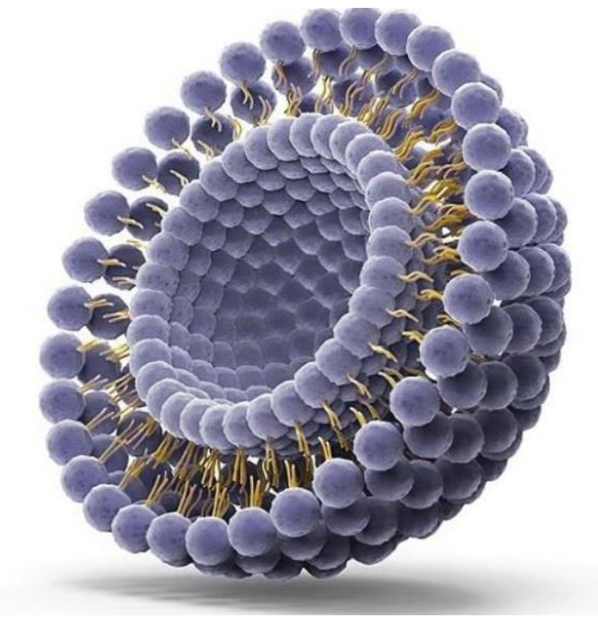
Front. Microbiol. **2022**, *13*, 815622; *Front. Microbiol.* **2022**, *13*, 846959; *Antibiotics* **2022**, *11*, 1728; *Heliyon* **2024**, *10*, e27601; *Dalton Trans.* **2024**, *53*, 9433.

Liposomal gold metalloantibiotics

- ✓ High stability and particle size and zeta potential values suitable for drug delivery
- ✓ Mantain the bactericidal action with respect to the free drug
- ✓ No appreciable effect on the viability of mammalian cells: optimal Therapeutic Index
- ✓ Reduced potential liabilities (inhibition of hERG and cytochromes)

	GLM804[a]	Lipo	Lipo-GLM804
MIC (mg/mL)			
S. aureus	0.5	>50	0.5
S. epidermis	1.0	>50	1.0
Citotoxicity (mg/mL)			
CCDC-1064-sk	0.9	>50	>50
THLE-2	1.0	>50	>50
hERG (mg/L)			
	6.2		26%

[a] GLM804: (C^S)-cyclometallated gold(III) complex

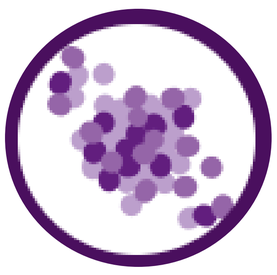


Dalton Trans. **2024**, *53*, 15205

	MIC (mg/L)						
	Free drug		Liposomal formulation				
	GEN[a]	AMK[b]	Lipo-GEN	Lipo-AMK	Lipo-Au	Lipo-Au-GEN	Lipo-Au-AMK
S. aureus							
162065-705	2	8	0.5	2	0.5	<0.25	2
162057-148	>64	>64	>64	>64	1	2	4
162058-967	>64	>64	>64	>64	1	2	4
S. epidermidis							
FG03015	0.25	2	<0.25	1	0.5	<0.25	<0.25
FG14013	>64	16	>64	16	1	8	1
FG22014	32	4	16	2	2	0.5	0.5

[a] GEN: Gentamicin; [b] AMK: Amikacin

Lipo-Au-AMK
AMK 170 mg/L, GLM804 30 mg/L
Lipo-Au-GEN
GEN 175 mg/L, GLM804 25 mg/L



Staphylococcus spp.
multidrug-resistant
methicillin-resistant

Antibiotic liposomal formulation against *Staphyloccocus* spp.

- ✓ Innovative lipoformulation co-encapsulating a gold(III) complex and gentamicin or amikacin
- ✓ Significantly reduced MIC compared to free drugs or single-loaded liposomes
- ✓ Liposomes effectively fuse with bacteria, facilitating antibiotic drug release directly into the bacterial cell
- ✓ Effective strategy for sensitizing resistant *Staphyloccocus* spp. against gentamicin and amikacin

In vivo **proof of concept in murine model for *S. aureus* skin infection**

- ✓ Significantly reduced bacterial load in the site of infection

A CORUÑA // 2025
19th - 21st - November
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