3rd Meeting of the International Consensus Meeting
8-10 of May, 2025 Istanbul

Are There Any Technological Advances in Creating Smart Antibiotic Carriers in the Fight Against Biofilms?

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Why this topic is important

1) Bacterial biofilms contribute to orthopedic implant failures and chronic musculoskeletal infections, hindering antibiotic penetration and immune responses.
2) Innovative drug delivery systems can enhance antibiotic penetration and achieve localized drug release at bacterial biofilms.

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SPECIAL ISSUE ARTICLE

2023 International Consensus Meeting on musculoskeletal infection: Summary from the treatment workgroup and consensus on treatment in preclinical models

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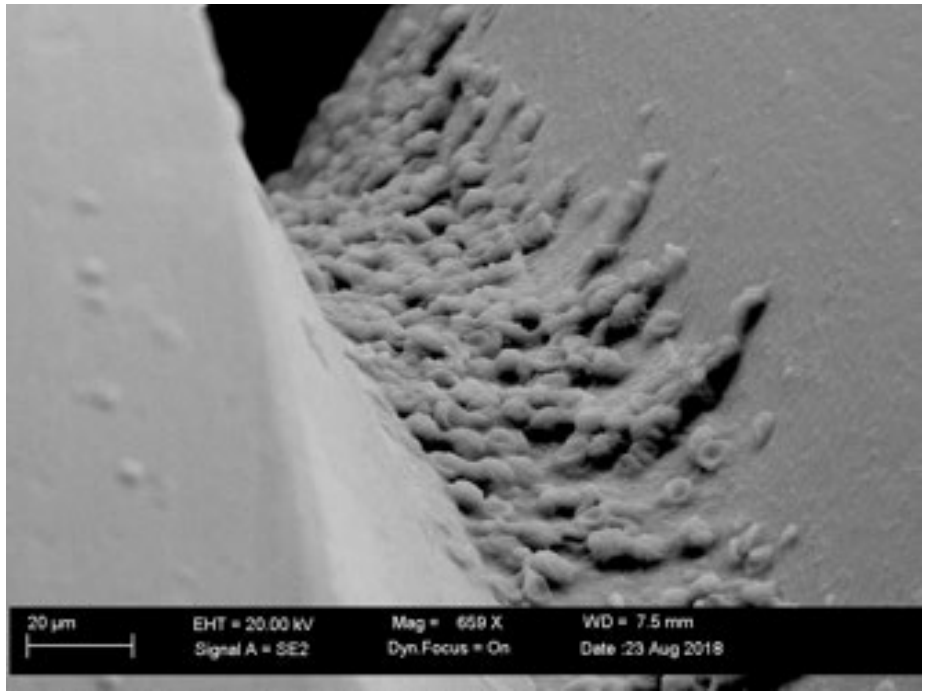
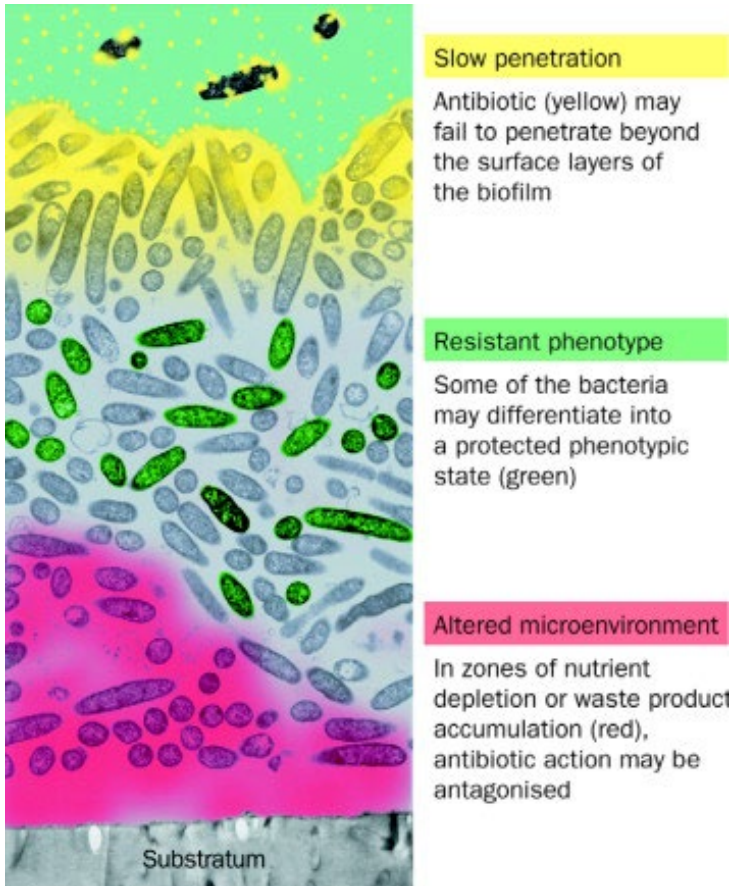
The Role of Biofilm in Orthopedic Implant Failures and Chronic Musculoskeletal Infections



Cobb, L. H., et al. "Therapeutics and delivery vehicles for local treatment of osteomyelitis," J Orthop Res, 2020



Stewart & Costerton, "Antibiotic Resistance of Bacteria in Biofilms," The Lancet, 2001

Biofilm Resistance Mechanisms

Blocked penetration:
Antibiotics inactivated or bound at biofilm surface

Microenvironment:
Low oxygen, low pH, and nutrient depletion reduce drug activity

Dormant cells:
A subset of bacteria enter a highly protected, non-growing state

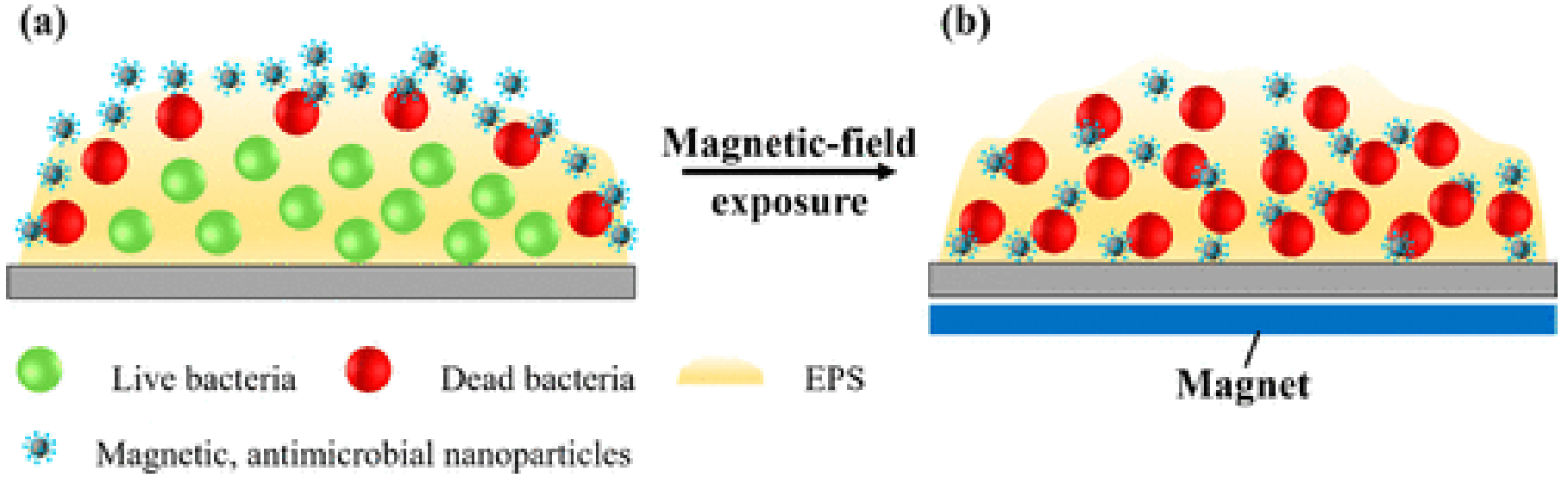
Literature Review/Process

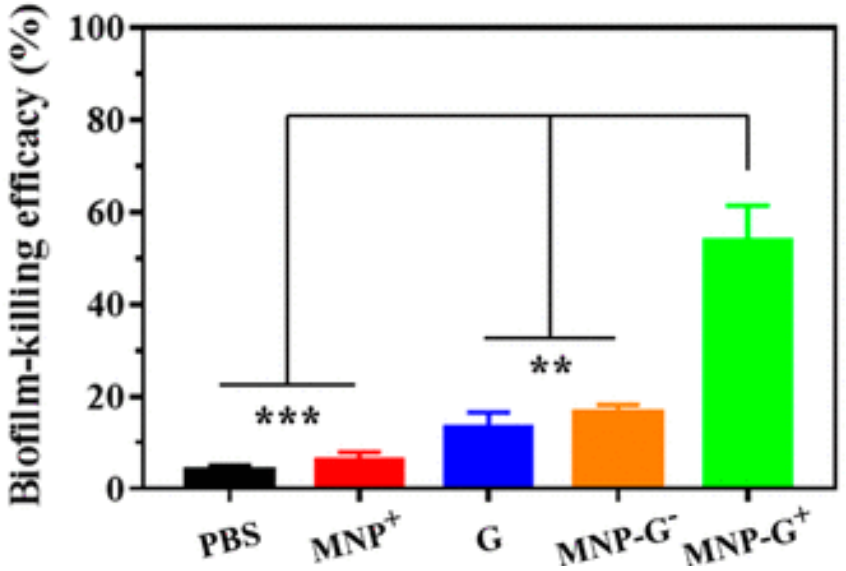
- Number of articles retrieved: 66
- Screening: 66
- Final number of publications: 30

Stimuli-Responsive Smart Antibiotic Carriers

Smart carriers that respond to stimuli:

- pH
- Enzyme
- ROS
- Light
- Heat
- Ultrasound
- **Magnetic field**





- **MNPs-G$^+$ (gentamicin-loaded magnetic nanoparticles + magnetic field) showed the highest *S. aureus* biofilm-killing efficacy (~60%)**

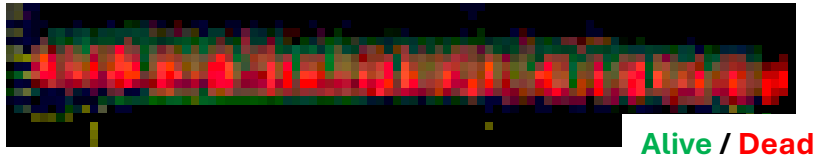
Quan et al., "Homogeneous Distribution of Magnetic, Antimicrobial-Carrying Nanoparticles Enhances Biofilm-Killing," ACS Biomater Sci Eng, 2020

Smart Antibiotic Carriers That Enhance Biofilm Targeting

Carriers that target biofilms:

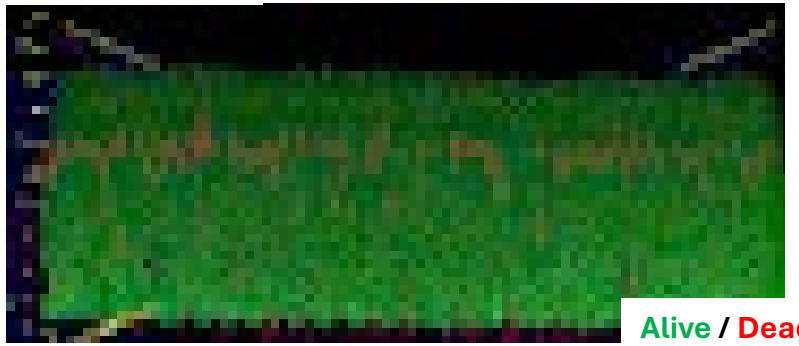
- **Enhance biofilm penetration**
- Bind to tissue with biofilm
- Bind to biofilm

Vancomycin-LCH-NPs (lipid-coated nanoparticles)

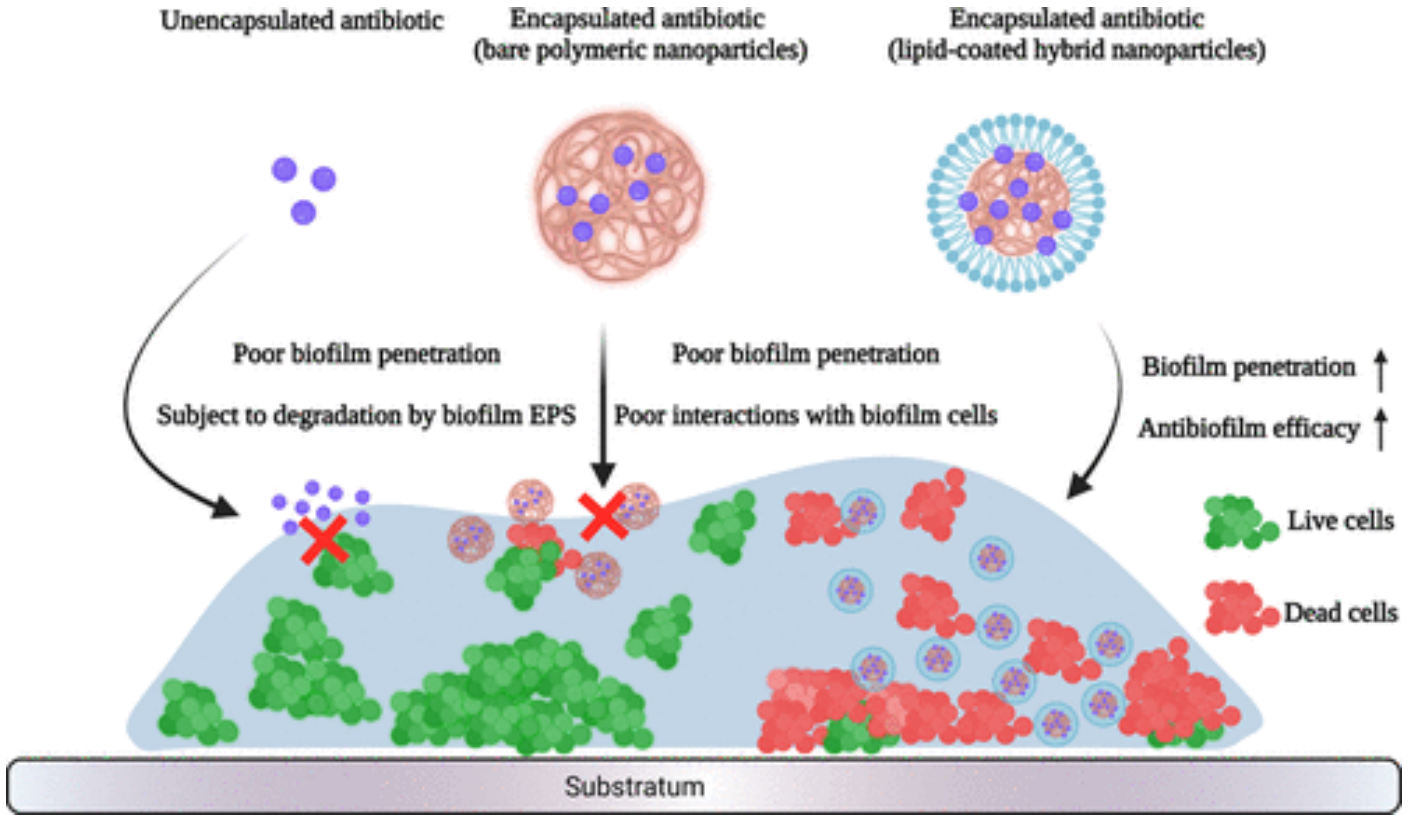


Alive / Dead

Vancomycin



Alive / Dead



- **Vancomycin-LCH-NPs** (lipid-coated nanoparticles) showed widespread MRSA biofilm cell death (red) at low doses
- **Free vancomycin** had minimal effect—most cells remained alive (green)

Lee et al., "Lipid-Coated Hybrid Nanoparticles for Enhanced Bacterial Biofilm Penetration and Antibiofilm Efficacy," ACS Omega, 2022

Smart Antibiotic Carriers that Enhance Biofilm Targeting

Carriers that target biofilms:

- Enhance biofilm penetration
- **Bind to tissue with biofilm**
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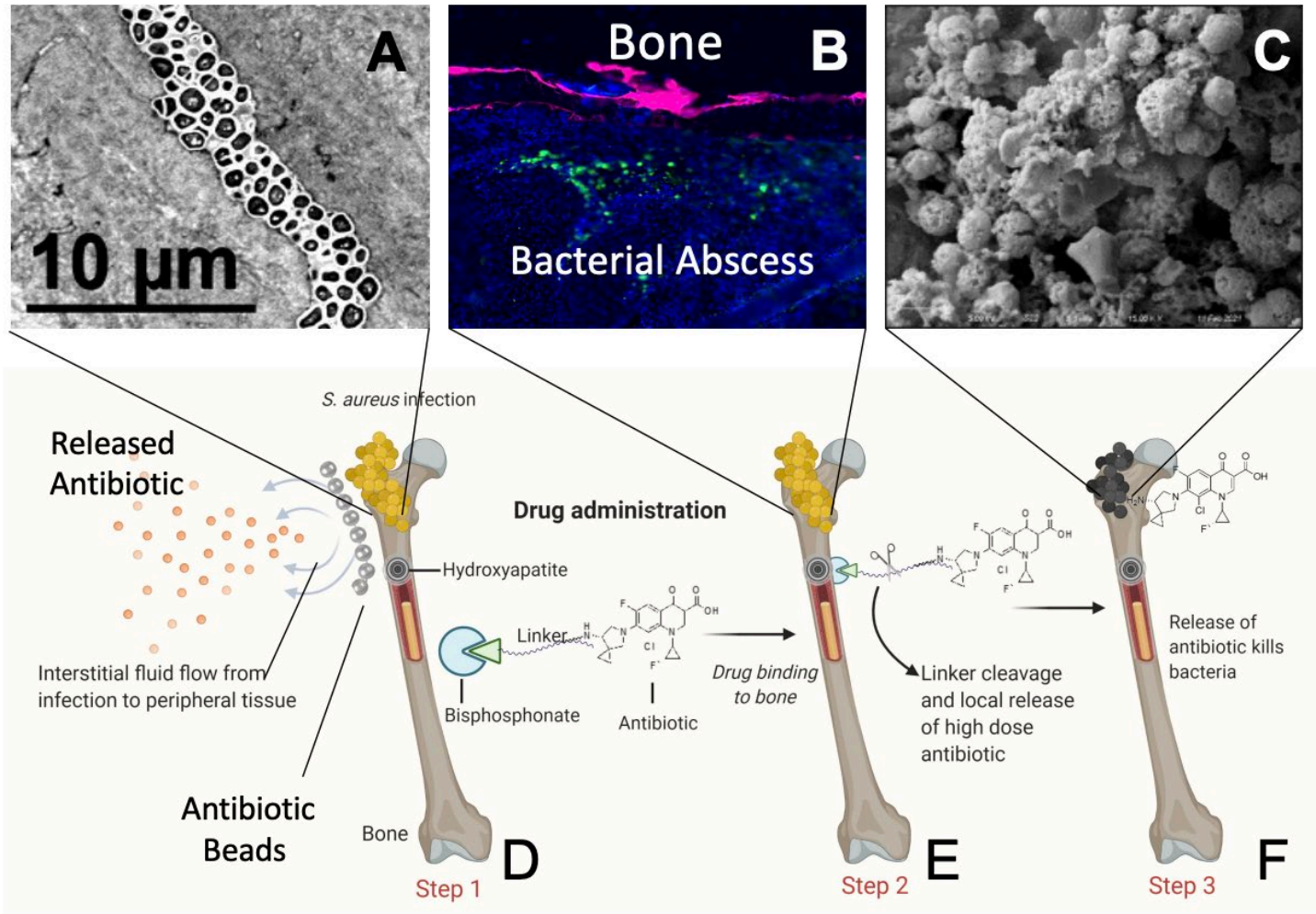
Bone-Targeted Bisphosphonate (BP)-Antibiotic Delivery

A: *S. aureus* invades bone canaliculi — inaccessible to standard antibiotics.
B: Fluorescent BP accumulates at infected bone surfaces.
C: Bacterial death after BP-antibiotic treatment.
D: **BP-antibiotic binds bone with high affinity**.
E: **Infection triggers drug release via linker cleavage**.
F: **Local antibiotic kills adjacent biofilm bacteria**.



Adjei-Sowah et al., "Bisphosphonate-Conjugated Antibiotics for Targeted Biofilm Eradication," Antibiotics, 2021.

Major Limitations

- **Only one liposomal antibiotic carrier has been clinically validated for bacterial infection treatment—and it is approved for use in a non-orthopedic setting.**
- **A gold-standard, minimally invasive biomarker for biofilm burden in clinical settings is needed for longitudinal evaluation of therapeutic efficacy.**

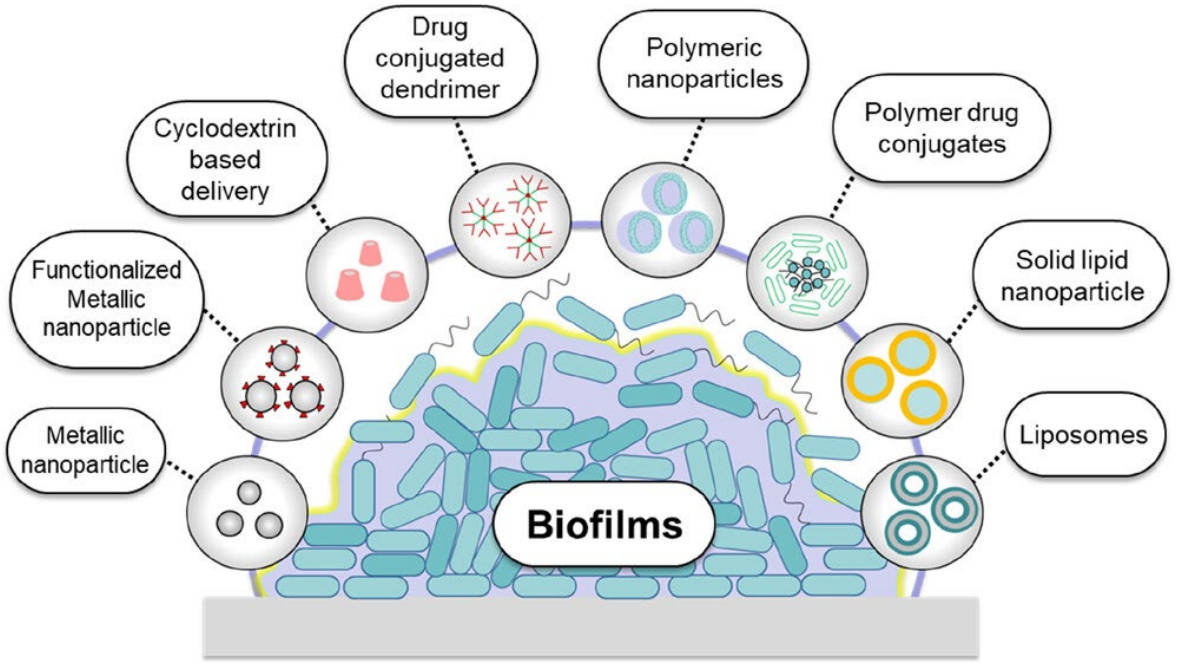
Question:

- Are there any technological advances in creating smart antibiotic carriers in the fight against biofilms?

❖Response:

Extensive preclinical evidence supports innovations that enhance antibiotic delivery, biofilm penetration, and overall anti-biofilm efficacy. Clinical validation remains necessary.

Level of Evidence: Strong



Kumar et al., "Advances in Nanotechnology for Biofilm Inhibition," ACS Omega, 2023

❖**Vote:**

Agree	**n=33; 100%**
Disagree	**0**
Abstain	**0**