



齊魯工業大學  
QILU UNIVERSITY OF TECHNOLOGY

# Semi-Synthetic Cationic Peptides Derived from Collagen: Potent Broad-Spectrum Antimicrobial Activity and High Biosafety

Speaker: Deyi Zhu

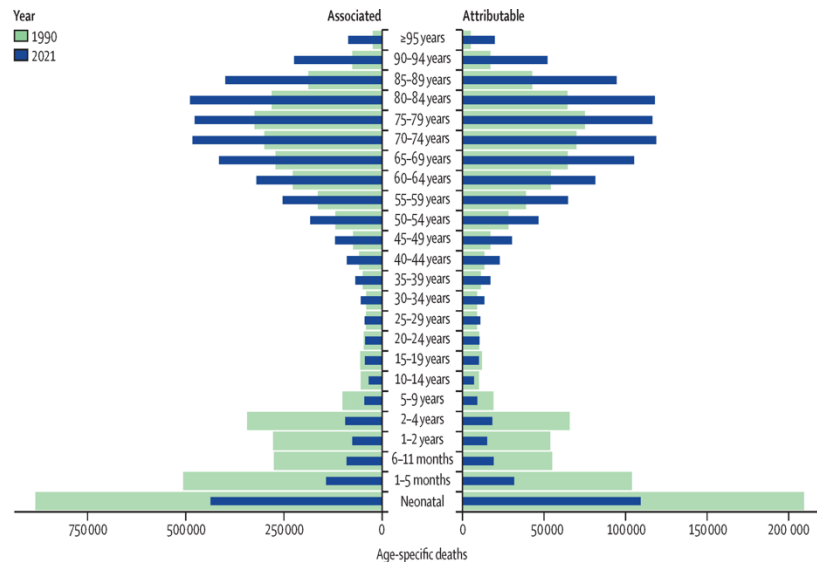
Qilu University of Technology

Sept., 2025

# Presentation Outline

- 01 Introduction & Background
- 02 The design and synthesis of collagen-based AMPs
- 03 Results & Discussion
- 04 Conclusions & Outlook

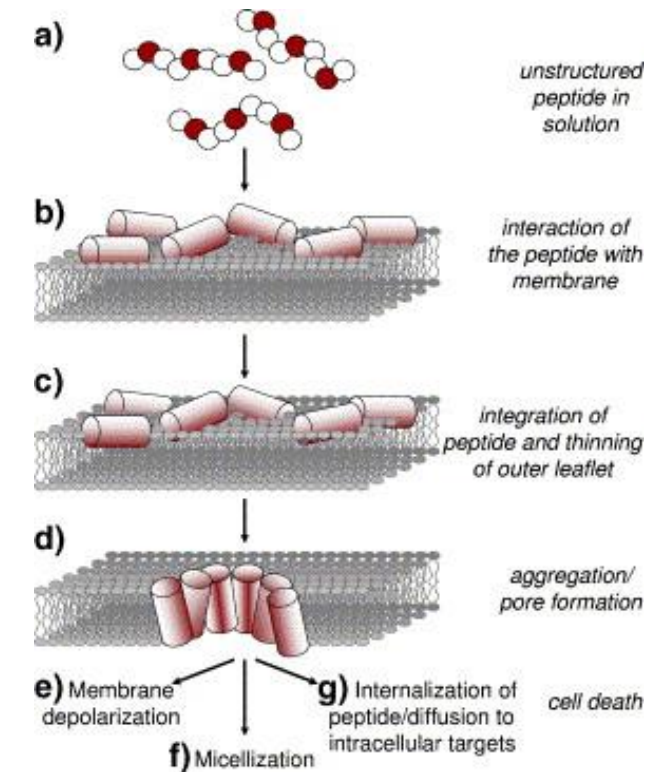
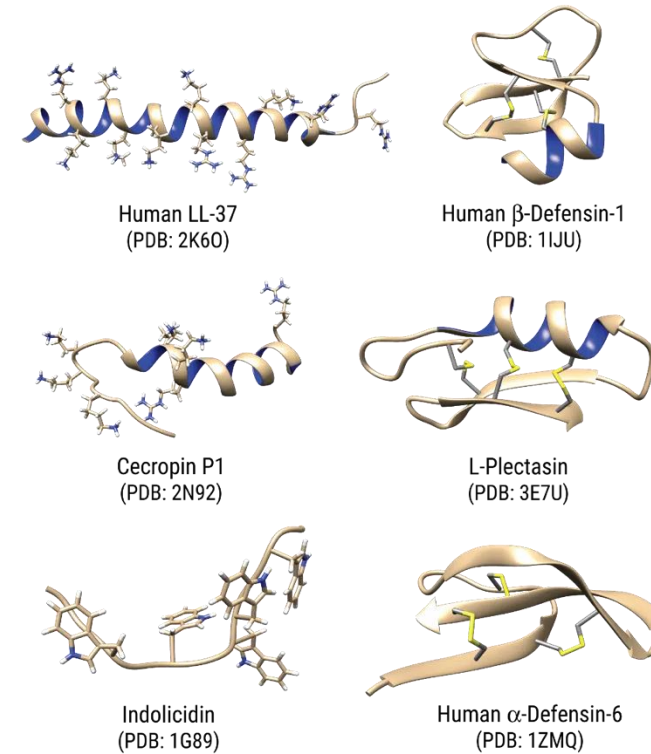
# Introduction & Background--AMPs



The Lancet, 2024, 404(10459): 1199-1226.

- Antibiotic resistance ↑
- Urgent need for new antimicrobials

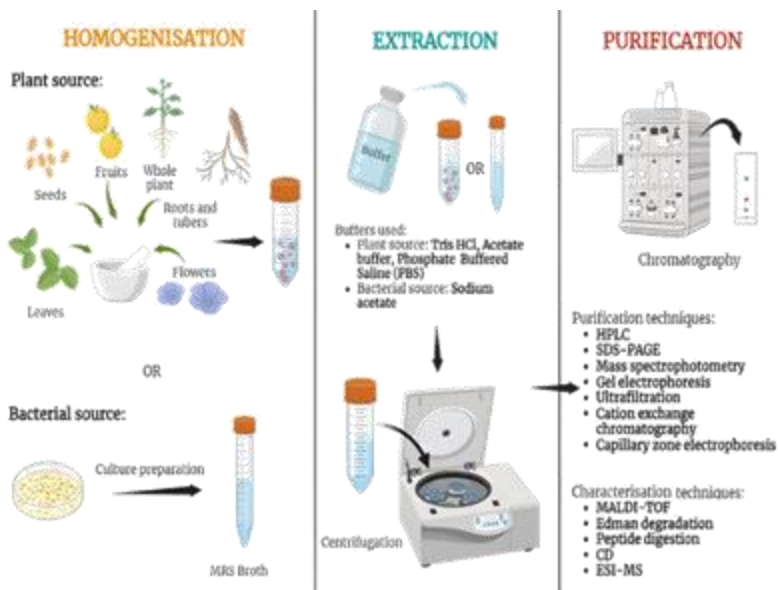
- AMPs: multi-target, hard to trigger resistance



- CAMPs: Rich in Lys/Arg, amphoteric, membrane disruption.

# Introduction & Background--Limitations

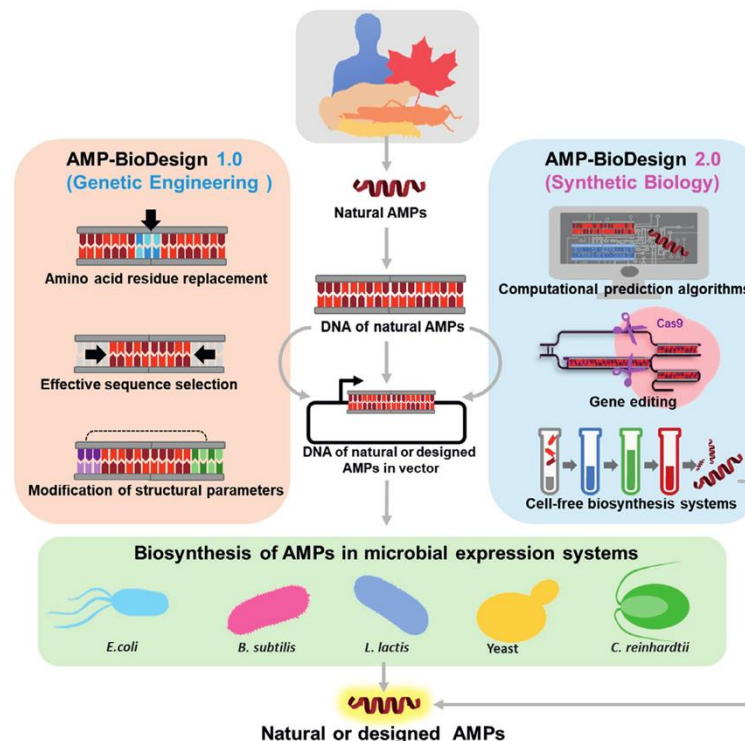
## ① extraction



Plant Pathology, 2024, 73(7): 1691-1707

- Low yields

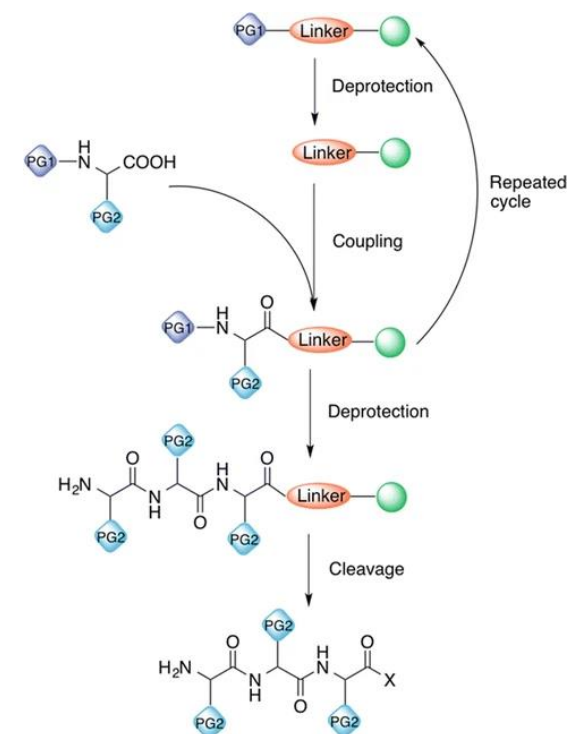
## ② biosynthesis



Biosafety and Health, 2022, 4(02): 118-134

- Low expression levels
- post-translational modification

## ③ chemical synthesis

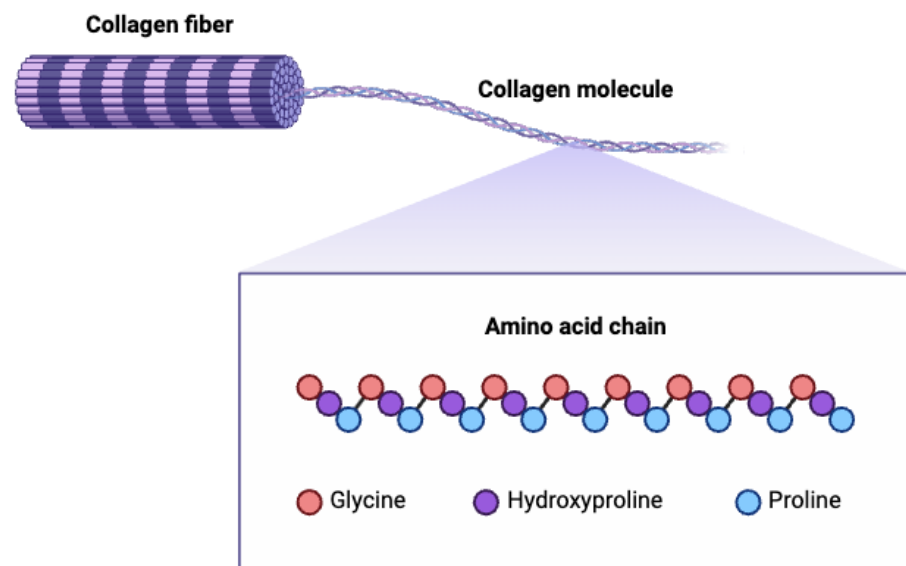


- High cost

Large-scale production of AMPs remains a major bottleneck

# Introduction & Background--Collagen as a Precursor

## Antimicrobial peptides from collagen hydrolysates



Antimicrobial and radical scavenging properties of bovine collagen hydrolysates produced by *Penicillium aurantiogriseum* URM 4622 collagenase. *Journal of food science and technology*. 2015;52(7):4459-4466.

GDHGETGEQGDR

Collagencin, an antibacterial peptide from fish collagen: Activity, structure and interaction dynamics with membrane. *Biochemical and biophysical research communications*. 2016;473(2):642-647.

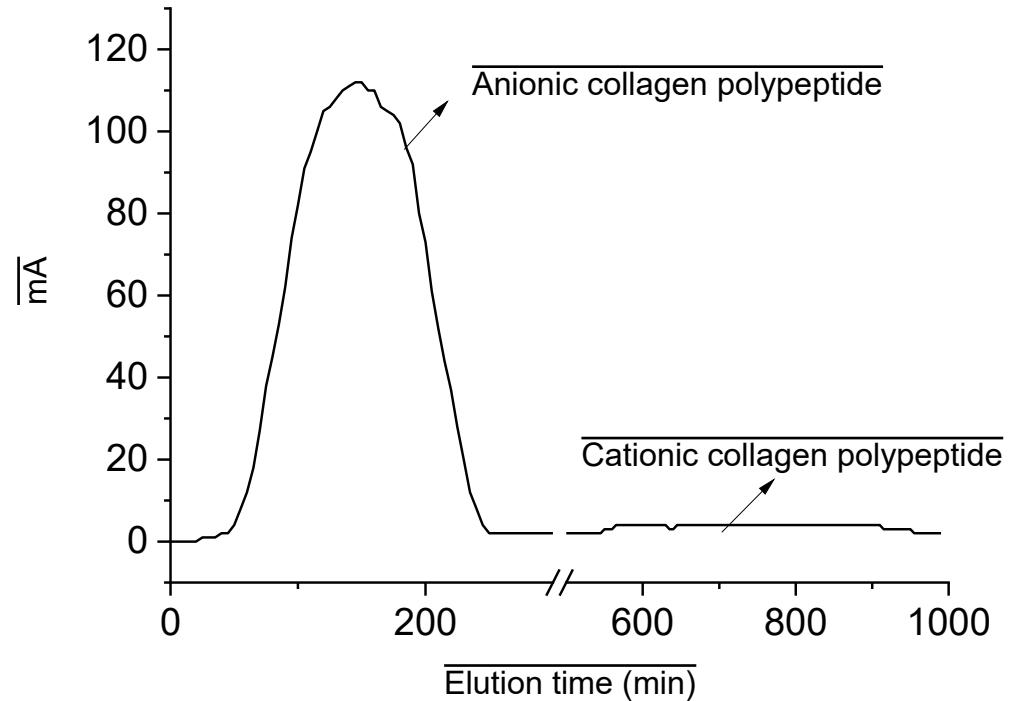
GLPGPLGPAGPK

- Collagen: Abundant, conserved G-X-Y repeats, biocompatible, low immunogenicity.

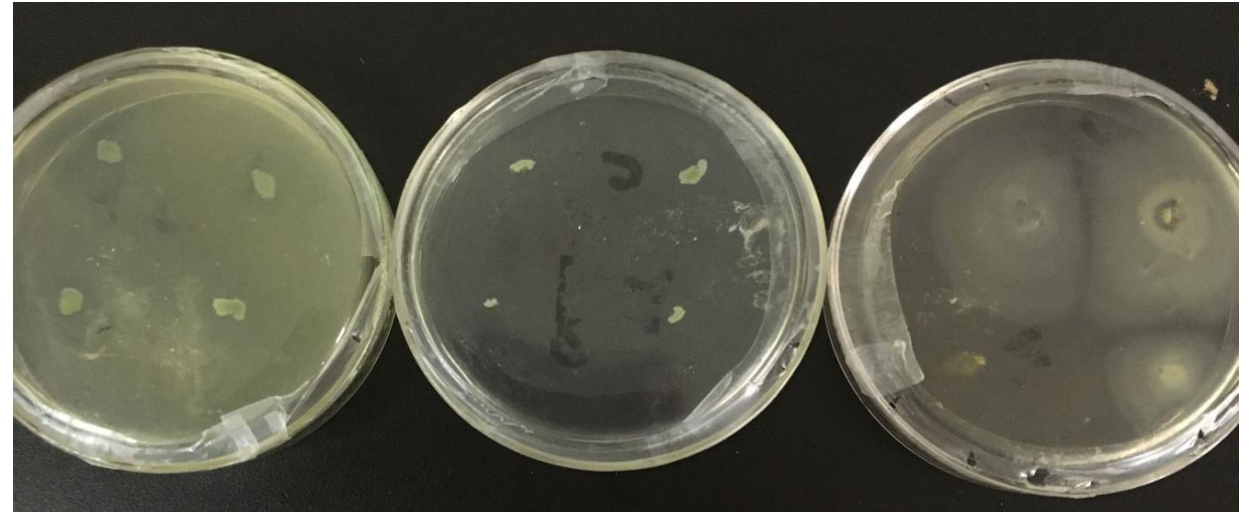
- The collagen-characteristic G-X-Y structure;
- Positively charged C-terminal residues



# Introduction & Background--Collagen as a Precursor



Separation of collagen hydrolysate by ion exchange chromatography



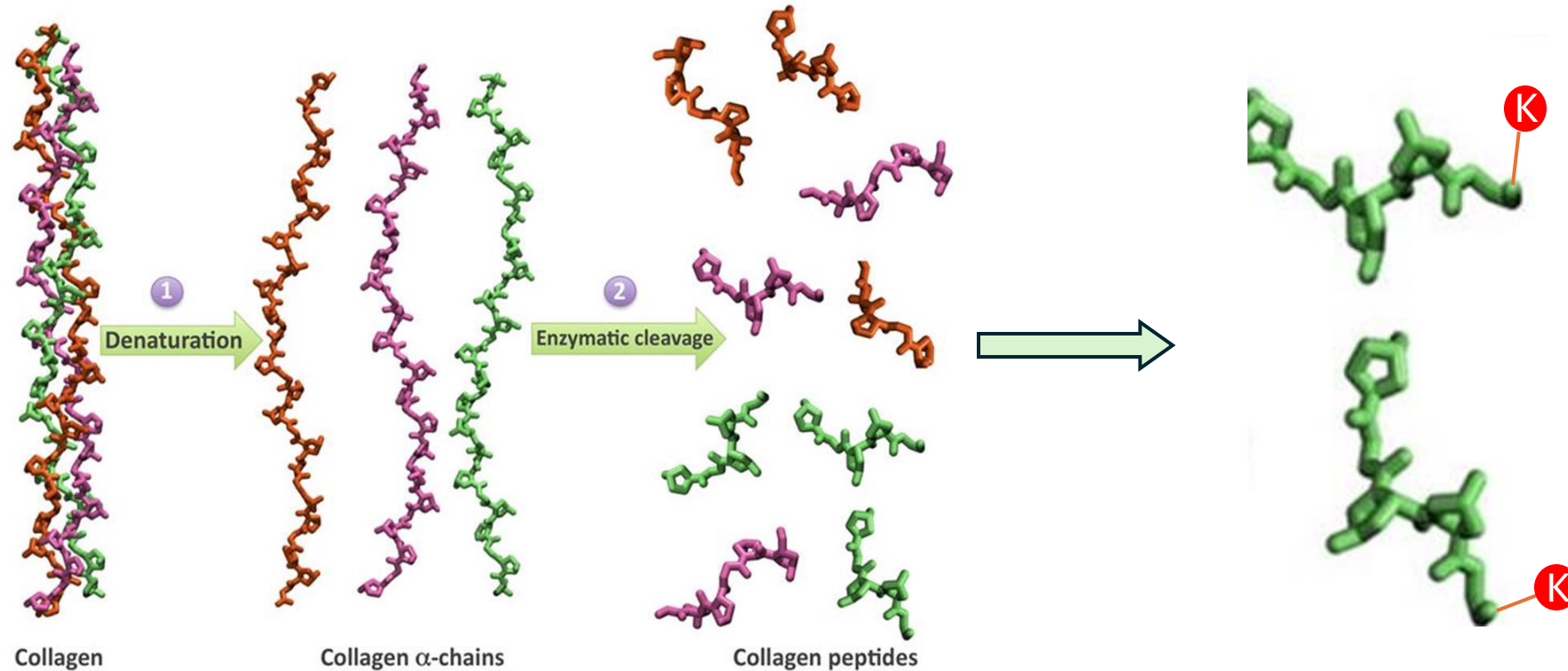
Collagen polypeptide

Cationic collagen polypeptide

Anionic collagen polypeptide

- The culture medium supplemented with the cationic portion of collagen hydrolysate had a certain inhibitory effect on the growth of *Escherichia coli*.

# Introduction & Background--Hypothesis

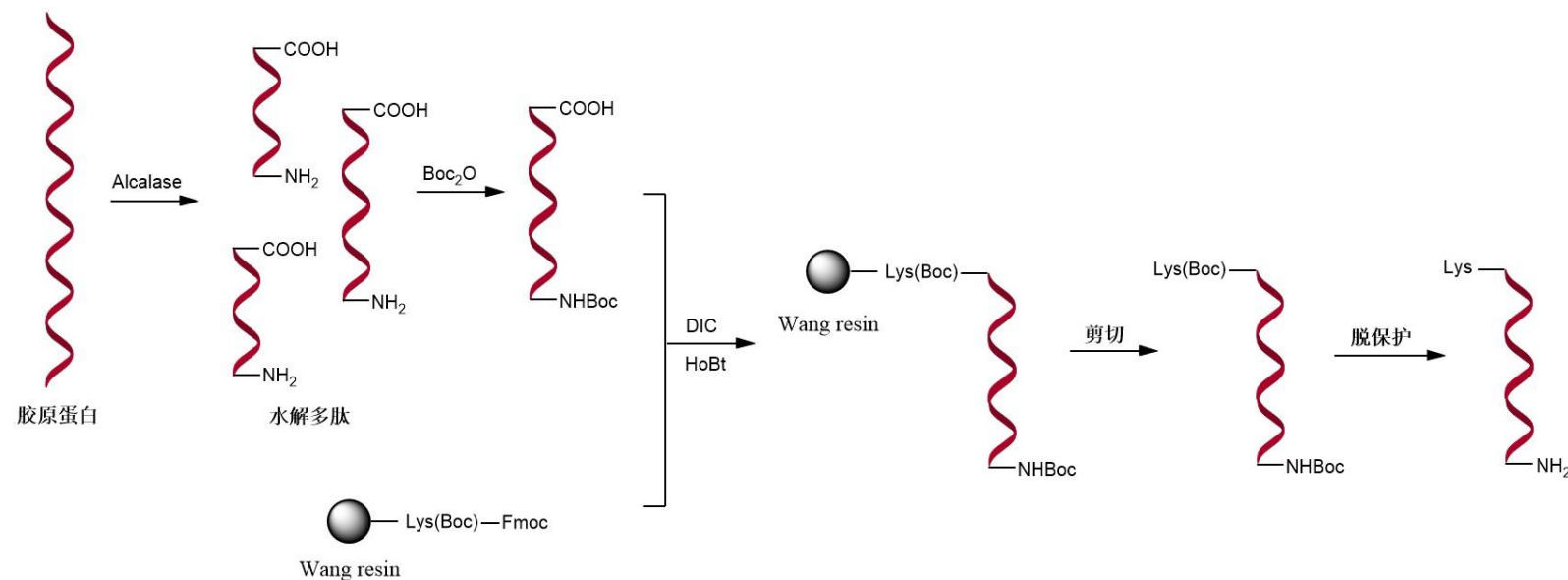


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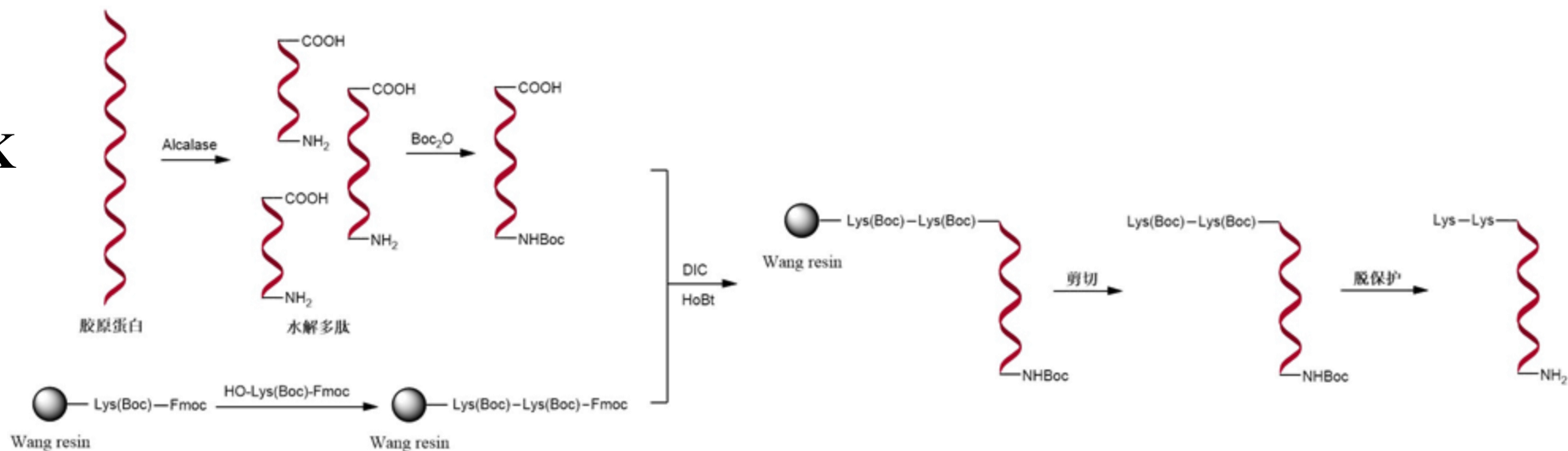
- We hypothesized that collagen peptides could be engineered into effective AMPs by covalently introducing cationic amino acids, such as lysine(K).

# Synthesis of collagen-based AMPs

## CP-K

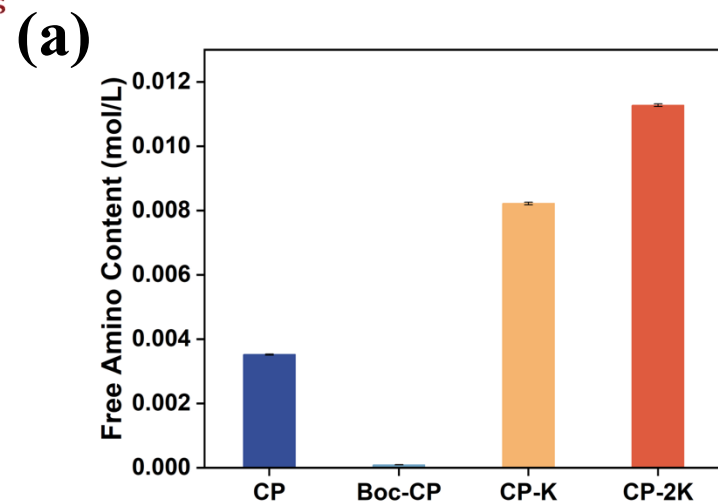


## CP-2K

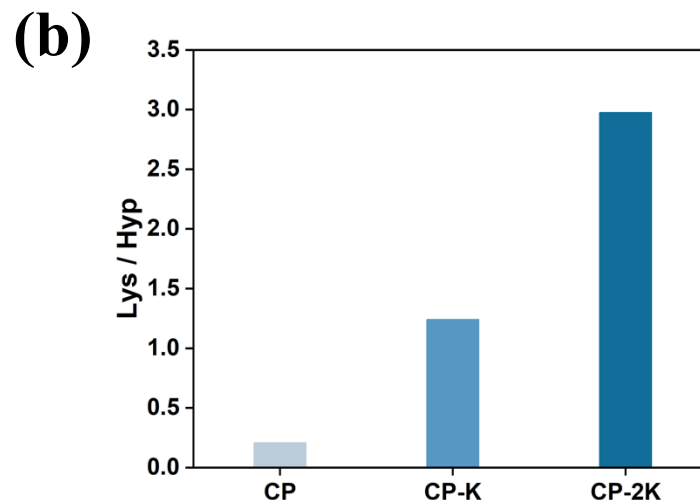




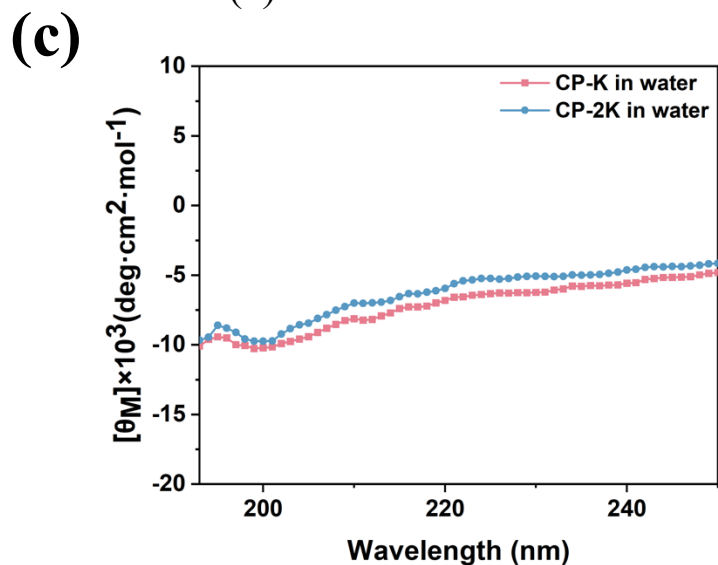
# Results & Discussion--Characterization



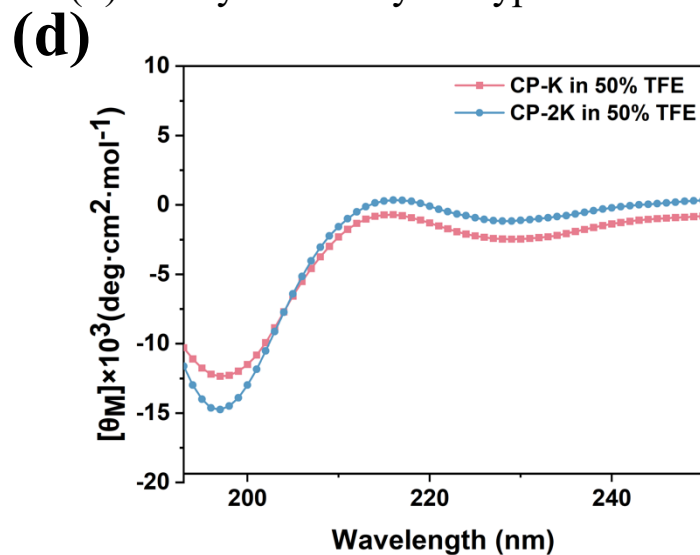
(a) Free amino content



(b) The lysine-to-hydroxyproline molar ratio



(c) CD spectrum (in water)



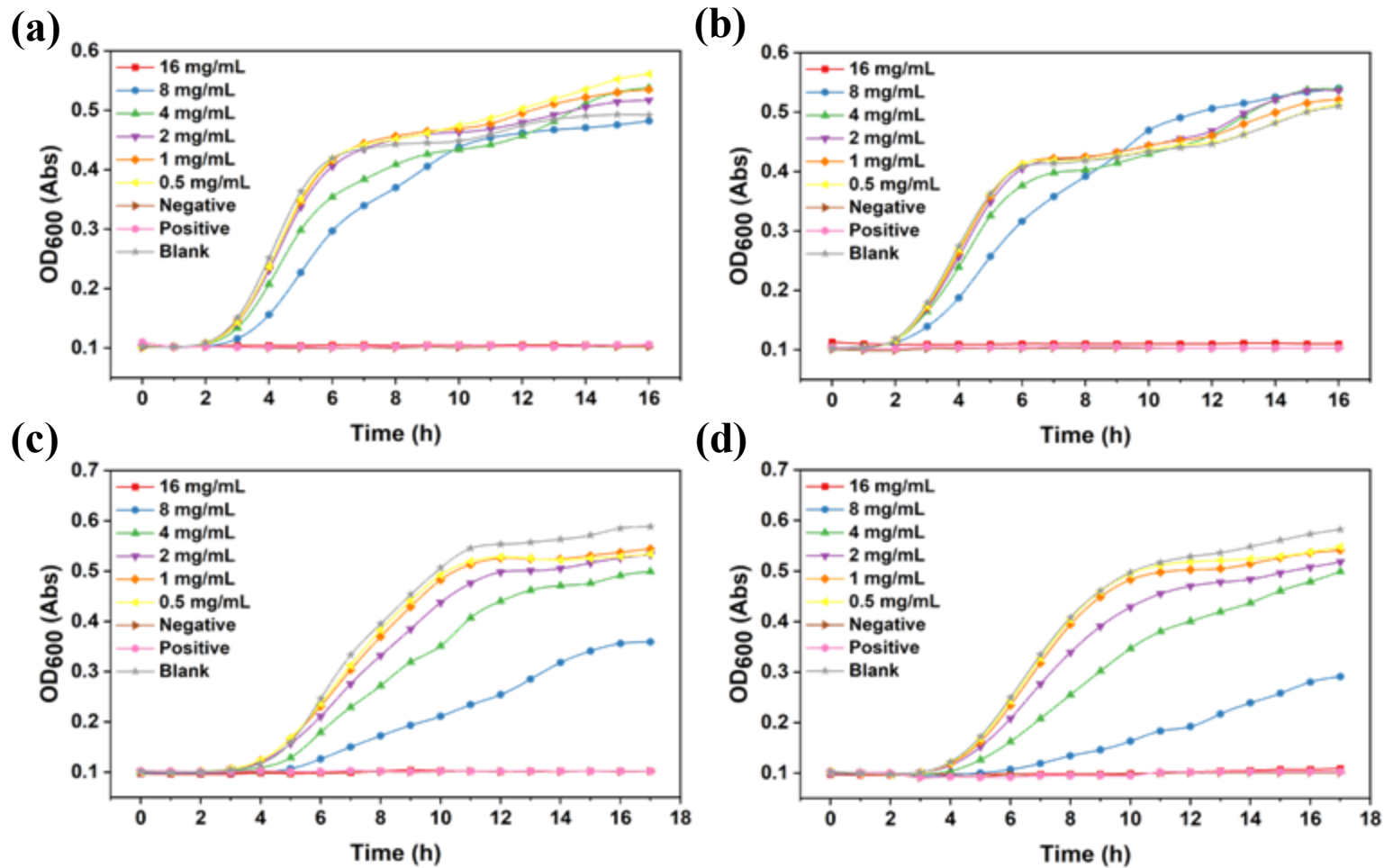
(d) CD spectrum (in 50% TFE solution)

□ Lysine was successfully linked to the polypeptide

□ Presents a disordered conformation in water

□ PPI helical secondary structures were presented in 50% TFE

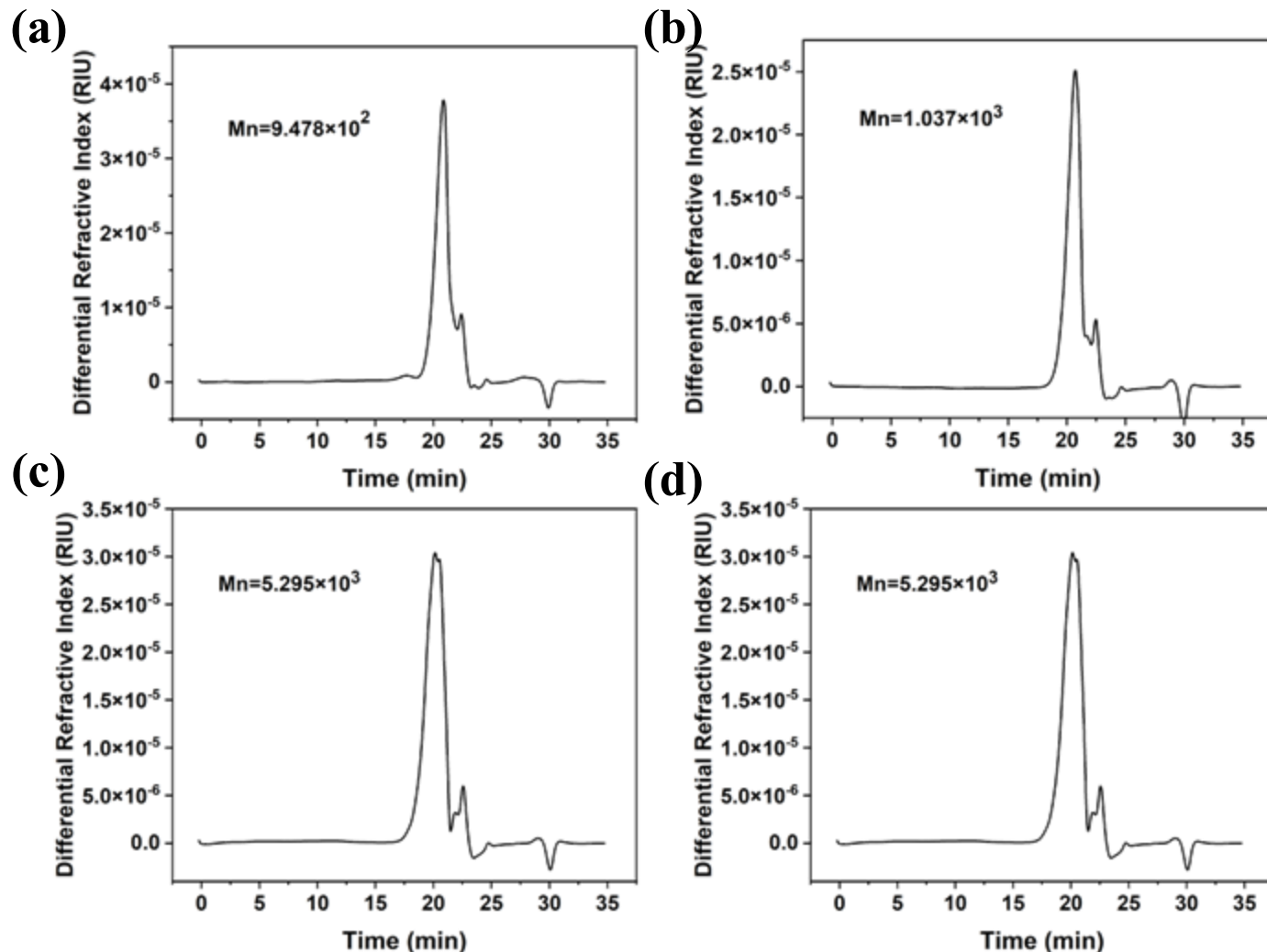
## Results & Discussion—Antibacterial Activity



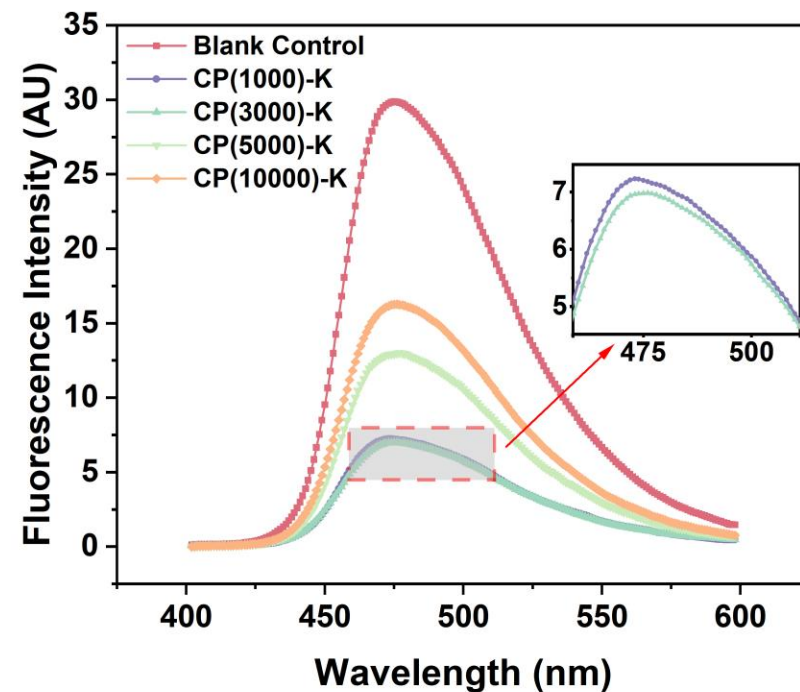
- Dose-dependent inhibition: Complete at 16 mg/mL for *E. coli* & *S. aureus*.

- CP-2K slightly stronger than CP-K.

# Results & Discussion—Effect of Molecular Weight

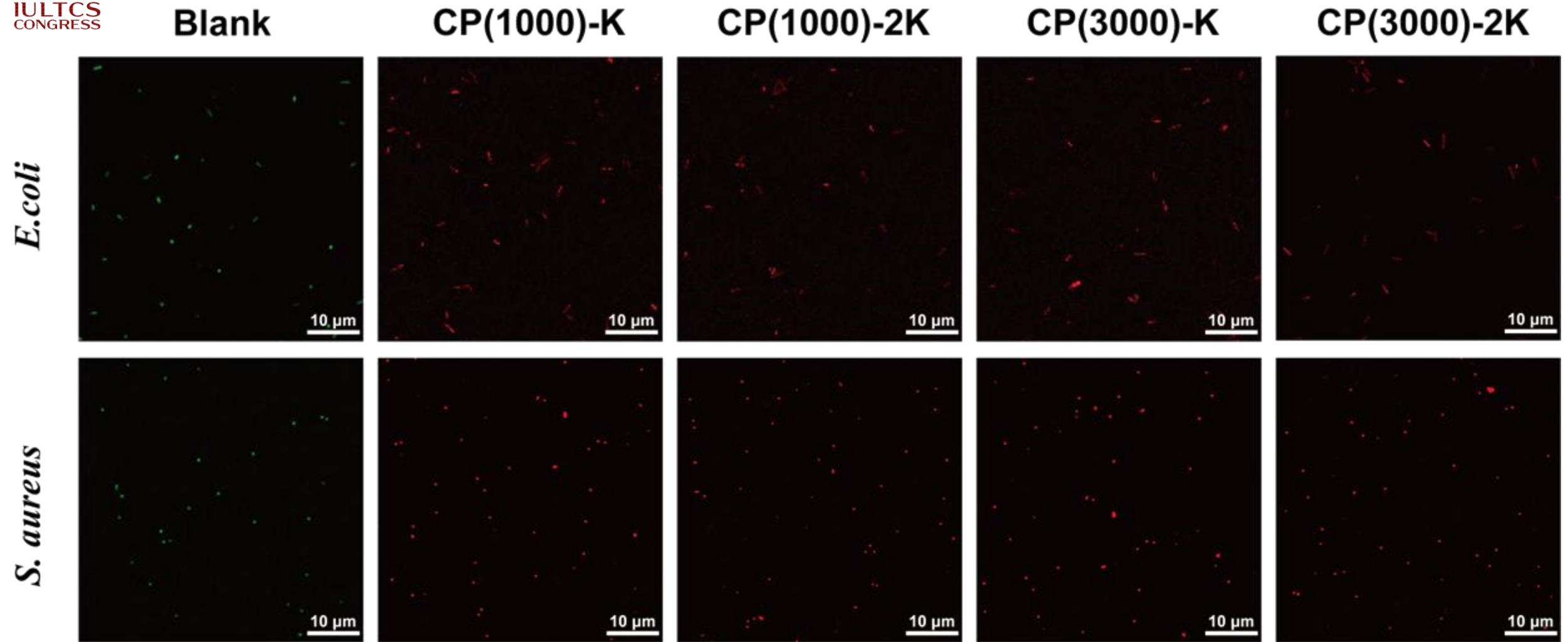


(a) CP(1000)、(b) CP(3000)、(c) CP(5000)、(d) CP(10000)



- Optimal: 1000-3000 Da (CP(1000)-K, CP(3000)-K).
- Stronger luminescence inhibition in *P. phosphoreum* T3.

## Results & Discussion—Mechanism



Live/Dead: Red fluorescence indicates membrane damage.



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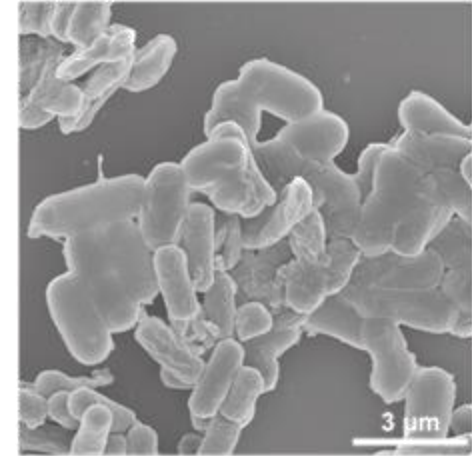
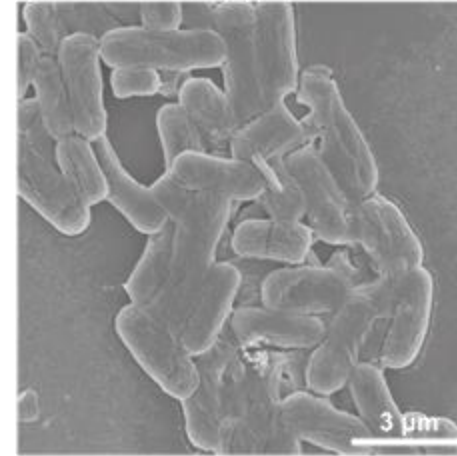
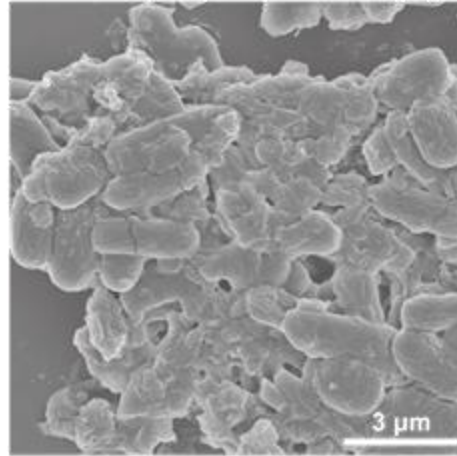
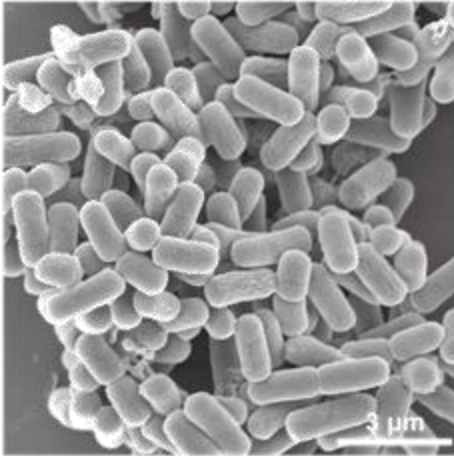
**CP(1000)-K**

**CP(1000)-2K**

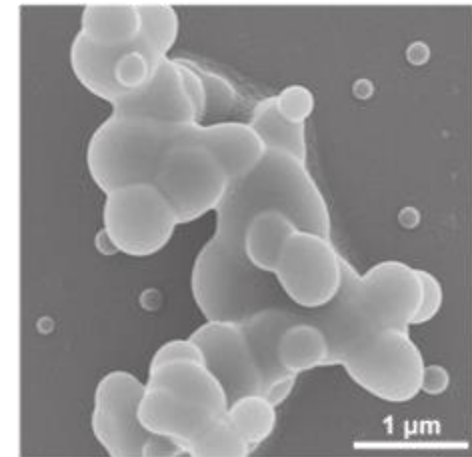
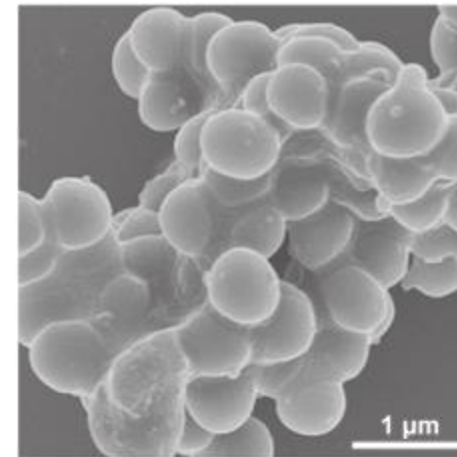
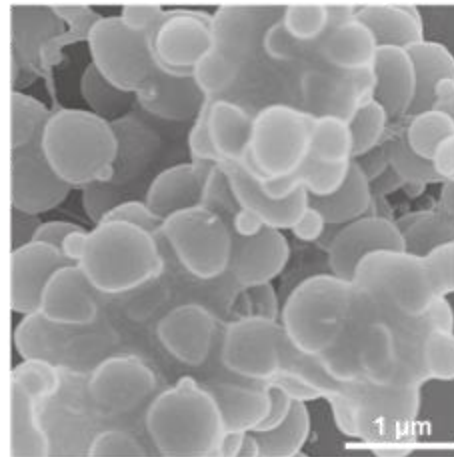
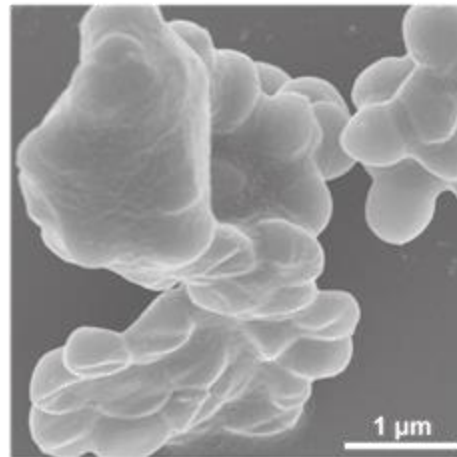
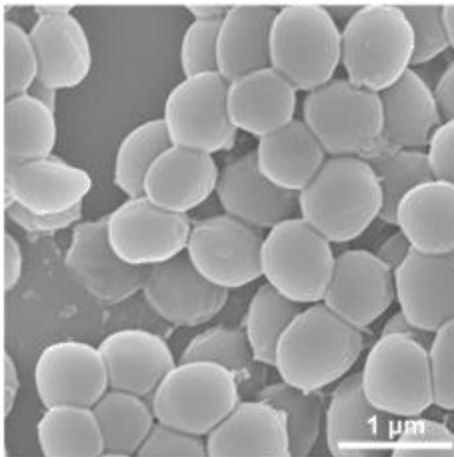
**CP(3000)-K**

**CP(3000)-2K**

*E. coli*



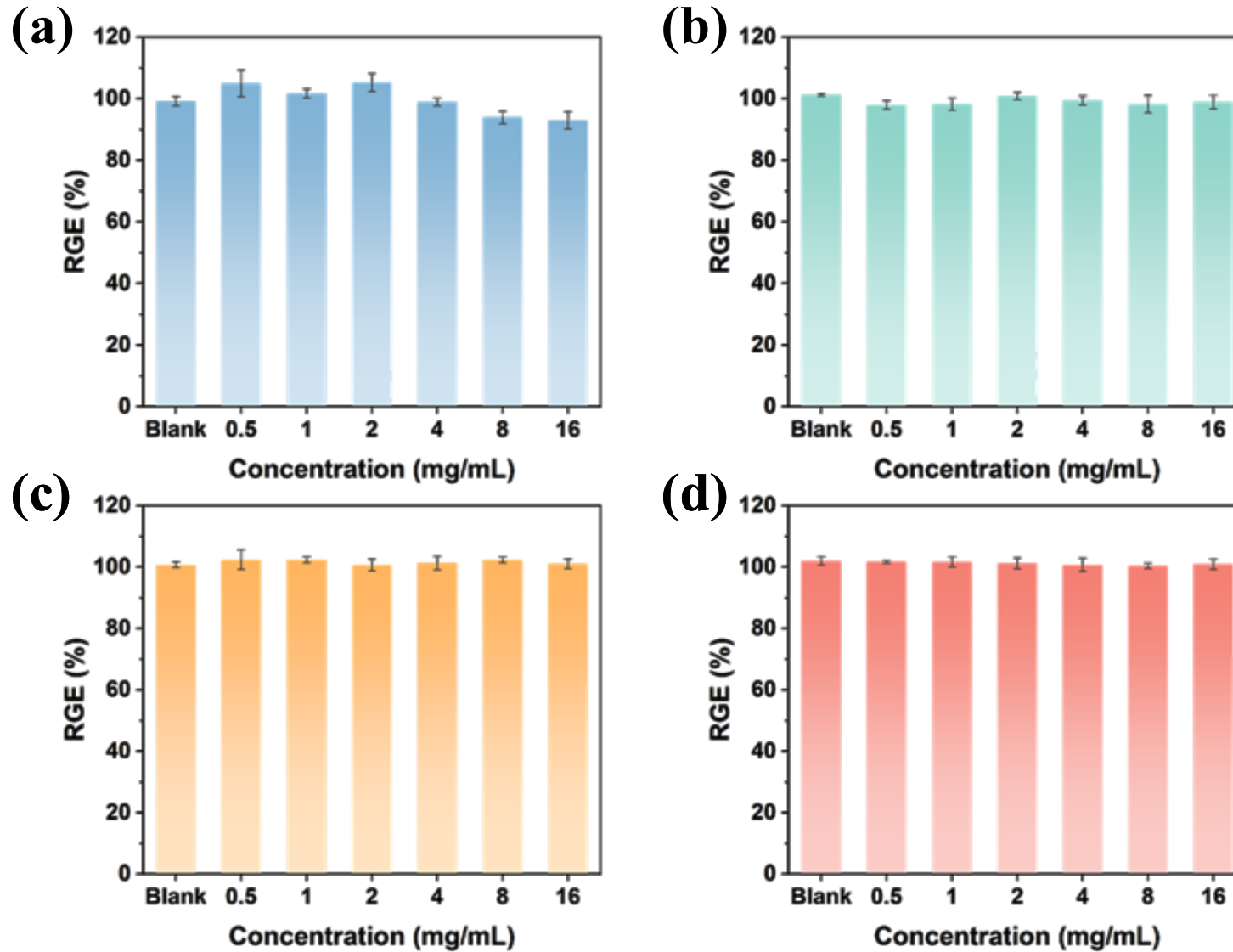
*S. aureus*



SEM – intact vs ruptured membranes



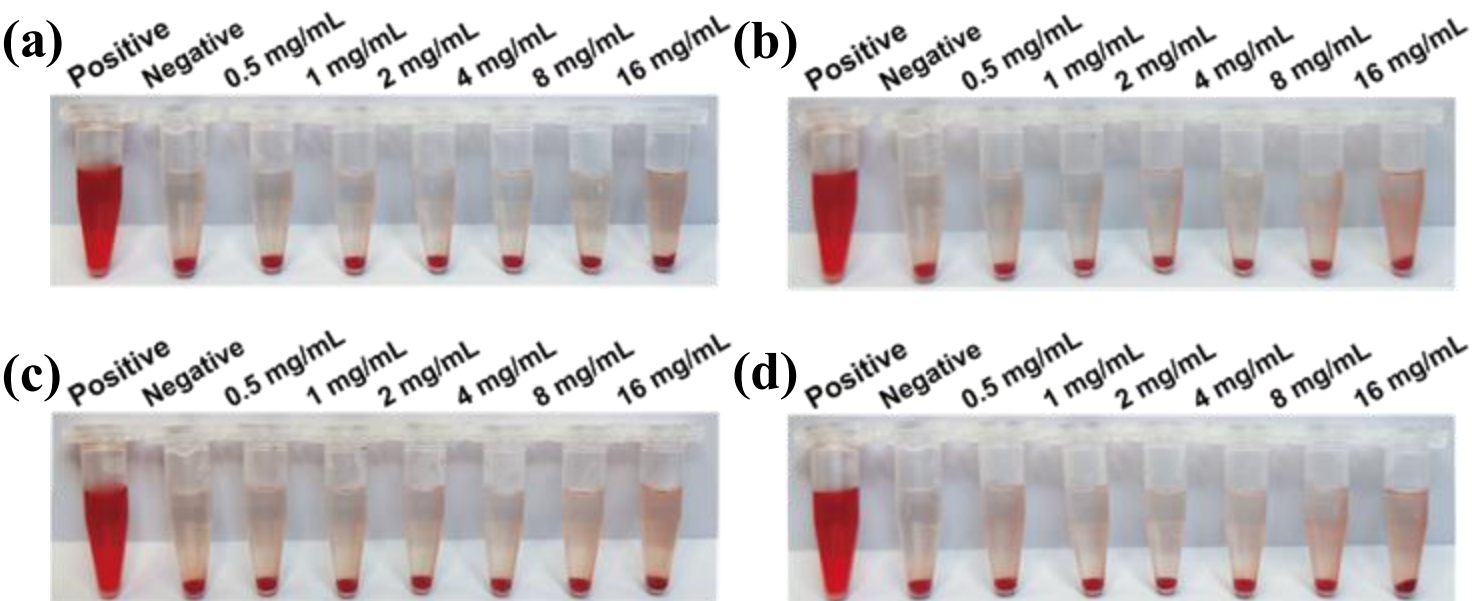
## Results & Discussion—Biosafety



HepG2 viability > 98 % at 16 mg mL<sup>-1</sup>

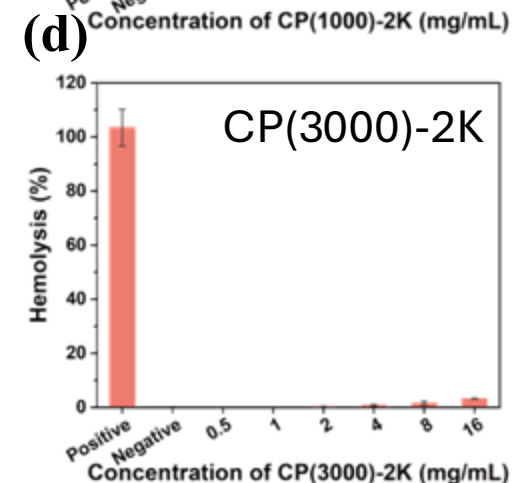
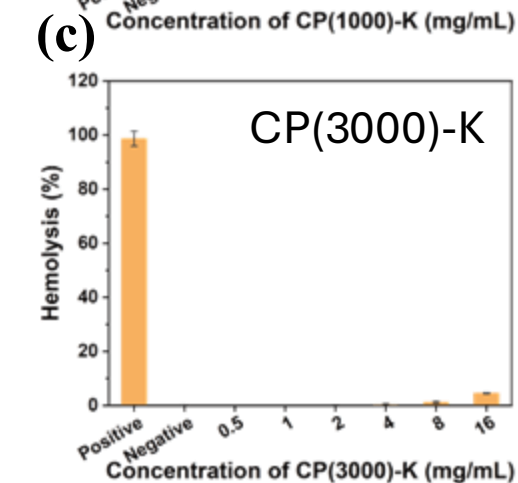
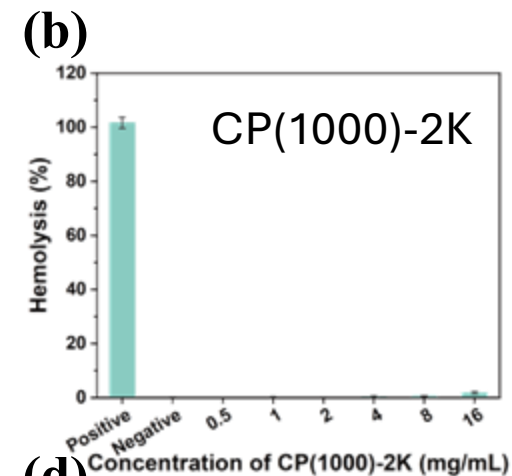
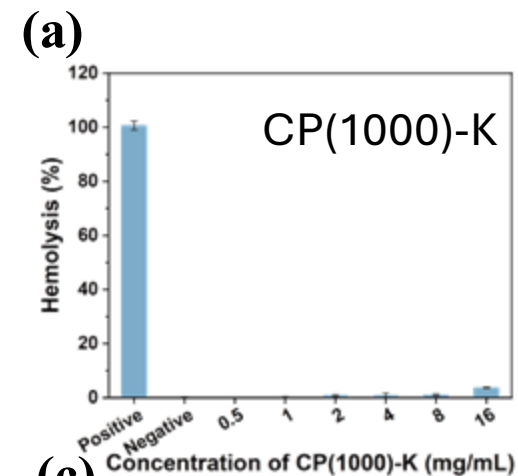
MTT assay results .(a) CP(1000)-K, (b) CP(1000)-2K, (c) CP(3000)-K, and (d) CP(3000)-2K.

# Results & Discussion—Biosafety

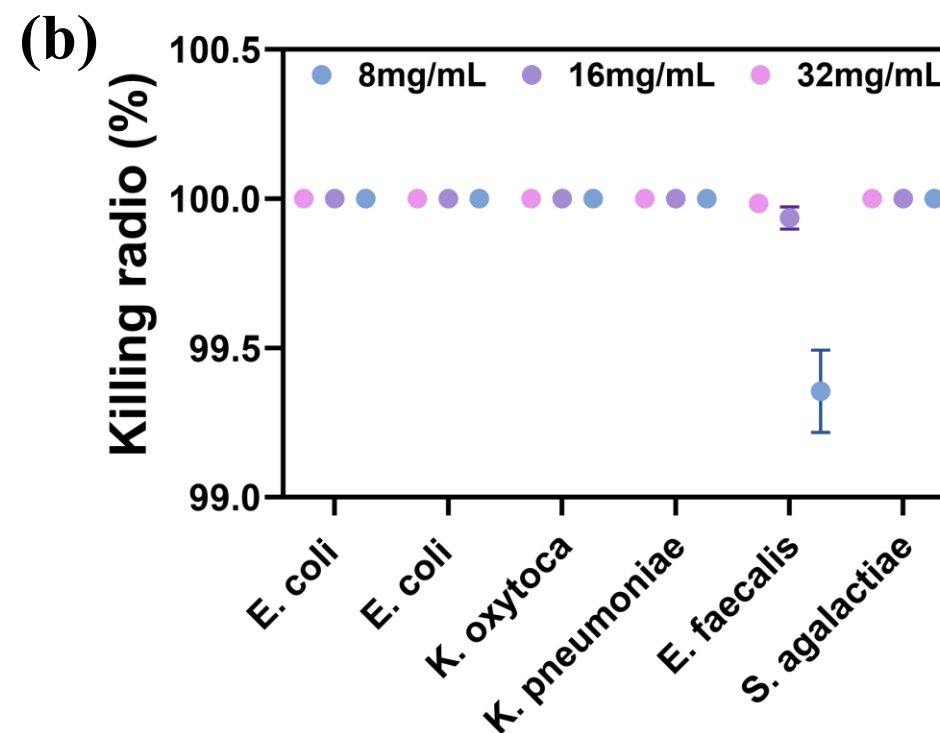
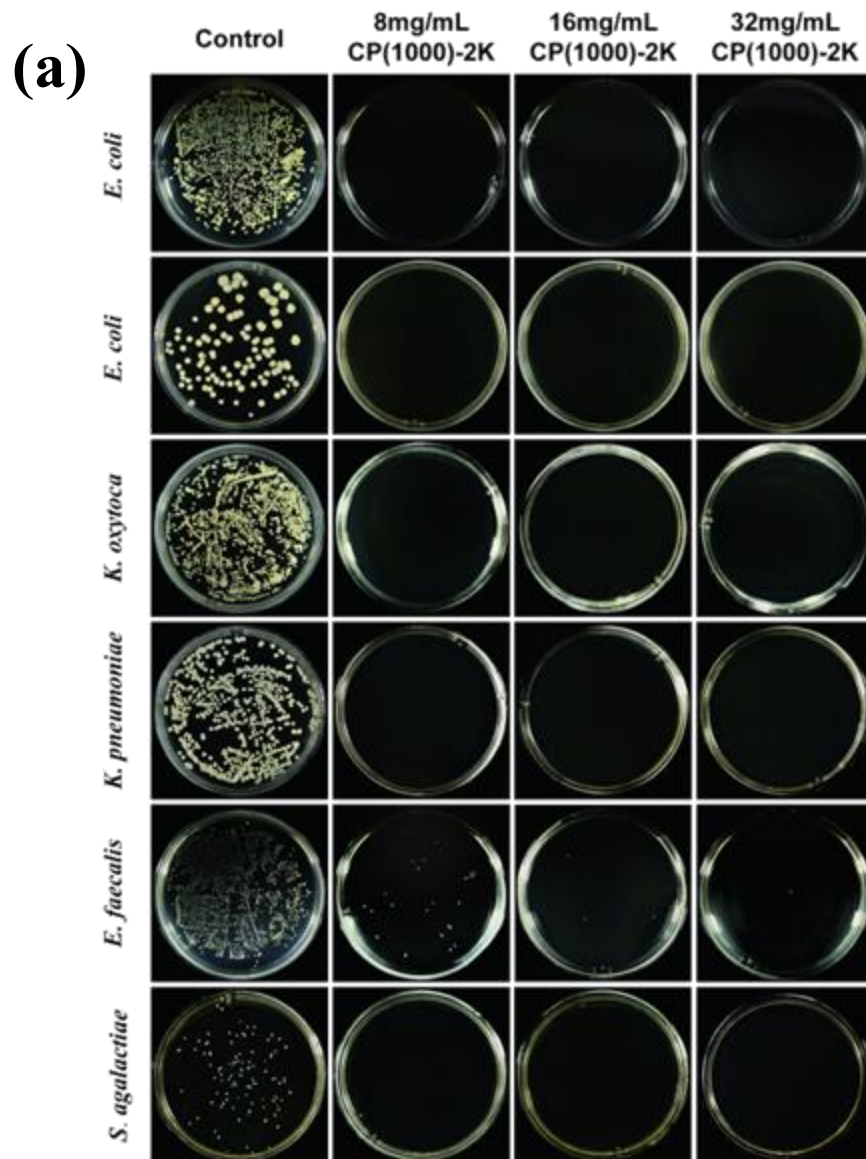


Hemolytic toxicity of CP(1000)-K (a) ,CP(1000)-2K (b),CP(3000)-K (c) and CP(3000)-2K(d).

- ❑ No hemolysis observed at low concentrations.
- ❑ At 16 mg/mL, a slight hemolysis occurs, the hemolysis rates were all less than 10%



# Results & Discussion—Inhibition of Vaginal Pathogens



□ >99% inhibition at 8-32 mg/mL for 6 strains.

## Conclusions & Outlook

- Semi-Synthetic Cationic Peptides Derived from Collagen: scalable, low-cost.
- Broad-spectrum activity via membrane disruption.
- High biosafety; promising for clinical applications



## Acknowledgements



Shuo Wang



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Ruxin Zhang





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# Thank you for your attention!

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