Lipidic Nanoparticle for Brain-targeted Treatment in Bacterial Meningitis

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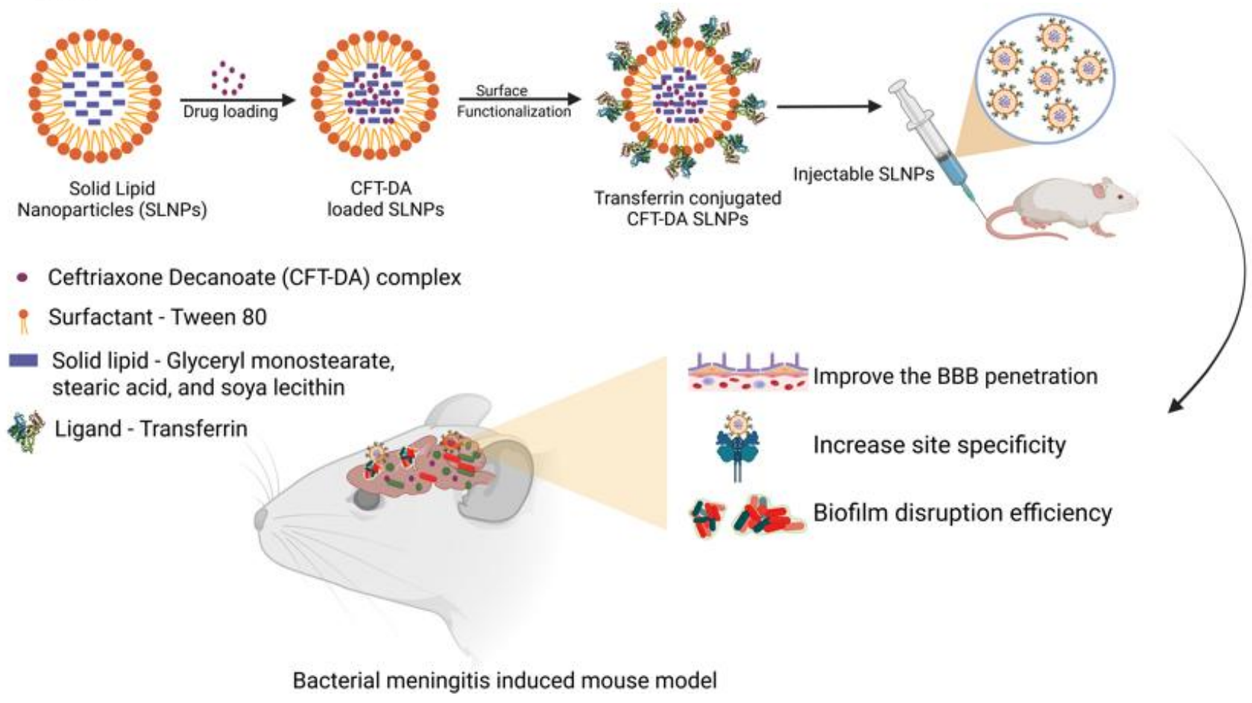
Introduction

- Bacterial meningitis (BM) is a critical, life-threatening infection characterized by inflammation of the meninges, and the protective membranes surrounding the central nervous system, necessitating immediate diagnosis and intervention.
- This inflammation spreads across the subarachnoid region of the spinal cord and brain. Due to the limited penetration of several antibacterial agents through the blood-brain barrier, the mortality rate of bacterial meningitis is high.
- The well-known bacterial species that are the main sources of infection that result in meningitis are Streptococcus pneumoniae, Staphylococcus aureus, Neisseria meningitidis, Haemophilus influenzae, and E.coli.

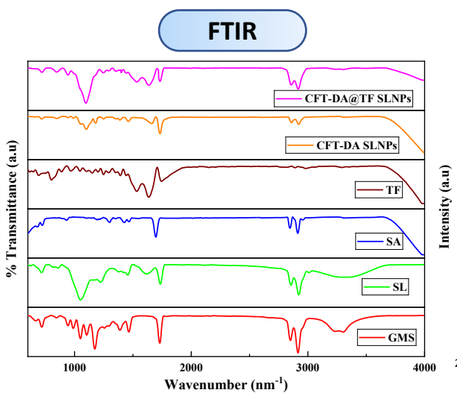


Learning Objectives

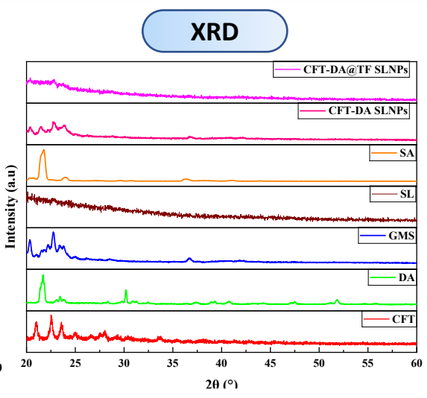
- To synthesize and characterize transferrin-conjugated ceftriaxone solid lipid nanoparticles (CFT-DA@TF SLNPs) that improve the BBB's permeability in treating bacterial meningitis.
- To evaluate the *in vitro* antibacterial and antibiofilm activity of SLNPs and to investigate the in vivo therapeutic efficacy of SLNPs in bacterial meningitis-induced mouse models.

Physicochemical Characterization

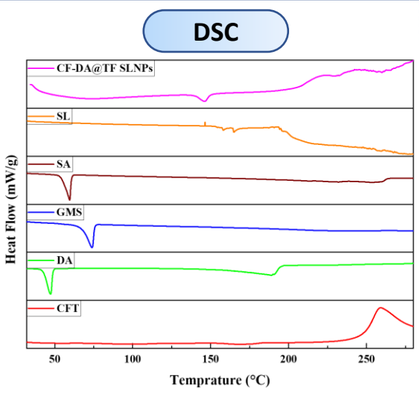
FTIR



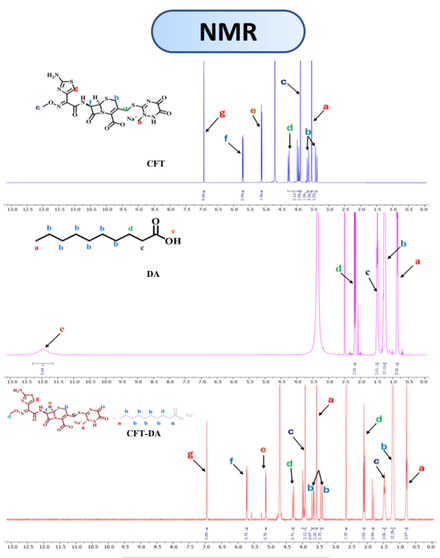
XRD



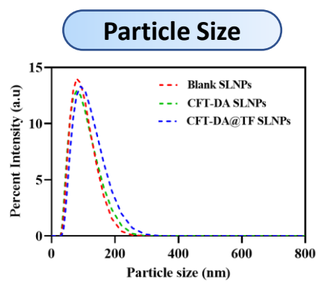
DSC



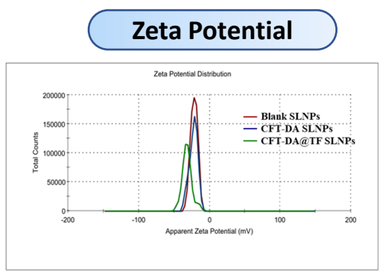
NMR



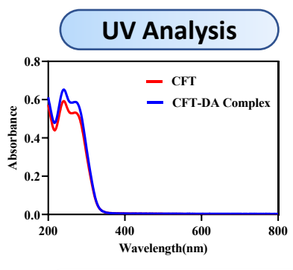
Particle Size



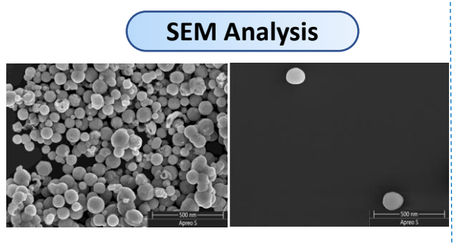
Zeta Potential



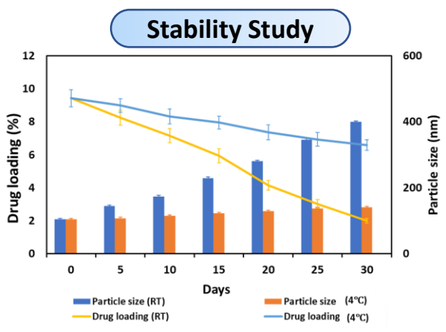
UV Analysis



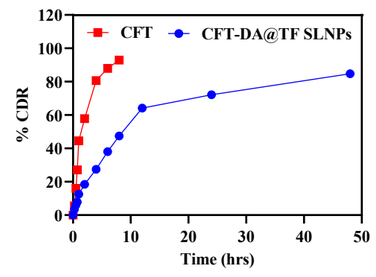
SEM Analysis



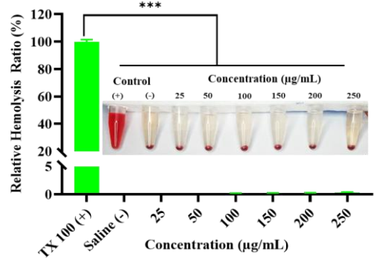
Stability Study



In Vitro Drug Release

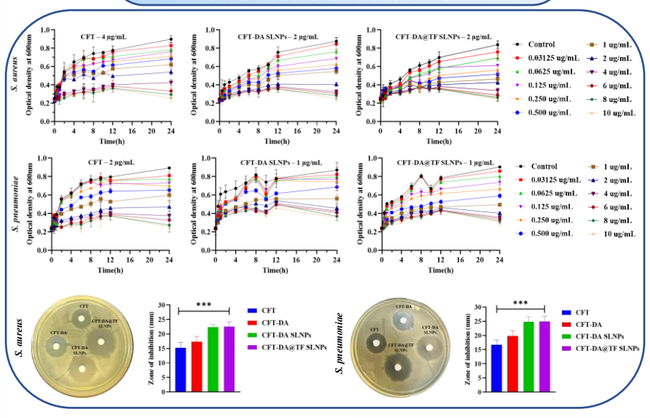


Hemolysis Study

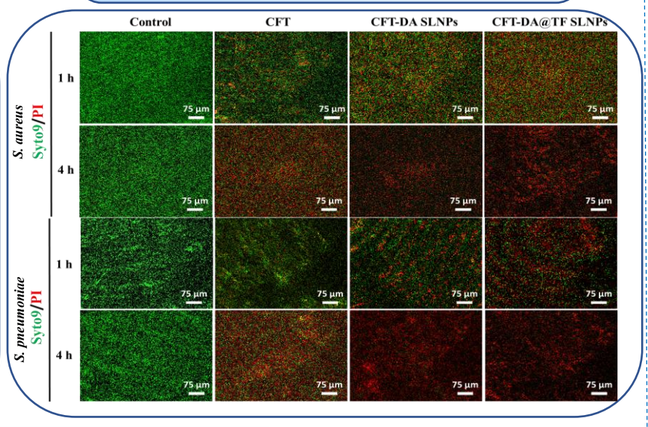


In vitro bacterial studies

Minimum Inhibitory Concentration and Zone of Inhibition

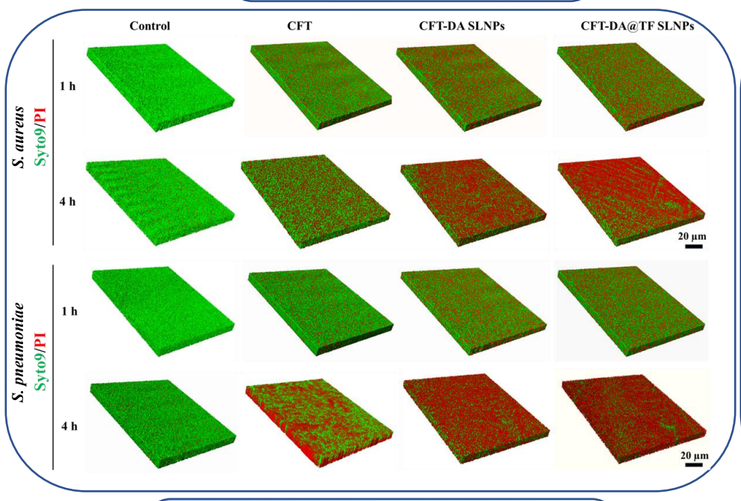


Live/Dead assay for Planktonic Bacteria

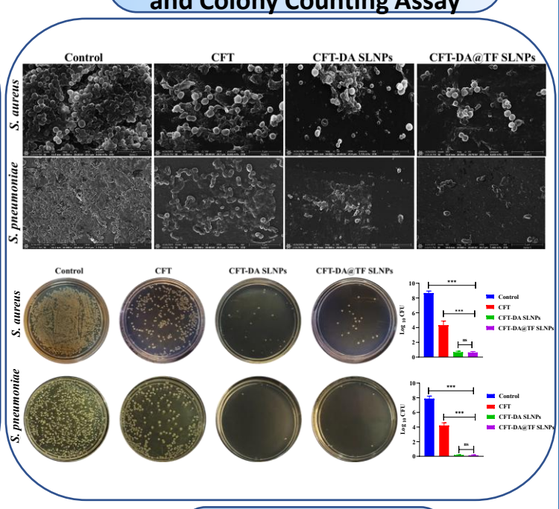


Quantitative Analysis of Live/Dead Cells by FACS

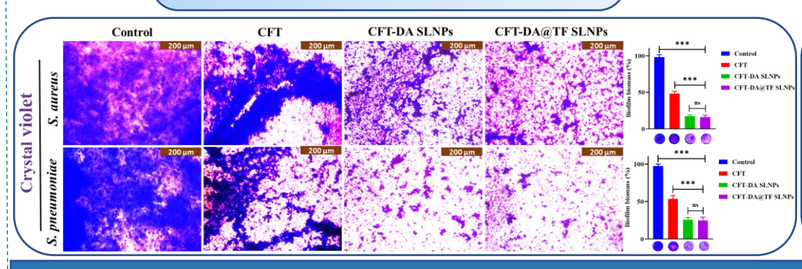
Biofilm Live/Dead Assay



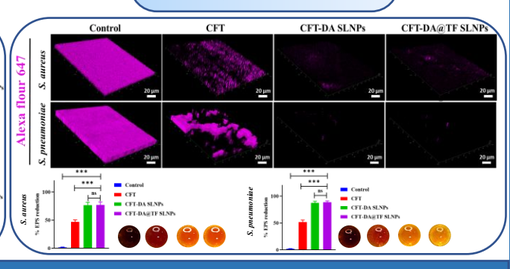
Biofilm Eradication by SEM and Colony Counting Assay



Biofilm Quantification by CV Assay

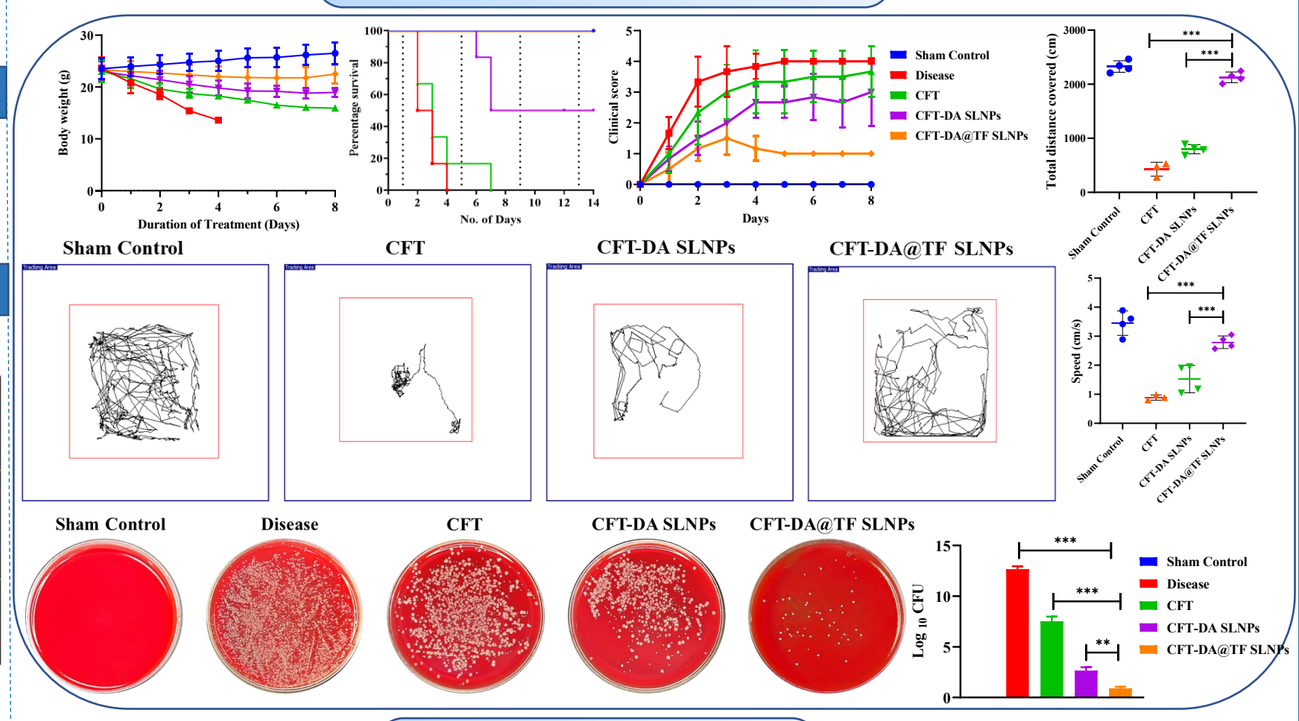


EPS Quantification

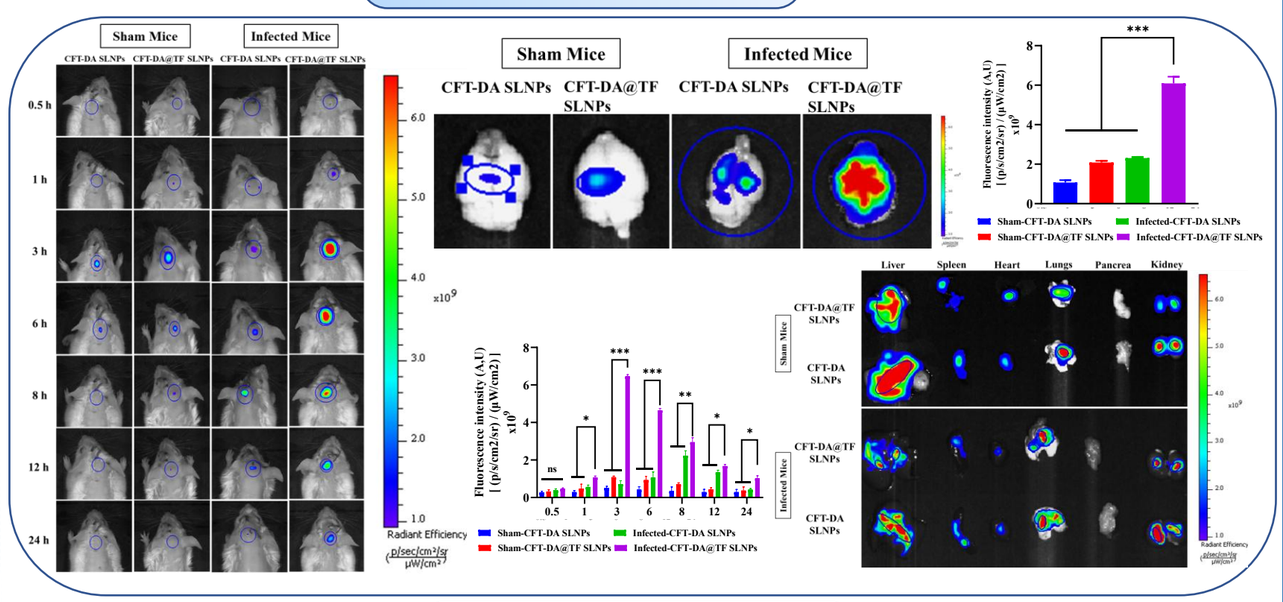


Efficacy against *in vivo* BM-induced *mouse model*

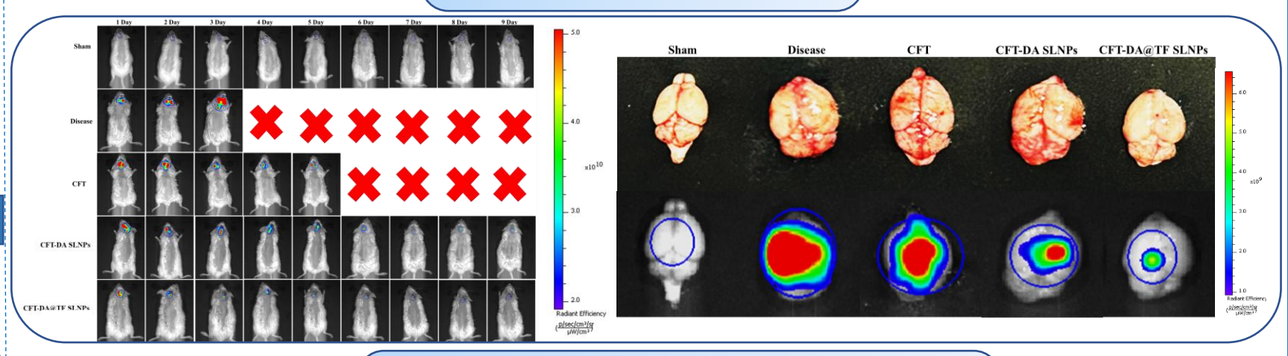
Open Field Test, Survival Study and CFU/mL



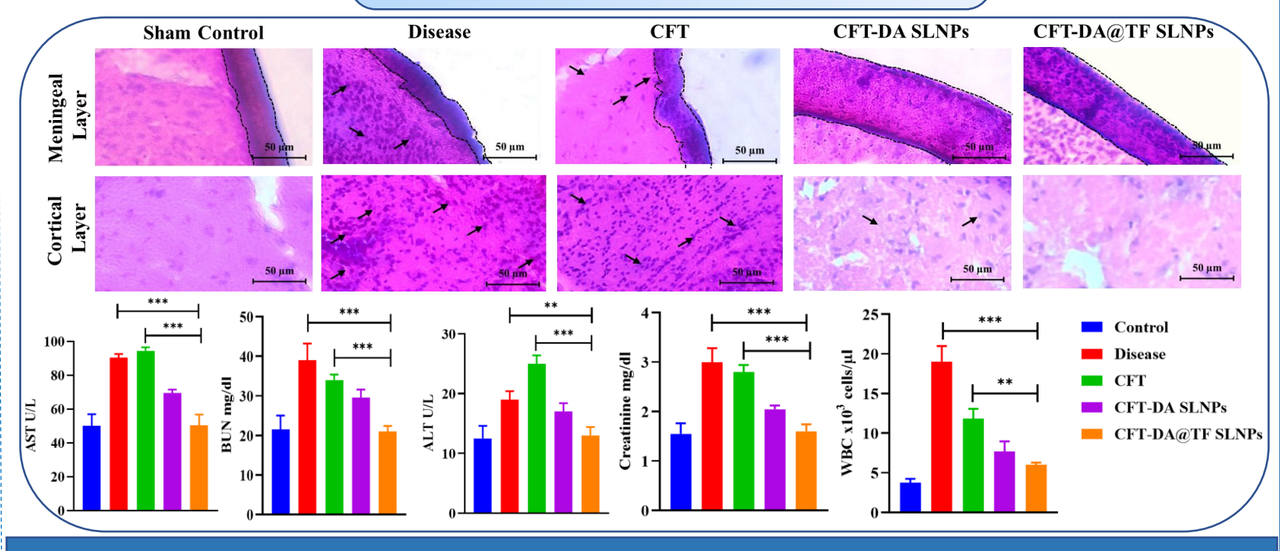
Biodistribution study by IVIS



In vivo ROS analysis by IVIS



Histological and Biochemical Parameters Analysis



Conclusion

- The physicochemical characterization confirmed the successful functionalization of SLNPs with transferrin (TF), and in vitro antibacterial studies demonstrate their potential as a promising strategy for enhancing brain targeting in the treatment of bacterial meningitis.
- The presented work demonstrates CFT-DA@TF SLNPs) achieve significantly efficient biofilm-disruption capabilities, and enhanced blood-brain barrier penetration, resulting in superior brain accumulation of the antibiotic and marked reduction of bacterial load in Streptococcus pneumoniae-induced meningitis mouse models.
- These findings highlight the potential of CFT-DA@TF SLNPs as a transformative approach for effective CNS delivery and treatment of bacterial meningitis.

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