Antibacterial activity of N^{α}-benzoyl-arginine-based surfactants and their possible mechanism of action

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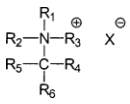


Disinfectants in COVID-19 times!

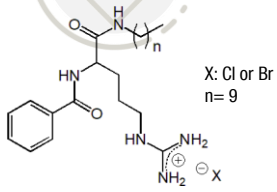
Surfactants are ingredients in many cleaners, cosmetic and pharmaceutical formulations as stabilizers and preservatives.

Cationic surfactants, such as Quats have antimicrobial properties, but are toxic to users and the environment.

Cationic amino acid-based tensioactives could be considered excellent alternatives.

We have synthesized by means of a biocatalytic eco-friendly strategy the arginine-based tensioactive Bz-Arg-NHC_{10}.

Papain



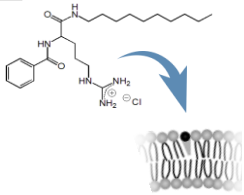
1. Antimicrobial Activity

Microorganism	Bz-Arg-NHC_{10}·HX X=Cl MIC	X=Cl MBC	X=Br MIC	X=Br MBC
Micrococcus	31	62	31	62
B. subtilis	62	62	62	62
S. aureus	62	62	62	125
Salmonella	62	125	125	250
P. aeruginosa	125	250	125	125
E. coli	125	125	125	125

Concentrations are expressed in μM

Both compounds inhibit the growth of Gram positive and Gram negative bacteria. In contrast, other arginine-based surfactants have shown good activity only against Gram positive bacteria.

2. Interaction of Bz-Arg-NHC_{10} with DPPC membranes



Insertion of Bz-Arg-NHC_{10}·HCl into lipid membranes composed of 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC) was investigated in order to elucidate the antimicrobial mechanism of action.

2.1 Monolayer penetration experiments

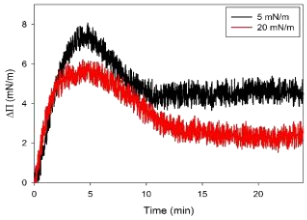


Fig. 1. Kinetics of insertion of Bz-Arg-NHC_{10} into lipid monolayers of DPPC. Once incorporated into the lipid film, the surfactant was able to remove lipid molecules from it.

2.2 Differential Scanning Calorimetry

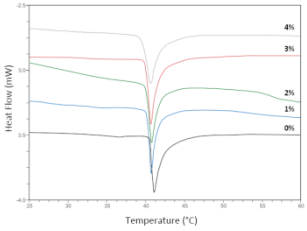


Fig. 2. DSC curves obtained with DPPC–Bz-Arg-NHC_{10} systems. Fluidification of the DPPC membrane induced by the surfactant was evidenced by a decrease in the transition temperature.

2.3 Atomic Force Microscopy Findings

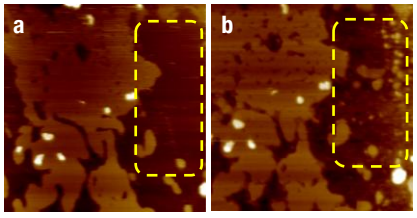
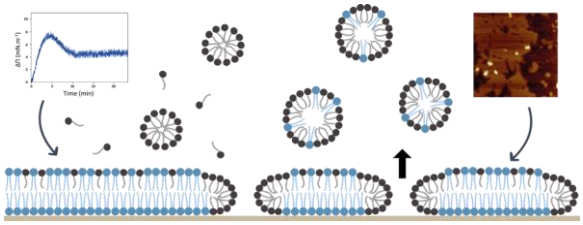
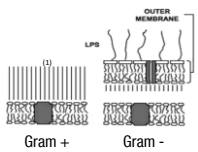


Fig. 3. Material was removed and re-adsorbed onto the mica surface after the interaction of the surfactant with DPPC supported bilayers.

3. Proposed mechanism for membrane interaction



N^{α}-benzoylated arginine-based surfactants showed broad spectrum bactericidal activity.



Disruption of the DPPC bilayer and lipid-surfactant mixed micelles releasing was observed.

The benzoyl group attached to the polar head of the surfactant would cause disorganization of the outer membrane of Gram negative bacteria, enhancing its antibacterial effect.