

Description for the general public

The rapid growth of bacterial resistance to conventional antibiotics puts an increased challenge to the search of alternative treatment strategies. Antimicrobial peptides (AMPs) constitute part of the host innate immunity of living organisms of all types and are one of the most promising classes of compounds exhibiting broad-spectrum of antimicrobial activities. Based on their specific structure one can design analogues with enhanced activities and improved pharmacokinetic properties. Short synthetic lipopeptides containing cationic amino acids and fragments of fatty acids seem to be an interesting group of antimicrobial compounds. They satisfy the amphipathicity and total positive charge conditions, essential features of antibiotic peptides. Moreover, in addition to the antibacterial activity they exhibit surface-active properties. Thus, they can act as preservatives and surfactants allowing to obtain and secure the multiphase system stability.

The main goal of this project is to determine the interplay between structure, biological activities and surface-active properties of three types of lipopeptides: single-chain, double-chain and double-head ones. By changing the balance in size between the hydrophilic head and hydrophobic tail of the lipopeptides we believe to control the morphology, characteristics, surface chemistry and finally the antimicrobial activity of lipopeptides' aggregates. The project includes synthesis, antimicrobial activity and cytotoxicity assays, studies of self-assembling processes and their effect on biological activities and mechanism of action of the lipopeptides.

The project uses the isothermal titration calorimetry and surface tension measurements to estimate the critical micellar concentrations (*cmc*) and as well as the NMR spectroscopy to estimate the size and dynamics of the lipopeptide aggregates. ITC, FTIR and confocal fluorescence microscopy will be employed to study the lipopeptide-membrane interactions. Finally, the molecular dynamics simulations will be performed to explore self-assembly, micellar properties and interactions of the lipopeptides with the bacterial membrane.

The results obtained in this project will be an important contribution to understanding the role played by self-assembly in antimicrobial activity. Getting the knowledge of the self-assembling regularity, the design of particular self-assembling antimicrobial peptides will be vital for their applications in the field of medicine and pharmaceutical industry.