Abstract

Lipophosphonoxins are small synthetic antimicrobials targeting the cytoplasmic membrane of bacteria. This thesis focuses on comparison of three lipophosphonoxins which differ in the number of carbons in its modules and in antimicrobial and hemolytic activity. The most promising candidate compound is lipophosphonoxin 7072 showing good antimicrobial activity as well as low hemolytic activity. Other two tested lipophosphonoxins are 7070 displaying high hemolytic activity and weakly antibacterial lipophosphonoxin 7107. The pore-forming activity of lipophosphonoxins is investigated using model membranes as well as living bacteria *Staphylococcus aureus* and *Escherichia coli*. The results show that small difference in structure can fundamentally affect the activity of these molecules. Lipophosphonoxins 7072 a 7070 display equal antibacterial activity against tested bacteria by forming pores in the bacterial membrane. Bacteria rapidly die of loss of membrane potential caused by lipophosphonoxins. The high hemolytic activity of the compound 7070 is probably related with its preference for uncharged membranes. The weak antimicrobial activity of 7107 is caused by its capability to form only small pores and its incapability to overcome and disrupt the outer membrane.

Key words: antimicrobial agents, lipophosphonoxins, cytoplasmic membrane, pore-forming activity