Abstract

Surfactin is a cyclic lipoheptapeptide produced by *B. subtilis*. It is a surface-active compound capable of interfering with the barrier function of the cytoplasmic membrane. With increasing concentration, it can disorganize the membrane, form conductive pores and eventually disintegrate the membrane in a detergent-like manner. The details of this mode of action are not well understood, nor is the mechanism by which the producer defends itself against its own toxic product. We have previously shown that *B. subtilis*, when exposed to surfactin, changes the lipid composition of its membranes, mainly increasing the amount of cardiolipin at the expense of phosphatidylglycerol. In this work, we have shown that the increase in cardiolipin content leads to a reduced susceptibility to permeabilization by surfactin in a concentration-dependent manner. This applies for membranes composed of synthetic phospholipids, membranes reconstituted from lipid isolates, and even living cells, as demonstrated by the propidium iodide test performed on *B. subtilis* cells deficient in cardiolipin production. However, we have not yet been able to prove whether this protective effect is at the level of surfactin insertion into the membrane or its action once inside the membrane. Besides that, we found that the stock solution used had a disproportionate effect on the effectiveness of surfactin, which we explained by differences in micellization behavior. In addition, we were able to visualize surfactin pores using electron microscopy. Based on the above, we conclude that target site modification, manifested as a change in the lipid composition of the cytoplasmic membrane, is an important part of the mechanism by which *B. subtilis* defends itself against surfactin.