

## Di- $\beta$ -alanine derivatives: crystal packing, self-assembly, silver nanoparticle formation, and antimicrobial properties

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The biological activity of proteins is determined by their three-dimensional structure. One example is the protein self-assembly into fibers, which can form continuous networks resulting in the formation of hydrogels. These biocompatible hydrogels are of special interest for various medical applications.

The production of a large amount of protein-based hydrogels can be difficult and expensive. Therefore, short  $\alpha$ -peptide based hydrogels are preferred over protein-based hydrogels, as they are easier to synthesize and less expensive. Nevertheless,  $\alpha$ -peptide based hydrogels can be degraded by proteases and are restricted to short term applications. A new promising group of peptides to study protein self-assembly are  $\beta$ -peptides which cannot be degraded by proteases and are thus excellent compounds with which to design long-lasting hydrogels. The overall goal of this project was to design an ultrashort  $\beta$ -peptide hydrogel with the purpose to be used for wound dressings. Ideally being doped with silver nanoparticles to enhance the dressings antimicrobial properties. Therefore, in a first section, 11 ultrashort  $\beta$ -peptides were designed, which consisted of two  $\beta$ -alanines. They differed in their N- and C-termini, to study the influence of hydrophobic-, aromatic-interactions and hydrogen bonding. The six obtained crystal structures confirmed that hydrogen bonding at the C-terminus, aromatic interactions and bulky hydrophobic groups have a big impact on crystal packing. Furthermore, for one of the di- $\beta$ -alanine derivatives, crystalline fibers or cuboids could be formed and studied. In a second section, the silver nanoparticle formation with the di- $\beta$ -alanine derivatives was studied. The investigation revealed that an interaction with  $\text{Ag}^+$  on the C-terminus was crucial for silver nanoparticle formation. Furthermore, the pH, temperature, solvent, and  $\beta$ -peptide concentration influenced silver nanoparticle formation, shape, and agglomeration.

In section three, the minimum inhibitory and bactericidal concentration of the references: ampicillin,  $\text{AgNO}_3$  and  $\text{Cu}_2^+$ -salts were established and the antimicrobial effect of the di- $\beta$ -alanine derivatives was investigated. The results revealed that the di- $\beta$ -alanine derivatives are not antimicrobial. Still, some di- $\beta$ -alanine derivatives caused a reduced growth.

Due to the results obtained we are convinced that by further step-by-step adaptations of the di- $\beta$ -peptide, specifically the residues, a hydrogel with suitable properties for wound dressings can be designed.

Jury:

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