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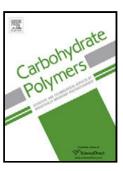
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ACCEPTED MANUSCRIPT

Tethering antimicrobial peptides onto chitosan: optimization of azide-alkyne "click" reaction conditions

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Highlights

- Chitosan's amines were converted into azides via the diazo-transfer reagent ISA.HCl
- An alkyne-modified derivative of the potent antimicrobial peptide Dhvar-5 was produced
- Peptide was tethered onto chitosan via copper-catalyzed alkyne-azide coupling (CuAAC)
- THPTA and aminoguanidine hydrochloride additives were critical for success of CuAAC
- FTIR and XPS confirmed success of all reaction steps
- A peptide load of 2 mg per gram of chitosan was obtained by amino acid analysis (AAA)

Abstract

Antimicrobial peptides (AMP) are promising alternatives to classical antibiotics, due to their high specificity and potency at low concentrations, and low propensity to elicit pathogen resistance. Immobilization of AMP onto biomaterials is an emergent field of research, towards creation of novel antimicrobial materials able to avoid formation of biofilms on the surfaces of medical devices. Herein, we report the chemical route towards one such material, where chitosan was used as biocompatible carrier for the covalent grafting of Dhvar-5, a well-known potent AMP, *via* the chemoselective ("click") Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC). The material's structure, as well as

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