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N-modified chitosans with non-randomly distributed functional groups by combining regioselective biocatalysis with efficient ?click? chemistry

AUTHORS
Max LINHORST / IBBP WWU, SCHLOßPLATZ 8, MUENSTER

PURPOSE OF THE ABSTRACT

Chitin- or chitosan-based polymers are promising candidates for renewable materials, as chitin is highly abundant in nature. Chitin is a polysaccharide composed of ?-(1,4)-linked N-acetyl-D-glucosamine-units (GlcNAc) and is a structural component e.g. of the exoskeletons of crustaceans and in the cell walls of filamentous fungi. Thus, it is available in Mt-scale as waste material from food and biotechnology industry. The most interesting chitin-derivatives are chitosans, which can be produced by partial de-N-acetylation of GlcNAc units to D-glucosamine-units (GlcN). The free amino groups of chitosans, in contrast to chitin, impart solubility in slightly acidic aqueous solutions (pH <6), facilitating further modification or formulation. Chitins and chitosans are structurally defined by their degree of polymerization (DP), fraction of N-acetylation (FA), and pattern of acetylation (PA)[1,2].

Therefore, a broad variety of applications can be developed for biopolymers from the chitin/chitosan family by varying the different molecular parameters. Chitosan applications can be found in the fields of plant protection[3], wound healing[4], or drug-release nano-formulations[5], to mention just a few. In many cases, further chemical functionalization can help tuning physico-chemical properties or bioactivities of chitosans[6,7]. The chemical nature of the GlcN building block of chitosans calls for modification strategies that balance high reactivity to yield high degrees of substitution on the one hand, and high selectivity between O- and N-functionalization on the other hand. Most of the strategies described in literature fail to yield high degrees of substitution or high selectivity of modification, or they include complex protection group strategies[8].

An alternative approach reported here is enzymatic modification of chitosans. Enzymes can combine high chemo- and regioselectivity with high reactivity. With chitins/chitosans being biomolecules, nature already provides enzymes capable of modifying them. One class of chitin/chitosan modifying enzymes catalyzes the N-deacetylation of chito-oligomers or ?polymers[9]. The in vivo roles of such chitin deacetylases (CDAs) range from the biosynthesis of chitosan from chitin as a molecular stealth strategy of fungal pathogens to the production of partially acetylated chitosan oligomers as signaling molecules. Biotechnologically, the CDA-catalyzed ?reverse' N-acetylation by addition of excessive amount of acetate in vitro has reported for the preparative production of defined paCOS[10,11].

Here, we present the exploitation of the chemo- and regioselective N-acylation activity of CDAs for the introduction of functional moieties to the chitosan backbone, by using different carbonic acids as co-substrates. First, the co-substrate promiscuity of two CDAs was tested to investigate the structure function relationship of these CDAs for the conversion of chitosan oligomers (FA = 0; DP = 4). Next, the use of co-substrates that bear moieties for subsequent ?click? chemistry reactions were investigated and their conversion was optimized for preparative purposes. Eventually, the work aims to access selectively N-modified chitosan-polymers with non-randomly distributed functional groups by combining regioselective biocatalysis with efficient ?click? chemistry.

FIGURES

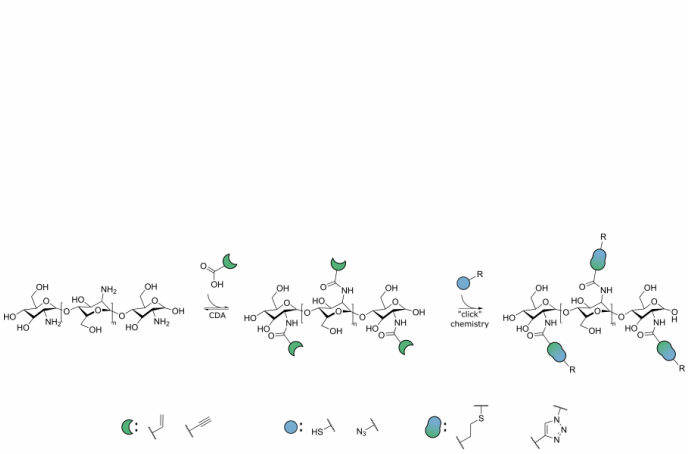

FIGURE 1

Scheme for the introduction of functional moieties (e.g.: -Br, -alkene, -alkyne) to chitosan via N-acylation catalyzed by CDAs, followed by ?click? reactions.

FIGURE 2

KEYWORDS

Biopolymers | Biocatalysis | Click chemistry | Chitosan

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