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Molecular weight and pH aspects of the efficacy of oligochitosan against methicillin-resistant *Staphylococcus aureus* (MRSA)

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ABSTRACT

Oligochitosan samples varying in molecular weight (M_w) and having narrow polydispersities were p
pared by means of depolymerization of chitosan in hydrochloric acid, and their antibacterial activ
against methicillin-resistant *Staphylococcus aureus* (MRSA) was measured at pH values 5.5–8.0. T
antibacterial testing of oligochitosans obtained showed that oligochitosans having M_w in the range
0.73–20.0 kDa could be used both at slightly acidic and neutral pH values, and that the activity agai
MRSA remained moderate for oligochitosan samples having M_w about 3–5 kDa even at slightly basic
values. The self-assembling behavior of oligochitosan macromolecules in the dilute solution at vari
pH values as a function of chain length was investigated. At first it was shown that oligochitosans form
supramolecular aggregates in dilute solutions below the critical pH value 6.5. Despite the aggregat
phenomenon, the formation of nano-sized aggregates did not prevent oligochitosan from demonstrat
the bactiostatic activity.

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1. Introduction

Among Gram-positive bacteria the mostly collected in hospitals, public buildings, and aircraft cabins is Gram-positive *Staphylococcus aureus* that can cause a wide variety of diseases in humans and animals. *S. aureus* is becoming more and more resistant to many commonly used antibiotics including penicillin, amoxicillin, tetracycline, erythromycin, linezolid, vancomycin, and methicillin (Gandara, 2006). Increased problems with human allergy also have been observed in the patients receiving antibiotic agents for treatment. As a result, benefits and safety of many biocides are the subjects of debates among regulators specializing in medicine, food, cosmetics, environmental sciences, and toxicology (Donadio, Maffioli, Monciardini, Sosio, & Jabes, 2010). Therefore, there is a need for new non-toxic biocides that could be active against broad spectrum of invasive and noninvasive human pathogens and could reduce the level of administration of classic antibiotics.

Chitosan produced by a partial or complete deacetylation of chitin represents a collective name for a group of polysaccharides consisting of glucosamine and *N*-acetylglucosamine or glucosamine only. Chitosan and chitooligosaccharides ha
attracted considerable interest due to their different biologi
activities (Xia, Liu, Zhang, & Chen, 2011). Numerous investigatio
of antimicrobial activity of chitosan, its derivatives and analogu
named oligochitosan and chitooligosaccharides against many ba
teria, including *S. aureus* (Muzzarelli et al., 1990), filamentous fu
and yeasts have been published so far, and nowadays it is co
monly accepted that the activity depends on molecular weig
(M_w), degree of deacetylation (DD), target microorganism, a
experimental conditions. As to DD, the higher DD is, the high
activity occurs. On the other side, the controversial evidences
a correlation between biocidal activity and M_w of chitosan ha
been found so far. It was shown in some studies that the increa
in chitosan molecular weight led to the decrease in biocidal act
ity of chitosan (Hernández-Lauzardo et al., 2008; Jung, Chung
Lee, 2002; Tikhonov et al., 2006; Xu, Zhao, Han, & Du, 2007; Yu
Kim, & Lee, 1999; Zheng & Zhu, 2003). In the others an increas
activity of high molecular weight chitosans in comparison w
low molecular weight chitosans was found (Hirano & Nagao, 198
Kim, Thomas, Lee, & Park, 2003; Li, Feng, Yang, Wang, & Su, 200
Lin, Lin, & Chen, 2009; Liu, Guan, Yang, Li, & Yao, 2001; Qin et
2006; Shahidi, Arachchi, & Jeon, 1999; Zhang, Tan, Yuan, & R
2003). It was only ones that the bell-like dependence of fungista
activity versus molecular weight was found (Tikhonov et
2011). The M_w-activity relationship is also found dependent on t

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