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Antifungal activity of oligochitosans (short chain chitosans) against some *Candida* species and clinical isolates of *Candida albicans*: Molecular weight–activity relationship

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ABSTRACT

A series of oligochitosans (short chain chitosans) prepared by acidic hydrolysis of chitosan and characterized by their molecular weight, polydispersity and degree of deacetylation were used to determine their anticandidal activities. This study has demonstrated that oligochitosans show a high fungistatic activity (MIC 8–512 μg/ml) against *Candida* species and clinical isolates of *Candida albicans*, which are resistant to a series of classic antibiotics. Flow cytometry analysis showed that oligochitosan possessed a high fungicidal activity as well. For the first time it was shown that even sub-MIC oligochitosan concentration suppressed the formation of *C. albicans* hyphal structures, cause severe cell wall alterations, and altered internal cell structure. These results indicate that oligochitosan should be considered as a possible alternative/additive to known anti-yeast agents in pharmaceutical compositions.

1. Introduction

The ascomycete yeast *Candida* is the most common cause of opportunistic mycosis worldwide.

Among *Candida* species, *Candida albicans*, *Candida tropicalis*, *Candida parapsilosis*, *Candida glabrata*, *Candida kruisei*, *Candida scotti*, and *Candida guilliermondii* are the most widespread ones. *Candida* species can be found in the oral cavity, throat, gastrointestinal tract, vagina, nails, and skin, and they are responsible for most (>91%) yeast infections with *C. albicans* being their major cause [1]. Over the last decades, the predominant pathogenic *Candida* species have changed, and infections caused by non-albicans *Candida* species have grown increasingly [2,3]. Conversely, the prominence of non-albicans, such as *C. kruisei*, *C. parapsilosis* and *C. tropicalis*, has increased their antibiotic resistance bringing challenges for effective antifungal therapy [4,5].

Moreover, misuse of antibiotics and the growing number of diseases caused by fungi not susceptible to antibiotics have increased problems with human allergy and have become a big problem globally [6], especially taking into account that there are a limited number of antifungal drugs [3]. Therefore, there is a need for new non-toxic fungicides which would be active against invasive and noninvasive human pathogens and could, at least, reduce the level of administration and side effects of classic antibiotics [7].

Chitin, poly[β-(1 → 4)-2-acetamido-2-deoxy-D-glucose], is the most abundant among the natural amino polysaccharides and represents a constituent of the cell walls of most fungi, algae, insects and crustaceans. Term "chitosan" belongs to a group of polysaccharides consisting of glucosamine and *N*-acetylglucosamine or glucosamine only, which are derived from chitin and are soluble in an acidic aqueous media. Conditionally, chitosans can be distinguished by their molecular weight (MW): high molecular weight chitosan (HMW), low molecular weight (LMW) chitosan,

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