

Current Opinion on Chitosan and its Derivatives: Biological Impact in Antimicrobial Applications From Nature to Chitosan and It Derivatives: How it is Working?

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Cédric Delattre. Current Opinion on Chitosan and its Derivatives: Biological Impact in Antimicrobial Applications From Nature to Chitosan and It Derivatives: How it is Working?. Advances in Biotechnology & Microbiology, 2017, 6 (2), 10.19080/AIBM.2017.06.555684 . hal-01657856

HAL Id: hal-01657856
https://uca.hal.science/hal-01657856

Submitted on 7 Dec 2017

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Advances in
Biotechnology & Microbiology
ISSN 2474-7637

Juniper Publishers
key to the Researchers

Opinion
Volume 6 Issue 2 – september 2017
DOI: 10.19080/AIBM.2017.06.555684

Adv Biotech & Micro
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Current Opinion on Chitosan and its Derivatives: Biological Impact in Antimicrobial Applications

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Submission: September 16, 2017; **Published:** September 20, 2017

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Abstract

Currently, lots of medical applications are investigated by using natural biopolymers such as polysaccharides. In this field chitosan is probably one of the most employed polysaccharides possessing very high pharmaceutical potential due to its chemo-physical and biological properties. The recent progresses in chemistry and biotechnologies apply to chitosan such as chemical and enzymatic modification allowed us to synthesize lot of biodegradable and biocompatible chitosan derivatives with huge impact in antimicrobial area. This present opinion describes the most widely described strategies for generate antimicrobial chitosan and derivatives by chemical/enzymatic structural macromolecular modification.

Keywords: Antimicrobial; Bioactivity; Chitosan; Chemical derivatives; Polysaccharide

From Nature to Chitosan and It Derivatives: How it is Working?

If we take a look on Scopus website from the last 5 years, we could see that chitosan and its chemical/enzymatic derivatives are ranked in one of the first bio-polysaccharide described for pharmaceutical applications. As for example, in 2012 using "chitosan" and a combination of "chitosan and pharmaceutical" we found, respectively, 4027 and 1588 publications whereas for 2016 we found respectively, 5327 and 2289. The continue evolution of publications on this very interesting topic between 2012 and 2016 is presented in Figure 1.

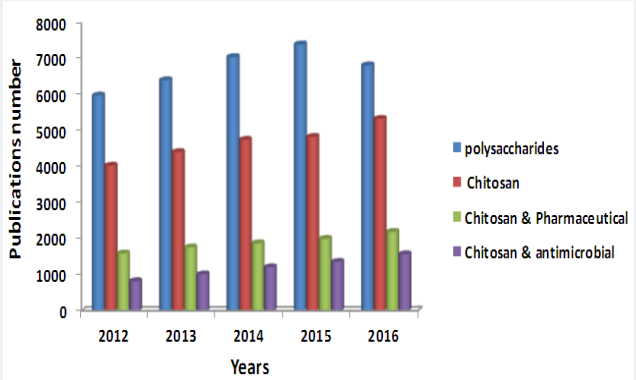


Figure 1: Evolution of publications number from 2012 to 2016 in Scopus web site with search using the words: (i) Polysaccharides, (ii) Chitosan, (iii) Chitosan & pharmaceutical and (iv) Chitosan & antimicrobial.

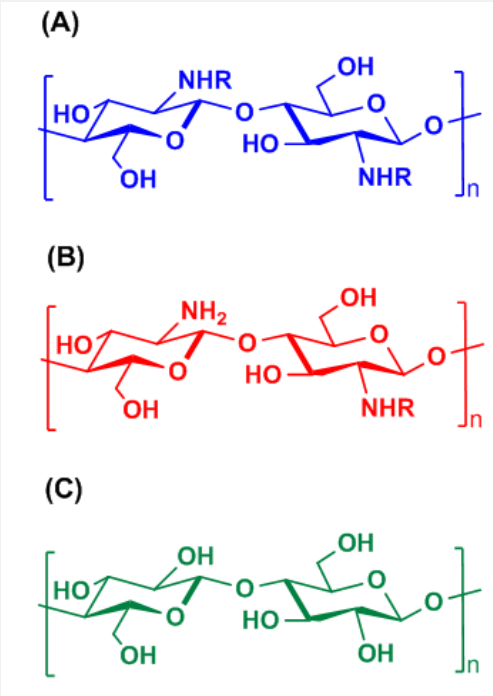


Figure 2: Chemical structure of (A) Chitin, (B) Chitosan and, (C) Cellulose with R= $COCH_3$ and/orH.

Generally speaking, this incredible bioactivity is possible due to the very particular macro-structure of chitosan which is the unique highly basic and cationic polysaccharide derived from alkaline N-deacetylation of chitin (Figure 2). After cellulose, chitin which is made-up of a β-(1,4)-2-acetamido-2-deoxy-D-glucose repeating units structure is the most abundant polysaccharide in the world found in fungal mycelia, insect cuticles, mollusks and crustacean shells [1]. As reported in literature [2,3] around 1000 tons/years of chitin is produce all over the world. Chitin is generally composed of high amount of N-acetylglucosamine groups (up to 90%mol) whereas chitosan contains around 40%mol of N-acetylglucosamine groups [4]. Contrary to chitin and cellulose, chitosan is very soluble in acid solution according to its low degree of N-acetylation. It is a highly biodegradable, biocompatible, renewable and environmentally non-toxic polysaccharide. Therefore, chitosan is largely employed in solution or material as bioactive molecules in lot of applications such as for example: anti-oxidant agent, anti-tumoral agent, drug delivery agent, tissular regenerating agent and anti-microbial [1,2]. Moreover, due to its reactive groups such as hydroxyl (-OH) and amine ($-NH_2$), several modifications/grafting have been largely described the last decades in order to build new generations of bioactive chitosan derivatives such as: acylated carboxyalkylated, hydroxyalkylated, phosphorylated, sulfated, thiolated, alkylated, trimethylated, etc. polysaccharides (Figure 3).

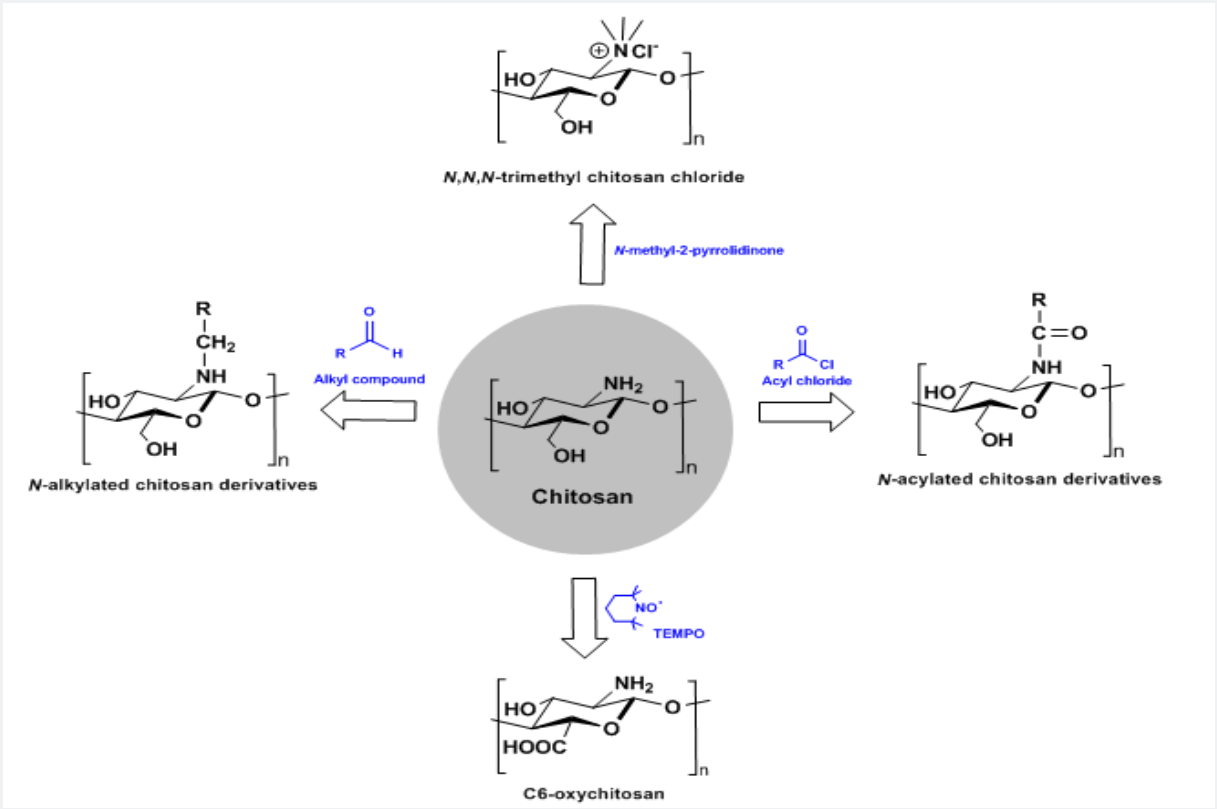


Figure 3: General ways to build new generation of bioactive chitosan derivatives.

All these specific modification coupled or not with depolymerization of chitosan derivatives (by enzymatic and chemical processes) were carried out to improve and highly modulate the native physico-chemical and biological properties [2]. As a general rule, the biological activities described in literature for all these chitosan derivatives are related to a broad range of structural parameters as solubility, molecular weight, global charge (cationic/anionic ratio), acetylation degree, etc. These chemical/enzymatic processes allowed generating new antimicrobial biomolecules as related in the following paragraph.

Antimicrobial Applications Using Chitosan and its Derivatives

The last years, the booming of natural biomolecules used as antimicrobial agent became a very interesting scientific challenge for academic and industry research due to the fact that lot of pathogen increased theirs antibiotic resistance. Because of this, chitosan is the number one candidate in the quest for new antimicrobial substance. When we talk about antimicrobial activity we have to talk about the mechanism involved with biomolecules. Then the question comes, why chitosan and

How to cite this article: Delattre Cédric. Current Opinion on Chitosan and its Derivatives: Biological Impact in Antimicrobial Applications. Adv Biotech & Micro. 2017; 6(2): 555684. DOI: 10.19080/AIBM.2017.06.555684

derivatives could be considered as natural antimicrobial agent? During the last decades lot of publications try to give the possible impact of chitosan and derivatives on antimicrobial activities. Nevertheless, the antimicrobial mode of action of chitosan is not clearly understood. In view of the last scientific knowledge [2,5-8] (some authors reported different responses about the possible mechanism involved during antimicrobial chitosan treatment :

(i) Ionic and electrostatic interactions between the negative charge from surface cell membrane of bacteria/fungi and the cationic charge of chitosan and derivatives (-NH_3+, N,N;N-trimethyl chloride derivative, quaternary ammonium derivatives, carboxymethyl derivatives, etc.),

(ii) The increasing release of cellular components from bacteria,

(iii) The possible disruption of energy generation pathways,

(iv) The specific chelation of metal ions,

(v) The specific precipitation/agglutination of bacteria with chitosan. Generally; lot of authors shown that the specific microbial inhibition caused by chitosan treatment is the consequence of molecular processes leading to microbial cell inhibition and death.

Very recently, the news advances using chitosan as antimicrobial supported material are the synthesis of new generation of functionalized biomaterial made up of chitosan with antibiofilm and antimicrobial agents. In this context, works presented by Elchinger et al. [9,10] were very interesting since for the first time, protease such as neutrase, proteinase K, and alcalase were immobilized in chitosan film in order to propose to the scientific community novels highly efficient antibiofilm material with very good adhesives properties against nosocomial infecting microbial agent such as *Listeria monocytogenes, Pseudomonas aeruginosa* and *Staphylococcus aureus.*

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DOI: 10.19080/AIBM.2017.06.555684

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