Chitosan and chitosan-based nanoparticles for antibacterial control

F.M. Goycoolea

*1School of Food Science and Nutrition. University of Leeds. Woodhouse Ln. Leeds, LS2 9JT, United Kingdom*

Antimicrobial resistance (AMR) is a rampant global problem that demands novel approaches alternative to the use of antibiotics to fight pathogenic microorganisms. There has been substantial research undertaken on the antimicrobial properties of chitosan. However, systematic studies are needed that address the role of the structure of chitosan and whether applied as a polymer or as a carrier of other antimicrobial payloads. In a series of collaborative studies, we have aimed to investigate the antibacterial activity of chitosans of varying structural characteristics, namely Mw, degree of acetylation (DA), and pattern of acetylation (PA). We have addressed the role of these properties on the antibacterial activity against *E. coli* and *Pseudomonas syringae* of relevance in food, health and agriculture. We have also studied the quorum sensing (QS) inhibition (or “quorum quenching”) and biofilm inhibitory activity for chitosan-based nanoparticle and nanocapsules formulations. The average hydrodynamic diameter of these systems ranges from d.~150 – ~270 nm and the -potential ~+20 – ~+50 mV. To this end, we have examined both blank and bioactive loaded systems. We have demonstrated experimentally and using computational simulations, that drug-free chitosan-based oil-core nanocapsules bind “stoichiometrically” to a *E. coli* Top 10 GFP QS reporter strain [1,2]. This is the consequence of bacterial aggregation while reducing the QS activity [2]. Ionotropic and covalent co-gelled chitosan nanoparticles exhibit similar bioactivity [3,4]. Different type of phytochemicals such as cinnamaldehyde [1,5], baicalein, quercetin and naringenin [6-8], have been loaded in chitosan-based nanocapsules. Also, novel natural and synthetic compounds have been screened and identified with potent quorum quenching activity [9-11]. Our results consistently show that the association of different types of bioactive compounds in nanoparticles results in the reduction and modulation of the bacterial network communication via quorum quenching and possibly also by enhancement of the anti-biofilm activity. Block-PA chitosan modified enzymatically showed stronger antibacterial activity than the chemically N-acetylated random-PA polymer against the Gram-negative bacterium *Pseudomonas syringae* in liquid culture, while both chitosans were equally active against the biofilm-forming Gram-positive bacterium *Bacillus licheniformis*. We have compared the antibacterial activity of conventional chitosans with a random distribution of N-acetyl glucosamine residues and block-PA chitosans against and found that it is inverselyrelated to the DA. However, the longer blocks of glucosamine residues in block-PA chitosans, confers them stronger antibacterial activity [12].

These findings contribute towards a better understanding on the role of the structure of chitosan and chitosan-based nanomaterials on its antibacterial and QS-inhibition activity, of relevance in the future development of innovative formulations for use in food, medicine and agriculture.

**References**

[1] Vila-Sanjurjo *et al*. (2016) *biorXiv*. Preprint <https://doi.org/10.1101/074369>

[2] Qin *et a*l. (2017) *Colloids and Surfaces B: Biointerfaces*.149, 358-368. <https://doi.org/10.1016/j.colsurfb.2016.10.031>

[3] Vila-Sanjurjo *et al.* (2019) *J. Colloid. Interface Sci.*, 556: 592-605. <https://doi.org/10.1016/j.jcis.2019.08.061>

[4] Vila-Sanjurjo *et al*. (2020) *J. Colloid. Interface Sci.*, 578: 171-183. <https://doi.org/10.1016/j.jcis.2020.05.075>

[5] Qin *et al*. (2017) *Colloids and Surfaces B: Biointerfaces*. 169: 453-461. <https://doi.org/10.1016/j.colsurfb.2018.05.054>

[6] Omwenga *et al*. (2018) *Colloids and Surfaces B: Biointerfaces*. 164: 125-133. [https://doi.org/10.1016/j.colsurfb.2018.01.019](https://doi.org/10.1016/j.carbpol.2016.05.014)

[7] Qin *et a*l.(2020) *Bioorg. Chem.* 98, 103698. <https://doi.org/10.1016/j.bioorg.2020.103698>

[8] Nguyen *et al.* (2022) *Colloids and Surfaces B: Biointerfaces.* 211: 112281. <https://doi.org/10.1016/j.colsurfb.2021.112281>

[9] Qin *et al* (2020), *Pharmaceuticals* 13, 263; <https://doi:10.3390/ph13090263>

[10] Kaur *et a*l. (2015) *Front. Microbiol*. 07/2017. [https://doi.org/10.3389/fmicb.2015.00832](https://doi.org/10.1016/j.bioorg.2020.103698)

[11] Collado *et al*. (2020) *Biomimetics*. 5, 36 https://doi.org/10.3390/biomimetics5030036

[12] Sreekumar *et al*. (2023) *Nature Comm.* 13, 7125 https://doi.org/10.1038/s41467-022-34483-3

*The research leading to these results has received funding from the European Union’s Seventh Framework Programme for research, technological development, and demonstration under grant agreement no. 613931.*