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O0434 Antimicrobial and oxygenating nonconventional nanotherapies for the management of chronic wound infections

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Background: Chronic wounds (CWs) are typically characterized by persistent tissue hypoxia, exacerbated inflammation, and impaired matrix remodeling. Moreover, CWs are often worsened by microbial infections, with antimicrobial therapies being hindered by emerging resistant strains.

The known benefits of nanotechnology combined with the advantages of antimicrobial properties of natural polysaccharides such as chitosan have paved the way for the development of new oxygen-based therapies to treat infected CWs. The specific aim of this work was to assess the antimicrobial effects of chitosan-based nanocarriers against bacteria.

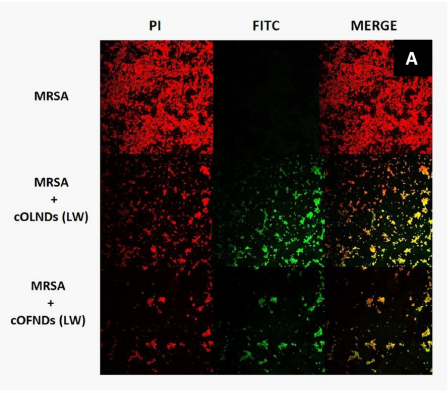
Materials/methods: Shell/core-structured oxygen nanocarriers [perfluoropentane (PFP)-cored nanobubbles and 2H,3H-decafluoropentane (DFP)-cored nanodroplets] were alternatively shelled with two chitosan molecules of different molecular weight [medium weight (MW) or low weight (LW) chitosan]. After manufacturing, MW chitosan-shelled oxygen-loaded nanobubbles (cOLNBs), as well as MW or LW chitosan-shelled oxygen-loaded nanodroplets (cOLNDs) were comparatively characterized for morphology and physico-chemical properties by microscopy and dynamic light scattering, respectively. *In vitro* oxygen releases from cOLNBs and cOLNDs or from control oxygen saturated-solution were comparatively measured through an oxymeter. Their biocompatibility and their ability to promote wound healing in human hypoxic skin cells were challenged by using keratinocyte, fibroblast, and/or endothelial cell lines. Their antimicrobial activity was investigated towards methicillin-resistant *Staphylococcus aureus* (MRSA) and *Streptococcus pyogenes* clinical strains and measured by monitoring bacterial growth over time. For each microorganism, the mechanical interaction with nanocarriers was also assessed by confocal microscopy.

Results: All carriers displayed spherical morphology, cationic surfaces, and diameters in the nanometer range.

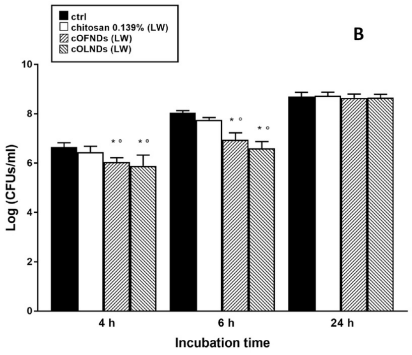
rom OLNBs. Additionally, LW cOLNDs displayed lower toxicity to skin cells than MW chitosan-shelled carriers. Compared to MW cOLNBs/cOLNDs, LW cOLNDs displayed in general similar or better efficacy in promoting wound healing under hypoxic conditions and in inhibiting both staphylococcal and streptococcal growth, in a long-term manner as a consequence of early cellular internalization (Figure 1).

Conclusions: Based on these findings, LW cOLNDs appear to be the most promising nanocarriers among those tested here to be potentially employed as innovative, nonconventional, and cost-effective medical devices for the treatment of hypoxic and infected CWs.

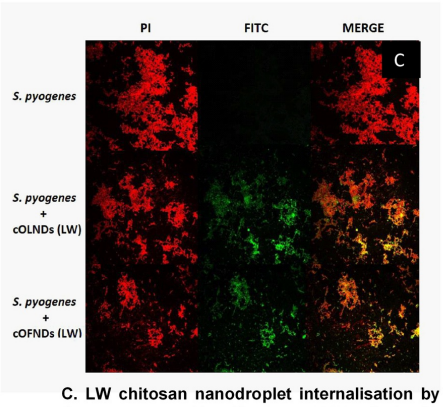
Figure 1



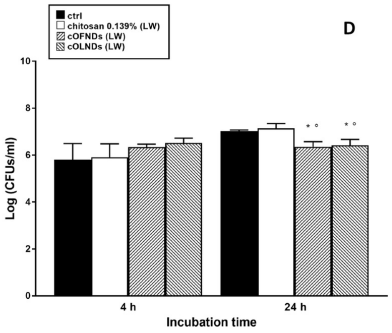
A. LW chitosan nanodroplet internalisation by MRSA. Magnification: 100X. Red: PI. Green: FITC.



B. Antibacterial activity of LW chitosan nanodroplets on MRSA.
*p <0.0001 *vs* controls; °p <0.05 *vs* LW chitosan solution.



C. LW chitosan nanodroplet internalisation by *S. pyogenes*. Magnification: 100X. Red: PI. Green: FITC.



D. Antibacterial activity of LW chitosan nanodroplets on *S. pyogenes*. *p<0.01 *vs* controls. °p <0.0001 *vs* LW chitosan solution.