Development of hydrogels containing protein-loaded PLGA nanoparticles for wound healing applications

Ana S. Macedo [a,b,c], Inês Duarte[b,c], Francisca Mendes[d], Salette Reis[a], Pedro Fonte [b, c, e, f,*]

[a] LAQV, REQUIMTE, Department of Chemical Sciences - Applied Chemistry Lab, Faculty of Pharmacy, University of Porto, Rua de Jorge Viterbo Ferreira, 228, 4050-313 Porto, Portugal
[b] iBB—Institute for Bioengineering and Biosciences, Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049-001 Lisboa, Portugal
[c] Associate Laboratory i4HB—Institute for Health and Bioeconomy at Instituto Superior Técnico, Universidade de Lisboa, Av. Rovisco Pais, 1049-001 Lisboa, Portugal
[d]Faculdade de Ciências, Universidade de Lisboa, Campo Grande, 1749-016 Lisboa, Portugal
[e] Center for Marine Sciences (CCMAR), University of Algarve, Gambelas Campus, 8005-139 Faro, Portugal
[f] Department of Chemistry and Pharmacy, Faculty of Sciences and Technology, University of Algarve, Gambelas Campus, 8005-139 Faro, Portugal
*Email: prfonte@ualg.pt

An effective treatment to improve life quality for patients suffering from wounds, and the astonishing budget spend for wound care, are what significantly drives the research for better wound healing (WH) alternatives (1). One promising strategy is to administer growth factors either pro-healing molecules and/or suppressors of elevated protease activity. However, due to their protein nature, they are easily degraded by the proteolytic environment in the wound bed, requiring frequent administrations. In this work, we suggest the use of insulin as a growth factor encapsulated in a multifunctional nanoparticle hydrogel delivery system to accelerate wound healing. PLGA nanoparticles were produced using a solvent emulsification-evaporation method based on a water-in-oil-in-water (w/o/w) double emulsion technique (2). The optimization of the hydrogel composition was achieved following a quality by design approach using chitosan (0.25, 0.5 and 0.75%), sodium alginate (1, 1.5 and 2%) and glycerin (5, 7.5 and 10%) and the number of freeze-thawing cycles (1, 2 and 3). Nanoparticles were characterized by dynamic light scattering and scanning electron microscopy, and hydrogels by FTIR. Insulin structure was evaluated by circular dichroism (CD). After the analysis of the formulation matrix, the sodium alginate was the variable with more statistical significance ($p<0.05$) in the zeta potential, viscosity and spreadability value, and no independent variable was statistically significant in the size of the nanoparticles. The results revealed that insulin structure was preserved upon encapsulation and production of the hydrogel. The association efficiency was above 90% for both formulations. The nanoparticles had a characteristic round shape and smooth surface shown by SEM. CD spectroscopy was performed showed two minima at 208.5 and 222 nm, which are distinct of the α-helix structure of the protein. A maximum was also observed at 197 nm. The CD spectra of the samples showed the that the insulin extracted from the hydrogel-nanoparticle formulations maintained its secondary structure and bioactivity (2). The results revealed that insulin structure was preserved upon encapsulation and production of the hydrogel and further characterization of the *in vitro* and *in vivo* bioactivity will be performed.

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References

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