Development of collagen nanoparticles for cartilage regeneration

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Introduction

Human articular cartilage is an avascular structure, which, when injured, presents significant hurdles to repair. Many cartilage repair methods have been developed so far, however, many of them are very invasive and do not bring a long-term solution. The use of nanotechnology and tissue engineering in cartilage regeneration has been shown to be very promising for the treatment of cartilage diseases.[1] Compounds from marine resources have been studied as raw materials for the construction of drug delivery systems for biomedical applications and tissue engineering due to several properties, such as biocompatibility, biodegradability and specific capacity to target and mimic human natural tissues.[2]

In this work, collagen from marine resources (jellyfish and blue shark) was used to produce nanodelivery systems for the incorporation of growth factors (GFs) for cartilage regeneration.

Experimental

The collagen nanoparticles preparation was based on a method of emulsifying and cross-linking of native collagen assisted by ultrasonication.

After the synthesis, the NPs suspensions were freeze-dried and ressuspended for further characterization and cytotoxicity assessment.

Results

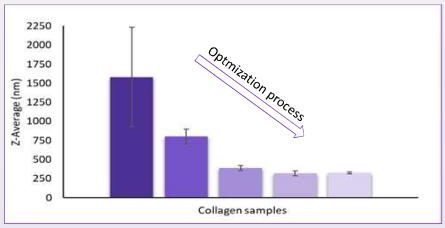

Figure 1 – Size optimization. Dynamic Light Scattering measurements.

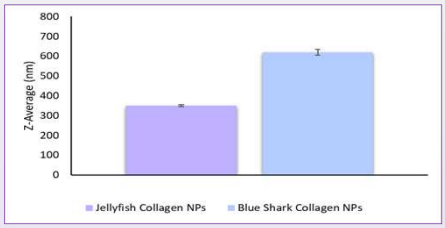

Figure 2 - Jellyfish and Blue Shark Collagen nanoparticles average size. All data represent the mean ± standard deviation (n = 3).

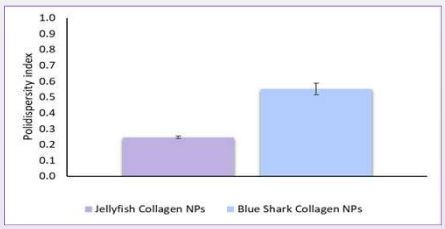

Figure 3 - Jellyfish and Blue Shark Collagen nanoparticles polydispersity index. All data represent the mean ± standard deviation (n = 3).

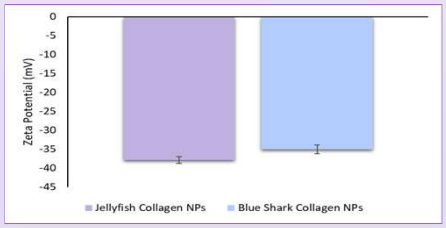

Figure 4 - Jellyfish and Blue Shark Collagen nanoparticles zeta potential. All data represent the mean ± standard deviation (n = 3).

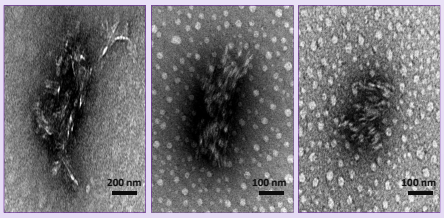

Figure 5 – Transmission Electron Microscopy Images of Jellyfish Collagen nanoparticles.

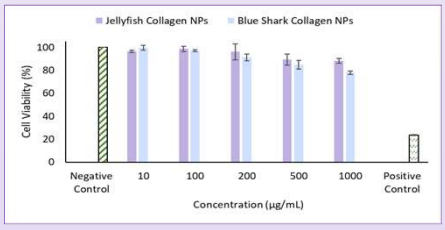

Figure 6 - Cytotoxicity evaluation of Collagen nanoparticles after 24h of exposition to hMSC cells (Resazurin reduction assay). All data represent the mean ± standard deviation (n = 4).

Conclusions

The **jellyfish collagen NPs** had approximately **300 nm** while **blue shark collagen NPs** reached almost **600 nm**, with **jellyfish collagen NPs** having a **lower PDI** as well as slightly **more negative charge**, enabling a repulsive effect between NPs, **avoiding** their **aggregation** and granting a **higher stability** in aqueous dispersions.

TEM confirm that **jellyfish collagen NPs maintained the triple helix conformation of collagen** and revealed images of NPs with similar size range as the above reported values obtained by DLS.

The **resazurin reduction assay** confirms that nanoparticles are **non-cytotoxic**, after 24h of exposition to hMSC cells, at least at the concentrations tested (from 10 to 1000 µg/mL of collagen). The **ideal concentration** that can be used for further efficacy assays without compromising cells viability is around **100 µg/mL.**

References

1. Lim, E.H.; Sardinha, J.P.; Myers, S. *Arch Plast Surg.* **2014**, 41:231–40.
2. Gao, Y.; Li, B.; Kong, W.; *et al. Int J Biol Macromol.* **2018**, 118:2014–20.

Acknowledgments

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