S2.4-O1

Green nanomedicine and sustainable drug-releasing systems for regenerative medicine.

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Abstract

Environmental sustainability is a key challenge driven by an increasing consumption of natural resources. Waste materials from agriculture are promising as renewable resources due to their high availability, renewability and low-cost. Hence, more efforts are needed to the study of plant-derived materials for biomedical and pharmaceutical applications. Particularly, efficient and safe nanocarriers are demanded to exploit RNA therapies for new applications, e.g. cardiac regeneration[1]. Zein is a by-product of corn industries, representing almost 50% of corn protein. Zein nanoparticles (ZNPs) have been mostly used for the release of lipophilic drugs. Only few recent studies have proposed ZNPs for plasmid DNA release[2,3]. Pectin is a biocompatible low-cost polysaccharide extracted from citrus peel waste, promising for regenerative medicine. However, it lacks bioactivity and proper biodegradability.
Herein, we designed sustainable and efficient ZNPs for microRNA (miRNA) therapy to be embedded into injectable and printable chemically-modified pectin/gelatin hydrogels for controlled release.
Green ZNPs loaded with miRNAs were prepared by a novel method able to minimize the use of organic solvents. Physicochemical (DLS analysis, encapsulation efficiency, release kinetics) and biological (*in vitro* biocompatibility, and uptake efficacy using siRNA-Cy5 loaded ZNPs) properties of ZNPs were analyzed. Pectin was modified to introduce reactive groups and obtain crosslinkable hydrogels by blending with gelatin. Optimal pectin/gelatin compositions were selected by rheological characterizations and *in vitro* cell tests. ZNPs loaded with curcumin were also produced to provide anti-oxidant and anti-inflammatory effects.
ZNPs/miRNA showed higher encapsulation efficiency than previous ZNPs/plasmid DNA reported in the literature[2,3] (more than 90% compared to 40-65%) and high biocompatibility. Anti-oxidant activity of ZNPs/curcumin was assessed by *in vitro* cell tests. Optimised pectin/gelatin hydrogels showed injectability and printability and supported cell viability.
In conclusion, green ZNPs were optimized for the delivery of small oligonucleotides (miRNAs, siRNAs) and anti-oxidant agents (curcumin). In the future, ZNPs will be embedded into pectin/gelatin hydrogels, obtaining new green and efficient controlled drug delivery systems for advanced therapies.

Acknowledgement: This work was supported by Research and Innovation NOP 2014-2020 for Doctoral Research programmes with specific reference to Action IV.5 “PhD programmes on sustainability-based topics” and the European Research Council (ERC) under the European Union’s Horizon 2020 research and innovation programme (BIORECAR, grant agreement No. 772168).
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