Novel drug delivery systems for regenerative medicine applications for perspective valorization of agricultural-derived waste products

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Environmental sustainability is a key challenge nowadays. Agricultural-derived waste materials are promising as renewable resources for biomedical and pharmaceutical applications, thanks to their availability, renewability and low-cost. Among them, zein is a protein extracted from corn while pectin is a polysaccharide extracted from plant walls. Herein, our ambition is to exploit green polymers to address one of the main challenges in drug delivery, the need for optimal carriers for RNA therapy. So far zein nanoparticles (ZNPs) have been mostly used for lipophilic drug release. Only few recent studies have proposed ZNPs for plasmid DNA release. Pectin is easily tunable for hydrogels, but it lacks bioactivity and *in vivo* degradability.
Therefore, we designed sustainable and efficient ZNPs for microRNA (miRNA) and curcumin delivery and their combination with an injectable pectin/gelatin hydrogel to achieve safe, efficient and controlled drug release.
ZNPs loaded with miRNAs were prepared by a novel method that minimizes the use of organic solvents. ZNPs/miRNA showed higher encapsulation efficiency (90-95%) than previous ZNPs/plasmid DNA reported in the literature (40-65%) and high biocompatibility towards human fibroblasts. In parallel, ZNPs were loaded with curcumin, a natural antioxidant able to enhance miRNA therapeutic efficacy. ZNPs/curcumin were produced through nanoprecipitation and antioxidant activity was assessed by reduced ROS production after hydrogen peroxide-induced oxidative stress. Pectin was oxidized to introduce reactive groups and obtain chemically crosslinked hydrogels through Schiff-base formation with modified-gelatin. Pectin/gelatin hydrogels showed tunable rheological properties (G' 50-300 Pa) by varying pectin:gelatin ratio (30:70-70:30). All compositions showed high injectability and supported fibroblast viability. Preliminary assessments of ZNPs embedding into injectable hydrogels are under investigation.
In conclusion, novel green ZNPs were optimized for the delivery of miRNA and curcumin. In the future, ZNP release behaviour from pectin/gelatin hydrogels will be further characterized, validating new green and efficient drug delivery systems for advanced therapies.

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