

Sustainable drug delivery systems for regenerative medicine applications

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Environmental sustainability is a critical concern due to the rising consumption of finite natural resources. Agricultural-derived waste materials are promising as renewable resources for biomedical and pharmaceutical applications, due to their availability, renewability and cost-effectiveness. Therefore, 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. Among these environmentally friendly biomaterials, zein has emerged as a promising candidate. Indeed, being the main protein of corn, zein may be derived from agricultural waste. Furthermore, it is biocompatible, biodegradable and FDA approved for medical use. To date, zein nanoparticles (ZNPs) have been mostly used for the delivery of lipophilic drugs, with only few studies investigating their potential for DNA release^{1,2}. Therefore, we designed sustainable and efficient ZNPs for microRNA (miRNA) and curcumin delivery.

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%) compared to previous ZNPs/plasmid DNA reported in the literature (40-65%)^{1,2}, along with high biocompatibility and uptake by human fibroblasts after 24h of culture. In parallel, ZNPs were loaded with curcumin, a natural antioxidant and anti-inflammatory compound derived from *Curcuma longa* plants. Literature reports that curcumin is able to enhance miRNA therapeutic efficacy since it mitigates oxidative stress. ZNPs/curcumin were produced through nanoprecipitation and results showed high yield (90%) and encapsulation efficiency (80%). High biocompatibility was reported after 24h of culture with human fibroblasts and antioxidant activity was assessed by reduced ROS production after H₂O₂-induced oxidative stress.

In conclusion, novel green ZNPs were optimized for the delivery of different drugs, such as miRNA and curcumin. In the future, ZNPs loaded with therapeutic miRNA and curcumin will be delivered *in situ* through a hydrogel depot for advanced regenerative therapies³.

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References:

- [1] Regier et al., J. Nanobiotechnology, 10, 2012
- [2] El Sharkawi et al., J. Drug Target., 25, 2017
- [3] Paoletti et al., Front. Bioeng. Biotechnol., 8, 2020