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Polysaccharide nanoparticles: Unveiling applications in mucosal drug delivery

Nanomedicines as a whole have been gathering tremendous attention. Many of the proposed formulations are based on natural polymers and, among these, polysaccharides have been a privileged category. They are particularly suited for nanoparticle preparation, offering advantages like high flexibility and propensity to comply with requisites of biocompatibility and biodegradability. Nevertheless, while some polysaccharides have been exhaustively explored, such as chitosan and hyaluronic acid, many others remain quite unknown [1]. The reduced dimensions of nanoparticles provide increased surface-to-volume ratio and maximal epithelial contact, permitting the concomitant protection of the encapsulated therapeutic agents from pH and enzymes. Nanoparticles have been frequently proposed as vehicles of drugs to the lungs, taking benefit of the characteristics provided by the lung route for either systemic or local delivery. Importantly in this regard, nanoparticles have demonstrated the ability to delay or avoid uptake by alveolar macrophages an effect that is more efficient for sizes below 500 nm [2]. Naturally, considering the small size of nanoparticles, inhalation requires a strategy to provide suitable aerodynamic properties. The microencapsulation of nanoparticles has been proposed for this end [3]. Applications of nanoparticles in other routes are also proposed often, particularly in oral delivery.

Considering the need to explore the potential of less explored polysaccharides, we have developed several nanoparticle formulations (Figure 1) based on polysaccharides such as pullulan, locust bean gum, chondroitin sulfate and fucoidan. All nanoparticles were produced using the method of polyelectrolyte complexation, which requires the presence of charged groups in the polymers. Therefore, some of the polysaccharides (pullulan, locust bean gum) had to undergo chemical modification to provide the necessary charges.

The physicochemical characteristics of the developed nanocarriers were easily modulated according to their composition, resulting in suitable characteristics for mucosal administration. Sizes around 180 – 300 nm were obtained for the various formulations and zeta potential shifted from strongly negative (-35 mV) to highly positive (+60 mV), depending on particle composition. Insulin and bovine serum albumin were associated with efficiencies up to 60% to several carriers proposed for lung delivery of biopharmaceuticals. Additionally, ovalbumin and an extract of *Salmonella* Enteritidis were used as model antigens in locust bean gum nanoparticles proposed for oral mucosal vaccination (association efficiencies up to 30%). *In vitro* biocompatibility assays in oral and pulmonary epithelial cells generally evidenced absence of toxicological effect of nanoparticles.

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References

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Figures

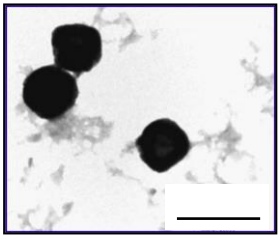

Figure 1: TEM microphotograph of representative polysaccharide-based nanoparticles produced by polyelectrolyte complexation.