CHITOSAN-BASED NANOCAPSULES: EFFECT OF THE DEGREE OF ACETYLATION AND Mw ON THE PHYSICOCHEMICAL CHARACTERISTICS AND STABILITY BEHAVIOR

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Colloidal nanocapsules (NCs) comprised by an oily core, lecithin and a hydrophilic coat of chitosan (CS) have been a focus of extensive research due to their promising potential as a drug delivery platform for transmucosal administration of peptides and lipophilic drugs [1-3]. In this regards, it has been recognized that CS significantly improves the ability of NCs to transport drugs accross the corneal epithelium [1]. Further evidence has shown that CS–coated NCs are excellent prototypes for the nasal [2] and oral [2,3] delivery of biologically active peptides, such as salmon calcitonine (sCT).

In this study, we have investigated the role of the degree of N–acetylation (DA) of chitosan (CS) of low and high M_w (~10 and ~110 kDa denoted here as LDP CS and HDP CS, respectively), on the physicochemical properties and biological stability of CS-coated NCs. The harnessed NCs had a rather constant average particle size (~150-200 nm) and spherical morphology, irrespective of CS's DA and M_w. The surface charge zeta potential (ζ) was invariably highly positive and exhibited a monotonic decreasing trend as the CS's DA increased and greater ζ values were recorded for HDP CS–coated NCs than for LDP CS-coated ones. We hypothesize that LDP CS arranges itself at the NC's surface in a flat conformation, while HDP CS does it forming loop-like ("train") assemblies. Synchrotron SAXS studies have revealed that diffraction peaks appear only in the systems coated with CS, while not in the naked nanoemulsión (Fig.1). The calculated Bragg distances for a series of NCs varied in the range (~55 – ~67 Å) and appeared to increase with CS's DA irrespective of its M_w. As an interpretation we venture to suggest that CS's hydrophobic domains perturb the phospholipid membrane by the penetration of of CS into the oily phase, thus effectively increasing the distance between polar lecithin heads.

In general, all systems showed high stability during incubation in MEM and ECGM cell culture media, regardless of CS type, while in RIPM-1640, only HDP27 and HDP56 and all LDP CS did exhibit so. The influence of the different conformations of CS adsorbed onto the oily core along with subtle differences in the composition of the biological media, are believed to influence the stability in biological conditions.

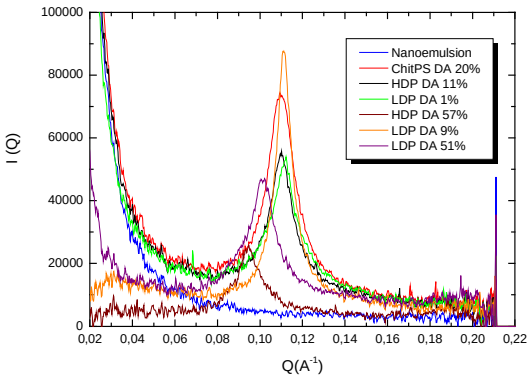

Fig. 1. SAXS scattering curve for CS-coated nanocapsules and naked nanoemulsión in water at 25ºC

The results of this work reveal that varying CS's characteristics allows fine tuning of the physical properties and biological stability of CS–coated nanocapsules. The significance of these properties on the biopharmaceutical performance of these systems is yet to be fully understood.

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