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Self-assembled hyaluronic acid nanoparticles: effect of molecular weight and two different chemical approaches

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INTRODUCTION: Natural polyssacharides, such as hyaluronic acid (HyA) have been widely used for biomedical and pharmaceutical applications. Hya has multiple functional groups available for chemical conjugation that can convert HyA into nano-sized carriers. We prepared self-assembled HyA nanoparticles by two different chemical derivatization techniques and used two different molecular weights HyA. Our aim was to compare these two techniques and evaluate the influence of molecular weight in the properties of HyA nanoparticles.

METHODS: HyA must be rendered soluble in non-aqueous solvents by exchangingthe sodium ion with a lipophilic ion – Tetrabutylammonium - using a cationic exchange resin. One of the chemical derivatization techniques used involve the transesterification of HyA-TBA with glycidyl methacrylate (GMA) in the presence of 4-dimethylaminopyridine (DMAP), as described by Oudshoorn et al [1]. Then, HyA-MA reacts with 1-hexadecanethiol by a Michael addition in the presence of Triethylamine (Fig. 1) [2].

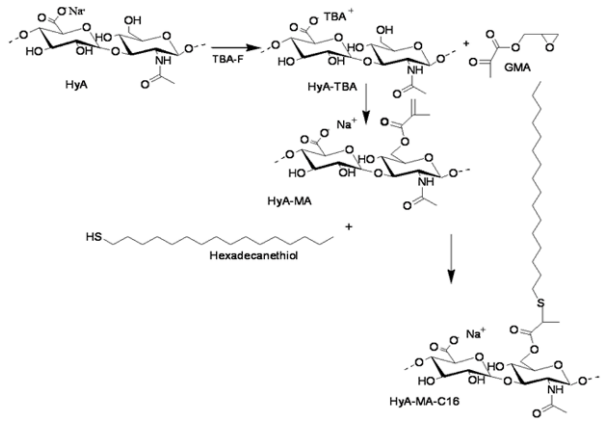

Fig. 1: Synthesis of Hya-MA-C16.

The other technique employed for the synthesis of nanoparticles was the chemical conjugation with 1-hexadecylamine in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) and N-hydroxysuccinime(NHS) (Fig. 2) [3]. In both techniques, the samples were dyalised firstly against a sodium chloride solution to remove the TBA ions and then against deionised water. The two chemical derivatizations were performed using both a low (7460 Da) and a high molecular weight HyA (0.5-2 MDa). The samples obtained were characterized by H-NMR spectroscopy, dynamic light scattering (DLS) and UV-VIS spectroscopy of a hydrophobic compound (curcumin) that asses the existence of hidrofobic moieties.

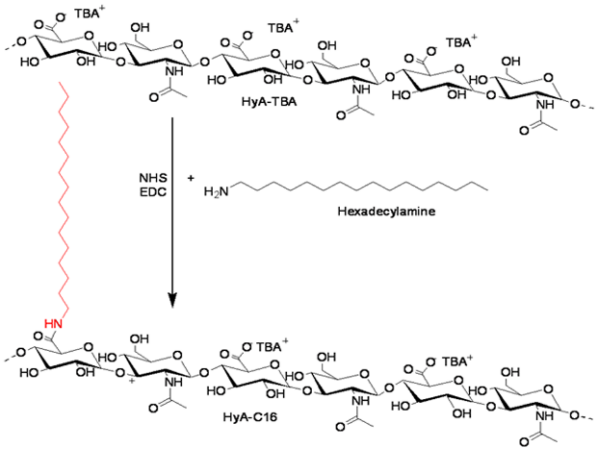

Fig. 2: Synthesis of HyA-C16

RESULTS: For the synthesis of HyA-MA-C16, we tested different molar ratios of grafting moiety: HMW/LMW and obtained different substitution degrees. Regardless of that, both materials presented good stability in aqueous solution at different pH through a period of nearly two months. The DLS analysis revealed a small difference (170 nm HMW: 140 nm, LMW) in the average size of the nanoparticles. The HMW HyA nanoparticles were able to incorporate a higher percentage of curcumin. A comprehensive characterization of both kinds of nanoparticles will be presented.

DISCUSSION & CONCLUSIONS: The chemical conjugation revealed a simpler approach with a more tailored degree of substitution.

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