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Molecular weight influence of superficially exposed hyaluronic acid on nanoparticles cell internalization kinetics

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In the engineering of nanodevices intended for active tumor targeting, hyaluronic acid (HA) plays a significant role due to its tropism for CD44 and RHAMM receptors [1,2]. Here, it has been investigated the molecular weight influence of HA on cell internalization kinetics. Biodegradable poly(lactic-co-glycolic acid)-based nanoparticles (NPs) have been decorated with HA at three different molecular weights: 200, 800 and 1437 kDa (NP formulations were named HA2, HA8 and HA14, respectively). NPs were produced by nanoprecipitation with no chemical reaction. The produced NPs were characterized for their morphology, z-potential and thermal properties. Moreover, NP internalization kinetics CD44-overexpressing breast carcinoma cells (HS578T) were evaluated, using healthy mouse fibroblast (L929) cells as a control. Finally, experimental results were compared with the numerical simulations obtained with a kinetic internalization model based on a cell membrane adsorption-desorption pseudo-stoichiometric balance [3]. NPs with a mean size < 200 nm and strongly negative ZP values were obtained, thereby indicating HA arrangement on NP surface. The results of thermal analysis show that, for PLGA and poloxamers, glass transition temperature (Tg) is lower than that of PLGA, suggesting a plasticizing effect of poloxamers in the organic blend. Results of cell internalization showed that uptake by cancer cells was promoted for all three formulations, with an approximately 2, 2.3 and 1.3-fold increase for HA2, HA8 and HA14 NPs, respectively. HA8 NPs were internalized faster and more effectively than HA2 and HA14 NPs, confirming that the differences in HA chain length can affect the binding and the internalization rate.

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