Cationic Polymeric Nanoparticles for Biomedical Applications

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Chronic inflammation diseases are ranked as the first cause of morbidity and mortality worldwide. They also cause long-term suffering, disability reduction on the quality of life and high cost to the society. Actual anti-inflammatory drugs present a limited effectiveness due to their hydrophobicity, low bioavailability, and lack of specific targeting. Moreover, anti-inflammatory treatments have associated several side effects limiting their safe use in the clinic. Our group has dedicated great efforts to the preparation of more efficient derivatives of these drugs: drug conjugates [1], drug combinations showing synergistic effects [2] and nanometric drug delivery systems (NDDS) [3].

In this presentation the application of polymer nanoparticles as drug delivery systems for the treatment of inflammatory diseases will be presented. In particular, non-steroidal anti-inflammatory drugs, NSAID (*i.e.* naproxen or ketoprofen) were chemically modified and the methacrylic derivative of the correspondent NSAID was prepared (*i.e.* HNAP or HKT, respectively). These synthetic monomers were used for the synthesis of polymer drugs with a pseudo-gradient microstructure by free radical copolymerization with 1-vinylimidazole (VI). These amphiphilic pseudo-block copolymers self-assembled in aqueous media by nanoprecipitation forming nanoparticles with spherical shape, nanometric size (between 100 and 200 nm) and positive surface charge. These physico-chemical properties demonstrated non-toxicity and a fast sequestration by macrophages which favors accumulation and retention at inflamed areas.

These **cationic anti-inflammatory NPs** have not only been studied as DDS [2,3], but also have been immobilized on surfaces by layer-by-layer (LbL) methodology [4] to avoid foreign body reaction, have been coated with hyaluronic acid in order to achieve active targeting toward CD44 receptor (overexpressed in M1 pro-inflammatory macrophages and cancer stem cells) [5], have been incorporated in self-assembling gels to obtain scaffolds with anti-inflammatory properties and have been used as genetic vetors.

References

[1] P. Suárez, L. Rojo, A. Gonzalez-Gomez, J.S. Román *Macromolecular Bioscience* 2013, **13**: 1174-1184
[2] E. Espinosa-Cano, M.R. Aguilar, Y. Portilla, D.F. Barber, J. San Roman. *Macromol. Biosci.* 2020, **20**: 2000002
[3] E. Espinosa-Cano, M.R. Aguilar, Y. Portilla, D.F. Barber, J. San Roman. *Pharmaceutics* 2020, **12**: E723
[4] H. AlKhoury, E. Espinosa-Cano, M.R. Aguilar, J. S. Roman, F. Syrowatka, G. Schmidt, T. Groth. *Biomacromolecules*, 2019, **20**: 4015-4025
[5] Eva Espinosa-Cano, Miguel Huerta-Madronal, Patricia Camara-Sánchez et al. *Materials Science & Engineering C* 2021, **124**: 112024