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Microfluidic-based development of thermo-responsive porous magnetic microparticles for cancer treatment

Luis F. Bravo-Duque, Jesús Gracia-Mora, Luis F. Olguin-Contreras, Guillermina Gonzalez-Mancera and **Josefa Bernad-Bernad**
National Autonomous University of Mexico (UNAM), Mexico

Multiparticle polymer systems (nano or micrometric) have gained great importance within the development of drug delivery systems (DDS), due to their great versatility and biocompatibility. Conventional manufacturing techniques are generally based on the formation of simple or multiple emulsions to use the drops as a template. The polymer particles prepared by these conventional methods exhibit a great variation between batch and batch in their physicochemical properties, such as average particle size, size distribution, surface charge and release profile. A manufacturing alternative is the miniaturization of the emulsification process by using microchannels to control the droplet size and their size distribution. The handling of fluids with microchannels is also called Microfluidics. The aim of this project is developed a multifunctional system for a more efficient treatment of tumors, obtained with a robust manufacturing process to control the physicochemical properties of the particles and thus reduce the variation in the manufacturing batches. We have obtained a multiparticle polymeric system with magnetic properties for the treatment of tumors, manufactured with microfluidic devices. This system consists of magnetic iron oxide nanoparticles embedded in porous polymer microparticles of poly-ε-caprolactam (PCL) and coated with a temperature sensitive co-polymer of poly-N-isopropylacrylamide (pNIPAM), N,N-Methylenebisacrylamide (MBA) and methacrylc acid (MA). The polymer coat has a transition phase temperature around 43°C where the polymer collapse and the microparticle inside is exposed. We pretend load Methotrexate (MTX) within the particles pores and by applying an alternating magnetic field (AMF), the nanoparticles will generate an increase in the temperature of the system resulting in the MTX release. The magnetic nanoparticles will also serve to do an *in vivo* monitoring of the system and tumor by Magnetic Resonance Imaging (MRI).

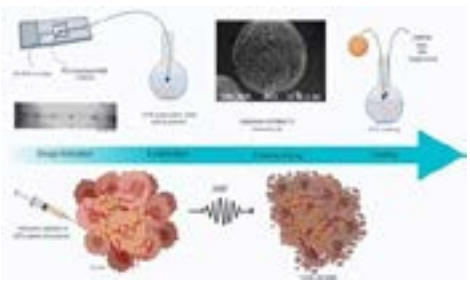

Figure 1: Graphic representation of the fabrication of Porous Microparticles and their coating with thermos-responsive polymer (above arrow), and the effect of AMF after intratumor administration (below arrow).

Recent Publications

1. Guisasola, E. *et al.* Beyond Traditional Hyperthermia: *In Vivo* Cancer Treatment with Magnetic-Responsive Mesoporous Silica Nanocarriers. ACS Appl. Mater. Interfaces 10, 12518–12525 (2018).
2. Park, J. H., Han, C. M., Lee, E. J. & Kim, H. W. Preparation of highly monodispersed porous-channeled poly(caprolactone) microspheres by a microfluidic system. Mater. Lett. 181, 92–98 (2016).

3. Alsuraifi, A., Curtis, A., Lamprou, D. A. & Hoskins, C. Stimuli responsive polymeric systems for cancer therapy. Pharmaceutics 10, 1–17 (2018).
4. Li, J. *et al.* Fabrication of uniform-sized poly-ε-caprolactone microspheres and their applications in human embryonic stem cell culture. Biomed. Microdevices 17, (2015).
5. Kosinski, A. M., Brugnano, J. L., Seal, B. L., Knight, F. C. & Panitch, A. Synthesis and characterization of a poly (lactic-co-glycolic acid) core + poly(N-isopropylacrylamide) shell nanoparticle system. Biomatter 2, 195– 201 (2012).
6. Tarabukina, E. *et al.* Thermoresponsive properties of N- isopropylacrylamide with methacrylic acid copolymer in media of different acidity. Macromol. Res. 25, 680–688 (2017).

Biography

Luis F. Bravo-Duque has exposed interest for Pharmaceutical Technology, Physical Chemistry, Cancer Research, and Drug Delivery System research. He has collaborated in both, privet investment and academic institution, research projects to develop Drug Delivery Systems. One of them was the development and manufacture of an oral polymeric multiparticle system, for the release of a chronic use drug against obesity. Also, he was teacher assistant in the Pharmaceutical Technology Laboratory at the Faculty of Chemistry, where he supported in the realization of experimental practices, focused on the integration of knowledge of sterile liquid pharmaceutical forms and modified release systems. Currently he is studding a Science Master at the National Autonomous University of Mexico.

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