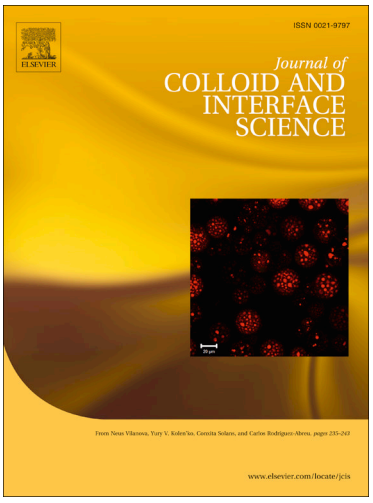

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Effects of Chemical and Processing Variables on Paclitaxel-Loaded Polymer Nanoparticles Prepared Using Microfluidics

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Abstract

For paclitaxel (PAX)-loaded polymeric nanoparticles PNPs prepared in a two-phase gas-liquid microfluidic reactor, the effects of microfluidic flow rate on the multiscale structure, loading efficiency and release rate are determined for three different copolymer compositions and two orders of magnitude variation in the PAX loading ratio. All experiments are carried out in the limit of low drug-to-polymer loading ratios ($r \leq 0.01$, w/w). In this range of r, PCL crystallinity, loading efficiency and release rate are not significantly affected by the amount of PAX dissolved in the core. These results are in sharp contrast to microfluidic PNPs prepared in a range of high loading ratios ($r \geq 0.1$), where the amount of added PAX has a strong influence on the multiscale structure and properties of drug delivery PNPs. For the case of $r = 0.01$, we show that flow rate strongly affects PNP morphologies for all three block copolymer compositions. For the shortest and longest PCL block lengths, the relative number of cylindrical morphologies increases and then decreases with increasing flow rate, whereas for the intermediate PCL block length, the number of cylinders steadily increases as the flow rate increases. Internal PCL crystallinities and PAX loading efficiencies show similar trends, both parameters increasing and decreasing with increasing flow rate for the extreme PCL block lengths and steadily increasing for the intermediate PCL block length. PAX release profiles indicate a marked slowing of PAX release as either the PCL block length or the microfluidic flow rate increase. Working in the limit of low loading ratio, this work provides clarity on separating the relative effects of copolymer composition and processing along with perturbations caused by the molecular cargo on the structure and function of drug delivery PNPs. These critical insights thus inform controlled microfluidic preparation of more medically-relevant PNPs at higher therapeutic loading levels.