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RESEARCH PAPER

Mass production of highly monodisperse polymeric nanoparticles by parallel flow focusing system

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Abstract Nanoparticles can be prepared through nanoprecipitation by mixing polymers dissolved in organic solvents with anti-solvents. However, due to the inability to precisely control the mixing processes during the synthesis of polymeric nanoparticles, its application is limited by a lack of homogeneous physicochemical properties. Here, we report that this obstacle can be overcome through rapid and controlled mixing by parallel flow focusing outside the microfluidic channels. Using the nanoprecipitation of methoxyl poly-(ethylene glycol)–poly-(lactic-co-glycolic acid) (MPEG–PLGA) block copolymers as an example, we prove that our parallel flow focusing method is a robust and predictable approach to synthesize highly monodisperse polymeric nanoparticles, and demonstrate that it improves the production speed of nanoparticles by an order of magnitude or more compared with previous microfluidic systems. Possible aggregation on the surface of PDMS wall and clogging of microchannels reported previously were avoided in the synthesis process of our method. This work is a typical application combining the advantages of microfluidics with nanoparticle technologies, suggesting that microfluidics may find applications in the development and mass production of polymeric nanoparticles with high monodispersity in large-scale industrial production field.

Keywords Mass production · Polymeric nanoparticles · High monodispersity · Microfluidics · Parallel flow focusing

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1 Introduction

Over the past decade, microfluidics has attracted enormous attention in different application fields because of its various advantages over traditional technologies (deMello and deMello 2004; deMello 2006) such as precise operations of fluid, high mixing speed, and massively parallel processing with very small amounts of reagents. One of the application field is the development of inorganic nanoparticles (Shestopalov et al. 2004; Chan et al. 2005; Wagner and Kohler 2005; Krishnadasan et al. 2007; Lo et al. 2010; Jahn et al. 2010) and microparticles (Xu et al. 2005) which has been greatly promoted by the combination of microfluidics and particle technologies. In the past few years, there has been an increasing interest in the development of organic nanoparticles by microfluidics, especially polymeric nanoparticles, for drug delivery (Soppimath et al. 2001; Peer et al. 2007; Davis et al. 2008; Farokhzad and Langer