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Controlled Synthesis of Water-Dispersible Conjugated Polymeric Nanoparticles for Cellular Imaging

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Abstract: Fluorescent water-dispersible conjugated polymeric nanoparticles (WDCPNs) were synthesized for cellular imaging. Sonogashira polycondensations of various combinations of symmetric monomers (A_x+B_y , $x>2$, $y\geq 2$) were firstly conducted in confined nanoreactors to produce soluble conjugated polymeric nanoparticles (SCPNs) with narrow size distribution and tunable fluorescence emission. The subsequent click reaction between the terminal alkyne groups in the SCPNs and azide terminated PEG₁₀₀₀ endowing good dispersity of the WDCPNs in aqueous solutions and stable fluorescence emission. The WDCPNs exhibited bright fluorescence in cellular imaging and showed good biocompatibility as revealed by cell variability assay, demonstrating them as ideal fluorescent probes for biological imaging and detection.

Introduction

The tremendous efforts taken in studying the complex and dynamic cellular processes have made great progresses in the last decades.¹⁻³ In this regard, cellular imaging based on fluorescent probes is an essential strategy, which allows for *in situ* investigation of cellular activities such as drug delivery, signal mRNA particles tracking and gene expression.⁴⁻⁶ So far, traditional fluorescent probes including fluorescent proteins⁷, organic dyes⁸, inorganic semiconductor quantum dots (QDs)⁹ and carbon nanodots¹⁰ suffer from some inherent limitations including poor photostability, fluorescence brightness and cytotoxicity in the *in vitro* and *in vivo* fluorescence imaging. Taking the widely used QDs for example, although they possess strong luminescence, narrow emission and great photo stability, their potential toxicity that mainly caused by the degradation of the heavy metal components or surface interaction is still under debate in the long-term study.¹¹⁻¹³ In this regard, fluorescent nanoparticles like polymer dots¹⁴⁻¹⁶ and conjugated polymer^{17,18} have emerged as a new class of fluorophores with the potential to overcome these limitations.

Conjugated polymers (CPs) are a class of macromolecules with π -electronic delocalized backbones, which facilitate semi-conductivity, photo and electroluminescence.¹⁹ In the past decade, CPs with great features including easy synthesis, tunable properties, bright fluorescence and low cytotoxicity have been used for biosensor and cellular imaging.²⁰⁻²² However, most CPs are hydrophobic, their low water solubility and insufficient cell uptake behavior severely hinder their biological imaging applications. Generally, two strategies have been developed to enhance the water solubility of the CPs, including fabricating the CPs into conjugated polymers nanoparticles (CPNs) and conjugated polyelectrolytes (CPEs).^{23,24} CPEs typically require many complicated synthetic steps; in addition, the charged side chains of CPEs might cause nonspecific interactions with biomolecules.²⁵⁻²⁷ Regarding to the facile operation and universality, CPNs with modified hydrophilic groups is

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