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Novel quantum dots–carboxymethyl chitosan nanocomposite nitric oxide donors capable of detecting release of nitric oxide in situ

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ABSTRACT

Nitric oxide (NO) donor compounds are primarily monofunctional in that they release NO under the requisite conditions. To detect the amount and duration of NO released, subsequent analysis methods are required. It would be advantageous if a NO donor compound could both release and detect NO at the same time. This would eliminate potential errors in the analysis. In this paper, novel cadmium telluride quantum dots (CdTe QD)–carboxymethyl chitosan (CMCS) nanocomposite NO donors, including both diazeniumdiolates and fluorescence probes, were fabricated by first synthesizing CdTe QD in CMCS aqueous solution and then reacting NO as well as ethyl bromide with the resultant CdTe QD–CMCS nanocomposites. Transmission electron microscopy, scanning electron microscopy and particle size analysis were used to examine the morphology and size distribution of the CdTe QD–CMCS nanocomposite NO donors. The donors are nanospheres with CdTe QD encapsulated and have dimensions of ~300 nm. Fourier transform infrared spectroscopy, X-ray diffraction, X-ray photoelectron spectroscopy and contact angle tests were employed to characterize the chemical structure of the donors, and the results also show that CdTe QD are well incorporated into CMCS, and many of them are close to the surface of the donors. The precursors of the donors exhibit a fluorescent effect, and the fluorescence can be quenched by NO. The donors can release NO spontaneously in a phosphate-buffered saline solution similar to a physiological environment, and can quantitatively detect the release of NO in situ based on fluorescence quenching of the donors by the NO.

1. Introduction

Nitric oxide (NO), a free radical molecule possessing very important functions in biological systems, is generated in various tissues from the amino acid L-arginine by different forms of NO synthase [1]. Many NO donors have been designed and synthesized, among which diazeniumdiolates are of great interest [2,3]. Diazeniumdiolates represent a class of compounds containing the anionic $[N(O)NO]^-$ functional groups, typically synthesized by reactions of a nucleophile with NO at elevated pressure [4]. They can generate NO under physiological conditions at different rates. Some diazeniumdiolate carriers, however, are found to be toxic and harmful to the human body, which limits their application in treatment of relevant diseases. Chitosan is a natural polysaccharide composed of β-(1 → 4)-2-amido-2-deoxy-D-glucan (glucosamine) and β-(1 → 4)-2-acetamido-2-deoxy-D-glucan (acetyl glucosamine) units, produced by deacetylation of chitin extracted from the exoskeleton of crustaceans [5]. Chitosan and its derivatives are biodegradable and biocompatible cationic polymers, which have been widely used in biomedical areas [6]. They have excellent chelating and adsorption characteristics owing to the high hydrophilicity and activity of hydroxyl and amino groups, which can react with metal cations and uptake metal cations by chelation mechanism. Also, the flexible structure of the polymer chains enables them to adopt suitable configuration for complexation with metal ions [7,8]. The secondary amine groups in some chitosan derivatives can act as a nucleophile to which NO is attached. The resultant chitosan–NO adduct has the $[N(O)NO]^-$ groups and is capable of releasing NO sustainably [9]. This polymeric diazeniumdiolate has proved an effective and reliable source of NO in a physiological environment.

Semiconductor quantum dots (QD) have unique properties and advantages over conventional organic fluorophores, such as broad excitation spectra, excellent photochemical stability, and narrow, symmetric and tunable emission spectra as a result of quantum confinement effect [10–15]. QD are usually prepared in aqueous solutions under alkaline conditions [16,17]. As a new class of fluorescent probes, QD are currently under intensive study in biosensing and biolabeling [18–22]. To reduce biological toxicity as well as enhance water solubility, QD are often modified by a variety of small molecules and biomacromolecules. Chitosan or chitosan

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