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Turn-off fluorescence of amino-functionalized carbon quantum dots as effective fluorescent probes for determination of isotretinoin

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ABSTRACT

Amino-functionalized carbon quantum dots (N-CQDs) as effective fluorescent probes were synthesized by a facile one-pot hydrothermal method via gluconic acid and N-methylethylenediamine as carbon and nitrogen sources respectively. Then the N-CQDs were applied to determine isotretinoin (INN). The synthesized N-CQDs were characterized using X-ray diffraction (XRD), transmission electron microscopy (TEM), dynamic light scattering (DLS), Fourier-transform infrared spectroscopy (FT-IR), UV-vis absorption and photoluminescence spectroscopy. As the emission of N-CQDs is efficiently quenched by INN, the as-prepared N-CQDs are employed as a highly sensitive and selective probe for INN detection. Under the optimal conditions, linear response was observed in the range of 0.08–70.0 μmol L^{-1} for INN determination. The calculated detection limit was 0.03 μmol L^{-1}. The established method showed a good selectivity for INN among several kinds of ions and biomolecules. The results of this study showed that the as-synthesized N-CQDs could be successfully applied to determine INN in blood serum and pharmaceutical samples.

1. Introduction

Isotretinoin (INN) chemically 3, 7-dimethyl-9 (2, 6, 6trimethylcyclohex-1-enyl) nona-2, 4, 6, 8 tetraenoic acid (Scheme 1), is a retinoid classified as vitamin A. It is used in the treatment of skin disease including acne vulgaris as a topical keratolytic agent. The mechanism of action is believed to inhibit the secretion of sebum and alter the lipid composition of the skin surface. Its effect on regulating cell differentiation led to use of it to treat cystic and nodular acne and also to inhibit neoplastic cells proliferation during past decades [1]. Several techniques have been applied to determine INN such as high-performance liquid chromatography with ultra-violet detection [1–3], gas chromatography (GC) [4] and others high-performance liquid chromatography with mass spectrometric detection [5–7]. Most of these methods depend on lengthy sample preparation schemes including extraction using an organic solvent, evaporation of solvent and reconstitution prior to HPLC analysis or need column switching techniques (online solid-phase extraction) or require expensive instruments such as LC–MS–MS [3].

Carbon quantum dots (CQDs) are a group of nanoparticles which consist of carbon with a size below 10 nm. Since the discovery of fluorescent fragments of a batch of single-wall nanotubes in 2004, numerous of papers have investigated the synthetic methods, properties, and application of CDs [8]. Unlike the conventional semiconductor quantum dots (QDs) containing toxic heavy metal elements and chalcogens, CDs are mainly composed of non-toxic C, O, and N elements, so are superior in the aspects of good water solubility, high quantum yield (Φs), outstanding photoluminescence (PL) properties, large stokes shifts, robust chemical inertness, low cytotoxicity, ease of functionalization, and excellent biocompatibility [9]. These are acceptable reasons for wide use of CQDs in the fields of biological labeling, bioimaging, and drug delivery recently.

Doping is a common approach to tune the PL properties of photoluminescent materials. Various doping methods with dozens of elements such as P, S, and N have been reported to tune the features of CQDs. N-doping is the most studied a way to increase the emission of the CQDs by inducing an upward shift in the Fermi level and electrons in the conduction band. It was demonstrated that only the nitrogen bonding to carbon can really enhance the PL emission of CQDs with quantum yields of more than 20% [10–12]. The excitation-dependent emissions are general features of CQDs. Several possibilities are proposed including an optical selection of nanoparticles with different size (quantum effect); different distributions of emissive trap sites on each CQD; free zigzag sites

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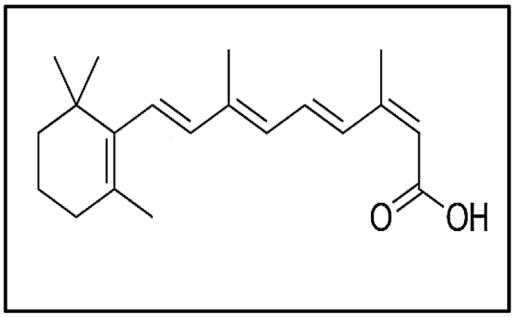

Scheme 1. Chemical structure of INN.

with a carbene-like triplet ground state; radiative recombination of excitons [13,14].

In this paper, a simple N-CQDs –based "turn-off" fluorescence method is proposed to determine INN. The N-CQDs were synthesized by a facile one-pot hydrothermal method with a quantum yield (QY) 35.2% using gluconic acid and N-methylethylenediamine as carbon and nitrogen sources, respectively. The morphology, size, and structure of the synthesized N-CQDs were characterized using different techniques. The effective parameters were evaluated and INN was determined under the optimal conditions.

Scheme 1

2. Experimental

2.1. Chemicals and reagents

All reagents and materials were obtained from Merck Company (Darmstadt, Germany) or Aldrich Company (St. Louis, MO, USA) and used without further purification. Gluconic acid and N-methylethylenediamin were purchased from Merck Company (Darmstadt, Germany) or Aldrich Company (St. Louis, MO, USA). INN stock solution (1.0×10^{-3} mol L^{-1}) was prepared in double distilled water (DDW) and stored at 4°C. Phosphate buffer solution (PBS, 0.1 mol L^{-1}) of pH 7.0 was used for pH adjustments. For recovery tests, INN tablets (20.0 mg, Roche Company) were purchased from a local pharmacy, and fresh human serum samples were provided from Bessat Hospital Lab. (Hamedan, Iran). DDW was used throughout the work.

2.2. Apparatus

A Perkin Elmer (LS50B) luminescence spectrometer was used for INN spectrofluorometric concentration determination. The absorption spectrum was recorded using a single beam UV-mini-WPA spectrophotometer. A transmission electron microscope (TEM, Philips-CM10–300 kV) was performed to characterize the morphology of the N-CQDs. The crystal structure of the synthesized N-CQDs was determined using an X-ray diffractometer (XRD, 38066 Riva, d/G. via M. Misone, 11/D (TN) Italy). Size distribution of the N-CQDs in water was measured by using dynamic light scattering (DLS, Nano ZS (red badge) ZEN 3600). The mid-infrared spectra of the synthesized N-CQDs in the 400–4000 cm^{-1} region were recorded by an FT-IR spectrometer (Perkin Elmer model Spectrum GX) using KBr pellets. A Metrohm model 713 pH meters was used for pH measurements. Also, a 40 kHz universal ultrasonic cleaner water bath (RoHS, Korea) was used.

2.3. Synthesis of amino-functionalized carbon quantum dots

The N-CQDs were prepared by a hydrothermal method [15]. Gluconic acid (1.0 g) and N-methylethylenediamin (2 mL) were dissolved in DDW water (10 mL). Then the solution was transferred to a Teflon-lined autoclave (100 mL) and heated at 200 °C for 5 h. Carbonization of the reactants was detected through colour changing of the solution to dark brown. The reaction mixture was cooled down to room temperature. Next, the aqueous solution was centrifuged at 15000 rpm for 15 min to dislodge the non- fluorescent deposit and got the upper N-CQDs aqueous solution for use. As prepared dark brown solution was further purified through a 0.2 μm membrane filter. Finally, the N-CQDs were diluted using DDW until appropriate signal was obtained

2.4. Procedure for spectrofluorometric detection of INN

To study the quenching effect of INN on the fluorescence intensity of N-CQDs, 50 μg mL^{-1} of N-CQDs solution, 1.5 mL of 0.1 mol L^{-1} PBS (pH 7.0) and different amounts of INN were successively added into a 5 mL volumetric flask, diluted to the mark with DDW and sonicated for 2 min until the solution was fully mixed. The fluorescence spectra were recorded from 300 nm to 700 nm. The fluorescence intensity of the solution at the maximum emission wavelength at 450 nm (λ_{ex} = 350 nm) was used for quantitative analysis.

2.5. Pharmaceutical sample solution preparation

For pharmaceutical analysis, seven INN capsules were opened carefully using a sharp blade and the content of these capsules was extracted. Then calculated amount (equal to weight of one capsule) of homogenized liquid was imported into a 25 mL volumetric flask and was dissolved in 5 ml of methanol. Afterward, it was sonicated to dissolve it completely and diluted up to the volume with DDW. The content of the flask was sonicated for 15 min and centrifuged

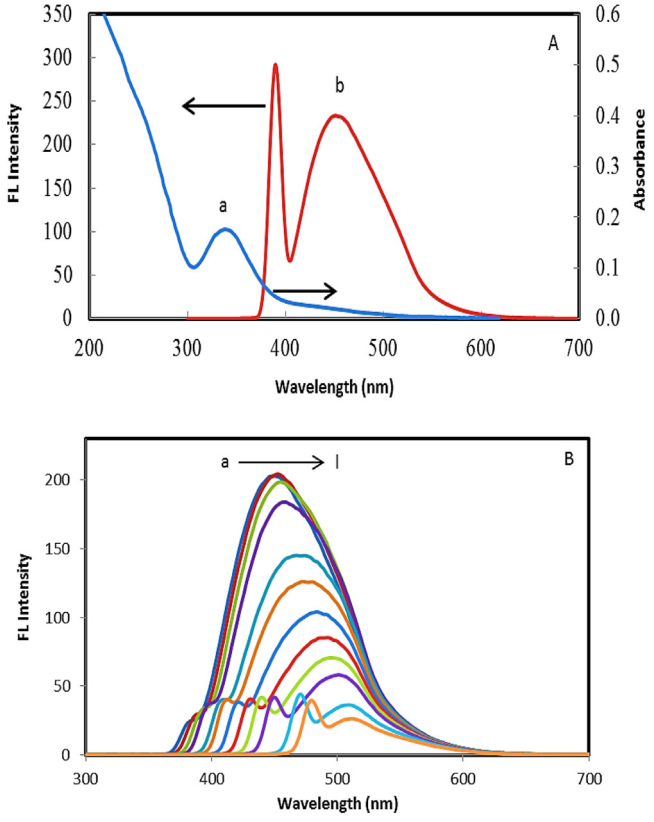

Fig. 1. (A) UV–vis absorption (a) and emission (b) spectra of the N-CQDs. (B) Emission spectra of the N-CQDs with excitation at different wavelengths.