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Sensitive Determination of Cetirizine Using CdS Quantum dots as Oxidase Mimic-mediated Chemiluminescence of Sulfite

Reza Hoseinpour Kouhestany, *Seyed Naser Azizi, Parmis Shakeri and Shaghyegh Rahmani

Faculty of Chemistry, University of Mazandaran, P.O. Box 47416–95447, Babolsar, Iran

ABSTRACT

A new chemiluminescence (CL) method using cadmium sulfide quantum dots (QDs) as sensitizers is proposed for the chemiluminometric determination of cetirizine pharmaceutical formulation. CdS QDs were synthesized by using water soluble route. The nanoparticles were structurally and optically characterized by X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), Ultra Violet-Visible (UV–Vis) absorption spectroscopy and scanning electron microscopy (SEM). In this study results shows that CdS quantum dots are enhancers of the weak CL emission. Trace amounts of cetirizine improved the sensitize effect of CdS quantum dots yielding a significant chemiluminescence enhancement of the Ce(IV)–SO_3^{2-}–CdS QDs system. So, a new CL analysis system was selected for the determination of cetirizine. There is a good linear relationship between the relative chemiluminescence intensity and the concentration of cetirizine in the range of 1×10^{-9}– 1×10^{-6} $molL^{-1}$ with a correlation coefficient (R^2) of 0.9963 at the optimum conditions. The limit of detection (LOD) of this system was found to be 5×10^{-11} M. This method is simple, sensitive and cost effective, and also is accommodating for pharmaceutical applications.

***Key Words*:** CdS quantum dot, Sensitized chemiluminescence, Ce(IV)–sulfite, Cetirizine.

INTRODUCTION

Cetirizine (figure 1) is a long acting antihistamine with some mast-cell stabilizing activity widely used in the comprehensive management of allergic rhinitis, the symptoms of which include itching, sneezing and nasal congestion (Haghighi *et al.*, 2013). Its molecular formula is $C_{21}H_{27}C_{l3}N_2O_3$. Cetirizine is an H1-receptor antagonist in a group of the cyclizine class of compounds. It is an active metabolite of hydroxyzine, a first generation H1-receptor antagonist. Marked affinity of cetirizine for peripheral histamine H1 receptors results in anti-allergic properties, but has the advantage that it lacks the CNS depressant effects often encountered in anti-histamines. Cetirizine is a potent and well tolerated nonsedating anti-histamine drug for the treatment of seasonal and prennial allergic rhinitis and chronic urticarial (Slater *et al.*, 1999).

In recent years, semiconductor nanocrystals, known as quantum dots (QDs), are in high-demand as inorganic fluorophores (Medintz *et al.*, 2005). Luminescent properties of semiconductor nanocrystals are usually inspected by photoluminescence (PL) produced using photoexcitation (Qu and Peng, 2002), electrochemiluminescence (ECL) generated by electron injection (Zou and Ju, 2004) and cathodoluminescence given from electron impact (Dabbousi *et al.*, 1997). In recent years, CL and relatedanalysis techniques have been utilized in different fields such as biology, bioimaging, biotechnology and analytical technology because of their widespread liner range, simple instrument and lack of background scattering light interference (Roda *et al.*, 2004). Several advantages, including flexible photoexcitation, sharp photoemission, and excellent resistance to photobleaching have made them more attractive than conventional organic fluorophores as luminescent molecular probes (Parak *et al.*, 2005). Thus, fluorescence or chemiluminescence (CL) based chemical sensing involving QDs have been developed for different chemical species such as ascorbic acid, urea, sulfadiazine (Yazid *et al.*, 2013), as well as a ions, such as fluoride, chloride and acetate ions (Callan *et al.*, 2008). In most QDs applications, the detection is based on signal quenching, while more newly attention has been focused on signal enhancing, mainly related to QD ability to sensitize different chemiluminescent systems (Sun *et al.*, 2008). Sensitized chemiluminescence is an expeditious policy to exploit CL reactions with low quantum efficiencies for analytical purposes. The weak created energy is transferred to a sensitizer, usually an organic fluorophore with high quantum yield, which is able to magnify it. Any species that selectively interacts with the fluorophore could quench the CL emission. To our knowledge, up to know, there is no report on sensitize effect of CdS QDs on distinct chemiluminescent systems. In the present study, we have found that the oxidation of sulfite by Ce(IV) and in the presence of CdS QDs that act as sensitizers produces strong CL signal to allow the development of detection systems. This paper presents a rapid, simple and sensitive method for determination of cetirizine in pharmaceutical formulation.

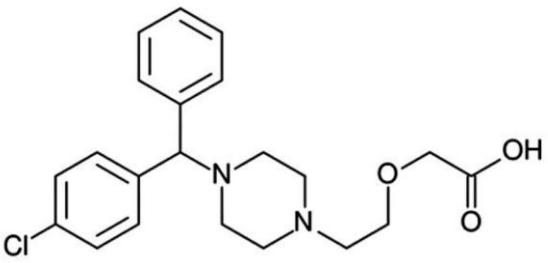

Figure1: Structural formula of cetirizine.

***Corresponding Author**:
Prof. Seyed Naser Azizi
Faculty of Chemistry, University of Mazandaran,
P.O. Box 47416–95447
Babolsar, Iran
E-mail: *s.n.azizi1975@gmail.com*
Contact No.: +98 113 534 2301

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MATERIALS AND METHODS

Reagents and chemicals

All the reagents or solvents were of analytical grade and used without further purification. Ultrapure water (deionized and doubly distilled) was used throughout. Na_2SO_3, Cadmium chloride hydrate, sodium hydroxide and H_2SO_4 were purchased from Merck (Darmstadt, Germany). Na_2S .$9H_2O$ was from Acros (Geel, Belgium). Cetirizine (99%) and $Ce(SO_4)_2$.$4H_2O$ were purchased from Sigma-Aldrich. The 1×10^{-3} $molL^{-1}$ stock solution of cetirizine was prepared in methanol and the working standard solutions were prepared by diluting stock solution with H_2O to an appropriate volume.

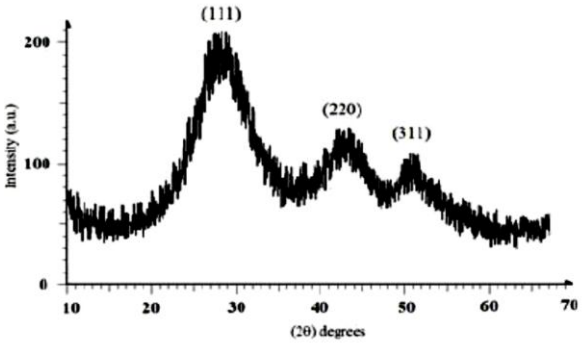

Figure 2: XRD pattern of the CdS nanoparticles.

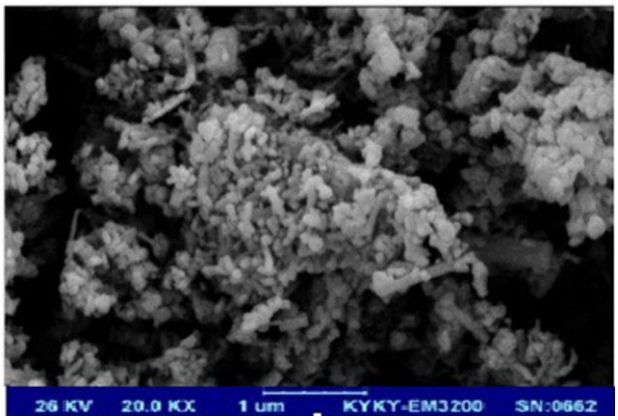

Figure 3: SEM image of CdS nanoparticles.

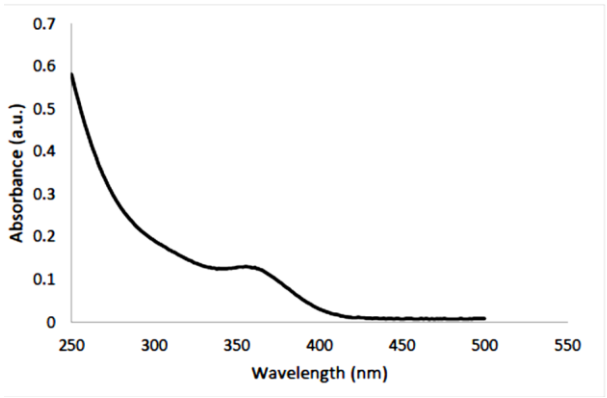

Figure 4: UV-Visible absorption spectra for CdS nanoparticles.

Apparatus

X-ray diffraction (XRD) patterns were recorded on a Bruker AXS D8 Advance X-ray diffractometer (Bruker, Germany) with Cu Kα radiation (λ = 1.5418 Å). Size of CdS QDs was performed on scanning electron microscope (SEM). The FT-IR spectra (4000–400cm^{-1}) were recorded using an FT-IR spectrometer (Tensor 27-Bruker). UV– Vis absorbance spectra of CdS nanocrystals were obtained from CdS QDs dispersive solutions using a UV-Vis spectrophotometer (Cambridge, UK). Photoluminescence (PL) measurements were recorded on a Perkin-ElmerL S-3B Luminescence Spectrometer (Waltham, USA) using 10 mm quartz cuvettes. All optical measurements were carried out at room temperature.

Preparation of TGA-Capped CdS QDs nanoparticles

Thioglycolic acid (TGA)-stabilized CdS QDs were synthesized via arrested precipitation in water as described previously. Nano crystals were prepared from a stirred solution of $CdCl_2$ (5 mM) in 100 mL of pure water. The pH was lowered to 2.15–2.30 with thioglycolic acid and by dropwise addition of 10 M NaOH to pH 4.5, followed by further dropwise addition of 1 M NaOH to obtain a final desired pH of 7.0±0.05. The solution was stirred vigorously under nitrogen atmosphere for 30 min. Then, 20 mL of 12 mM $Na_2S.9H_2O$ aqueous solution was added to this solution with rapid stirring, in order to set the molar ratio of $Cd^{2+}/S^{2-}$to 1: 0.4. The reaction mixture was stirred for 4 h prior to analysis. Particles were obtained by either the pH before adding the $Na_2S{\cdot}9H_2O$ solution or the [$CdCl_2$]: [Na_2S] molar ratio. The final concentration of the CdS QDs was approximately $4\times10^{-3}molL^{-1}$ (according to the Cd^{2+} concentration). For purification of CdS QDs, the colloid was dialyzed with 0.01 M NaOH solution for 2 days. A membrane with a molecular weight of cutoff 7000 was used for the purification of CdS QDs (Chen *et al.*, 2000).

Procedure for CL detection

Solution A was made by mixing 100 µL of CdS QDs (appropriate concentrations in water), 100 µL of sulfite and 50 µL water or 50 µL cetirizine (various concentrations in water). Solution A was delivered to the instru-instrument quartz cuvette via polypropene syringes. The mixture was shaken thoroughly and equilibrated at room temperature for10 min. Then 50 µL proper concentration of Ce(IV) solution was injected in to the quartz cuvette and the chemiluminescence spectrum was recorded.

RESULTS AND DISCUSSION

Characterization of CdS QDs

XRD pattern of the CdS nanoparticles illustrated in Figure 2 can be indexed as hexagonal wurtzite structure of CdS with prominent peaks corresponding to the reflections at (111), (220) and (311) planes. The broadened peaks are showing that the sizes of the particles are in nanorange (Suryanarayana and Norton, 1998).

Figure 3 represents the SEM image of CdS nanoparticles. This picture confirms the formation of CdS nanoparticles. This picture shows the spherical shape to the nanoparticles, and most of the particles exhibit some covering. From the pictures, it also can be seen that the size of the nanoparticle is less than 50 nm which was in agreement with the particle sizes (16.21 nm) calculated from the Debye-Scherrer formula.

The UV–Visible absorption spectra of CdS nanoparticles are shown in Figure 4. Although the wavelength of

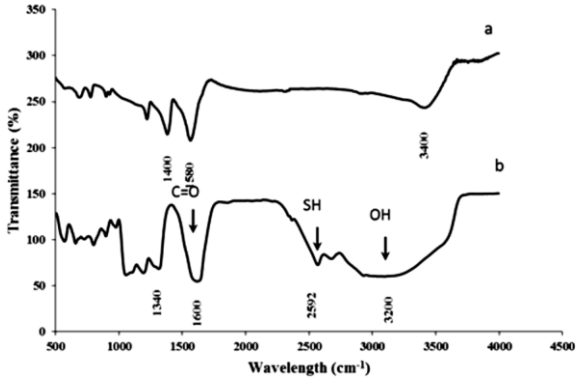

Figure 5: the FT-IR spectra of TGA capped (a) and free TGA (b) CdS nanoparticles.

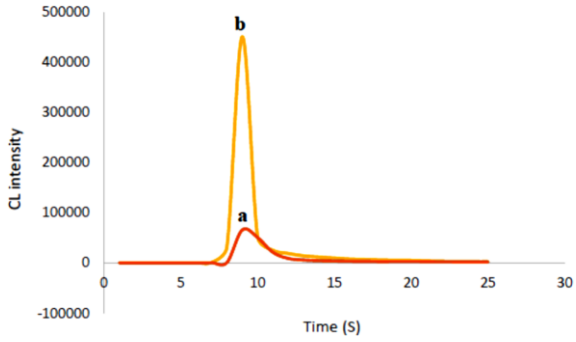

Figure 6: CL intensity–time profiles of Ce(IV)–SO_3^{2-} (a), Ce(IV)–SO_3^{2-} CdS QDs (b).

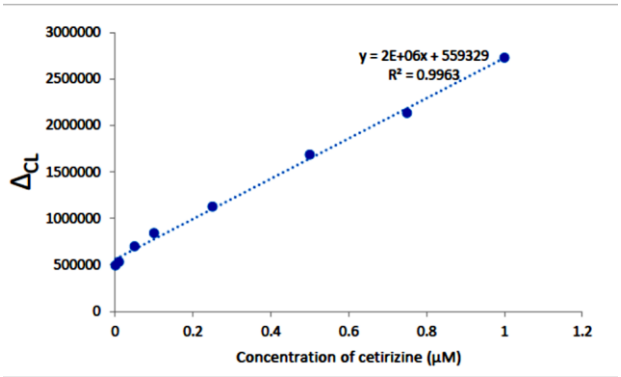

Figure 7: The linear dependence of relative chemiluminescence intensity ΔICL as a function of cetirizine concentration (μmol L^{-1}).

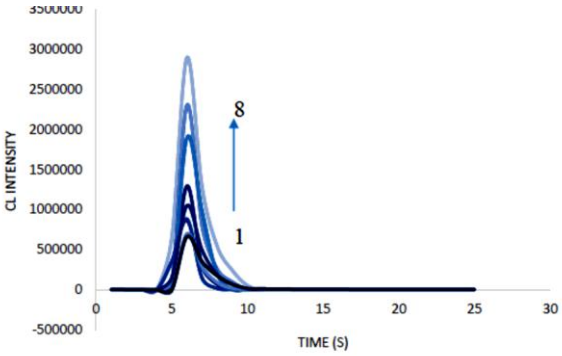

Figure 8: The changes of the CL spectra of Ce(IV)–SO_3^{2-}–CdS QDs system after addition of various concentrations of cetirizine. The solution conditions were: 50 μL 5×10^{-4} M Ce(IV) was injected into a mixture of 100 μL 1.0×10^{-3} M SO_3^{-2} plus 100 μL 1 M CdS QDs solution with different concentrations of cetirizine: (1) 0.001, (2) 0.01, (3) 0.05, (4) 0.1, (5) 0.25, (6) 0.5, (7) 0.75, and (8) 1 μmol L^{-1}.

Table 1: Determination of cetirizine in pharmaceutical sample by the proposed method.

Formulation	Claimed value (mg/ml)	Found (mg/ml)	Recovery (%)	RSD (%) (n=3)
Cetirizine injection (10mg/ml)	10	0.96	97.5	2.5

Table 2: Results of determination and recoveries in pharmaceutical formulation.

Sample	Added (10^{-7})	Observed (10^{-7})	Recovery (%)	RSD (%) (n=3)
1	1	0.97	96.6	3.2
2	5	5.85	101	2.5
3	10	10.4	103	2.8

our spectrometer is omitted by the light source, the absorption band of the CdS nanoparticles shows a blue shift due to the quantum confinement of the excitations present in the sample as compared with the bulk CdS particles. This optical phenomenon shows that these nanoparticles have a quantum size effect (Azizi *et al.*, 2013; Berger, 1996).

In addition, Fourier transform infrared spectroscopy was carried out in order to confirm the bonding of thioglycolic acid (TGA) to the nanoparticle surface. Figure 5 shows the FT-IR spectra of TGA capped (a) and free TGA (b) CdS nanoparticles. The IR absorption band around 1550–1610 cm−1, 1300- 1450 cm^{-1} (sυ COO−), 3000–3500 cm^{-1} (mυ OH) and 2550-2750 cm^{-1}(sυ S-H) indicate these groups. Results showed that the stretching band of the S–H thiol group, (2550–2670 cm^{-1} wυ S–H), is not observed when the nanoparticles are evaluated. The reason for disappearance of S–H group vibration on the surface of CdS nanoparticles is due to the formation of covalent bonds between thiols and Cd^{2+} surface atoms (Wang *et al.*, 2011).

Chemiluminescence of CdS QDs

Chemiluminescence emission of CdS QDs was studied in Ce (IV)–SO_3^{2-}–CdS QDs system. It was reported that the oxidation of sulfite by Ce^{4+} in acidic medium yields a weak chemiluminescent emission, which can be enhanced in the presence of sensitizers or fluorophore compounds, one of which is QDs that attract special attention due to their high quantum yields (Wang *et al.*, 2009; Fortes *et al.*, 2011). Therefore, in this study we study the effects of CdS NCs on the Ce (IV)–SO_3^{2-} CL system. Figure 6 shows the dynamic CL intensity–time profiles of the Ce (IV)–SO_3^{2-} (curve a) and Ce (IV)–SO_3^{2-} –CdS QDs (curve b) were acquired in the static-injection mode. It indicated (Figure 6b) that the CL reaction was very quick and the CL intensity reached a maximum in about a second after the injection. It could be seen from Figure 6 that the CL intensity of Ce (IV)–SO_3^{2-} –CdS NCs (nanocrystallites) system is far stronger than that of Ce (IV)–SO_3^{2-}system, indicating the great sensitized effect of CdS NCs on Ce (IV)–SO_3^{2-} CL reaction. Useful arameters for the CL signals of Ce (IV)–SO_3^{2-} –CdS NCs system were then investigated systematically to establish the optimal conditions for the CL reaction. This optimization was carried out in the following experiment.

Calibration curves and performance characteristics

By adding different amounts of cetirizine proposed system (Ce(IV)–SO_3^{2-} CdS QDs) changes in chemiluminescence intensities (ΔI_{CL}) are quantitatively related to the concentration of cetirizine. Under the optimal experimental conditions described above, the calibration graph (i.e., the relationship between the concentration of cetirizine and the changes in the intensities) was shown (Figure 7) and following results were: the regression equation is ΔI_{CL}= 2E+06C + 559329 (where C is the concentration of cetirizine, in $\mu molL^{-1}$) with correlation coefficient (R^2) of 0.9963, the linear range is 1×10^{-9}– 1×10^{-6} $molL^{-1}$ and the detection limit (S/N=3) is 5×10^{-11} $molL^{-1}$ cetirizine (Figure 8). From Table 1, it can be found that the proposed method has a lower detection limit and larger linear range, compared with most of other methods.

Sample determination and recovery tests

To test the proposed method, it was applied to the analysis of cetirizine in injection. The samples were diluted appropriately with water before measurement. The results are shown in Table 1. As can be seen, the RSD was 2.5% and the recovery of the real samples was 97.5%, which suggested that there were no significant differences between the compared values, making this new chemiluminescence method applicable to these pharmaceutical formulations. Recovery tests were done to estimate the accuracy of this method. So a specific amount of standards was added to injection sample in three different levels. Results are given in Table 2. The recoveries ranged from 96.6% to 103%, with RSDs of < 4%. It shows that the proposed method was appropriate.

CONCLUSION

In summary, cetirizine inhibits strongly the CL intensity of the Ce (IV)–SO_3^{2-}–CdS QDs system. In fact, a simple and sensitive CL method for the determination of cetirizine is established, the increase in the CL signal being proportional to the concentration of cetirizine in the range of 5×10^{-9}-1×10^{-6} $molL^{-1}$. Moreover, the analytical results of real samples were accommodating. The proposed method has been applied to the determination of low levels of cetirizine in pharmaceutical products.

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