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A table of contents entry:

Modulating growth of CdS nanoparticles by copper as redox catalyst allows designing very simple and sensitive assays using disposable photoelectrochemical screen-printed electrodes (SPCEs) sensitized by conductive osmium complex.

Graphical Abstract

Photoelectrochemical detection of copper ions by modulating the growth of CdS quantum dots

*Ruta Grinyte, Javier Barroso, Beatriz Díez-Buitrago, Laura Saa, Marco Moller, Valeri Pavlov**

CIC biomaGUNE, Paseo de Miramón 182, 20014 Donostia-San Sebastián.

Corresponding Author

* To whom correspondence should be addressed

Dr. Valeri Pavlov,

Tel: (+34) 943005308, Fax: (+34)943005314

E-mail: vpavlov@cicbiomagune.es

Abstract

We discovered that copper ions (Cu^{2+}) catalyze the oxidation of cysteine (CSH) by oxygen (O_2) to modulate the growth of CSH-capped cadmium sulfide (CdS) nanoparticles (NPs). This new chemical process was applied to sensitive fluorogenic and photoelectrochemical (PEC) detection of Cu^{2+} ions in real samples of mineral and tap water using the photocatalytic activity of the resulting NPs. Disposable screen-printed electrodes (SPCEs) modified with electroactive polyvinylpyridine bearing osmium complex (Os-PVP) by cyclic voltammetry (CV) were employed for PEC analytical system. CdS NPs formed during the assay photocatalyze oxidation of 1-thioglycerol (TG) upon application of 0.3 V vs. Ag/AgCl to SPCEs. Os-PVP complex mediated the electron transfer between the electrode surface and CdS NPs. We proved that our assays did not suffer from interference from other ions accompanying Cu^{2+} and the sensitivity of our assays covers the European Union standard limit of Cu^{2+} ions in drinking water.

Keywords: Quantum dots, copper, fluorescence, photoelectrochemistry, cysteine.

1. Introduction

Nanomaterials based analytical assays are becoming a promising low cost approach for the detection of analytes. Usually, nanomaterials like metal and semiconductor nanoparticles (SNPs) were employed in analytical systems as fluorescent and electrochemical labels tethered to recognition elements such as antibodies and DNA oligomers [1-3], enhancers of raman scattering [4, 5], fluorescence quenchers [6, 7] or tracers [8, 9]. Moreover, metal nanoparticles (NPs) can be generated *in situ* in the course of biocatalytic processes catalyzed by different enzymes [10-12]. Unfortunately, metal NPs produced *in situ* in the above mentioned biocatalytical assays are not fluorescent thus the sensitivity of those assays is limited by the sensitivity of UV-vis spectroscopy employed to follow the formation of gold and silver NPs. SNPs used in bioanalytical assays are fluorescent and demonstrate quantum effects. They emit photons of light upon photoexcitation hence they are referred to as quantum dots (QDs). QDs allow to use much more sensitive fluorescence spectroscopy and photoelectrochemistry to follow the readout signal. Indeed, enzymatic assays based on *in situ* generation [13, 14] and etching [15] of semiconductor QDs are much more sensitive and cost efficient but they still require expensive and unstable enzymes. The employment of biocatalysts requires a very stringent control of their enzymatic activities in order to attain reproducible readout signals. Here, we present a new analytical methodology to overcome this intrinsic shortcoming of biocatalytical assays.

Cysteine (CSH) is an efficient stabilizer of CdS NPs [16, 17] due to the presence of thiol functional group, facilitating binding to the surface of CdS NPs, and hydrophilic amino and carboxylic groups, conferring solubility in aqueous solutions. On the other hand, CSH can be oxidized to form a dimer containing disulfide bridge between two CSHs, known as cystine

(CSSC) by oxygen (O_2) in the presence of copper ions (Cu^{2+}). Oxidation of CSH by O_2 catalyzed with Cu^{2+} ions proceeds through the following mechanism [18]:

Cu^{2+} ions are among heavy metal ions occurring in drinking water. Copper (Cu) plays a critical role in living organisms. Excessive consumption of Cu may increase gastrointestinal distress, even liver or kidney damage or increase the risk of Wilson's disease [19, 20]. Therefore, it is important to develop a rapid and simple method for monitoring low concentrations of Cu^{2+} ions in drinking water. A number of analytical techniques have been developed over the years for Cu^{2+} ions analysis, including chromogenic analytical assays [21], fluorogenic analytical systems [22], electrochemical sensors [23-26] and others [27-29]. We applied the technique of modulated growths *in situ* of CdS QDs pioneered by our group to detection of Cu^{2+} ions. For the first time, we combine oxidation of CSH catalyzed by Cu^{2+} ions modulating formation of QDs *in situ* and photoelectrochemical (PEC) measurements.

The process of PEC detection usually involves transformation of light into other forms of energy like electrochemical energy at the surface of the electrode, creating electrical readout signal. Exploiting the nature of light and electrochemical properties of SNPs, low cost PEC devices can be developed exhibiting high sensitivity and easiness of handling. Therefore, PEC assays finds broader application to analysis [30], substituting more expensive fluorescence spectroscopy.

We have designed the new very simple and inexpensive PEC analytical system based on disposable screen-printed carbon electrodes (SPCEs) and a standard laboratory UV lamp. The SPCEs were coated by the complex of poly(vinylpyridine) with $Os(bipyridine)_2Cl_2$ (Os-PVP complex), which facilitates electron transfer between the electrode surface and SNPs, thus

allowing for ultrafast PEC detection of copper using “wired” CdS NPs. Previously, this Os-PVP complex was used as the electrocatalyst to enhance the electron transfer between the electrode surface and active centers or cofactors of redox enzymes [31, 32].

2. Materials and Methods

2.1. Materials

Sodium sulfide (Na_2S), cadmium nitrate $\text{Cd}(\text{NO}_3)_2$, copper chloride (CuCl_2) and other chemicals were supplied by Sigma-Aldrich.

2.2. Spectroscopic and Optical Methods

Transmission electron microscopy (TEM) images were collected with a JEM-2100F-UHR (JEOL, Japan) equipped with a high-angle annular dark field (HAADF) detector and an energy-dispersive X-ray spectroscopy (EDX) system of type INCA (Oxford Instruments Analytical Limited, UK) for analysis of chemical composition. X-ray photoelectron spectroscopy (XPS) for chemical analysis was performed in a SPECS Sage HR 100 spectrometer with a non-monochromatic X-ray source (Aluminum Ka line of 1486.6 eV energy and 300 W). Fluorescence measurements were performed in a Varioskan Flash microplate reader (Thermo Scientific) using black flat-well (330 μL) NUNC 96 wells microwell plates at room temperature. The system was controlled by SkanIt Software 2.4.3. RE for Varioskan Flash. The acquisition of fluorescence spectra was optimized by selection of suitable operational parameters. In order to get better resolution, the excitation bandwidth was selected equal to 5 nm. Likewise, the gain was enhanced by increasing the measurements time until 100 ms.

2.3. Photoelectrochemistry

All electrochemical experiments were conducted on the Autolab Electrochemical Workstation (Model: PGSTAT302N, Metrohm Autolab, The Netherlands) equipped with NOVA 1.10 software. Disposable SPCEs incorporating carbon working electrode, Ag/AgCl reference electrode and carbon counter electrode were purchased from DropSens (model DRP-110, 4 mm diameter). Electrical contact to workstation was done with a special boxed connector supplied by DropSens. The illumination source was a compact UV Lamp emitting at 365 nm (UVP, Analytik Jena AG). The commercially available UV lamps and UV-illuminators are able to generate light with the peak intensity at 365 nm by default. They allow to illuminate large areas with the light of high intensity and high homogeneity. Of course, other sources of light like xenon or mercury-xenon lamps coupled to monochromators are available on the market, but they are very expensive, generate dangerous ozone, require a lot of space, specially trained personal, therefore they are not in the common use in general analytical laboratories. Usage of the standard UV lamp in PEC devices makes analytical assays based on PEC measurements much more available and cost efficient. All PEC studies were performed at room temperature. All the potentials reported in our work were against Ag/AgCl. Unless mentioned otherwise, all experimental results presented here are averaged from three independent measurements ($n = 3$).

2.4. CdS QD-mediated determination of Cu^{2+} ions

Different concentrations of Cu were incubated with 0.075 mM of CSH in citrate-phosphate buffer (pH 7.5). After 10 min Na_2S (18 μL , 1 mM) and $\text{Cd}(\text{NO}_3)_2$ (36 μL , 1 mM) were added to the samples of 146 μL . The emission spectra of the resulting suspensions were recorded after 5 min at $\lambda_{\text{exc}} = 300$ nm.

2.5. Quantification of Cu^{2+} ions in real samples (mineral and tap water)

Tap water samples (samples were collected in CIC biomagune, San Sebastián, Spain) and mineral water samples (Insalus, Tolosa, Spain) were spiked with different concentrations of Cu ($0\ \mu\text{M}$; $12.5\ \mu\text{M}$; $25\ \mu\text{M}$; $37.5\ \mu\text{M}$). Next, for measurements the samples were diluted by 100 times with standard citrate-phosphate buffer, pH 7.5. The results were plotted with the concentration standard added in the x-axis and the obtained fluorescence readings in the y-axis of calibration line.

2.6. Photoelectrochemical detection

SPCEs were initially pretreated electrochemically by cyclic voltammetry (CV) at a potential range of $0 - 0.8\ \text{V}$ in citrate-phosphate buffer (pH 7.5) for cleansing. Subsequently, a $40\ \mu\text{L}$ drop of Os-PVP complex ($1.375\ \text{mg mL}^{-1}$) was placed on the SPCEs and deposited by CV scanning (2 cycles, $50\ \text{mV s}^{-1}$). Later, SPCEs were rinsed out with ultrapure water and dried under argon atmosphere. Modified SPCEs were stored in fridge, submerged in buffer and protected from light. Finally, a $40\ \mu\text{L}$ of samples and TG ($20\ \text{mM}$) were placed on the SPCE and PEC measurements were carried out with UV lamp emitting at $365\ \text{nm}$ and the applied potential of $0.3\ \text{V vs. Ag/AgCl}$. The dependence of photocurrent on time was measured after reaching the steady state (5 min).

3. Results and discussion

3.1. CdS QD-mediated determination of Cu^{2+} ions

The oxidation of CSH can be easily applied for detection of Cu^{2+} ions. The principle of the QD based determination of Cu^{2+} ions is represented in Scheme 1 and can be described as follows. In

the absence of Cu^{2+} ions in the reaction mixture CSH interacts with Na_2S and $\text{Cd}(\text{NO}_3)_2$ to give CSH-stabilized CdS nanocrystals. On the other hand, when Cu^{2+} ions are present in the system, they catalyze oxidation of CSH by O_2 to CSSC reducing the amount of formed QDs and consequentially fluorescence intensity shown by the system.

Fig. 1A represents the effect of varying quantities of Cu^{2+} at constant CSH concentration on the fluorescence registered in the system. The UV-vis spectrum shows increasing absorption below 500 nm and the adsorption peak at 298 nm (Fig. S1 in the Supplementary Material). Upon excitation at 300 nm of those CdS QDs, a characteristic fluorescence emission spectrum is observed with the peak between 450 and 650 nm and a maximum emission at about 540 nm. As one can see in Fig. 1B the increase in the concentration of Cu^{2+} ions up to 375 nM is linearly related with the decrease in the intensity of fluorescence. TEM was used to confirm the presence of spheroidal CdS QDs in the reaction mixture in the absence of Cu^{2+} ions as it is depicted in Fig. S2 in the Supplementary Material. TEM images confirmed that the average diameter of CSH-CdS QDs is 2.18 ± 0.20 nm. The size decreased when Cu^{2+} ions were added, finding a diameter of 1.50 ± 0.39 nm at concentration of 125 nM. CdS QDs were not found at all when Cu^{2+} ions concentration was saturating (500 nM). The chemical composition of stabilized CdS QDs was acquired by EDX using TEM in scanning mode (STEM) and XPS measurements. These studies are presented in the Supplementary Material.

According to European Union Drinking Water Directive the Maximum Contaminant Level (MCL) of Cu^{2+} ions in tap water is 2 mg/L (32 μM). So, our assay is suitable for quantification of Cu^{2+} ions in drinking tap water. The lowest Cu^{2+} ions amount that could be detected by this analytical assay was found to be 6.83 nM. In comparison with other analytic methods like colorimetric detections based on aggregation of Au NPs [33] or Ag NPs [34], fluorogenic

detection [22], electrochemical assay [23] and others [28, 29] for detection of Cu^{2+} ions, the fluorogenic method proposed by us is more sensitive and does not require neither any complicated procedures nor expensive fluorogenic dyes.

Next, in order to check out the selectivity of the proposed assay we conducted additional experiments with the heavy metal ions (Co^{2+} , Fe^{3+} , Fe^{2+} , Pb^{2+} , Cr^{2+} , Hg^{2+} , Ni^{2+}) usually accompanying Cu^{2+} ions in tap water. We also studied the influence of other ions (Na^+ , SO_4^{2-} , Cl^- , I^- , CH_3COO^-) on the response of our system. All components were used at 500 nM concentrations taking into account that this amount of Cu^{2+} ions can oxidize CSH completely under the experimental conditions (according to the calibration plot in Figure 1B). The diagram in Fig. 2A does not show any influence on the readout signal of other ions added to the system. In order to demonstrate that the decrease in the fluorescence intensity in the presence of Cu^{2+} ions is not caused by simple quenching effect, the following control experiment was performed. Cu^{2+} ions (375 nM) were added to CSH-capped CdS QDs which were pre-formed in the absence of Cu^{2+} ions. The emission peak upon the addition of 375 nM Cu^{2+} ions still retained 88% of the initial emission peak. Taking into consideration that 3 independent measurements of fluorescence peaks were performed with 10% relative standard deviation (RSD) no significant quenching was observed upon addition of Cu^{2+} ions.

We also checked out the effect of Cu^{2+} ions on *in situ* generation of CdS QDs in the presence of other capping agents, such as reduced glutathione and orthophosphate using the optimum experimental conditions reported elsewhere [14, 35] in the presence of 500 nM of Cu^{2+} ions. According to Fig. 2B CdS QDs capped by reduced glutathione demonstrate higher emission intensity but reduced glutathione-capped QDs obtained in the presence of 500 nM of Cu^{2+} still retain 60% of the readout signal. It means that Cu^{2+} ions are able to catalyze oxidation of reduced

glutathione [36] but this reaction is much slower than the oxidation of CSH. When CdS QDs were formed using another stabilizing agent (orthophosphate), Cu^{2+} ions did not show any effect on fluorescence intensity and consequently formation of QDs confirming that Cu^{2+} ions catalyze only the oxidation of thiolated products and do not quench efficiently CdS QDs under our experimental conditions. We also evaluated our assay for detection of Cu^{2+} ions with real samples. As it was mentioned before, the MCL of Cu^{2+} ions in tap water is 32 μM . Keeping this value in mind, we validated the developed fluorogenic method employing bottled mineral water and tap water samples containing different known concentrations of copper close to MCL value (spiked concentrations of Cu^{2+} were 0 μM ; 12.5 μM ; 25 μM ; 37.5 μM).

The received calibration plot including the error bars for three different measurements is shown in Fig. 3. The calibration curves obtained using mineral water (dotted line) and tap water (dashed line) are very similar to the calibration line demonstrated previously by the system using buffered solutions (dark line). So, we demonstrated that the system is suitable for detection of Cu^{2+} ions in real samples taking into consideration the extreme sensitivity of our assay and MCL values.

3.2. Photoelectrochemical detection of Cu^{2+} ions

In addition to fluorescence, the other remarkable property of QDs is their capacity to act as photoelectrochemical catalysts. The designed QDs-based PEC system is depicted in Scheme 2. The oxidation of CSH promoted by Cu^{2+} ions provokes a decrease in the amount of formed QDs and consequently their photoelectrochemical activity. The latter is measured using SPCEs coated with Os-PVP complex and a standard laboratory UV lamp for excitation of CdS QDs. Photons emitted by the UV lamp are absorbed by CdS QDs to excite electrons from the occupied valence

band (VB) to the empty conduction band (CB) forming electron-hole pairs. Os-PVP complex immobilized on the surface of the SPCE facilitates the electron transfer of excited electrons to the electrode surface. In order to neutralize the holes on the surface of CdS QDs the electron donor, 1-thioglycerol (TG), exhibiting high affinity to CdS [37], was added to the assay mixture after formation of QDs. During this redox process TG is oxidized to bis(1-thio-2,3 propanediol).

Initial screening was focused on identifying the optimal parameters for the best performance of PEC assay. First of all, the surface of SPCE was photosensitized with Os-PVP complex by cyclic voltammetry (CV) applying varying potential in the range between 0.0 and 0.6 V vs. Ag/AgCl during two cycles. The surface coverage (Γ / nmol cm⁻²) of osmium moieties (Table S1) was determined by CV, revealing two specific redox waves related to the presence of the central osmium atom (Fig. S5 in the Supplementary Material). The saturating concentration of TG equal to 20 mM was selected for measurements (Fig. S6 in the Supplementary Material). The working potential of 0.3V vs. Ag/AgCl was selected taking into account the highest ratio (I_{QDs}/I_0) between photocurrents registered in the presence (I_{QDs}) and in the absence (I_0) of CdS QDs (Fig. S7 in the Supplementary Material) with the signal-to-noise ratio greater than 3. Having identified the optimal reaction conditions, the control experiments were performed using non modified SPCEs for the detection of anodic photocurrent in the presence of CdS QDs and TG in the assay mixture. No significant photocurrent was observed in the absence of Os-PVP complex.

As depicted in Fig. 4A and 4B the photocurrent intensities decreased in the presence of Cu²⁺ ions. The response shows linearity from 0 to 350 nM and saturation starting from 500 nM Cu²⁺ concentration. The LOD was found to be 2 nM (3 σ). The average RSD calculated from the Cu²⁺ calibration plot (obtained using at least three independent SPCEs with Os-PVP) was 6%. In the previously published PEC systems for detection of Cu the LOD was found to be 10 nM [38,

39]. Compared to the previously published electrochemical sensors [23, 40-43], our system demonstrated better sensitivity using the standard UV lamp emitting at 365 nm as the source of photons (see Material and methods).

The photocurrent responses are shown in Fig. 5A and 5B. The PEC assay was validated by determination of Cu^{2+} ions in real water samples: mineral and tap water (Fig. 5C). The LODs of Cu determination in mineral and tap water were 2.1 nM (RSD = 9%) and 3 nM (RSD = 7%), respectively. So, we demonstrated the simplicity and validity of developed SPCE for determination of trace amount of Cu^{2+} ions in real samples.

4. Conclusions

In summary, we have developed assays for copper ions (Cu^{2+}) based on the growth of CdS QDs modulated by oxidation of cysteine (CSH). The sensitivity of our assays meets the European Union standard limit of Cu^{2+} ions in drinking water. Besides, this assay did not suffer from interference from other ions accompanying Cu^{2+} cations. We believe that the present approach shows high potential for monitoring Cu^{2+} ions in environmental samples. Furthermore, exploiting the photoelectrochemical properties of *in situ* formed QDs opens up new possibilities in the field of nanotechnology exploiting formation of nanoparticles *in situ* modulated by redox reactions.

Conflict of interest

The authors declare no conflict of interest.

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Author Contributions

R. Grinyte and J. Barroso contributed equally to this work. All authors have given approval to the final version of the manuscript.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version.

Figures Captions

Fig. 1. (A) Fluorescence emission spectra of the system containing cysteine (0.075 mM), Na_2S (0.09 mM), $\text{Cd}(\text{NO}_3)_2$ (0.18 mM) and different concentrations of Cu: a) 0 nM; b) 25 nM; c) 125 nM; d) 250 nM; e) 375 nM; f) 500 nM; (B) Calibration curve of copper obtained using, F_{540} .

Fig. 2. (A) Effect of different ions on peak fluorescence intensity, F_{540} , in the system composed of cysteine (0.075 mM), Na_2S (0.09 mM), $\text{Cd}(\text{NO}_3)_2$ (0.18 mM) and 500 nM of ions. (B) Effect of 500 nM of Cu^{2+} ions on formation of QDs capped with different agents: I. CdS NPs stabilized with reduced L-glutathione (reduced L-glutathione 0.075 mM, Na_2S 0.09 mM, $\text{Cd}(\text{NO}_3)_2$ 0.18 mM, Tris-HCl 10 mM, pH 8); II. Cysteine stabilized CdS NPs (Cysteine (0.075 mM), Na_2S (0.09 mM), $\text{Cd}(\text{NO}_3)_2$ (0.18 mM)); III. Orthophosphate stabilized CdS NPs (Na_3PO_4 0.3 mM, Na_2S 0.3 mM, $\text{Cd}(\text{NO}_3)_2$ 1.25 mM, Tris-HCl 50 mM, pH 9.8).

Fig. 3. Fluorescence quantification of Cu^{2+} ions in buffer (dark line), in mineral water (dotted line) and tap water (dashed line) using peak fluorescence intensity at 540 nm (F_{540}) in the system composed of cysteine (0.075 mM), Na_2S (0.09 mM), $\text{Cd}(\text{NO}_3)_2$ (0.18 mM).

Fig. 4. (A) Photocurrent responses of CdS QDs in the system containing cysteine (0.075 mM), 1-thioglycerol (0.02 M), Na_2S (0.09 mM), $\text{Cd}(\text{NO}_3)_2$ (0.18 mM) and different concentrations of Cu: a) 0 nM; b) 25 nM; c) 125 nM; d) 250 nM; e) 375 nM; f) 500 nM; (B) Calibration curve of Cu obtained at 0.3 V (vs. Ag/AgCl) and 365 nm excitation light.

Fig. 5. Photocurrent responses of the system containing cysteine (0.075 mM), 1-thioglycerol (0.02 M), Na₂S (0.09 mM), Cd(NO₃)₂ (0.18 mM) and different concentrations of Cu: a) 0 nM; b) 125 nM; c) 250 nM; d) 375 nM for (A) mineral and (B) tap water. (C) Photoelectrochemical quantification of Cu²⁺ ions in buffer (dark line), in mineral water (dotted line) and tap water (dashed line).

Scheme 1. Fluorogenic determination of Cu^{2+} ions using formation of QDs.

Scheme 2. Electrochemical detection of Cu^{2+} ions using formation of CdS QDs “wired” by Os-PVP complex to the surface of SPCE.

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Highlights

- CdS QDs growing in aqueous buffered solutions are stabilized by cysteine (CSH).
- Copper ions (Cu^{2+}) modulate the growth of CSH-capped CdS QDs.
- This system allows quantification of Cu^{2+} in real samples: bottled mineral and tap water.
- Photoelectrochemical (PEC) analysis was performed using SPCEs modified with Os-PVP polymer.
- PEC method for detection of Cu^{2+} ions outperforms the optical assays.