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Review

Recent Advances in Electrochemiluminescence Sensors for Hg^{2+} Ion Detection: A Review

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Abstract- As one of the most sensitive detection methods, electrochemiluminescence (ECL) has received great attention due to its unique properties such as extremely low background, high sensitivity, wide dynamic range, simple, rapid and inexpensive instrumentation and ability to measure in in the area of environmental, biochemical and pharmaceutical matrices. Electrochemiluminescent sensors are able to detect the presence and evaluate the content of various toxic substances (pesticides, heavy metals, etc.) both in water and in food. Among the heavy metal ions, mercury ion (Hg^{2+}) is one of the most stable forms in mercury pollution. It is a widely investigated analyte since it is a toxic element at very low concentrations and its determination is very important for environmental purposes. This article reviews key advances in electrochemiluminescence measurements of Hg^{2+} ions over the past decade. The categorization of different ECL sensors is done on the basis of different luminophores including luminol, ruthenium(II) complexes and quantum dots.

Keywords- Electrochemiluminescence; Heavy metals; Mercury ion; Luminophore

1. INTRODUCTION

Heavy metal ions are significantly harmful for humans and the environment and cannot be biodegraded. The have widespread presence in our lives, and can be found in water, soil, food, and many organisms. As one of the most toxic metal, mercury has polluted the environment to a significant extent and threatens the health of many organisms. The fact that mercury ions can cause numerous adverse health effects in humans has also further exacerbated the condition. Being exposed to Hg^{2+} leads to lung damage and severe neurological and psychological problems including changes in personality, anxiety, depression and sleep disorders [1,2]. Thus, there is a need for reliable methods to detect these metal ions. Several analytical methods (based on spectroscopy) have been developed for the determination of trace mercury in industrial wastes and environmental aqueous samples [3]. However, these techniques for the detection of heavy metal contamination have many disadvantages such as being highly expensive and tedious, and requiring trained personnel. Electrochemiluminescence is a process in which light emitting excited states are formed through high-energy electron-transfer reactions of electrode-generated species [4]. Because of the combination of electrochemical and spectroscopic methods, ECL displays several advantages, including high sensitivity, fast response, high spatial resolution, high throughput, simple and low-cost instrumentation setups [5-12]. Signal-amplification strategies based on nanomaterials have received great attention due to their good electrical conductivity and biocompatibility and the possibility of the high loading of signal molecules for synergistic amplification of the target response [13-24]. In this review, we focus on classifying different varieties of luminophores reported for Hg (II) ion detection.

2. ECL SYSTEMS BASED ON RUTHENIUM (II) COMPLEXES

$Ru(bpy)_3^{2+}$ is a luminophore widely employed in ECL sensors. In practical applications, co-reactants are commonly used to amplify the ECL intensity of $Ru\ (bpy)_3^{2+}$ and simplify the ECL methodology [25]. Saqib et al. found that the cathodic ECL signal of $Ru\ (bpy)_3^{2+}$ can be greatly enhanced by Hg^{2+} [26]. They reported that N-hydroxysuccinimide (NHS) and N hydroxysulfosuccinimide (NHSS) could be used as efficient co-reactants of $Ru\ (bpy)_3^{2+}$ to produce ECL signals. In 2018, Wang and co-workers proposed a novel ECL assay in “turn-on” mode for Hg^{2+} analysis based on the different adsorption behavior of ssDNA and target-dependent dsDNA on gold nanoparticles (AuNPs) [27]. In the presence of AuNPs, the electrochemical reaction of $Ru\ (bpy)_3^{2+}$ /TPA can be catalyzed. Using ECL assays, the target analyte was determined in a dynamic concentration range from 8 pM to 2 nM with the limit of detection being around 2 pM. The application of mercury-specific oligonucleotide on the surface of ITO/AuNPs electrode allowed Huang et al. to use an ECL approach for the detection of the Hg^{2+}ions, as shown in Fig. 1 [28]. In this work, the application of signal-generating molecules (Ru-dppz, dppz=dipyrido [3,2-a:2′,3′-c] phenazine as ECL probe showed a 4-fold lower detection limit than the method using $Ru(phen)_3^{2+}$. Liu et al. developed a remote, label-free paper-based bipolar electrode- ECL switch system [29]. The presence of Hg^{2+} ions led to the label-freely intercalation of the “light-switch” molecule $[Ru(phen)_2dppz]^{2+}$ within the base pairs of the dsDNA, causing an intense ECL emission. The proposed biosensor could detect Hg^{2+} within a broad linear range from 0.1 to 50 nM, with a detection limit of 0.1 nM.

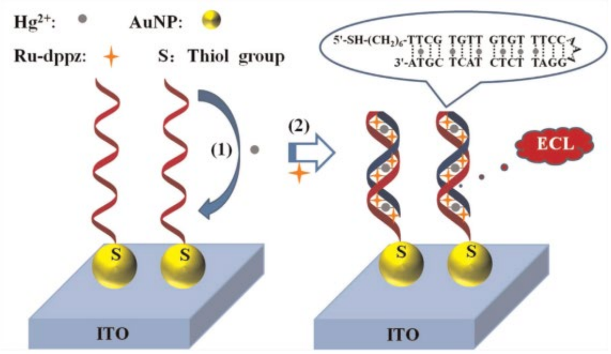

Fig. 1. Illustrative electrochemiluminescence DNA sensor for the detection of Hg^{2+} ion based on analyte-induced conformational change of oligonucleotide [28]

Cheng et al. developed an ECL mercury(II) biosensor by modifying $Ru(bpy)_3^{2+}$ /Cyclodextrins-Au nanoparticles(CD-AuNps)/Nafion complexes on the surface of glass carbon electrodes (GCEs) [30]. This ECL biosensor employed a ferrocene-tagged hairpin-DNA as Fc-probe DNA, in which the ferrocene could interact with CD and quench the ECL signal of the Ru $(bpy)_3^{2+}$. After incubation with Hg^{2+}, the probe prefers to form the thymine-Hg^{2+}- thymine structure, leading to a significant recovery of the ECL signal of Ru $(bpy)_3^{2+}$. Wang et al constructed a DNA ECL biosensor for the identification of Hg^{2+} ions. In the presence of target, the conformation of ssDNA probes switched into a hairpin structure by forming T-Hg-T structure. $Ru(bpy)_3^{2+}$ embedded into the grooves of the hairpin DNA generated the ECL signal [31]. The calibration curve for Hg^{2+} concentration was linearly co-related between 10.0 fM to 1.0 mM with an LOD of 10.0 fM.

3. ECL SYSTEMS BASED ON QUANTUM DOT (QDS)

Quantum dots (QDs) are semiconductor nanoparticles having the size in the range of 2-10 nanometers [32-43]. He and colleagues proposed a sensitive ECL sensor for Hg^{2+} based on molybdenum disulfide/quantum dot (MoS_2–QD) composites and DNA/gold nanoparticle/glucose oxidase (DNA–AuNP–GOD) conjugates. The glucose oxidase bound to the electrode surface reduces dissolved oxygen to generate hydrogen peroxide, a co-reactant of the QDs, in the presence of glucose [44]. Feng et al. designed an ECL aptasensor based on MIL-53(Al)@CdTe for the determination of heavy-metal ions ($Hg^{2+}$and Pb^{2+}) in fish and shrimp samples [45]. The T-rich aptamers labelled with gold nanoparticles were used to identify Hg^{2+} ion. The as-fabricated ECL-sensor provided a linear signal response for Hg^{2+} ions (1.0×10^{-11} to 1.0×10^{-7}M), with an LOD of 4.1×10^{-12} M. Shi and co-workers constructed a signal-on ECL aptasensor using QDs-aptamer bioconjugates for the detection of mercury [46]. Herein, core-shell CdTeSe@CdS QDs-DNA were prepared, which were then coated onto the gold electrode. This sensor showed a remarkable linear range of 1.0×10^{-11} to 1.0×10^{-6} M for the target and a detection limit of 3.5×10^{-12} M. In other work, Cai et al. constructed a sensitive and rapid ECL immunoassay for detecting Hg^{2+} based on the poly (diallyldimethylammonium chloride)-graphene-CdSe composites (PDDA-GN-CdSe) and AuNPs marker [47]. This sensing platform displayed a low detection limit of 0.06 ng mL^{-1}, which was lower than the WHO and US EPA defined toxicity level of Hg^{2+} ions in drinking water (6 ppb and 2 ppb).

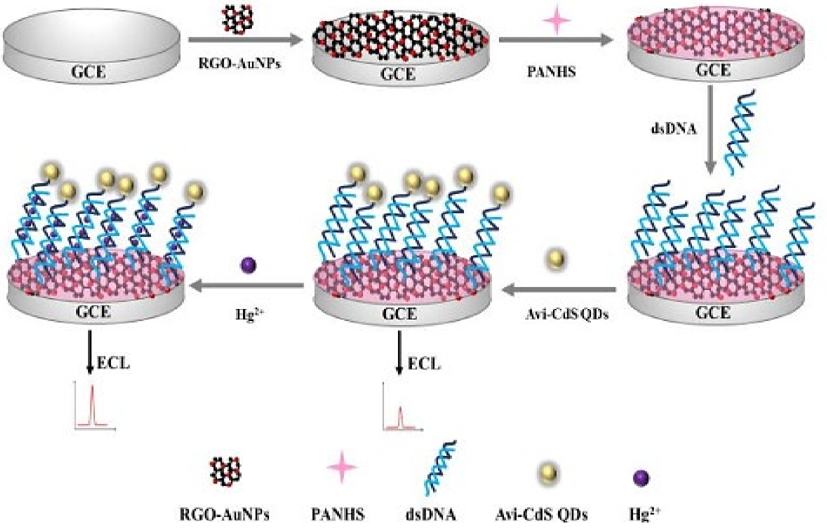

Fig. 2. Schematic representation of ECL biosensing strategy for Hg^{2+} ion detection [50]

In 2016, Li and co-workers reported an ECL based on analyte-induced DNA hybridization sensing device with high-intensity electron transfer for Hg^{2+} detection [48]. CdSe quantum dots (QDs) were used as the ECL indicator on the surface of the electrode. With the use of specific T-rich double-stranded (ds) DNA, higher Hg (II) concentrations increases the ECL intensity. The increase of ECL signal was logarithmically linear with the concentration of Hg^{2+} (1.0×10^{-11} to 1.0×10^{-8} M) with a detection limit of 1.0×10^{-11} M. Zhang and colleagues developed a specific and noticeably sensitive ECL immunoassay for the detection of Hg^{2+} based on CdSe quantum dots (QDs) and specific monoclonal antibody (mAbs) [49]. Methylmercury-6-mercaptonicotinic acid-ovalbumin was used as the coating antigen. Binding competition for specific sites of mAb-QDs, which binds specifically to Hg^{2+} ions, between the Hg^{2+} ions in the sample solution and the immobilized coating antigen takes place. Under optimal conditions, the ECL signal decreased linearly with the logarithm of Hg^{2+} ions concentration within the 0.02 to 100 nM range, with a limit of detection of 6.2 pM. In 2018, Hu et al. proposed a novel ECL mercury (II) biosensor based on reduced graphene oxide-Au nanoparticles (RGO-AuNPs) composites modified glassy carbon electrode functionalized with double-stranded DNA (dsDNA) linked to CdS quantum dots [50]. Discernibly sensitivity was achieved as a result of the high electrical conductivity of RGO-AuNPs nancomposites and fast charge transfer of dsDNA with T–Hg^{2+}–T (T = thymine) structures (Fig. 2). The signal intensity of the biosensor increased with the addition of mercury ions into the detection solution. The linear range of the sensor was 0.5pM – 1nM with a detection limit of 0.2 pM.

4. ECL SYSTEMS BASED ON LUMINOL

Because of excellent light efficiency, luminol is frequently used as an ECL reagent for the identification of numerous analytes [51-55]. However, because of the lack of effective immobilization methods on an electrode which do not lower the light-yielding efficiency of luminol, its use in ECL sensors has been restricted. Based on DNA-linked luminol-Au NPs superstructures, Wan et al. designed a sensitive ECL biosensor using 3-aminopropyl-triethoxysilane (APS) as the signal enhancer [56]. It was reported that ECL system could detect Hg^{2+} ion within the range of 2.0×10^{-10} to 2.0×10^{-8} M, and a limit of detection of 1.05×10^{-10} M was reported**.**

In 2019, Hu and co-workers developed a dual-signal ratiometric ECL sensor for Hg^{2+} detection. CdS QDs and luminol@Au were immobilized on the electrode surface, acting as cathodic and anodic ECL emitters, respectively [57]. It was seen that, as a result of the resonance energy transfer between QDs and luminol, the signal intensity of the CdS QDs–H_2O_2 system was promoted. The logarithm of the ratio of ECL intensity of CdS QDs and luminol was linearly proportional to the logarithm of Hg^{2+} concentrations ranging from 0.005 to 2.5 nM with a detection limit of 0.002 nM**.**

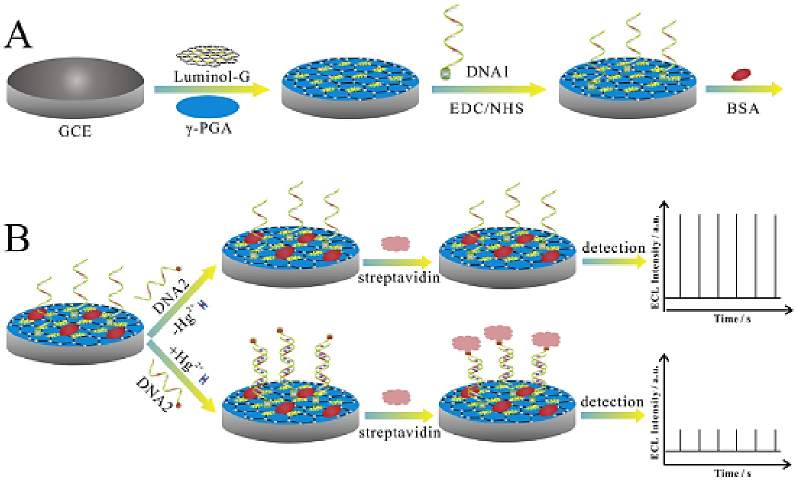

Fig. 3. (A) Construction process and (B) detection mechanism of the ECL sensor for mercury(II) ions [59]

Liu et al. proposed a detection system based on the Hg^{2+} induced surface-tethered (AIST) of ECL signal nanoparticles for the first time [58]. In this research, luminol@Au-cysteamine-thymine (luminol@Au-Cys-T) multifunctional nano-architecture was reported as the ECL signal probe. The linear response range of this method for Hg^{2+} was from 0.005 nM to 5 nM with a detection limit of 0.002 nM. Guo et al. designed a novel ECL biosensor for the detection of Hg^{2+} using gamma-polyglutamic acidgraphene-luminol (-PGA-G-luminol) composites coated on the glassy carbon electrode and T-rich oligonucleotides [59].

Two oligonucleotides can hybridize via the T–Hg^{2+}–T coordination, leading to the combination of streptavidin and reduction of ECL signal (Fig. 3). The increase of the ECL signal was logarithmically proportonal with the concentration of Hg^{2+} in a wide linear range from 0.01 to 100 nM. Several nanostructures have been used as luminophores in different ECL systems. Table 1 lists different types of luminophores for mercury ion.

Table 1. Various ECL-sensors for mercury ion

Electrode	luminophores	Linear Range	Detection Limit	Reference
GCE [1]	g-C_3N_4 NSs[2]	0.01–600 nM	5 pM	[60]
GCE	peroxydisulfate/oxygen	0.05–1000 nM	0.016 nM	[61]
GCE	copper nanoclusters	0.5–10 nM	0.01 nM	[62]
GCE	ABEI [3]	10 pM - 1 µM	3.8 pM	[63]
Pt	Ir(III) complex	0–40 µM	170 pM	[64]
GCE	PTCA[4]	0.001 pM-0.1 nM	0.0001 pM	[65]
GCE	PTCA	0.1 pM to 0.1 µM	33 fM	[66]
GCE	ABEI	10 pM to1 mM	3.1 pM	[67]

1-glassy carbon electrode
2- Graphite-like carbon nitride nanosheets
3- N-(4-Aminobutyl)-N-ethylisoluminol
4-Perylenetetracarboxylic acid

5. CONCLUSION

As one of the most effective methods in electrochemical sensors, ECL sensors can be applied to detect various compounds, such as metal ions. Recently, due to development of nanotechnology in sensing systems, the efficiency of ECL sensors will be improved using various nanomaterials. Up to now, several reagents have been reported to generate an ECL signal. In this review, we showed how the main groups of luminophores, such luminol, ruthenium (II) complexes and quantum dots, enable ECL systems to benefit from higher sensitivity towards the detection of mercury ions.

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