Recent Advances in Chemiluminescence

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Recent Advances in Chemiluminescence

Yingying Su, He Chen, Zhimeng Wang, and Yi Lv
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Abstract: This article reviews the development and application of chemiluminescence (CL) published in the literature between January 2004 and October 2006, with regard to instrumentation, systems, applications, and conclusions.

Keywords: Chemiluminescence, review, application

INTRODUCTION

It is well known that the first application of chemiluminescence as an analytical tool was developed in the early 1950s, employing several substances such as luminol, lophine, and lucigenin as volumetric indicators (1). In the following years, many researchers have focused on chemiluminescence analysis and brought significant progress, such as the innovation of instrumentation, the development of theoretical concepts, and the creation of methodologies. Owing to the simple measuring devices and the high versatility for the determination of a wide variety of species, chemiluminescence was usually acknowledged to be one of the most highly sensitive and most useful analytical techniques and can now be routinely used to solve diverse qualitative and quantitative analytical problems. However, the development of new or enhanced analytical methodologies based on the use of chemiluminescence phenomenon is still a very active area of current research.
Chemiluminescence is generally defined as a phenomenon of emitting visible light during the process of chemical reaction. There are three requirements for CL emission: (1) sufficient energy to form the electronically excited state; (2) a reaction pathway to induce the energy for the formation of an electronically excited state; and (3) the efficiency of generating molecules in the excited state for releasing photons (2–4).

The reason that CL reaction can be used in analysis is the CL emission intensity ($I_{CL}$), to a certain extent, is relative to the rate of the reaction, i.e., $I_{CL} = \phi_{CL} \cdot (-dA/dt)$, where $I_{CL}$ is the CL emission intensity (photons/seconds), $\phi_{CL}$ is the CL quantum yield, and $(-dA/dt)$ is the rate at which the CL substance is consumed (2, 4). Because the reaction rate is a function of the chemical concentration, the above equation also can be shown as $I_{CL} = \phi_{CL} \cdot C_A$, where $C_A$ is the concentration of the substance (4).

In general, the objects of CL analysis can be catalogued into three groups (4): the first is the reactant of CL reaction; the second is the catalyst, enhancer, or inhibitor of CL reaction; and the third is the catalyst, enhancer, or inhibitor of coupling reaction. Furthermore, many other substances can be analyzed by some indirect techniques. It is noteworthy that CL is very sensitive because the absence of a light source reduces noise and eliminates Rayleigh and Raman scattering, allowing photon detectors to be operated at high gains to improve the signal-to-noise ratio.

In the last two years, several reviews have been published relating to:

- analysis of pesticides (5, 6), pharmaceuticals (6), and proteins (7);
- analysis of phosphorus (8, 9) and ofloxacin (10);
- analytical applications of peroxoxyxalate chemiluminescence (11) and electrochemiluminescence of tris-(2,2'-bipyridyl) ruthenium and its derivatives (12);
- reactive oxygen species and their chemiluminescence-detection methods (13);
- chemiluminescence imaging in analytical chemistry (14);
- chemiluminescence sensors (15, 16); and
- hyphenation of chemiluminescence detection to separation techniques, such as liquid chromatography (LC) (17) gas chromatography (GC) (17), capillary electrophoresis (CE) (17, 18), and microchip capillary electrophoresis (MCE) (18).

The purpose of this review is to provide the reader with a wide overview of the CL instrument and CL systems improved and reported in recent years, with emphasis on its recent application in environmental, biological, clinical, food, and pharmaceutical analysis. Gas chromatography–chemiluminescence (GC-CL) and miniaturized total analysis system ($\mu$-TAS) are not covered in this review.
INSTRUMENTATION

Basic Instrumentation

One of the most important advantages of CL as an analytical technique is the simplicity of instrumentation. It usually includes a light-tight chamber, a reaction cell (RC), a device for introducing and mixing the reagents or samples, an optical detector, and a signal-processing system, as shown in Figure 1. In fact, most of the instruments used today are still based on this basic instrumentation, but with the development of relatively new flow injection technique and evolution of microelectronics, optoelectronics, fiber-optics, assemble techniques, and robotics. For example, recently CCD has been widely used in bioanalytical analysis owing to its efficient imaging performance.

Electrochemiluminescence

Electrochemiluminescence (ECL) is the process whereby a chemiluminescence emission is produced directly as a result of electrochemical reactions. Unlike conventional CL, commercial ECL instrumentation is not available. Compared to the basic instrumentation, a conventional electrode system used for the electrolytic system must be included.

Three main electrode configurations have been used in ECL work: rotating ring-disk (RRD) and dual (19) and single electrodes. The materials used for the working electrode where the ECL reaction takes place include platinum (20), gold (20), aluminum (21, 22), glassy carbon (23), paraffin-impregnated graphite electrode (PIGE) (24), carbon paste (25), indium tin oxide (ITO) (26), and silicon (27).

One important area in ECL is that of surfactants, such as X-100 (polyethylene glycol tert-octylphenyl ether), which can change the property of the surface of the working electrode. Richter et al. (20) found increases in ECL efficiency and TPrA oxidation current due to the adsorption of surfactant
on the electrode surface. Compared with Triton X-100, its hydrocarbon analogue (Zonyl FSN) not only rendered the electrode surfaces more hydrophobic but also significantly retarded the growth of the electrode oxide layers. As a result, oxidation potential and ECL signal change.

Another important area in ECL is modified electrodes. ECL properties of the working electrodes modified with poly(4-vinylpyridine) (PVP)-bound Ru(bpy)$_2$Cl$^+$ (where bpy = 2,2-bipyridine), clay nanoparticles/Ru(bpy)$_3$Cl$^+$ (28), negatively charged SiO$_2$ nanoparticles/positively charged (Ru(bpy)$_3$)$^{2+}$ (29), polyelectrolyte complex (30), CdSe nanocrystal (24), RuDS nanoparticles/Ru(bpy)$_3$$^+$ (31), nickel(II) tetrathalocyanine (NiTSPc)/Nafion (32), zeolite Y (25), and Fe$_3$O$_4$ magnetic nanoparticles/Nafion (33) have been studied in detail. It is found that ECL signal can be enhanced greatly with the modified electrodes, thus improving the sensitivity.

Carbon nanotube (CNT) has received considerable attention in various fields because of its unique properties such as high electrical conductivity, physical rigidity, and chemical stability. Based on the composite films of single-wall (SWCNT) and Nafion, Dong’s group reported on the preparation and characterization of the Ru(bpy)$_3$$^{2+}$ ECL sensor (34). The ECL sensor based on the SWCNT-Nafion composite films exhibited enhanced ECL sensitivity compared to that based on pure Nafion films. Two years later, a new and simple method for the fabrication of CNT-based Ru(bpy)$_3$$^{2+}$ ECL sensor using sol-gel–derived titania-Nafion mesoporous composite films was first reported (23). The proposed ECL sensor showed better long-term stability without signal loss for four months.

HPLC-CL

Chemiluminescence has been used as a detector for high-performance liquid chromatography (HPLC) since the 1980s, and it is rapidly growing due to its high sensitivity, wide linear working range, and simplicity of instrumentation. HPLC-CL techniques play an attractive and important role in the determination of analytes in complex matrices; e.g., for the analysis of environmental and biological samples. Serrano and coworker (35) have reported an HPLC-CL method for the determination of amikacin in body fluid on the basis of its complex formation reaction with Cu(II), the catalyst of the luminol/hydrogen peroxide chemiluminescence system. In order to detect erythromycin A in rat plasma and urine, Hori et al. (36) have established an HPLC method in which the electrogenerated chemiluminescence detection using Tris(2,2'-bipyridine)ruthenium(II) was employed.

It is also worth noting that the HPLC-CL technique is often reported for the determination of the homologous, because homologous compounds sometimes have a similar possibility of CL emission in a given CL system. Zhang et al. (37) have developed an HPLC method for the determination of four Sudan dyes in hot chilli pepper and chilli tomato sauce, with on-line
electrogenerated BrO\textsuperscript{−}-luminol chemiluminescence detection. With CL detector, an HPLC method for 20 phenolic compounds has been reported by Cui and coworkers (38). The CL detection method is based on the chemiluminescent enhancement by phenolic compound of the cerium(IV)-rhodamine 6G system in sulfuric acid medium. Lloret et al. (39) reported a sensitive method for the determination of six short aliphatic amines in water by high-performance liquid chromatography with chemiluminescence detection. These aliphatic amines are dansylated on solid sorbents and then chromatographed and post-column-detected with a typical CL reaction of peroxoxyxalate (TCPO) and H\textsubscript{2}O\textsubscript{2}.

Recently, photochemical reactions have been introduced to an HPLC-CL system for the determination of photoactive analytes, and many of them have been adopted as post-column detection schemes in liquid chromatography. Figure 2 shows a typical instrumental diagram of an HPLC-CL based on a post-column photochemical reaction system. With this hyphenated system, a sensitive method for the measurement of nine pyrethroid insecticides has been developed by Galera and coworkers (40). After a post-column irradiation with UV light, photolyzed pyrethroids take part in a chemiluminescent reaction in presence of K\textsubscript{3}Fe(CN)\textsubscript{6} and NaOH, whose signal increases with the percentage of acetonitrile in the reaction medium. The proposed method has been successfully applied to the determination of pyrethroids in tomato with good results. With the chemiluminescence detection based on photochemical reaction, Perez-Ruiz et al. (41) successfully accomplished the analysis of the five nitrosamines in water samples and organic compounds such as citric, lactic, malic, oxalic, and tartaric acids in different real samples, including wines, beer, milk, fruits, and soft drinks.

![Figure 2. Instrumental diagram of an HPLC post-column photochemical reaction system for the CL detection.](image-url)
Kuroda et al. (42) found that with a UV irradiation (254 nm, 15 W), quinines would generate hydrogen peroxide and a fluorescent product, and then the two resulting photoproducts mixed with diaryloxalate to produce CL emission. Based on this phenomenon, an HPLC-PO-CL method for the determination of four quinines was established.

CL generated based on catalytic oxidation of analytes on the surface of solid materials is a very interesting phenomenon called “cataluminescence” (15). Recently, based on this phenomenon, Lv et al. (43) have established a novel aerosol chemiluminescence detector, which can be coupled to HPLC for the detection of the compounds without or with only weak UV-visible absorption. The aerosol chemiluminescence detector is composed of three main components that individually govern three successive processes: nebulization of HPLC effluent, CL reaction on the surface of porous alumina, and optical detection by PMT. A stainless steel capillary tube (0.35-mm i.d., 0.80-mm o.d.) is used for the continuous sampler, through which the effluent from the liquid chromatography is introduced into the aerosol chemiluminescence detector. The aerosol chemiluminescence detector is shown in Figure 3. Many organic compounds, without or with only weak UV-visible absorption, such as saccharides, poly(ethylene glycol)s, amino acids, and steroid pharmaceuticals in solution, could be detected by the present aerosol chemiluminescence detector. The aerosol CL detector offers advantages of wide linear response, satisfied stability, simplicity, low cost, minimal size, ease of fabrication, and less interference from mobile phase or preparation of sample solutions. Subsequently, the aerosol chemiluminescence detector was also used for CE (44).

![Schematic diagram of the aerosol cataluminescence detector hyphenated to HPLC.](image-url)

Figure 3. Schematic diagram of the aerosol cataluminescence detector hyphenated to HPLC.
The advantages of high resolution, relatively short analysis time, and low operational cost make CE an ideal separation technique when compared to HPLC. Because of ultra-small volume sample at the nanoliter level in CE analysis, chemiluminescence has become an attractive detection mode to CE, since chemiluminescence detectors are characterized by simple inexpensive optical systems requiring no light sources and providing low background and high sensitivity compared with other optical detectors.

Since the most formidable challenges in applying CL detection to CE is the on-line introduction of one or two reagents into the system, suitable interfaces are very important to establish a successful CE-CL system. Here, we only discuss the interfaces in the recent two years. There are several different designs including on-column, off-column, and end-column. For on-column configuration, coaxial flow is the most popular detection mode in CE-CL systems due to its simplicity and sensitivity. In the coaxial flow configuration, the separation capillary tube is inserted into a reaction capillary of larger inner diameter (i.d.) than the outer diameter (o.d.) of the separation capillary. The larger diameter coaxial capillary is connected to an additional reservoir containing CL reagents. Indirect chemiluminescence (ICL) detection for capillary electrophoresis (CE) of monoamines and catechol using a luminol-K₃[Fe(CN)₆] system was described. The CL detection interface utilizes a conventional on-column coaxial flow design (45). Recently, an improved interface was reported, which makes the CE-CL system more simple and reliable for potential commercial development (46). In the same year, using a modified on-column coaxial flow detection interface, Chen’s group (47) developed a new method for pressurized capillary electrochromatography (pCEC) coupled with chemiluminescence (CL) detection. To evaluate the feasibility and reliability of the experimental setup, CL compounds luminol and isoluminol were separated and detected using this pCEC-CL system. At last, the mixture of amino acids was efficiently separated with satisfactory results. In the off-column configuration, the detection region was isolated from the CE HV supply. Cheng’s group (48) developed an off-column CL-CE system, which belongs to the coaxial flow mode. In the system, all capillaries and a grounding electrode were fixed in a four-way tee. The separation capillary was inserted into a reaction capillary. The end of the reaction capillary sloped down 2 cm to cause the solution to flow out of the reaction capillary more quickly. In this improved method, satisfactory reproducibility was achieved even at a higher concentration of hydrogen peroxide. In the end-column configuration, the CL signal produced is detected at the end of the capillary as analytes exit the capillary and react with CL reagents in the outlet buffer reservoir. Tsukagoshi and coworkers (49–52) have studied several variations of end-column CE-CL detection. The interface of microchip capillary electrophoresis (MCE) and chemiluminescence (CL) detection is also investigated in these two years.
Su et al. (53, 54) and Ren’s group (55) have employed similar MCE-CL systems. CL light was directly collected by a PMT without additional light focusing and reflection.

CHEMILUMINESCENCE SYSTEMS

Hitherto, various CL or ECL systems have been investigated and widely applied in many fields. In this review, they were approximately defined as the conventional system note and the new systems.

Conventional System Note

In the last two years, work has been performed to improve the conventional CL systems. Surfactants, complexes, and nanomaterials have been widely used in this research. Nonionic surfactants, such as Triton X-100, can effectively enhance the ECL intensity of lucigenin (56) and the Os(phen)$_2$(dppene)$_2^{2+}$ (phen = 1,10-phenanthroline and dppene = bis(diphenylphosphino)ethene) system (20). The experiments showed that the addition of surfactants can improve the detection limit of the analyte. A novel effect of a nonionic fluoro-surfactant (Zonyl FSN) on the electrogenerated chemiluminescence (ECL) of the Ru(bpy)$_3^{2+}$/TPrA system at gold and platinum electrodes was described by Li et al. (57). Using the surfactant, a low oxidation potential ECL signal can be obtained, resulting in a more efficient ECL analysis. Complexes, such as phthalocyanine (Pc) compounds, are also used to enhance the intensity of CL or ECL and improve the sensitivity (32, 58, 59). In 2006, Stedman’s group (60) investigated chemiluminescent reactions of nickel, iron, and cobalt carboxyls with ozone, which have the potential of improving conventional CL systems.

Recently, nanomaterials attract much attention to chemiluminescence systems to improve the sensitivity and the stability, mainly resulting from the high surface area and special structure. Cui’s group (61) found that gold colloids with nanoparticles of different sizes enhance the chemiluminescence of the luminol-H$_2$O$_2$ system, and they supposed that the enhancement effect originated from the catalysis of gold nanoparticles. This system was successful in determining some compounds at the nanomole per liter level with the inhibited CL and was of great analytical potential in developing new immunoassay and CL detectors with a wide response to a range of compounds for HPLC and CE. Subsequently, Li’s group (62) synthesized specially shaped, irregular gold nanoparticles (IGNPs) and found their catalytic efficiency on luminol CL to be 100-fold greater than that of spherical gold nanoparticles (Au-NPs). Using the IGNPs-functionalized DNA oligomers and the IGNPs-modified anti-IgG as in situ chemiluminescent probes, they established sandwich-type analytical methods for rapid, simple, selective, and sensitive
sequence-specific DNA detection and human plasma IgG immunoassay, respectively.

Dong’s group developed a series of novel ECL systems with SiO$_2$ nanoparticles (29), carbon nanotube (CNT) (34), and doped silica (RuDS) nanoparticles (31), in turn based on Ru(bpy)$_2^{3+}$ reaction. They assembled positively charged Ru(bpy)$_2^{3+}$ and negatively charged SiO$_2$ nanoparticles on ITO (tin-doped indium oxide on glass) electrodes by a layer-by-layer method, and the multilayer films were investigated in detail. In the same year, the CNT/Nafion composite films were also measured with TPA, and they found that the composite film had more open structures and a larger surface area, allowing faster diffusion of Ru(bpy)$_2^{3+}$, and that the CNT could adsorb Ru(bpy)$_2^{3+}$ and also acted as conducting pathways to connect Ru(bpy)$_2^{3+}$ sites to the electrode. According to this, the sensitivity of the ECL system at the CNT/Nafion film-modified electrodes was more than two orders of magnitude higher than that observed at a silica/Nafion composite film–modified electrode and three orders of magnitude higher than that at pure Nafion films. Two years later, they worked on the application of RuDS nanoparticles into the field of ECL. Homoplastically, magnetic Fe$_3$O$_4$ nanoparticles were used by Kim et al. (33) to fabricate a sensitive and novel Ru(bpy)$_2^{3+}$ ECL sensor. The most remarkable feature of the work was using an external magnet.

In addition, microwave (63) and ultrasound (64) techniques have been used to improve the intensity of CL. A novel platform technology named microwave-triggered metal-enhanced chemiluminescence was established by Geddes’s group (63). This approach has significant advantages over traditional chemiluminescence techniques. Greenway et al. (64) found chemiluminescence obtained from the luminol-H$_2$O$_2$-cobalt(II) reaction was enhanced by applying 120 W of ultrasound for a period of 4 s. Due to the high sensitivity, the method was applied to the determination of trace amounts of H$_2$O$_2$ in purified water and natural water samples without any special pretreatments.

New Systems

Sorouraddin et al. (65) reported a new CL reagent, thiosemicarbazide (TSC). Based on catalytic activity of copper on thiosemicarbazide (TSC)-H$_2$O$_2$ CL system in the presence of the surfactant cetyltrimethylammonium bromide (CTMAB), they established a novel method for the determination of nanogram per milliliter amounts of copper.

Cyclometalated Ir(III) complexes have been studied as new ECL reagents instead of Ru(bpy)$_2^{3+}$, since they have high photoluminescence efficiencies compared to the low photoluminescence efficiency of Ru(bpy)$_2^{3+}$. Kim et al. (66) investigated the origin of the low ECL on the basis of the energetics of the $fac$-Ir(ppy)$_3$/TPrA system. By controlling the relative positions of HOMO and LUMO levels (oxidation potential and reduction potential) of
Ir(III) complexes, higher ECL, about 77 times than Ru(bpy)$_3^{2+}$/TPrA, can be obtained. ECL properties of F(Ir)pic [bis(3,5-difluoro-2-(2-pyridyl) phenyl-(2-carboxypyridyl)) iridium(III)] and (btp)$_2$Ir(acac) [bis[2,(2'-benzothienyl)-pyridinato-\(N,C_3\)](acetylacetonate) Ir(III) in aqueous, nonaqueous (MeCN), mixed solvents (50:50 v:v, MeCN/H$_2$O), and in the presence of surfactant are reported by Muegge and Richter (67). The blue emission of F(Ir)pic, the red emission of (btp)$_2$Ir(acac), and the green emission of Ir(ppy)$_3$ reported previously give a wide color range of possible emitters, which can raise the possibility of internal standards and the analysis of multiple analytes in the same solution.

Zhu et al. (68, 69) designed and synthesized 4,5-dimethylthio-4'-[2-(9-anthryloxy) ethylthio] tetrathiafulvalene as a highly selective and sensitive chemiluminescence (CL) probe for singlet oxygen ($^1$O$_2$), which makes it possible to be used widely for $^1$O$_2$ detection in many chemical and biological systems and even in light water environments. Moreover, the probe exhibits both strong CL response to and high selectivity for $^1$O$_2$ only, rather than the other ROS, allowing $^1$O$_2$ to be determined in the presence of other ROS, such as hydrogen peroxide, hypochlorite, superoxide, hydroxyl radical.

Wightman et al. (70) described two systems that form emissive states in ECL with different properties than those when formed with photoluminescence. The first system involves the reaction of the anthracene radical anion with the radical cation of 4,N,N-trimethylaniline. In the second system, the benzophenone radical anion reacted with the radical cation of either phenoxathiin or 4-methoxythioanisole; the ECL emission was from the benzophenone triplet state and an excimer. The results investigated from these two systems clearly demonstrate that the radical ion annihilation pathway of ECL can generate different emissive states than those formed following photoexcitation. In the same year, Bard’s group (71) found two weak electrogenerated chemiluminescence (ECL) signals of OH-terminated PAMAM dendrimers. This new ECL product is believed to have a potential application in analysis.

APPLICATIONS

In recent years, interest in the use of CL systems in analytical chemistry has been growing exponentially, mainly in environmental, biological, clinical, food, and pharmaceutical analysis.

Environmental

Pesticide Residues

Pesticides are used for chemicals, synthetic or natural, that are applied for the control of insects, fungi, bacteria, weeds, nematodes, rodents, and other pests.
Public concern over pesticide residues has risen markedly and their accurate determination in fruits, vegetables, and related matrices in food analysis and in environmental samples is increasingly important. In the last few years, CL, as a detection tool, has offered interesting and promising alternatives to the traditional detection techniques for pesticides. The application of pesticides by CL in the last two years is summarized in Table 1. As can be seen from the table, a new technique, the photolysis provided by low-pressure mercury lamps, permits an increase in the number of compounds of environmental interest to be determined by direct chemiluminescence.

Compounds in Air or Vapor

On the basis of various CL phenomenon, novel sensors for various compounds in air or vapor, including S-containing (72, 73), N-containing (74), and organic compounds (75–77) CL in environment have been established. Methyl mercaptan (CH₃SH) and dimethyl sulfide (DMS) can emit strong chemiluminescence by reaction with ozone. Based on this phenomenon, Azad et al. (72) established a simple, automated CL method for the measurement of these two sulfur gases. In toilet air analysis, sulfur gases at ppb level are successfully measured by the simple procedure without much interference. CL analysis is also one of the most sensitive methods for the determination of NO₂. A sequential injection chemiluminescence (SI-CL) method has been satisfactorily applied to the determination of nitrogen oxide in air samples in wide concentration range with a minimum consumption of reagent, higher sample throughput, and waste generation (74).

Formaldehyde is the most abundant gas-phase carbonyl compound in the atmosphere, originating from both emissions from combustion sources and photooxidation of hydrocarbons. Many years ago, the chemiluminescence (CL) method for the determination of formaldehyde in natural and wastewater based on the modified Trautz-Schorigin reaction was described. However, the method at proposed configuration is not convenient for flow-injection application, and the sensitivity of the method is not sufficient for the measurement of formaldehyde in ambient air. A renaissance of Trautz-Schorigin chemiluminescence reaction from the point of view of the determination of gaseous formaldehyde in air was brought by Mikuska et al. (78).

One of the groups who studied the catalytic CL sensors is Zhang’s group. In their laboratory, several nanosized materials, owing to their advantages of high surface areas, good adsorption characteristics, and high activity, are employed as catalyst for cataluminescence (CTL) sensors, such as H₂S sensor (73), ethanol sensor (76), and a trimethylamine (TMA) sensor (75). Okabayashi and coworkers (79) have also established a new CTL method for identification of 11 types of gases, based on the difference in the CTL intensities during transition from physisorption to chemisorption state on the catalyst.
Table 1. Summary of the determination of pesticides by CL in the last two years

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Matrix</th>
<th>System</th>
<th>Detection limit</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nine pyrethroid insecticides</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Tomato</td>
<td></td>
<td>Acetonitrile-K$_2$Fe(CN)$_6$-NaOH</td>
<td>0.013–0.049 μg mL$^{-1}$</td>
<td>(40)</td>
</tr>
<tr>
<td><strong>Simazine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Surface water and fruit juice</td>
<td></td>
<td>(m-ISLMA)</td>
<td>1.29 $\times$ 10$^{-3}$ μg L$^{-1}$</td>
<td>(120)</td>
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<tr>
<td><strong>Asulam</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water samples</td>
<td></td>
<td>Potassium permanganate</td>
<td>40 μg L$^{-1}$</td>
<td>(121)</td>
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<tr>
<td><strong>Aldicarb</strong></td>
<td></td>
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<tr>
<td>Mineral water samples</td>
<td></td>
<td>Potassium permanganate-quinate sulphate</td>
<td>0.069 μg L$^{-1}$</td>
<td>(122)</td>
</tr>
<tr>
<td><strong>Carbaryl</strong></td>
<td></td>
<td></td>
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<tr>
<td>Water and cucumber samples</td>
<td></td>
<td>Luminal-potassium permanganate-OH</td>
<td>4.9 ng mL$^{-1}$</td>
<td>(123)</td>
</tr>
<tr>
<td>Soil and grain samples</td>
<td></td>
<td>Ce(IV)-rhodamine 6G</td>
<td>45.6 and 28.7 ng mL$^{-1}$ for peak height and peak area, respectively</td>
<td>(124)</td>
</tr>
<tr>
<td>Natural waters, vegetal food,</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>and cucumber</td>
<td></td>
<td>UV- peroxoxyalate</td>
<td>0.026 μg mL$^{-1}$</td>
<td>(125)</td>
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<tr>
<td><strong>N-nitrosodimethylamine</strong></td>
<td></td>
<td></td>
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<tr>
<td>Water and different cured</td>
<td></td>
<td>UV-tris(2,2'-bipyridyl) ruthenium (III)</td>
<td>0.29 ng mL$^{-1}$</td>
<td>(128)</td>
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<tr>
<td>meat products</td>
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<td><strong>Parabens</strong></td>
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<tr>
<td>Wash-off cosmetic</td>
<td></td>
<td>Cerium(IV)-rhodamine 6G</td>
<td>1.9 $\times$ 10$^{-9}$–5.3 $\times$ 10$^{-9}$ g mL$^{-1}$</td>
<td>(129)</td>
</tr>
<tr>
<td><strong>17β-Estradiol</strong></td>
<td></td>
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<tr>
<td>Wastewater</td>
<td></td>
<td>Chemiluminescence enzyme immunoassay (fluorescein-iso-thiocyanate (FITC)–anti-FITC)</td>
<td>1.5 pg mL$^{-1}$</td>
<td>(130)</td>
</tr>
<tr>
<td><strong>Glyphosate</strong></td>
<td></td>
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<tr>
<td>Industrial and commercial</td>
<td></td>
<td>Tris(2,2'-bipyridyl)ruthenium(II)</td>
<td>7 $\times$ 10$^{-9}$ mol L$^{-1}$</td>
<td>(131)</td>
</tr>
<tr>
<td>formulations</td>
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<tr>
<td><strong>Carbofuran</strong></td>
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<tr>
<td>Spiked water and lettuce samples</td>
<td></td>
<td>Luminol</td>
<td>0.02 μg mL$^{-1}$</td>
<td>(132)</td>
</tr>
<tr>
<td><strong>Propanil</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water samples</td>
<td></td>
<td>UV-potassium permanganate-sulphuric acid</td>
<td>8 μg L$^{-1}$</td>
<td>(133)</td>
</tr>
</tbody>
</table>
Inorganic Compounds in Liquid

The determination of nitrite, sulfite, hypochlorite, silicate, and phosphate concentration in liquid is of great importance for environmental protection. The CL methods for these salts account for the CL emission produced by salts oxidation using oxidants. Lin et al. (80) found peroxynitrous acid (ONOOH) was produced by the on-line mixing of acidified hydrogen peroxide with nitrite in a flow system, and a strong chemiluminescent (CL) emission was observed when ONOOH reacted with carbonate without any special CL reagents. In the presence of cotton, using the CL system, a sensitive and selective determination of nitrite in tap and well waters was demonstrated. In the same year, based on the emission produced by sulfite-induced autoxidation of Ni(II)/tetraglycine complex in the presence of luminol, Coichev et al. (81) established a sensitive method for determination sulfite. For the determination of hypochlorite, Claver et al. (82) developed a monolayer test strip procedure, which was based on the measurement of chemiluminescence produced in its reaction with fluoresceinate anion. The experimental result shows that the test strip proposed offers enough selectivity for its application to waters. A flow-injection (FI) manifold based on luminol chemiluminescence (CL) detection for the determination of silicate in freshwaters has also been described (83). Several CL methods for phosphate have been reported in the last two years. Based on the oxidation of luminol by heteropoly acid, a flow-injection–chemiluminescence method for the rapid determination of phosphate at nanomolar concentrations using a simple FI manifold was reported in 2004 (84). The determination of ultratrace orthophosphate in freshwater has been achieved by application of the CL technique based on oxidation of 3-aminophthalhydrazide (luminol) with vanadomolybdophosphoric heteropoly acid (VMoP) or MoP. The CL method based on the formation of VMoP adopted a flow-through solid-phase–based optical sensor with a detection limit of 129 nmol L$^{-1}$ for a 1.8 mL sample. This method has been successfully applied to the determination of trace levels of orthophosphate in the environmental samples such as mineral, ground, tap, and pond waters as well as samples from a water–steam cycle of an incineration plant. A simple and rapid flow-injection method has been developed on the oxidation of luminol by MoP, and the detection limit was 1 nmol L$^{-1}$ for a 0.18 mL sample (85). Both VMoP and MoP could act with luminal to produce CL light. The analysis of orthophosphate in seawater using the CL technique was not successful because of the seawater matrix interference. Subsequently, a novel on-line solid-phase extraction method coupled with flow-injection analysis and luminol chemiluminescence detection was successfully established to determine ultra-trace orthophosphate in seawater (86).

Ozone is one of the most powerful oxidizing agents and has become the disinfecting agent of choice for water treatment. CL can be used in the determination of ozone, because ozone is such an energetic oxidant that many of its reactions result in products in the excited state that emit light. It was found that
great enhancement of the CL signal can be induced reproducibly by modest exposure of the chromotropic acid (CA) solution to UV light en route to its reaction with ozone. Based on this, a system was established for the monitoring of ozonation status of playa lake water that exhibited significant ozone demand (87).

Hydrogen peroxide can also be widely found in the environment. The luminol chemiluminescence reaction within a microfluidic device was investigated to produce a miniaturized analytical system for the determination of hydrogen peroxide in rainwater (88).

Organic Compounds in Liquid

Inorganic phosphorus in the form of orthophosphate has long been regarded as the focus of many environmental studies. However, organic phosphorus species, such as phosphatidylcholine, may also constitute a sizeable proportion of the total phosphorus. A sensitive and selective flow-injection method for the determination of phosphatidylcholine (PC) in sediment pore waters and extracts has been described (89). The final product of the enzymatic reaction of phosphatidylcholine is hydrogen peroxide, and this is detected by measuring the chemiluminescence emission resulting from cobalt(II)-catalyzed reaction with luminol. The method has been applied to the determination of phosphatidylcholine in sediment extracts and sediment pore waters.

The pollution of environmental water by linear alkylebenzene sulfonates (LASs), which are widely used as anionic surfactants in detergents, has created a serious environmental problem. A chemiluminescent immunoassay using magnetic microbeads in an SIA system equipped with a magnet was proposed for the highly sensitive and rapid determination of LAS (90).

Benzenediols and benzenetriols are environmentally important phenolic compounds. Based on the sensitizing effect of formic acid on the chemiluminescence (CL) reaction of polyhydroxybenzenes with acidified potassium permanganate and the combination technique of high-performance liquid chromatography (HPLC), a sensitive, selective, and simple post-column CL detection method for simultaneously determining catechol, resorcinol, hydroquinone, and 1,2,4-benzenetriol was described (91). The proposed method has been successfully applied to the determination of the polyhydroxybenzenes in river water.

The CL intensity of luminol-DMSO-OH could be enhanced or inhibited by aromatic compounds. Based on this phenomenon, a sensitive HPLC-CL method was developed for the determination of intermediates such as p-phenylenediamine (PPDA), o-phenylenediamine (OPDA), p-aminophenol (PAP), o-aminophenol (OAP), resorcinol (RE), and hydroquinone (HQ) in oxidative hair dyes and wastewater of shampooing after hair dying (92).

Chemical oxygen demand (COD) is widely used as one of the most important measurable parameters for water quality. In many countries, such
as China and Japan, it has been accepted as a national standard for organic pollution evaluation. Up until now, chemiluminescence methods for determining COD were reported by only three groups (93–95). Zhang’s group (94) established a method for the determination of COD by using the CL system of luminol-H$_2$O$_2$-Mn$^{2+}$. Hu and Yang (95) developed a cost-efficient chemiluminescence photodiode detector that measures chemiluminescence emission produced by the luminol-H$_2$O$_2$-Cr$^{3+}$ reaction. Using a flow-injection ozonation chemiluminescence method involving ozone and UV oxidation of R-naphthol, Jin et al. (93) also determined COD in natural water. However, in these works, the oxidative degradation must be performed by use of strong oxidizing agents, dichromate, permanganate, or UV-O$_3$. The accuracy and reproducibility were diluted by the various factors in these systems, so there is still room for significant improvement.

Metal Ions and Nonmetal Ions

Quantification of metal ions and nonmetal ions is important in environmental monitoring of pollution from agricultural and industrial sources. In ground and surface waters, arsenic is generally found in the inorganic forms of arsenite, As(III), and arsenate, As(V), both of which are acutely toxic if swallowed. A novel chemiluminescence flow-injection procedure for the determination of As(III) in aqueous samples was proposed by Satienperakul et al. (96). The method involved injection of As(III) samples into a 1% (m/v) sodium hexametaphosphate in 0.02 mol $\cdot$ L$^{-1}$ $\text{H}_2\text{SO}_4$ carrier stream, which then merges at a Y-piece with a reagent stream consisting of potassium permanganate ($5.0 \times 10^{-5}$ mol $\cdot$ L$^{-1}$).

CL has been used to the determination of other metal ions in the environment, such as vanadium(IV), Hg(II), Cu(II), Co(II), chromium(III), and total chromium. A new chemiluminescent flow-injection analysis (FIA) method has been proposed for the determination of vanadium(IV) ions in aqueous media based on the chemiluminescent reaction between cinchomeronic hydrazide (CH) and hydrogen peroxide in a strongly alkaline medium (97). In the CL reaction, vanadium(IV) acts as a catalyst. Similarly, based on luminescence produced by Na$_2$O$_2$-H$_2$O$_2$ CL system sensitized by [Eu(EDTA)] and chemiluminescence intensity of the luminol-H$_2$O$_2$ reaction enhanced by the presence of Hg(II), flow-injection chemiluminescence (CL) analysis was used for the determination of europium in mineral samples (98) and Hg(II) (99), respectively. Cu(II) was investigated by several research groups in the past two years. In 2004, based on peroxalate chemiluminescence reaction using coproporphyrin I as a fluorophor compound to provide selectivity and a simple flow-injection (FI) chemiluminescence detector (CLD), an automatic method was proposed for the screening of water samples containing Cu(II) (100). Analysis of labile Cu$^{2+}$ in freshwaters using the Cu$^{2+}$-catalyzed oxidation of 1,10-phenanthroline by superoxide anion radical was investigated in the same year (101). In 2005, a novel chemiluminescence (CL) reaction,
thiosemicarbazide (TSC)-H₂O₂, for the determination of copper at nanogram per milliliter level in batch type is described (65). Zhang’s group (102) proposed a flow-injection chemiluminescence (CL) system for simultaneous determination of Co²⁺ and Cu²⁺ using partial least-squares (PLS) calibration. This method was based on the fact that both Co²⁺ and Cu²⁺ catalyze the CL reaction of luminol-H₂O₂. A simple flow-based procedure with chemiluminescence (CL) detection was proposed for a nonmetal ion, bromide ion determination in seawater (103). The procedure was based on the oxidation of bromide to bromine by chloramine-T followed by the reaction of bromine with luminol to produce CL emission.

**Biological and Clinical**

The most important applications of chemiluminescence in the biological and clinical analysis are mainly immunoassay and nucleic acid assays.

**Immunooassay**

Chemiluminescence immunoassay (CLIA) is the marriage of CL analysis and immunoassay. In CLIA, the three major chemiluminescent technologies are: (1) acridinium ester and sulfonamide labels in chemiluminescent immunoassay; (2) chemiluminescent detection techniques for horseradish peroxidase labels and glucose oxidase labels; and (3) chemiluminescent detection techniques for alkaline phosphatase labels in enzyme immunoassay. Automated immunoassay analyzers have been developed and commercialized by several major companies. Thus, CLIA (including ECL Immunoassay and CL) was applied in many fields, especially in biological and clinical analysis (Table 2).

**Nucleic Acid Assays**

In recent years, various nonradiochemical methods utilizing chemiluminescence reactions have been developed to enhance the sensitivity and speed of detecting nucleic acid probes or nucleic acid itself.

Sensitivity in DNA hybridization and other bioassays is important in clinical diagnostics. ECL methods have been widely used in such studies because of their high sensitivity, wide dynamic range, and selectivity. Bard and coworkers (104) reported an ultrasensitive DNA hybridization detection methodology that utilizes polystyrene microspheres/beads (PSB) as the carrier of a large number of the electrogenerated chemiluminescence (ECL) labels, namely, Ru(bpy)₃²⁺ species. Compared with the previously reported ECL determination of immobilized DNA, it has a number of advantages: (a) high sensitivity/low detection limits (as low as 1.0 fM t-ssDNA can be detected); (b) high selectivity/low nonspecific adsorptions complementary:
Table 2. The application of CLIA in the last two years

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Labeled complex/derivatization reagent</th>
<th>System</th>
<th>Detection limit</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone morphogenic protein-2 (BMP-2)</td>
<td>HRP-Ab2-mAb-BMP-2 complexes</td>
<td>HRP-luminol-H2O2-p-iodophenol</td>
<td>6.2 pM (75 zmol)</td>
<td>(48)</td>
</tr>
<tr>
<td>Bovine serum albumin</td>
<td>Tetra-substituted sulphonated cobalt(II) (CoTSPc)</td>
<td>Luminol-H2O2</td>
<td>0.25 µg mL⁻¹</td>
<td>(58)</td>
</tr>
<tr>
<td>IgG</td>
<td>Irregular gold nanoparticles (IGNPs) labeled IgG</td>
<td>Luminol-Au-NPs</td>
<td>17 pmol L⁻¹</td>
<td>(62)</td>
</tr>
<tr>
<td>Human IgG and IgA</td>
<td>Poly(N-isopropylacrylamide) (PNIP) and magnetic beads</td>
<td>Luminol-H2O2-HRP</td>
<td>2.0 and 1.5 ng mL⁻¹</td>
<td>(134)</td>
</tr>
<tr>
<td>Carcinoembryonic antigen (CEA)</td>
<td>HRP-labeled anti-CEA</td>
<td>Luminol- HRP-H2O2</td>
<td>0.5 ng mL⁻¹</td>
<td>(135)</td>
</tr>
<tr>
<td>Alpha-fetoprotein (AFP)</td>
<td>HRP-labeled anti-AFP</td>
<td>Luminol- HRP-H2O2</td>
<td>0.5 ng mL⁻¹</td>
<td>(136)</td>
</tr>
<tr>
<td>Estriol</td>
<td>HRP-labeled anti-estriol antibody</td>
<td>Luminol- HRP-H2O2</td>
<td>5.0 ng mL⁻¹</td>
<td>(137)</td>
</tr>
<tr>
<td>Human serum albumin (HSA) and immunosuppressive acidic protein (IAP)</td>
<td>Isoluminol isothiocyanato (ILITC)</td>
<td>ILITC-microperoxidase-H2O2</td>
<td>1×10⁻⁷ mol L⁻¹</td>
<td>(138)</td>
</tr>
<tr>
<td>Human chorionic gonadotropin beta (hCGβ)</td>
<td>Superparamagnetic polymers (SPMP) microbeads labeled anti-hCGβ</td>
<td>AMPPD-ALP</td>
<td>0.22 mIU·m⁻¹</td>
<td>(139)</td>
</tr>
<tr>
<td>Haptoglobin</td>
<td>Hp-hemoglobin (Hb) complex</td>
<td>Luminol-H2O2</td>
<td>1.21 ng</td>
<td>(140)</td>
</tr>
<tr>
<td>C-reactive protein (CRP)</td>
<td>Ru(bpy)₃-[B(C₆F₅)₄]₂/ bead</td>
<td>Ru-(bpy)₃²⁺-ECL</td>
<td>0.010 µg mL⁻¹</td>
<td>(141)</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Analyte</th>
<th>Labeled complex/derivatization reagent</th>
<th>System</th>
<th>Detection limit</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA125 antibody (Ab) and Ab-antigen</td>
<td>HRP-labeled antibody</td>
<td>Luminol-H₂O₂-HRP (CE-CL) (HRP)</td>
<td>1.0 × 10⁻¹² mol L⁻¹</td>
<td>(142)</td>
</tr>
<tr>
<td>Clenbuterol</td>
<td>Molecularly imprinted polymer (MIP) prepared by methacrylic acid (MAA)</td>
<td>Potassium permanganate-formaldehyde</td>
<td>3.0 × 10⁻¹⁰ g mL⁻¹</td>
<td>(143)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Luminol-BSA-digoxin conjugate Avidin–biotin system and Fluorescein-isothiocyanate (FITC)-anti-FITC system</td>
<td>Luminol (ECL-IA) 4-methoxy-4-(3-phosphatethenyl)-spiro(1,2-dioxetane-3,2′-adamantane)</td>
<td>2.8 × 10⁻¹⁰ g mL⁻¹</td>
<td>(144)</td>
</tr>
<tr>
<td>Albumin</td>
<td></td>
<td></td>
<td>0.089 µg mL⁻¹</td>
<td>(145)</td>
</tr>
<tr>
<td>Human tumor necrosis factor-α (rh TNF-α)</td>
<td>Horseradish peroxidase (HRP)</td>
<td>Luminol (ECL)</td>
<td>1 pg mL⁻¹</td>
<td>(146)</td>
</tr>
<tr>
<td>IgG</td>
<td>IgG-functionalized gold nanoparticles</td>
<td>AuCl₄⁻-luminol-H₂O₂</td>
<td>1.5 ng mL⁻¹</td>
<td>(147)</td>
</tr>
<tr>
<td>Carp vitellogenin (Vg)</td>
<td>Labeled with magnetic beads or HRP</td>
<td>Luminol-H₂O₂-HRP-p-iodophenol</td>
<td>2 ng mL⁻¹</td>
<td>(148)</td>
</tr>
<tr>
<td>Terbutaline</td>
<td>Molecularly imprinted polymer (MIP) prepared by methacrylic acid (MAA)</td>
<td>Luminol-ferricyanide</td>
<td>4.0 ng mL⁻¹</td>
<td>(149)</td>
</tr>
<tr>
<td>Human papillomavirus (HPV)</td>
<td>Horseradish peroxidase–labeled antidigoxigenin antibody</td>
<td>Luminol-peroxide-enhancer</td>
<td>—</td>
<td>(150)</td>
</tr>
</tbody>
</table>
Recent Advances in Chemiluminescence

two base pair mismatched and noncomplementary DNA hybridizations can be distinguished and no complicated treatment to eliminate nonspecific adsorption of Ru(bpy)$_3^{2+}$ is required; and (c) high stability and the possibility of multiple measurements, because the solution containing the ECL label, Ru(bpy)$_3^{2+}$ can be used to make many ECL measurements without loss of signal. Since the property of electrical conductivity, biocompatibility, and easy self-assembly through a thiol group, gold nanoparticle has received a considerable interest. A highly sensitive ECL method for the detection of DNA hybridization based on multiple reporters per hybridization event using gold nanoparticle as a carrier for ECL label and ss-DNA has been developed recently (105). A detection limit of $5.0 \times 10^{-12}$ mol L$^{-1}$ for target ss-DNA was achieved.

A new FI-CL method for the determination of ctDNA and hsDNA in dilute sulfuric acid was developed by Ma et al. (106). In their work, imidazole-HCl buffer solution is firstly applied to activate DNA; the complicated thermally denatured procedure for DNAs is therefore avoided and the response range is broadened further to five or seven orders of magnitude. Kang et al. (107) used a commercial chemiluminescence generating system to evaluate the validity of quantitative measurements of biotin-labeled tRNA and single-stranded DNA.

Recently, Fan et al. (108) used magnetic beads for DNA hybridization detection assay and reported a new oxidative gold metal dissolution–based CL method for the noncompetitive immunoassay of a human immunoglobulin G by taking advantage of a magnetic separation/mixing process and the amplification feature of colloidal gold label. Following this work, they established a new CL method for the detection of the specific DNA sequence by the coupling of DNAzyme CL detection route with an efficient magnetic isolation of the hybrid. Compared with previous DNAzyme-based methods, the new method has such characteristics as rapidness, ease of use, and high sensitivity. The entire assay can be completed within 2–3 h at a concentration of 0.02–2 pmol and a detection limit of $1 \times 10^{-10}$ mol L$^{-1}$ for the recognition of 30-base model oligonucleotide (109).

Li et al. (62) synthesized specially shaped, irregular gold nanoparticles (IGNPs) and found their catalytic efficiency on luminol CL to be 100-fold greater than that of spherical Au-NPs. Using the IGNPs-functionalized DNA oligomers and the IGNPs-modified anti-IgG as in situ chemiluminescent probes, they established sandwich-type analytic methods for rapid, simple, selective, and sensitive sequence-specific not only for human plasma DNA detection but also for IgG immunoassay, respectively.

Zheng et al. (110) performed single- and multiplex gene expression analysis with multiple hybridization probes to capture mRNA directly from blood lysate and used branched DNA to amplify the signal. The 96-well plate singleplex assay uses chemiluminescence detection. Both the singleplex and the multiplex branched DNA assays can quantitatively measure mRNA expression directly from a small volume of whole blood.
Food Analysis

The colorants known also as Sudan I-IV have shown potential in laboratory experiments to cause cancer to animals and humans. However, Sudan dyes have been found as a contaminant in chilli powder. Although various methods have been successfully applied to the analysis of Sudan dye residues in food products at trace levels, they suffer from a tedious procedure, time consumption or high cost. HPLC-CL assay of Sudan dyes was proposed by Zhang et al. (37). The method was based on the enhancement effect of Sudan dyes on the chemiluminescence reaction between luminol and BrO\(^-\), which was on-line electro-generated by constant current electrolysis. It has been successfully applied to the determination of four Sudan dyes in hot chilli products.

Catechins are always the main components in tea. Many CL analysis methods have been used for the determination of catechins. Recently, based on the fact aromatic compounds upon UV irradiation can cause CL upon mixing with Ru(bpy)\(^{3+}\), a novel HPLC method for the determination of aromatic compounds based on the on-line photochemical degradation and subsequent Ru(bpy)\(^{3+}\) chemiluminescence detection have been developed (111).

Phenolic compounds (38), praline (112), and trans-resveratrol (113) in wine can also be determined by CL method. In Cui et al.’s work (38), based on the chemiluminescent enhancement by phenolic compound of the cerium(IV)-rhodamine 6G system in sulfuric acid medium, a simple, selective, and sensitive determination method for 20 phenolic compounds in red wine has been developed using HPLC with chemiluminescence detection. They also established a novel method for the determination of trans-resveratrol in red wines based on a similar technique (113). Several CL methods have been satisfactorily applied to the determination of benzoyl peroxide in wheat flour (114, 115). A new simplified procedure for the enzymatic CL assay of glucose by means of a hybrid FIA/SIA method with soluble enzyme was proposed (116). This method is considered satisfactory for rapid screening of the glucose content in energy drinks and honey.

Food additives play a vital role in the modern food industry and are generally used for maintaining food quality and characteristics as well as promoting food safety. The alkyl esters of p-hydroxybenzoic acid (parabens) including methylparaben (MP), ethylparaben (EP), propylparaben (PP), and butylparaben (BP) are used as preservatives. Cui et al. (117) found the enhancement by parabens of cerium (IV)-rhodamine 6G chemiluminescence reaction in sulfuric acid medium. Based on this, a simple method for the determination of parabens was established.

Immunosorbent assay with chemiluminescence is widely applied in food analysis (118, 119). An enzyme-linked immunosorbent assay (ELISA) based on polyclonal antibody with enhanced chemiluminescent (ECL) detection of fumonisin B1 (FB1) in food samples has been first developed by Wang’s group (118). The method was about 10 times more sensitive compared to colorimetric ELISA using the same antibody and HRP-conjugate with rapid analysis.
<table>
<thead>
<tr>
<th>Analyte</th>
<th>System</th>
<th>Matrix</th>
<th>Detection limit</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>Lucigenin</td>
<td>Injection</td>
<td>$2.4 \times 10^{-8}$ mol L$^{-1}$</td>
<td>(56)</td>
</tr>
<tr>
<td></td>
<td>Luminol-K$_3$[Fe(CN)$_6$]</td>
<td>Urine</td>
<td>0.39 µmol L$^{-1}$</td>
<td>(45)</td>
</tr>
<tr>
<td>Benserazide</td>
<td>Luminol-K$_3$Fe(CN)$_6$</td>
<td>Tablets</td>
<td>1.85 µg mL$^{-1}$</td>
<td>(46)</td>
</tr>
<tr>
<td>Levodopa</td>
<td></td>
<td></td>
<td>0.12 µg mL$^{-1}$</td>
<td></td>
</tr>
<tr>
<td>97 Compounds</td>
<td>KMnO$_4$-sulphuric acid</td>
<td>—</td>
<td>—</td>
<td>(151)</td>
</tr>
<tr>
<td>Estrogens</td>
<td>Luminol-H$_2$O$_2$</td>
<td>Injections, tap water</td>
<td>$7.2 \times 10^{-9}$–$6.5 \times 10^{-8}$ mol L$^{-1}$</td>
<td>(59)</td>
</tr>
<tr>
<td></td>
<td>KMnO$_4$-formaldehyde</td>
<td>Tablets, tap water</td>
<td>$1.08 \times 10^{-9}$–$6.28 \times 10^{-9}$ g mL$^{-1}$</td>
<td>(152)</td>
</tr>
<tr>
<td>d-Thyroxine</td>
<td>Luminol-iron(II)</td>
<td>Tablets</td>
<td>0.08 mg L$^{-1}$</td>
<td>(153)</td>
</tr>
<tr>
<td>L-Thyroxine</td>
<td></td>
<td></td>
<td>0.1 mg L$^{-1}$</td>
<td></td>
</tr>
<tr>
<td>Diethylstilbestrol</td>
<td>Luminol-H$_2$O$_2$</td>
<td>Tablets</td>
<td>$6.42 \times 10^{-8}$ mol L$^{-1}$</td>
<td>(154)</td>
</tr>
<tr>
<td>Methimazole</td>
<td>Luminol-H$_2$O$_2$-Cu(II)</td>
<td>Tablets</td>
<td>2 mg L$^{-1}$</td>
<td>(155)</td>
</tr>
<tr>
<td>Carbimazole</td>
<td></td>
<td></td>
<td>1 mg L$^{-1}$</td>
<td></td>
</tr>
<tr>
<td>Cephalosporin antibiotics</td>
<td>KMnO$_4$-glyoxal</td>
<td>Tablets</td>
<td>2–10 ng mL$^{-1}$</td>
<td>(156)</td>
</tr>
<tr>
<td></td>
<td>Ru(bpy)$_3^{2+}$-KmnO$_4$</td>
<td>Tablets, injections</td>
<td>0.03–0.08 µg mL$^{-1}$</td>
<td>(157)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Peroxyoxalate-imidazole</td>
<td>Injections</td>
<td>1.18 µg mL$^{-1}$</td>
<td>(158)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Luminol-H$_2$O$_2$-Cu(II)</td>
<td>Tablets</td>
<td>2.97 mg L$^{-1}$</td>
<td>(159)</td>
</tr>
<tr>
<td>Cefadroxil</td>
<td>KMnO$_4$-formaldehyde</td>
<td>Tablets</td>
<td>25 ng mL$^{-1}$</td>
<td>(160)</td>
</tr>
<tr>
<td>Cefprozil</td>
<td>Ru(bpy)$_3^{2+}$-KmnO$_4$</td>
<td>Tablets</td>
<td>0.005 µg mL$^{-1}$</td>
<td>(161)</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Luminol-myoglobin</td>
<td>Capsules</td>
<td>0.03 ng mL$^{-1}$</td>
<td>(162)</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>KMnO$_4$</td>
<td>—</td>
<td>$2 \times 10^{-8}$ g mL$^{-1}$</td>
<td>(163)</td>
</tr>
<tr>
<td>Tetraclycline</td>
<td>Acetonitrile-H$_2$O$_2$</td>
<td>Tablets</td>
<td>60 nmol L$^{-1}$</td>
<td>(164)</td>
</tr>
<tr>
<td></td>
<td>Ru(bpy)$_3^{2+}$-KmnO$_4$</td>
<td>—</td>
<td>$1.0 \times 10^{-6}$–$2.0 \times 10^{-6}$ mol L$^{-1}$</td>
<td>(165)</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>H$_2$O$_2$-nitrite-sulfuric acid</td>
<td>Urine</td>
<td>$8.6 \times 10^{-8}$ mol L$^{-1}$</td>
<td>(166)</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Analyte</th>
<th>System</th>
<th>Matrix</th>
<th>Detection limit</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indomethacin</td>
<td>Mn (IV)-formaldehyde</td>
<td>Urine</td>
<td>$4 \times 10^{-8} \text{ g mL}^{-1}$</td>
<td>(167)</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Ru(bpy)$_2^{3+}$-KMnO$_4$</td>
<td>Tablets</td>
<td>0.2 $\mu$g mL$^{-1}$</td>
<td>(168)</td>
</tr>
<tr>
<td></td>
<td>Luminol-K$_3$Fe(CN)$_6$</td>
<td>Tablets, urine</td>
<td>$5.6 \times 10^{-10} \text{ mol L}^{-1}$</td>
<td>(169)</td>
</tr>
<tr>
<td>Analgin</td>
<td>MnO$_2$-Rhodamine B</td>
<td>Tablets</td>
<td>$2.7 \times 10^{-5} \text{ g mL}^{-1}$</td>
<td>(170)</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Luminol-K$_3$Fe(CN)$_6$</td>
<td>Injections</td>
<td>5 $\mu$g L$^{-1}$</td>
<td>(171)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Ru(bpy)$_2^{3+}$-PbO$_2$</td>
<td>Human serum</td>
<td>$1.0 \times 10^{-8} \text{ mol L}^{-1}$</td>
<td>(172)</td>
</tr>
<tr>
<td></td>
<td>SO$_3^{2-}$-SDBS</td>
<td>Tablet, urine</td>
<td>0.9 ng mL$^{-1}$</td>
<td>(173)</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>N-Bromosuccinimide-fluorescein</td>
<td>Tablets</td>
<td>$7.7 \times 10^{-8} \text{ mol L}^{-1}$</td>
<td>(174)</td>
</tr>
<tr>
<td>Puerarin</td>
<td>Ce(IV)-rhodamine 6G</td>
<td>Injection</td>
<td>$8.4 \times 10^{-10} \text{ g mL}^{-1}$</td>
<td>(175)</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Peroxynitrous acid</td>
<td>Tablets, drops</td>
<td>$4.5 \times 10^{-8} \text{ mol L}^{-1}$</td>
<td>(176)</td>
</tr>
<tr>
<td>Protocatechuic aldehyde</td>
<td>Luminol-K$_3$[Fe(CN)$_6$]</td>
<td>Injections</td>
<td>$7.0 \times 10^{-8} \text{ mol L}^{-1}$</td>
<td>(177)</td>
</tr>
<tr>
<td>Protocatechuic acid</td>
<td>K$_2$[Fe(CN)$_6$]-dioxane</td>
<td>Tablets</td>
<td>$5.0 \times 10^{-8} \text{ mol L}^{-1}$</td>
<td>(178)</td>
</tr>
<tr>
<td>Ergotamine tartrate</td>
<td>KMnO$_4$, Mn(IV)</td>
<td>Tablets</td>
<td>$6 \times 10^{-7} \text{ mg L}^{-1}$</td>
<td>(179)</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>Ce(IV)-photo irradiation</td>
<td>Tablets</td>
<td>0.005–0.06 $\text{ g mL}^{-1}$</td>
<td>(180)</td>
</tr>
<tr>
<td>Thiazides</td>
<td>RuBPS-Ce(IV)</td>
<td>Tablets</td>
<td>$1.0 \times 10^{-3} \mu$g mL$^{-1}$</td>
<td>(181)</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Furosemide</td>
<td>Tablets</td>
<td>$8.8 \times 10^{-3} \mu$g mL$^{-1}$</td>
<td>(182)</td>
</tr>
<tr>
<td>Aminophylline</td>
<td>N-bromosuccinimide-luminol</td>
<td>Plasma</td>
<td>$3.4 \times 10^{-8} \text{ g mL}^{-1}$</td>
<td>(183)</td>
</tr>
<tr>
<td>Clenbuterol</td>
<td>Luminol-H$_2$O$_2$-HRP</td>
<td>Urine</td>
<td>1.2 nmol L$^{-1}$</td>
<td>(184)</td>
</tr>
<tr>
<td>Syneprine</td>
<td>Luminol-K$_3$Fe(CN)$_6$</td>
<td>Herbal products</td>
<td>1.6 ng mL$^{-1}$</td>
<td>(185)</td>
</tr>
<tr>
<td>Drug</td>
<td>Reagent</td>
<td>Formulation</td>
<td>Concentration</td>
<td>Ref.</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------------------</td>
<td>-----------------</td>
<td>------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>Luminol-hypochlorite</td>
<td>Tablets</td>
<td>$8.7 \times 10^{-9}$ mol L(^{-1})</td>
<td>(185)</td>
</tr>
<tr>
<td>Dihydralazine sulfate</td>
<td>$K_2Fe(CN)_6$-eosin Y</td>
<td>Tablets</td>
<td>$0.012 \mu$g mL(^{-1})</td>
<td>(186)</td>
</tr>
<tr>
<td>Propranolol</td>
<td>$KMnO_4-H_2SO_4$</td>
<td>Tablets, injections</td>
<td>—</td>
<td>(187)</td>
</tr>
<tr>
<td></td>
<td>$KMnO_4$-pyrogallol</td>
<td>Injections</td>
<td>$3.74$ ng mL(^{-1})</td>
<td>(188)</td>
</tr>
<tr>
<td>Phentolamine</td>
<td>Luminol-$K_3Fe(CN)_6$</td>
<td>Injections, plasma, urine</td>
<td>$3.0$ ng mL(^{-1})</td>
<td>(189)</td>
</tr>
<tr>
<td></td>
<td>Ce(IV)-rhodamine 6G</td>
<td>Injections, plasma, urine</td>
<td>$4 \times 10^{-10}$ g mL(^{-1})</td>
<td>(190)</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>Luminol-periodate</td>
<td>Urine</td>
<td>$6 \times 10^{-10}$ g mL(^{-1})</td>
<td>(191)</td>
</tr>
<tr>
<td>Metoprolol tartrate</td>
<td>Ce(IV)-SO(_4)_2</td>
<td>Tablets, urine</td>
<td>$4.7 \times 10^{-9}$ mol L(^{-1})</td>
<td>(192)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Ru(bpy)$_3^{2+}$-peroxydisulfate</td>
<td>Injections, tablets</td>
<td>$0.28 \mu$g mL(^{-1})</td>
<td>(193)</td>
</tr>
<tr>
<td>Atropine sulfate</td>
<td>Ce(IV)-sodium sulfate</td>
<td>Tablets</td>
<td>$4 \times 10^{-7}$ g mL(^{-1})</td>
<td>(194)</td>
</tr>
<tr>
<td>Salbutamol</td>
<td>Luminol-$K_3Fe(CN)_6$</td>
<td>Urine</td>
<td>$1.6 \times 10^{-3}$ g mL(^{-1})</td>
<td>(195)</td>
</tr>
<tr>
<td>Naloxone</td>
<td>$KMnO_4-H_3PO_4$</td>
<td>Injections</td>
<td>$0.01 \mu$g mL(^{-1})</td>
<td>(196)</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Ru(bpy)$_3^{2+}$-Ce(IV)</td>
<td>Injection</td>
<td>$2.5 \times 10^{-2}$ $\mu$g mL(^{-1})</td>
<td>(197)</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Luminol-cyclohexane</td>
<td>Urine</td>
<td>$6$ ng mL(^{-1})</td>
<td>(198)</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Luminol-$H_2O_2$</td>
<td>Tablets</td>
<td>$4$ pg mL(^{-1})</td>
<td>(199)</td>
</tr>
<tr>
<td>Promethazine hydrochloride</td>
<td>Luminol-$K_3Fe(CN)_6$</td>
<td>Urine</td>
<td>$80$ ng mL(^{-1})</td>
<td>(200)</td>
</tr>
<tr>
<td>Promazine hydrochloride</td>
<td>Luminol-$K_3Fe(CN)_6$</td>
<td>Urine</td>
<td>$334$ ng mL(^{-1})</td>
<td>(201)</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Sodium sulphite-Ce(IV)</td>
<td>Injections, tablets</td>
<td>$0.7$ $\mu$g mL(^{-1})</td>
<td>(202)</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>Hydrogen peroxide-nitrite-sulfuric acid</td>
<td>Injections, serum</td>
<td>$1.8 \times 10^{-7}$ mol L(^{-1})</td>
<td>(203)</td>
</tr>
<tr>
<td>Cysteine</td>
<td>Luminol-cysteine-$NaIO_4$</td>
<td>Injections</td>
<td>$5 \times 10^{-9}$ mol L(^{-1})</td>
<td>(204)</td>
</tr>
<tr>
<td>Oxymetazoline hydrochloride</td>
<td>Luminol-$KmMnO_4$</td>
<td>Tablets</td>
<td>$1.21$ ng mL(^{-1})</td>
<td>(205)</td>
</tr>
<tr>
<td>Difenidol hydrochloride</td>
<td>Ru(bpy)$_3^{2+}$</td>
<td>Tablets</td>
<td>$1 \times 10^{-7}$ mol L(^{-1})</td>
<td>(206)</td>
</tr>
</tbody>
</table>
Zhang’s group (119) developed a sensitive, simple, and rapid technique for high-throughput simultaneous detection of staphylococcal enterotoxin C1 (SEC1) in milk. The proposed method adequately shows the specificity of ELISA.

Pharmaceutical

Owing to its high sensitivity, wide linear range, relatively low cost, and simple instrumentation, chemiluminescence methods coupled with other analytical approaches such as flow-injection or sequential injection (SI), high-performance liquid chromatography (HPLC), capillary electrophoresis (CE), or molecule imprinting (MIP) have been widely applied to pharmaceutical detection. The mechanism in pharmaceutical applications is primarily based on the enhancement effect or the inhibition effect of the studied drugs on the chemiluminescence emission of the employed chemiluminescence systems. The application of CL in pharmaceutical analysis in the last two years is summarized in Table 3.

CONCLUSION

Owing to the advantages of high sensitivity, wide linear range, simple instrumentation, and fast dynamic response, CL has continually received more and more attention in the last two years. CL has been used in various fields, including environmental, biological, clinical, food, and pharmaceutical analysis. Nevertheless, compared to other conventional, well-established, and commercial modes of detection such as UV, CL detection is a developing technique and further research is needed in order to implement CL routinely as a mode of detection.

It is worth mentioning here that miniaturization of CL instrumentation for special application should be further studied to extend the new technique to on-site, on-line, or real-time analysis in life science as well as other areas. The investigation of new and efficient catalysts such as complexes and nanoparticles for chemiluminescent reactions is of great analytical potential in developing new immunoassay and CL detectors with a wide response to a range of compounds for HPLC and CE. It is also necessary to synthesize new CL reagents with more effective CL quantum yield or look for new CL reactions to further improve the linear dynamic range and sensitivity of CL detection. Furthermore, the lifetime of the sensors, which can be increased with various materials such as nanosized materials, should be further improved.

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REFERENCES


Recent Advances in Chemiluminescence


