

Review

Flow Injection Technique for Biochemical Analysis with Chemiluminescence Detection in Acidic Media

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Received: 23 March 2007 / Accepted: 4 April 2007 / Published: 16 April 2007

Abstract: A review with 90 references is presented to show the development of acidic chemiluminescence methods for biochemical analysis by use of flow injection technique in the last 10 years. A brief discussion of both the chemiluminescence and flow injection technique is given. The proposed methods for biochemical analysis are described and compared according to the used chemiluminescence system.

Keywords: Flow injection, Chemiluminescence.

1. Introduction

Analysis in biochemistry includes pharmaceutical analysis, clinic analysis, food analysis, nucleic acid analysis, protein analysis, and so on. Over the past 20 years, owing to the wide use of such species, many techniques have been proposed for their determination in different matrices and at different levels. Conventional methods can handle only a limited number of samples due to the requirement for time-consuming procedures involving extraction, reaction and analysis. Also, the analyte in biochemical samples is often small-level, and for this reason it demands high-sensitive detection techniques.

Chemiluminescence (CL) is the light emission derived from a chemical reaction in which chemically excited molecules decay to the electronic ground state and emit photons [1]. In terms of the production mechanism of light emission, the CL technique can be divided into direct CL and indirect CL, in which the chemical energy is transferred from a product C* in an excited state to a fluorophore F, as illustrated in Fig.1. Measurement of light from a chemical reaction is very useful from an analytical point of view because, under appropriate experimental conditions, the light intensity is

directly related to the analyte concentration, thus allowing precise and sensitive quantitative analysis. Compared with the other spectrophotometric techniques such as spectrophotometry, fluorometry, resonance light scattering methods etc., the main attractions of CL for biochemical analysis show excellent sensitivity over a wide linear dynamic range and low limits of detection because no external excitation source is required and therefore, the background signal is very low. However, there is a drawback in CL methods that the lack of selectivity due to the fact that most CL reagents can produce emission for more than one analyte.

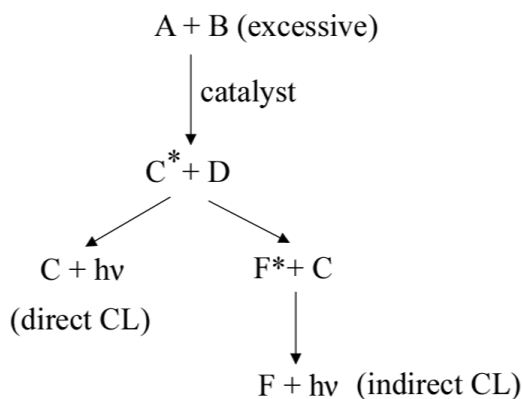


Figure 1. The main mechanisms leading to a chemiluminescent reaction: A, analyte; B, oxidant; C, D, product; F, fluorophore; *, the excited state; $h\nu$, luminescence.

Fortunately, the limited selectivity of CL reactions can be overcome by coupling with physical separations or a flow technique including flow injection analysis (FIA) as the most widely used technique. FIA is a simple analytical technique under non-equilibrium conditions, in which a discrete liquid sample is injected automatically into a liquid carrier stream to be transported to a flow-through detector [2]. Assays based on FIA reveals, in comparison to manual procedures, a better precision, a higher analysis throughput and a reduction in sample contamination. Thus, CL determinations coupled with FI technique have been the most successful approach to monitor CL reaction, combining the advantages of instrumental simplicity, rapidity (normally 0.1-10 s) and a high degree of reproducibility in signal detection, and being appropriate for on-line analysis of biochemical species. In Fig.2 schematic illustration of a typical FI-CL analysis apparatus is depicted [3].

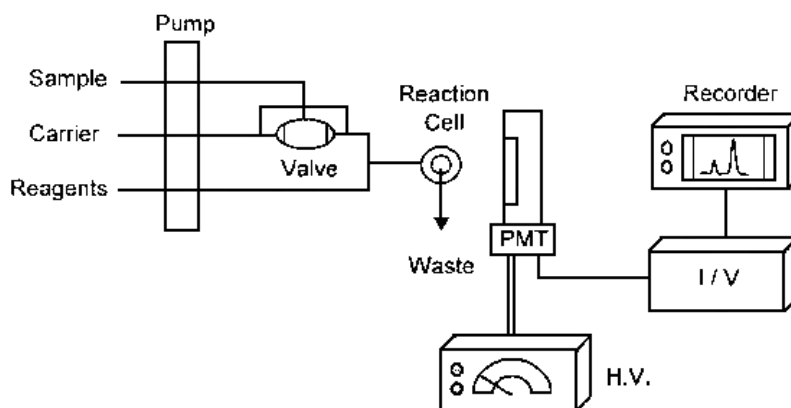


Figure 2. schematic illustration of a typical FI-CL analysis apparatus.

To date, many analysts have show great interests in flow injection technique with a CL detector. Although the most widely used CL system in FIA is luminol with hydrogen peroxide as oxidant, an acidic CL system involving potassium permanganate, cerium (IV) and rhodamine compounds seems more suitable for analysis of biochemical species since such substances are often not stable in basic media. In recent years, the use of FI methodologies with CL detection in an acidic media presents a great potential to perform the analysis for kinds of species in foods, drinks, pharmaceuticals and body fluids, and the proposed methods are described and compared according to the used CL detection system in this paper.

2. Applications of Different CL Systems in FIA

2.1. Permanganate-Based CL System in FIA

It is likely that Grinberg [4], in 1920, was the first to report the use of acidic potassium permanganate (KMnO_4) as a reagent for the oxidation of pyrogallol in the presence of hydrogen peroxide. The first analytical application of acidic potassium permanganate CL reaction was published in 1975 [5]. However, until 1986, this reagent was mainly focused on the determination of sulphur dioxide. The report of Townshend [6] on morphine determination blossomed the application of acidic potassium permanganate to the analysis of drugs and organic compounds. Now, acidic potassium permanganate has been successfully employed, generally with flow analysis, as a strong oxidant to generate chemiluminescence. Of the methodologies described, many have demonstrated that this chemistry is capable of detecting a wide variety of analytes with good sensitivity, using batch techniques, flow analysis, after separation by either liquid chromatogram or, more recently, capillary electrophoresis. The KMnO_4 -based FI-CL methods are mainly based on the direct oxidation of the analyte by KMnO_4 [7-14], or based on the enhancement of CL intensity of the KMnO_4 -sulfite system by the analyte [15-17], using quinine, formaldehyde, glyoxal, formic acid and some surfactants as a sensitizer. Among the wide range of compounds, the most analytes in KMnO_4 -based CL system possess either an amine or a phenolic moiety [18]. So far, KMnO_4 -based CL detection is overwhelming in the determination of pharmaceutical preparations (mainly antibiotics). The related review has focus on the analytical application and the mechanism discussion of the system published up until mid-2001 [19]. In a word, as one of a few of acidic CL systems, KMnO_4 -based CL holds still a wide potential applications with a deeper understanding of the mechanisms that lead to the production of light. In Table 1, a chronological survey of the analytical applications of acidic potassium permanganate CL with FI technique for the determinations of biochemical species are listed in the last 10 years.

2.2. Cerium (IV)-Based CL System in FIA

Compared with acidic KMnO_4 -based CL system, cerium (IV)-related CL reaction is not subject to the chloride ion [40]. Moreover, KMnO_4 has strong absorption to light emission and consequently the CL intensity could decrease when the concentration of KMnO_4 is too high. Instead, the sensitivity for cerium (IV)-based CL system can be improved by increasing cerium (IV) concentration since the self-absorption of light is reduced largely in the system. Therefore, the cerium (IV)-based CL reaction in an acidic media (generally in sulfuric acid medium) has also been carried out for the determination of

biochemical species in dosage forms. For example, a few of pharmaceuticals can reduce the Ce (IV) directly and produce luminescence. Given this, many FI-CL methods have been established for such species like naproxen [41], acetaminophen [42], fluphenazine hydrochloride [43], and so on. However, most determinations involving Ce(IV) as the oxidant are of the indirect type, which based on the enhancement effect of some analytes on the CL intensity of Ce (IV)-sulfite system, Ce (IV)-Ru(bpy)₃²⁺ system or Ce (IV)-Tween 20 system, etc. This type of process, named sensitization, is used to determine reducing compounds, such as cortisone [44], ofloxacin [45], nomoxacin, ciprofloxacin, lomefloxacin [46], flufenamic acid, mefenamic acid [47] and salicylic acid [48]. In particular, light emission resulting from the chemical reaction of Ce (IV) with some mercapto-containing compounds in pharmaceutical preparations can be enhanced by certain fluorometric reagents such as quinine^[49, 50], rhodamine B [43, 51] and rhodamine 6G [52, 53] or by lanthanide ions like Tb (III) and Eu (III), etc.[54-56]. Thus, a series of FI-CL methods have been developed for this kind of compounds determination. But in this paper, the determinations utilizing Ce (IV)-based CL that sensitized by rhodamine compounds are discussed as a separated section in consideration that rhodamine compounds have also been used as a CL reagent in the literatures [57-60]. Table 2 summarizes as the analytical applications of Ce (IV)-based FI-CL methods not including that involving rhodamine compounds, with respect to the analytes, the used detection system, samples and detection limits.

2.3. Rhodamine Compounds-Based CL System in FIA

Rhodamine compounds, as a series of xanthene dyes, have been extensively applied in analytical chemistry and especially in spectrometry, fluorescence analysis, catalytic and kinetic analysis since it has high efficiency to generate light emission [74-76]. In recent years, rhodamine compounds, including rhodamine B (RhB) and rhodamine 6G (Rh6G), have utilized gradually in FI-CL analysis. Nevertheless, rhodamine compounds are often considered as a sensitizer for other CL systems (especially for Ce (IV)-based CL system) and the detailed mechanism for the detection has little reports in the open literatures. In 1986, Zhang [77] observed that the redox reaction between RhB and hydrogen peroxide produced CL in alkaline aqueous solutions, and the effect of chromium (IV) concentration on the CL intensity was also discussed. In 2002, Ma and co-workers [57] discovered that the oxidation of RhB by cerium (IV) in sulfuric acid could produce strong light emission directly and a new CL system applying RhB as a CL reagent was established and applied for the determination of ascorbic acid in vegetables. Before long, the possible chemiluminescence mechanism of the system was investigated in detail. The formation of a complex in excited state between RhB and cerium (IV) was affirmed and the chemiluminescent emissive wavelength was indicated at ca. 425 nm [58]. Further, based on the enhancement of CL of RhB-Ce (IV) system in sulfuric acid medium, thermally denatured DNAs and DNAs activated previously by imidazole-HCl buffer solution were determined respectively [59, 60]. Similarly, the related reports involving rhodamine compounds-based CL with FI technique for the determination of biochemical species are described in Table 3. It is worth hoping that the development of the CL system of rhodamine compounds with Ce (IV) in an acidic media helps to broaden the analytical applications of CL methods with FI technique.

2.4. Other CL Systems in Acidic Media with FIA

In recent years, CL flow systems in acidic media with electrogenerated unstable oxidation reagents have received much attention and some analytical applications have appeared in the literatures [87-90]. In these systems, the unstable reagents were on-line electrochemically generated, resulting in the elimination of the instability of these reagents. For instance, Li et al [89] reported a new FI-CL system involving electrogenerated Mn (III) as oxidant for determination of isoniazid in sulfuric acid medium. In 2001, another novel CL flow system for captopril was described based on the direct CL reaction between captopril and electrogenerated Ag (II) in HNO₃ medium and the content of captopril in a pharmaceutical preparation was determined with a detection limit of 6×10^{-9} g/mL [90].

3. Conclusions

Applications of acidic chemiluminescence system coupled with flow injection technique for the assay of biochemical species are described and compared in this paper. CL represents a versatile, ultra-sensitivity analytical tool with a wide range of applications in diverse fields. As a powerful methodology, FI allows accurate and precise results for the detection. Besides, FI methodology is simple and inexpensive, in both reagent consumption and equipment involved. It is, therefore, suitable for determination in routine procedures and rapid analysis. The combination of sensitive CL detection in an acidic media with FI enhances the availability of this technique for the analysis in pharmaceuticals, foods and body fluids. An important recent trend for FI-CL analysis is towards the discovery of new CL systems especially in acidic media and the detailed study on reaction mechanism. With the development of other separation tools, it is hoped that in the future many new FI methodologies with CL detector would still play an important role for the determination of biochemical species at trace level in all kinds of complicated matrices.

Acknowledgements

The authors are gratefully acknowledge the financial support by the Tianjin Natural Science Foundation (No: 043806311, No:06YFJMJC07700) and the National Key Technologies R&D program of China (No: 200BAK02A09).

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