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Review

Chemiluminescence detection of opium poppy (*Papaver somniferum*) alkaloids

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ABSTRACT

A review with 98 references. The determination of the opium poppy (*Papaver somniferum*) alkaloids and their semi-synthetic derivatives has important applications in industrial process monitoring, clinical analysis and forensic science. Liquid-phase chemiluminescence reagents such as tris(2,2′-bipyridyl)ruthenium(II) and acidic potassium permanganate exhibit remarkable sensitivity and complementary selectivity for many *P. somniferum* alkaloids, which has been exploited in the development of a range of analytical procedures using flow analysis, high-performance liquid chromatography, capillary electrophoresis and microfluidic instrumentation.

Contents

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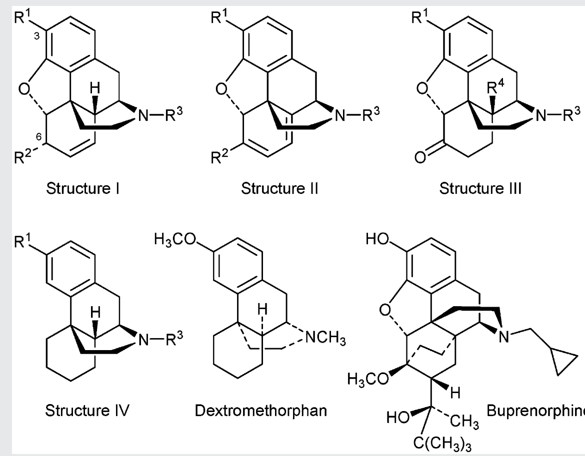
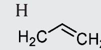
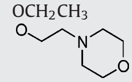
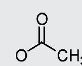
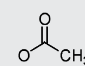
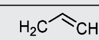
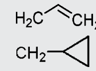
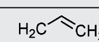
1. Introduction

Medicinal use of the opium poppy (*Papaver somniferum*) and opium – the alkaloid-rich latex exuded from surface incisions in the unripe seed heads – predates written history, but the isolation of morphine was not described until the early nineteenth century [1]. Many *P. somniferum* alkaloids are now known; the most significant in terms of their quantity within the plant are morphine, codeine, thebaine, noscapine, and papaverine [1]. Opiate alkaloids and their semi-synthetic derivatives (such as oxycodone, hydrocodone and pholcodine) are used extensively in medicine, and hundreds of tonnes of these compounds are produced by the pharmaceutical industry [2]. Accurate means to determine the *P. somniferum* alkaloids are therefore required for samples such as raw plant materials (to establish or monitor alkaloid abundance in different crops), industrial process streams (to optimise the extraction yields and reduce waste) and pharmaceutical formulations (for quality control and regulatory requirements). Furthermore, the misuse of opiate alkaloids, particularly the illegal trafficking and abuse of heroin (3,6-diacetylmorphine), has created the need to detect these substances on surfaces and in suspected illicit drug seizures, and identify and/or quantify the parent compounds and their metabolites in biological fluids and hair samples. General methodology for the determination of *P. somniferum* alkaloids has been discussed in previous reviews [3–7]; the determination of single or multiple analytes in complex sample matrices most commonly involves GC with mass spectrometric detection, or either HPLC or CE with UV-absorbance, fluorescence, electrochemical or mass spectrometric detection. Chemiluminescence (the emission of light from a chemical reaction) is an alternative mode of detection that provides high sensitivity using relatively simple instrumentation [8–11]. Chemiluminescence has been used to determine a wide range of *P. somniferum* alkaloids; many of their chemical structures are shown in Tables 1 and 2. It should be noted that these tables include derivatives and analogues that do not naturally occur in *P. somniferum*. The IUPAC numbering of relevant carbon atoms in Structure I (Table 1) has been shown to clarify the structure of some simple derivatives such as 6-monoacetylmorphine and 3-methoxycodeine, which were not included in the table.

Table 1
Selected morphinan alkaloids and their semi-synthetic derivatives



Structure I	R^1	R^2	R^3
Morphine	OH	OH	CH_3
Codeine	OCH_3	OH	CH_3
Normorphine	OH	OH	H
Nalorphine	OH	OH	
Ethylmorphine	OCH_2CH_3	OH	CH_3
Pholcodine		OH	CH_3
Heroin			CH_3
Structure II	R^1	R^2	R^3
Oripavine	OH	OCH_3	CH_3
Thebaine	OCH_3	OCH_3	CH_3
Structure III	R^1	R^3	R^4
Naloxone	OH		OH
Naltrexone	OH		OH
Hydrocodone	OCH_3	CH_3	H
Oxycodone	OCH_3	CH_3	OH
Noroxycodone	OCH_3	H	OH
Structure IV	R^1	R^3	
Levallorphan	OH		
Norlevorphanol	OH	H	

2. Chemiluminescence reagents

2.1. Potassium permanganate

Morphine was one of the first organic compounds to be detected with acidic potassium permanganate chemiluminescence [11,12], and although many other compounds have since been examined, very few can be detected at the exceedingly low concentrations reported for morphine and selected other *P. somniferum* alkaloids. The characteristic red emission from these reactions has been attributed to the production of an excited manganese(II) species and in corrected chemiluminescence spectra, the wavelength of maximum intensity is 734 ± 5 nm [13,14]. Polyphosphates and polyphosphoric acids are commonly used to enhance the chemiluminescence from reactions with acidic potassium permanganate. Interestingly, these enhancers shift the wavelength of maximum intensity to 689 ± 5 nm [13]. Polyphosphates have been employed extensively in the determination of *P. somniferum* alkaloids, but formic acid and formaldehyde, which have been shown to enhance the chemiluminescence with other analytes [11], have very rarely been used in the detection of these alkaloids.

Abbott et al. [15] and Barnett et al. [16] compared the chemiluminescence intensity from a range of *P. somniferum* alkaloids and other narcotic analgesics with acidic potassium permanganate, using flow injection analysis (FIA) methodology (Table 3). Compounds with a morphinan backbone, phenolic OH group at carbon-3 and furan bridge between C4 and C5 (Table 1; Structures I, II and III: R^1 = OH, and buprenorphine) were found to evoke a far more intense emission than all other compounds under investigation. For example, morphine and codeine differ only by their hydroxy and methoxy groups at carbon-3, but the response for codeine was only 2% of the response for morphine. The response for papaverine (a benzylisoquinoline alkaloid also found in *P. somniferum*) was 0.3%. Analgesics that shared little common structure with morphine, such as methadone, pethidine and fentanyl (not shown in table), gave a response of less than 0.1% [15].

However, a different relationship between analyte structure and chemiluminescence intensity was observed when *P. somniferum* alkaloids were treated with acidic potassium permanganate and sodium sulfite. Zhang and co-workers used these reagents to determine papaverine [17] and noscapine [18] (see Table 2) and found that morphine, codeine and heroin did not interfere at concentrations two orders of magnitude higher than that of the analytes.