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Comparison of three analytical methods for cocaine analysis of illicit powders[1]

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Abstract

A new cocaine-sensitive ISFET device based on a cocaine–reineckate ion-pair complex dispersed in a PVC–sebacate matrix has been fabricated. This sensor displays a linear range for cocaine hydrochloride between about 3×10^{-6} and 2×10^{-2} M and a fast response (≤ 25 s), which remains almost constant over the pH range 3–7. The sensor has been applied to the analysis of authentic illicit powders containing cocaine hydrochloride and other substances commonly associated with it, or of cocaine free base (crack).

Experimental results were compared with those obtained employing two more common instrumental methods of analysis: gas chromatography (GC), and UV absorption spectrometry (the latter applied directly or based on second derivative absorption spectroscopy).

Good agreement was found between results obtained by ISFET and GC methods, while UV absorption spectrophotometry proved suitable only in the case of pure cocaine hydrochloride and free base, or in samples also containing lidocaine, but using second derivative absorption spectroscopy.

Keywords: Analysis; Cocaine hydrochloride; Free base; ISFET

1. Introduction

The development of new methods of cocaine determination has taken on increasing importance in recent years, due to the world-wide diffusion of this drug.

The official method for cocaine hydrochloride analysis, proposed by the British and United States Pharmacopoeias, is based on titration by perchloric acid in a non-aqueous solution of 1,4-dioxane [1]. However, this method is seriously affected by interferences due to the presence of several organic bases.

Many analytical techniques can be used for detecting cocaine, such as high performance liquid chromatography (HPLC) [2], gas chromatography–mass spectrometry (GC–MS) [3], UV absorption derivative spectroscopy [4] and so on. However, many of these techniques, including the pharmacopoeia titration method using perchloric acid [1], have the drawback of being expensive,

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Table 1
Comparison of the working conditions and main characteristics of the responses of the cocaine–reineckate ISFET and classical ISE

Parameter	Cocaine-reineckate membrane ISFET	Cocaine–reineckate membrane ISE[a]
Membrane composition	Polymeric matrix:PVC Plasticizer: bis(2-ethylhexyl)sebacate	Polymeric matrix:PVC Plasticizer:dibutyl sebacate
Exchanger	Cocaine-reineckate	Cocaine-reineckate
pH	5	2.5–7.5
Working solution	Acetate buffer, 0.05 M	Potassium nitrate 0.1 M
Response time (s) (for $c = 10^{-3}$ M)	≤ 25	≤ 60
Slope (Δ mV/Δ log c) (c = M)	-53.9 (± 0.4)	53.5 (± 0.4)
Intercept (mV)	1114 (± 0.6)	170 (± 0.6)
Correlation coefficient (r)	-0.999	0.998
Linearity range (M)	3.3×10^{-6}–2.1×10^{-2}	1.0×10^{-5}–1.0×10^{-2}
Minimum detection limit (M)	$\approx 3 \times 10^{-6}$	7.0×10^{-6}
Repeatability of measurements	1.1%[b]	(0.4–0.6)%[c]

[a] Data reported in Ref. [6].
[b] As "pooled SD"%.
[c] As RSD%.

time-consuming and requiring the sample to be manipulated in several steps.

Recently, piezoelectric sensors [5] and classical ion-selective membrane electrodes [6] have been developed and applied to cocaine determination. On the basis of the experience acquired in the development of ISFET sensors [7,8], the present authors have, over the last year, carried out basis research into different ion-selective solid-state devices in order to develop a suitable cocaine-sensitive ISFET. The device based on cocaine–reineckate ion-pair complexes dispersed in a PVC–sebacate matrix was found to be the best [9].

The sensor has been applied to the analysis of several illicit powders containing cocaine hydrochloride, as well as to testing for free base (crack).

The results of tests using this ISFET are reported and compared with those obtained using GC and UV absorption spectroscopy (direct and second derivative methods).

2. Experimental

2.1. Materials

High-molecular-weight poly(vinylchloride) (PVC), bis(2-ethylhexyl)sebacate and Jeffamine D-230 were from Fluka, AG(Buchs, Switzerland); ammonium reineckate was from Sigma (St. Louis, MO); the standard cocaine hydrochloride was from S.A.L.A.R.S., (Como, Italy), with the authorisation of the Italian Minsitry of Health; tetrahydrofuran and all other solvents or reagents were of analytical-reagent grade and were obtained from Carlo Erba (Milan, Italy). The different illicit cocaine powders were obtained from the "Istituto di Medicina Legale", "La Sapienza" University of Rome (Italy), which also undertook to supply the composition and the nominal cocaine content of the powder[2].

2.2. Methods

2.2.1. Exchanger preparation

The ion association complex of cocaine with reineckate was prepared as described in Ref. [6] by mixing 10 ml of 10^{-1} M aqueous cocaine hydrochloride solution and 10 ml of 10^{-2} M ammonium reineckate. The precipitate obtained was filtered off, washed with distilled water and dried at room temperature. This complex was used as the exchanger in PVC membranes stratified on the ISFET gate area.

[2] Samples from the illegal market were analysed for legal purposes.

Table 2
Comparison of selectivity coefficients found for the cocaine-sensitive ISFETs and those reported in Ref [6] for classical ISEs. Cocaine ion as primary ion (*i*).

Interferent ion (*j*)	Selectivity coefficient ($-\log K_{ij}$)		
	ISFET using cocaine–reineckate as exchanger	ISE using cocaine–reineckate as exchanger	ISE using cocaine–TPB as exchanger
Caffeine	3.11	2.23	2.31
Nicotine	3.06	1.21	1.96
Papaverine	1.03	−0.70	−0.52
Alanine	3.55	2.12	2.23
Atropine	1.80	–	–
Lidocaine	1.00	0.67	0.74
Procaine	1.13	0.67	0.74
Ephedrine	0.42	1.09	1.53
Ca^{2+}	4.18	2.16	2.18
NH_4^+	3.52	2.27	2.31
K^+	3.80	2.04	2.23
Na^+	4.01	2.16	2.23

2.2.2. Polymeric ion-selective membrane and cocaine-sensitive ISFET preparation

The polymeric membrane was prepared by stirring for about 5 h a suspension consisting of 113 mg of PVC as base polymer, 279 mg of bis (2-ethylhexyl) sebacate as plasticizer, and 8 mg (2% by weight) of cocaine reineckate (i.e. the cocaine ion-pair complex used as the exchanger) in 3 ml of tetrahydrofuran. The solvent was allowed to partially evaporate in order to obtain a sufficiently viscous suspension. A drop of this suspension (about 40 μl) was deposited on the ISFET gate area, taking care to avoid air bubble formation, and left to dry at room temperature for 24 h.

2.2.3. FET device assembly, ISFET measurement procedure and apparatus

The integrated chips (UUO3 type) were supplied by HEDCO Laboratory of Utah University; each chip (overall dimension 1.28 mm × 2.16 mm) contained two (400 μm × 20 μm) gates and two metal gate-control devices. The chip was carefully washed with isopropylic alcohol and then mounted on a plastic stick subsequently connected to the electrical measurement system. After making the electrical connections with an ultrasonic wire-bonder (Kulicke and Soffa, model 4123; Switzerland), the device was encapsulated in an epoxy resin (EPON 825 + Jeffamine D-230) body, leaving only the two gates area free.

The ISFET measurements were carried out under steady-state conditions using equipment supplied by CPC Elettronica s.r.l., (Rome, Italy), which operated at constant applied drain voltage conditions, in feedback mode: the source-drain current (I_D) and the drain potential (V_D) were maintained constant at about 100 μA and 1.0 V, respectively, using an operational amplifier in a feedback loop as described in Ref. [10]. The readout of the gate output voltage (V_g) was then obtained directly in millivolts on a suitable display on the measurement apparatus.

For the measurements, the ISFET device, together with the reference electrode (saturated calomel), were immersed in 30 ml of 0.05 M acetate buffer solution at pH 5, contained in a thermostatted cell kept at 25°C under magnetic stirring. After the signal had been allowed to stabilise (about 10 min), fixed volumes of standard solutions of cocaine hydrochloride were successively added to 30 ml of the initial solution and, after 25 s, the gate output voltage variation of the ISFET was recorded.

Table 3
Cocaine hydrochloride or free base determination in illicit powders containing the most common local anaesthetics and sugars (nominal and found concentrations are the final ones in the analysed solution)

Mixture compostition (as % w/w)	Cocaine nominal value (μg ml^{-1}) (a)	Cocaine[a] found value (μg ml^{-1}) (%RSD in parentheses; $n = 5$) (b)	$(b-a)/a$(%)
Cocaine base (100%) (Crack)	49.9	49.1 (3.0)	−1.6
Cocaine hydrochloride (100%)	397.9	397.9 (2.8)	0.0
Cocaine[b] + lidocaine[b] (50%:50%)	397.9	404.5 (1.4)	+1.7
Cocaine[b] + procaine[b] (50%:50%)	397.9	407.7 (2.4)	+2.5
Cocaine[b] + lidocaine[b] + procaine[b] (50%:25%:25%)	397.9	401.3 (0.8)	+0.8
Cocaine[b] + caffeine[b] (50%:50%)	397.9	392.2 (2.2)	−1.0
Cocaine[b] + lidocaine[b] + caffeine[b] (50%:25%:25%)	397.9	424.7 (1.2)	+6.7
Cocaine[b] + D-glucose (50%:50%)	397.9	390.0 (2.3)	−1.5
Cocaine[b] + lidocaine[b] + D-glucose (50%:25%:25%)	397.9	385.3 (2.5)	−3.2
Cocaine[b] + mannitol (50%:50%)	397.9	390.0 (4.3)	−1.5
Cocaine[b] + lidocaine[b] + mannitol (50%:25%:25%)	397.9	407.7 (4.4)	+2.5

[a] Mean of at least five determinations.
[b] As hydrochloride.

All calibration graphs for cocaine hydrochloride and cocaine free base tested using ISFET devices were obtained by plotting the gate output voltage (V_g) variation (as Δ mV) vs. the cocaine final concentration values.

2.2.4. Spectrophotometric measurements

Spectra were carried out using a Perkin-Elmer Lambda 15 dual-beam UV–visible spectrophotometer. The instrument was furnished with quartz cuvettes of 1 cm pathlength and operated under the following conditions: wavelength range, 370–220 nm; absorption, or D^2 mode; scan rate 60 nm min^{-1}; slit 2 nm.

Standard water solutions (0.1 mg ml^{-1}) of cocaine-, caffeine-, lidocaine-hydrochloride, were prepared; in the case of free base, the powder was first dissolved in 2 M hydrochloric acid and the solution diluted with water until a final concentration of 0.1 mg ml^{-1} was reached.

Analyses were carried out using calibration curves obtained by reading the absorbance of standard cocaine hydrochloride solution at 233 nm, or by measuring the amplitude from positive and negative adjacent peaks of second derivative spectra, as recently proposed by Cruz et al. [4].

2.2.5. GC measurements

GC measurements were performed on a HP model 5890 gas chromatograph, furnished with a Megabore capillary column HP-1 [(methyl silicone gum) 10 m × 0.53 mm × 2.65 μm film], employing an FID (flame-ionisation detector) and He (12 psi) as gas carrier [11].

The cocaine hydrochloride-containing powders were dissolved in methanol and 1 μl of this solution was injected into the instrument.

The sample concentration was evaluated using a cocaine hydrochloride calibration curve from 0.5–3.0 mg ml^{-1} and ethyl morphine hydrochloride at 1.0 mg ml^{-1} as internal standard.

Table 4
Recovery of cocaine hydrochloride, by standard addition method, in different authentic illicit cocaine samples

Mixture composition (as % w/w)	Found value (mg ml^{-1}) (% RSD ≤ 4.0) ($n = 5$)	Standard cocaine hydrochloride added (mg ml^{-1})	Total value (mg ml^{-1})	Total found value (mg ml^{-1}) (% RSD ≤ 4.0) ($n = 5$)	Recovery of cocaine hydrochloride (%)
Cocaine[a] 50% + lidocaine[a] 50%	0.146	0.166	0.312	0.305	97.8
	0.146	0.330	0.476	0.469	98.5
	0.146	0.492	0.638	0.631	98.9
Cocaine[a] 50% + caffeine[a] 50%	0.149	0.167	0.313	0.309	98.7
	0.149	0.333	0.482	0.474	98.3
	0.149	0.497	0.646	0.643	99.5
Cocaine[a] 30% + lidocaine[a] 30% + caffeine[a] 30% + D-glucose 10%	0.177	0.166	0.343	0.344	100.3
	0.177	0.330	0.507	0.513	101.2
	0.177	0.492	0.669	0.682	101.9
Cocaine[a] 50% + lidocaine[a] 25% + caffeine[a] 25%	0.158	0.167	0.325	0.322	99.1
	0.158	0.333	0.491	0.481	98.0
	0.158	0.497	0.655	0.657	100.3

[a] As hydrochloride.

3. Results and discussion

First, with reference to the long-term stability of the cocaine sensors, the response of the developed ISFET device, stored without any special precautions, may be said to have remained almost stable over a period of at least 2 months of discontinuous (roughly daily) usage.

In Table 1 the main working conditions and data for a complete characterisation of the ISFET device employing cocaine-reineckate as exchanger are summarised. In this Table, the response time, slopes, linearity range, minimum detection limit, repeatability, accuracy of the measurements, reproducibility of the slopes and correlation coefficients of the calibration graphs, in the linear range, are shown and compared with corresponding data reported by Elnemma et al. [6] obtained using a classical ion-selective electrode (ISE) and the same exchanger.

In Table 2 the selectivity coefficient values [12], reported as $-\log K_{ij}$, of the most common organic interferents and inorganic cations obtained by the "mixed solutions" method [13,14] with respect to the cocaine hydrochloride as primary ion, for the polymeric membrane ISFETs and using cocaine–reineckate as exchanger, are compared with those reported by Elnemma et al. [6] for the classical ISE, employing dibutylsebacate as plasticizer and cocaine tetraphenylborate (TPB) or cocaine–reineckate as exchanger. Comparison of the data for the two sensors, contained in Tables 1 and 2, shows that ISFETs have a shorter response time than ISEs (25 s instead of 60 s), a better linear range and a selectivity of the same order or better.

In Table 3 the analysis of free base (crack) and of cocaine hydrochloride in illicit powders containing other local anaesthetics, such as procaine, lidocaine, caffeine, and sugars (e.g. D-glucose,

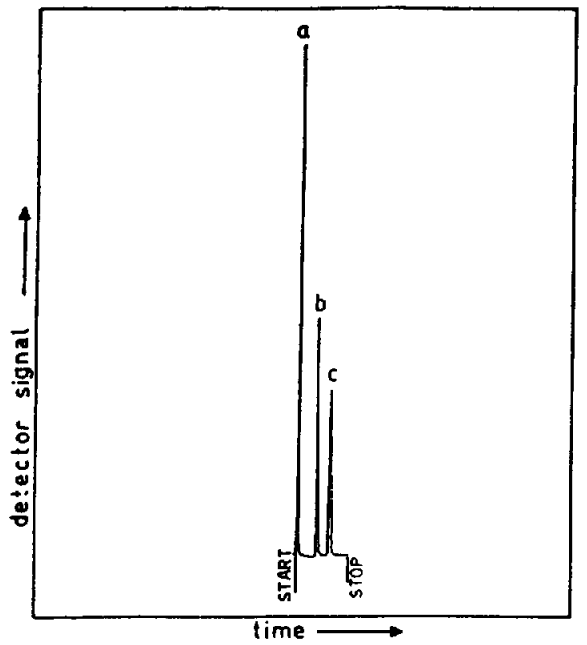

Fig. 1. Typical GC peaks obtained: (a) solvent peak (methanol); (b) cocaine hydrochloride peak (1.0 mg ml^{-1}); (c) ethyl morphine hydrochloride peak (1.0 mg ml^{-1}).

mannitol) is shown. The accuracy of measurements, as evaluated by cocaine hydrochloride recovery, using the standard addition method, is reported in Table 4 for different authentic illicit cocaine hydrochloride samples.

The results of the tests carried out using the ISFET and set out in the above Tables are definitely positive as regards both accuracy and precision of measurements (%RSD $\leq$ 4.0%). Nevertheless, as this is a new type of sensor and

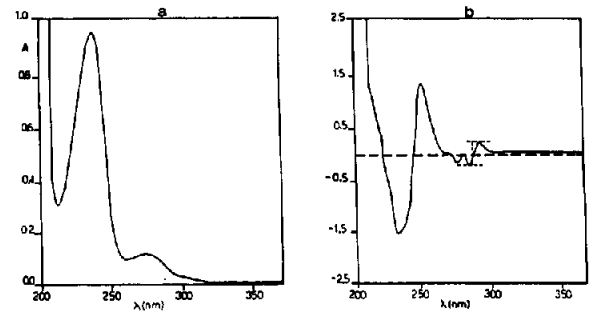

Fig. 2. (a) UV absorption spectrum; (b) second derivative spectrum of cocaine hydrochloride water solution (34.0 μg ml^{-1}); pathlength 1.0 cm.

in view of the very small number of real matrices containing cocaine hydrochloride or free base tested using sensors and described in the literature, it was deemed necessary to analyse the same samples (of illicit powders) using also two modern but more conventional instrumental methods (i.e. generally accepted and reliable methods). Only a true comparison of the results obtained using the same samples can provide an effective analytical validation of the proposed method.

The classical methods selected, which are described briefly in the preceding section, consist essentially of a classical GC method using a 10 m tall capillary column and a FID (a typical example of the gas chromatograms recorded is shown in Fig. 1). Subsequently, a spectrophotometric method (UV) was used. This method has recently been the subject of a considerable number of studies, particularly by Spanish researchers [4,15]. For determinations of complex matrices, these researchers have endeavoured to offset the recorded interferences, above all those due to anaesthetic substances in the illicit powders tested, by operating both directly by reading off the absorbance of the appropriate wavelength, and also using the second derivative. The present authors therefore attempted to analyse some of the illicit powder samples by using the direct spectrophotometric method, in which the absorption is read off at 233 nm (see Fig. 2(a)), or by using the second derivative. In the latter case, after carrying out a preliminary survey to ascertain the most suitable amplitude between adjacent peaks and troughs, it was decided to perform the determination by measuring the amplitude between 291 and 283 nm or between 291 and 370 nm, as proposed for the determination of cocaine hydrochloride by the above-mentioned authors [4] (see Fig. 2(b)). Amplitude determinations performed over other wavelengths, for instance, over the range between 291 and 283 nm, as done here, or between 291 and 370 nm, which was also proposed by the above-mentioned authors [4], proved totally unsuitable on the basis of the results obtained (except in the case of samples containing only cocaine hydrochloride or free base).

Table 5
Comparison of cocaine hydrochloride and cocaine free base determination in authentic samples (illicit powders), using the ISFET sensor, GC and spectrophotometric techniques

Mixture composition (as % w/w)	Cocaine hydrochloride and cocaine free base found (as % w/w) (%RSD in parentheses; $n = 5$)				
	ISFET sensor	GC	Spectrophotometry (Direct method[a])	Spectrophotometry (Second derivative method)[b]	
				(a)	(b)
Cocaine base (100%) (crack)	98.4 (3.0)	106.2 (2.3)	100.4 (0.8)	99.8 (2.2)	100.8 (1.9)
Cocaine hydrochloride (100%)	100.0 (2.8)	106.1 (2.2)	104.1 (0.8)	101.5 (2.7)	102.0 (2.2)
Cocaine[c] (50%) + lidocaine[c] (50%)	48.5 (2.0)	46.7 (1.2)	67.7 (1.8)	50.8 (3.2)	50.9 (2.7)
Cocaine[c] (50%) + caffeine[c] (50%)	48.0 (2.2)	49.7 (3.6)	88.4 (2.1)	287.2 (2.3)	210.2 (2.5)
Cocaine[c] (50%) + lidocaine[c] (25%) + caffeine[c] (25%)	50.8 (2.2)	49.5 (4.0)	79.5 (2.0)	221.2 (1.9)	171.2 (1.9)
Cocaine[c] (30%) + lidocaine[c] (30%) + caffeine[c] (30%)	31.1 (3.8)	29.8 (1.0)	78.0 (1.8)	163.3 (2.2)	116.2 (2.2)

[a] Reading the absorbance at 233 nm.
[b] (a) Reading the amplitude between 291 and 370 nm; (b) reading the amplitude between 291 and 283 nm.
[c] As hydrochloride.

The comparison of the main results for cocaine hydrochloride determination in authentic samples (illicit powders) using the ISFET sensor, GC and spectrophotometric techniques (direct absorption method and second derivative spectrophotometry) are summarised in Table 5.

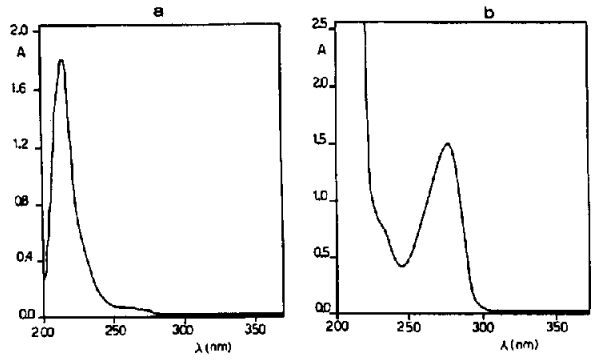

Fig. 3. (a) UV absorption spectrum of lidocaine hydrochloride water solution (34.0 μg ml^{-1}); (b) UV absorption spectrum of caffeine hydrochloride water solution (34.0 μg ml^{-1}); path-length 1.0 cm.

Comparison of the data obtained in the respective tests, as set out in Table 5, and among these and the respective nominal values of the various samples, definitely shows excellent agreement for data obtained using the ISFET, or by means of GC and the nominal values. However, the spectrophotometric method displays excellent agreement with the nominal values or with the other two methods only in the case of the analysis of solutions containing pure cocaine hydrochloride or free base. Values differing substantially from the nominal values are in fact found in the analysis of powders also containing lidocaine or caffeine. This is only to be expected as these substances also display absorption bands at 233 nm (see Fig. 3). Furthermore, the results of using the second derivative spectrophotometric method, which are shown in the last two columns of Table

5, indicate that only lidocaine interference can be eliminated by means of the second derivative. In the case of the presence of caffeine, the results obtained are comparable to, or even worse than, those obtained using the direct spectrophotometric method.

In conclusion, these comparisons show that using the ISFET in real matrices yields definite advantages over the spectrophotometric method, which is frequently affected by serious interferences. However, compared with the GC method, the results are practically the same in terms of accuracy and precision. However, the ISFET determinations are much simpler, cheaper and above all faster; for instance, the ISFET response time is only 25 s.

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