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Electrochemistry and analytical determination of lysergic acid diethylamide (LSD) via adsorptive stripping voltammetry

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ABSTRACT

Lysergic acid diethylamide (LSD) is hardly detectable and quantifiable in biological samples because of its low active dose. Although several analytical tests are available, routine analysis of this drug is rarely performed. In this article, we report a simple and accurate method for the determination of LSD, based on adsorptive stripping voltammetry in DMF/tetrabutylammonium perchlorate, with a linear range of 1–90 ng L^{-1} for deposition times of 50 s. LOD of 1.4 ng L^{-1} and LOQ of 4.3 ng L^{-1} were found. The method can be also applied to biological samples after a simple extraction with 1-chlorobutane.

1. Introduction

Lysergic acid diethylamide (LSD, Fig. 1) is a semisynthetic product of lysergic acid, a natural substance from the parasitic rye fungus *Claviceps purpurea*. Albert Hofmann, a natural products chemist at the Sandoz AG Pharmaceutical Company (Basel, Switzerland), synthesized LSD in 1938 while searching for pharmacologically active derivatives of lysergic acid. He accidentally discovered its dramatic psychological effects in 1943, and though he synthesized many lysergic acid derivatives, none had LSD's unique spectrum of psychological effects. During the 1950s, LSD (Delysid® Sandoz) was introduced to the medical community as an experimental tool to induce temporary psychotic-like states ("model-psychosis") and later to enhance psychotherapeutic treatments ("psycholytic" or "psychedelic" therapy) [1].

LSD is one of the most potent psychotropic drugs, only few micrograms (50–100) are required for pharmacological effects [1]. LSD is extensively metabolized, but a small fraction is found unchanged in biological fluids, so that the identification of LSD at 200 ng L^{-1} in urine is considered positive for LSD abuse [2]. The detection of very low concentrations of LSD and its metabolites requires the development of specific and sensitive analytical methods. Several gas chromatographic mass spectrometric methods [3] have been developed for LSD analysis providing specificity and high selectivity but they need time-consuming extraction, purification and derivatization procedures. More recently, liquid chromatography–mass spectrometry (LC–MS) methods for its determination have been proposed [4].

In this paper, the electroactivity of the ergot nucleus [5] was exploited to develop a rapid, sensitive and specific adsorptive stripping voltammetric method at glassy carbon electrode in DMF containing 0.1 M tetrabutylammonium perchlorate for the determination of LSD, alternative to LC–MS, less expensive and with comparable sensitivity.

2. Experimental section

2.1. General section

Reagents of the purest grade available were purchased from Sigma-Aldrich and used as received. All electrochemical measurements and characterizations were carried out with a BASI PWR-3 power module and a standard three-electrode EF-1085 C-3 cell with a glassy carbon (0.02 cm^2 geometrical area) electrode as the working electrode, a platinum wire as auxiliary electrode and a Ag/AgCl/NaCl (3 M NaCl saturated with AgCl) reference electrode.

Due to its photoreactivity [6], the synthesis and manipulation of LSD were carried out in a dark environment. Standards (in dimethylformamide: DMF) were prepared daily from a 1000 mg L^{-1} stock solution (in DMF), stable for at least 1 week when conserved at −18 °C, and stored in the dark.

Electrochemical potentials are referred to Ag/AgCl/NaCl (3 M NaCl saturated with AgCl). An Orion SA 520 pH meter was used for pH measurements.

In the following, the uncertainty on the last digit has been reported in brackets, when appropriate.

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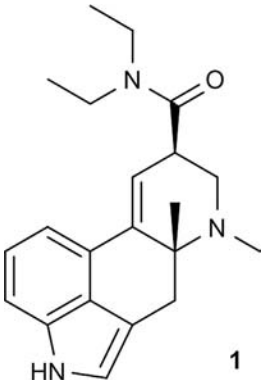


Fig. 1. Chemical structure of LSD (1).

Please notice that LSD tartrate was used for this study, but quantity reported below refer to the free base.

2.2. LSD synthesis

LSD was synthesized from the corresponding lysergic acid hydrate according to the well-known Hoffmann procedure [6]. The compound was purified by column chromatography (neutral alumina; eluent benzene/chloroform 3:1) and crystallized three times from methanol as L-(+)-tartrate [6]. The substance is highly physiologically active and its synthesis and manipulation require special precaution to avoid any contact, also with dilute solutions or samples contaminated with it.

2.3. Glassy carbon (GC) electrode pretreatment/characterization

Before use, following standard procedures, the GC electrode was abraded with successively finer grades alumina (from 1 μm to 0.05 μm), rinsed with 5% nitric acid and water and cleaned in an ultrasonic bath to remove any trace of alumina. Then the smooth surface was electrochemically cleaned by Cyclic Voltammetry (CV) in a 0.5 M H_2SO_4 solution (15 cycles, initial potential E_i=0.0 mV, final potential E_f=+1400 mV, scan speed ν=200 mV s^{-1}) in order to obtain low background currents and reproducible results [7]. Effective glassy carbon electrode area was determined by applying the Randles–Sevcik equation by CV in a 1.0 mM ferrocene/0.1 M tetrabutylammonium perchlorate solution in acetonitrile (E_i=+200 mV, E_f=+800 mV, scan speed ν=100 mV s^{-1}) [8,9].

2.4. Electrochemical investigations of LSD

Measurements in CV to evaluate the redox activity of the drug were performed in 0.1 M tetrabutylammonium perchlorate ($(Bu_4N)ClO_4$) in DMF, in the potential range from −600 mV to +1500 mV (accessible to the GC electrode in these conditions) with a title compound concentration of 1 mg L^{-1} at variable scan speeds, from 50 mV s^{-1} up to 1000 mV s^{-1}.

To evaluate whether the electrochemical processes were diffusion-controlled, plots of current intensity (i) vs. square root of the scan speed ($\nu^{1/2}$) or vs. scan speed (ν) were performed (CV, 0.05 M $(Bu_4N)ClO_4$ in DMF as described, E_i=+700 mV, E_f=+1500 mV, title compound concentration 50 mg L^{-1}, scan speeds from 10 to 200 mV s^{-1}). The scan window was limited only to $E > 700$ mV as no peaks were found at more negative potentials (see below). The relationships between log i and log ν in the same conditions, the behavior of $i/\nu^{1/2}$ vs. log ν and the peak's potential dependence with respect to the logarithm of scan speed were investigated as well, to better assess the nature of the electrochemical processes.

The number of electrons involved in the electrochemical rate-determining step was obtained by CV at different scan speeds (from 10 to 200 mV s^{-1}; potential range from +700 mV to +1300 mV) in 0.05 M $(Bu_4N)ClO_4$ in DMF as described, drug concentration of 50 mg L^{-1}; the equation for reversible processes was applied, being:

$$|E_p - E_{p/2}| = (2.218RT)/(nF) = [57.7/(n)]\,mV \quad (1)$$

where symbols have the usual meaning [10].

For further details, see Supplementary information.

2.5. Electrochemical determination of LSD

For the quantification of LSD, a method based on adsorptive stripping voltammetry (AdSV) was developed. The quantitative determination was done on the oxidation wave, by the standard addition method. Different supporting electrolytes, viz. $(Bu_4N)ClO_4$, $LiClO_4$, tetrabutylammonium tetrafluoroborate in different solvents (methanol, acetonitrile, *N*,*N*-dimethylformamide) were tested, as well as the effect of the presence of water in the media. The influence of the main parameters (namely, deposition potential, deposition time, scan speed) was verified.

2.6. Extraction of LSD from biological matrices and toons

Biological matrices were spiked with realistic amounts of LSD, taking into account the dose usually taken and metabolism [2,11] and half-life of the dose ingested [1].

For the extraction of LSD from biological matrices and toons, known procedures were followed, in particular:

- *Toons*: LSD was extracted from toons (2 × 3 cm^2, usual LSD content ranging from 50 μg to 100 μg) with 15 mL DMF (ambient temperature) in ultrasonic bath for 10 min.
- *Hairs*: Approximately 50 mg of hair, accurately weighted, were cut into small pieces of about 3 mm in length, and then washed with water, methanol and cyclohexane (5 mL each, to remove any residual detergent, dye or traces of grease). The sample was extracted with 5 mL DMF in ultrasonic bath at 50 °C for 10 min. A second extraction was performed to asses that recovery was quantitative.
- *Plasma and urine*: Following a known procedure [12] slightly modified and adopted, 1 mL of sample (adjusted to pH=9 with phosphate buffer in the case of plasma) was extracted with 1 mL 1-chlorobutane with strong agitation (Autovortex®) for 2 min; the solution was centrifuged at 4500 rpm for 10 min. The organic phase was diluted 1:100 with a 0.1 M $(Bu_4N)ClO_4$ solution and analyzed by the standard additions method by AdSV.

A known amount of each extract was added to 10 mL DMF 0.05 M $(Bu_4N)ClO_4$ in order to have a final concentration in the range 10–50 ng L^{-1}, and analyzed.

3. Results and discussion

3.1. Electrode characterization

Glassy carbon electrode area was estimated to be 0.083(1) cm^2, in good accordance with geometrically calculated area. This indicated that the surface was well polished and with low roughness.

3.2. Electrochemistry of LSD

Investigation of LSD behavior by CV showed two oxidation waves, each characterized by a two-electron process (see Fig. 2 and Supplementary Figs. S1a and S1b) with $E_{1/2}=860$ mV ($E_p=913$ mV, corresponding to path from *a* to *d* in Scheme 1, see below for details) and $E_{1/2}=1250$ mV ($E_p=1139$ mV, corresponding to path *e* and *f* in Scheme 1, see below for details). The broad cathodic wave with $E_{1/2}=1205$ mV suggests that the second oxidation process is reversible, while the first is not. However, if CV is performed in a narrow potential range to avoid the second oxidation step, a reversible wave is obtained (see Supplementary information Figs. S2a and S2b: the latter well shows the behavior described with the $E_{1/2}$ potential of the cathodic wave at 1010 mV), meaning that in the timescale of the CV (scan speed 10–200 mV s^{-1}) step *a* is reversible; the dimerization represents the not reversible chemical step, producing the intermediate radical cation $\mathbf{2}^{\bullet+}$ which undergoes further electron transfer and further chemical (deprotonation) steps. The CV in the wider potential window describes an electrochemical/chemical (EC) mechanism: the product of the first oxidation wave (path *d* in Scheme 1) is transformed by a second oxidation in a product which undergoes deprotonations in path *e* and *f* in Scheme 1 which reduce the apparent reversibility of the process (these data, those below reported and previous literature [5,13,14] allowed us to deduce the redox mechanism proposed in Scheme 1).

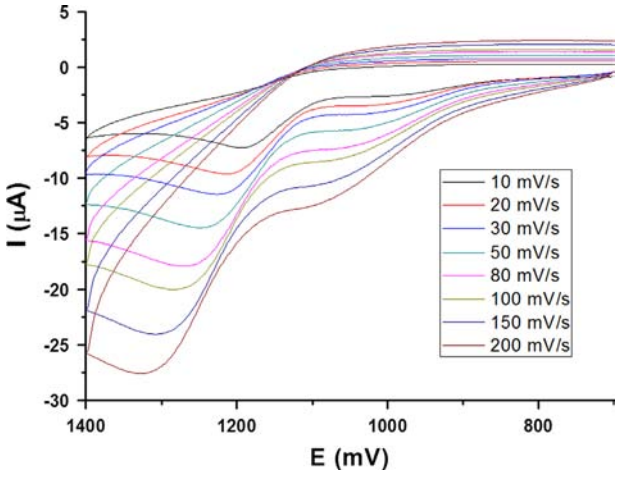
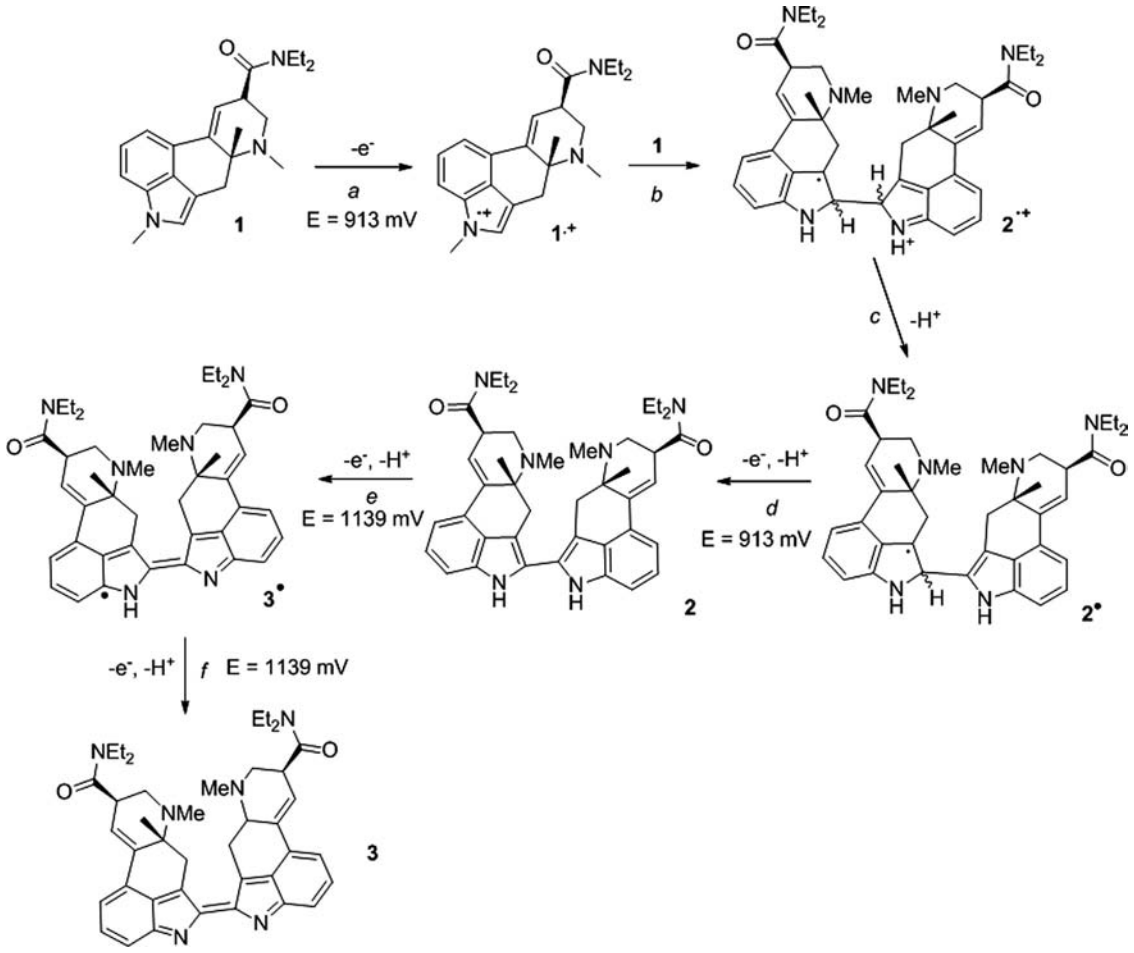


Fig. 2. CV scan of LSD at different scan velocity. Electrochemical conditions: DMF containing 0.1 M $(Bu_4N)ClO_4$. Drug concentration = 50 mg L^{-1}.

The first redox process appears to be controlled mainly by diffusion at the electrode, as the following relationship between square root of scan speed and *i* has been obtained: $i(\mu A)=0.4603(1)\nu^{1/2}$ (mV s^{-1})–0.34(3), $r^2=0.993$ [15,16].

It was noted that upon 10–15 scans peaks begin to broaden and become undefined, in accordance with a (partial) adsorption of the redox product(s) at the electrode surface.

The linear relationship between log *i* and log ν, $\log i(\mu A)=0.62(4)\log\nu$ (mV s^{-1})+0.035(1), $r^2=0.992$, confirms a diffusion-controlled reaction [17–19].



Scheme 1. Proposed mechanism for the electrochemical oxidation of **1**.

The value of $i/\nu^{1/2}$ ratio remains constant at different log ν, and this furthermore confirms that the process at the electrode surface at high LSD concentration was mainly diffusive; peak potential linearly depends on log of the scan speed, E(mV)=71(2)log ν (mVs^{-1})+877 (3), r^2=0.982. This is consistent with the EC mechanism, where the electron transfer at the electrode is coupled with a following irreversible chemical process [17,20], as said before.

The second oxidation wave ($E_{1/2}$=1059 mV) seems to be controlled mainly by diffusion at the glassy carbon, as the following relationship between square root of scan speed and current is obtained: i(μA)=0.473(2)$\nu^{1/2}$ (mV s^{-1})–0.14(2), r^2=0.992 [15,16].

The relationship between log i and log ν [17,18] is linear, as expected for a diffusion-controlled reaction [19,20]. The equation was: log i (μA)=0.74(3)log ν (mV s^{-1})–0.03(2), r^2=0.993.

The relationship between $i/\nu^{1/2}$ vs. log ν does not show any increment of the first term with respect to the second, and this furthermore confirms that the process on the electrode surface is mainly diffusive when high concentrations of LSD are used in solution; the linear dependence of peak potential on log of scan speed, with a regression line E(mV)=130.8(2)log ν (mV s^{-1})+1026(3), r^2=0.985, is consistent with the EC mechanism, where the electron transfer at the electrode is coupled with the following irreversible chemical process [17], as said before.

Concerning the cathodic wave ($E_{1/2}$=1075 mV), a linear relationship between square root of scan speed and i is obtained, i(μA)=0.888 (3)$\nu^{1/2}$ (mV s^{-1})–1.35(2), r^2=0.999 [15,16], and the process is diffusion controlled as log i vs. log ν [17,18] was linear: log i(μA)=0.37(2) log ν (mV s^{-1})+3.16(3), r^2=0.983. These data confirm that the reductive process is mainly diffusive, but the increase of $i/\nu^{1/2}$ vs. log ν is indicative of adsorption of the reactant (see Fig. S3). Peak potential linearly depends on log of scan speed with a linear regression line E(mV)=22.0(3)log ν (mV s^{-1})+1100(4), r^2=0.982, and is consistent with the EC mechanism, where the electron transfer at the electrode is coupled with a following irreversible chemical process [17,19].

The electrons involved in the rate determining step, determined in CV ($(Bu_4N)ClO_4$ 0.05 M in DMF, LSD 50 mg L^{-1}, E_i=700 mV, E_f=1400 mV) by applying Eq. (1) (see note in Supplementary information) are respectively 1.1(2) for the first oxidation peak and 0.9(1) for the second one. Both represent the mean value of 10 measurements carried out with scan speeds ranging from 10 to 200 mV s^{-1} (see Fig. 2). From these values and from data reported in literature [5,20,21] for similar structures, as the oxidation process consists in the dimerization of two LSD molecules, and as there is a consumption of one electron for mole of compound, it can be concluded that each redox peak involves two molecules of reactant, i.e. two moles of electrons. The indole core is the oxidation center, as it is more oxidizable than the amino one and the double bond [20–22].

The generated radical cation **1**$^{\bullet+}$ (path *a*) can add itself onto the double bond in the indole ring of a second LSD molecule (path *b*). Then, detachment of a proton from the dimer (path *c*) produces a neutral radical **2**$^{\bullet}$ [5,13]. Further one-electron oxidation followed by deprotonation takes place to produce the electronically neutral **2** obtained in the first oxidation wave (path *d*). Electrochemical oxidation of 2,2′ and 3,3′ bis-indoles has been investigated in literature. According to what suggested for 3,3′-bis-indole [21], the second oxidation wave and the following deprotonation result in the formation of highly conjugated aromatic radical **3**$^{\bullet}$ (path *e*). Further oxidation and loss of proton (path *f*) conduce to neutral **3** [5]. The electrochemistry of the compound remains unchanged if tartaric acid (up to 5 g L^{-1}) is added to the supporting electrolyte.

3.3. Electrochemical determination of LSD

The determination of LSD at glassy carbon electrode by AdSV was obtained on the second wave (E_{p2}=+1139 mV), by the external standard addition method with concentrations ranging from 5 to 90 ng L^{-1} (see Fig. S4).

The optimized electrochemical conditions are below reported. At low concentrations (ng L^{-1} concentrations), adsorption of the compound occurs at the electrode surface [5]; while shifting to non-aqueous (DMF) supporting media, the adsorption is weaker and during the anodic scan the compound accumulated on the surface during the deposition step could be stripped off. In the electrochemical conditions described *for the CV investigations*, the adsorption of LSD on the electrode surface is negligible, as illustrated before.

Sharper and well-defined peaks were obtained with 0.05 M $(Bu_4N)ClO_4$ in DMF. The concentration of the supporting electrolyte was shown to play a major effect on the definition and separation of the two peaks obtained. Although generally a diminution of a stripping signal is expected lowering the concentration of the supporting electrolyte [23], in this case we observed the contrary phenomenon; this is sometime observed and is attributed to the interaction between the target molecule (LSD) and the supporting electrolyte, which causes a shielding effect [24].

The deposition potential has a limited effect on the analytical signal: as a compromise, a deposition potential of +400 mV was chosen as the co-evolution of hydrogen and progressive damage of the GC surface are avoided; potentials less negative than –500 mV did not lead to an increase of the stripping signal and caused progressive diminution of the signal. Further chemical or physical cleaning of the electrode after each deposition cycle was not necessary as the oxidative scan is brought to 1.3 V, sufficient to clean the electrode.

The effect of scan speed was investigated in the range 10–200 mV s^{-1} and, as expected, it was found that high scan speeds increased the peaks height but also broadened the peaks and worsen the definition. A scan speed of 100 mV s^{-1} was chosen as the best compromise.

The choice of the deposition time is related to the concentration of LSD expected in the sample. By increasing the deposition time, the signal linearly increases until a complete monolayer is formed on the electrode surface and saturation of the signal is obtained (e.g. this is observed for 250 s deposition time at 5 μg L^{-1} LSD concentration). For deposition times of 50 s, a limit of detection (LOD) of 1.4 ng L^{-1} and a limit of quantification (LOQ) of 4.3 ng L^{-1} were obtained, and the signal was linear up to 90 μg L^{-1}. The calibration curve obtained under these conditions (10 data points) was: i(μA)=0.0308(3) (C, ng L^{-1})–0.008(5), r^2=0.995. At a concentration greater than 90 ng L^{-1} loss of linearity occurred.

Summing up, AdSV optimized parameters were E_i=+700 mV, E_f=+1300 mV, scan rate ν=100 mV s^{-1}, E_{dep}=+400 mV and deposition time 50 s. The other electrochemical parameters were constructor's default parameter of the chosen stripping techniques (BASi): pulse amplitude=50 mV, pulse width=50 ms and pulse period=200 ms (see Fig. 3 for a typical voltammetric curve).

Water, if present up to 10% with respect to DMF, did not interfere. At greater concentrations, peaks broadened and became undefined.

The most common excipients and drugs that can be administered together with LSD were investigated: sucrose, caffeine, mescaline, bromazepam, amphetamine did not change peak height and profile up to a 50 times the LSD concentration. Tartaric acid (up to 5 g L^{-1}) did not influence the performance of the method.

3.4. Validation of the proposed methods

The analytical method was validated according to the International Conference on Harmonization (ICH) guidelines [25]. A ten concentration (AdSV: 5–90 ng L^{-1} t_{dep}=50 s) calibration graph was obtained by least-square regression method and LOD and LOQ were calculated from the calibration curve. The repeatability

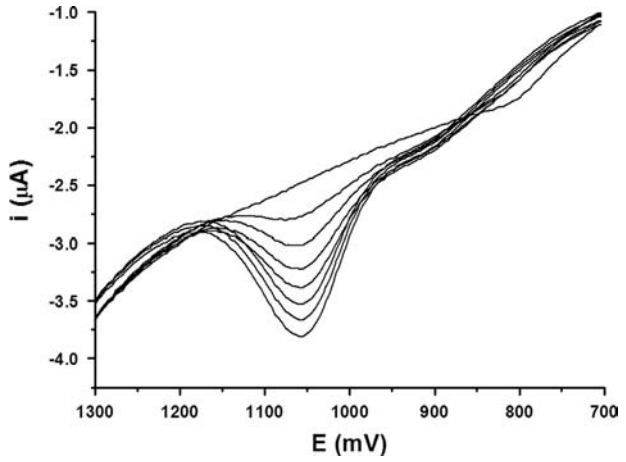


Fig. 3. AdSV curves obtained for LSD at 5, 10, 15, 20, 25, 30 and 35 ng L^{-1} concentrations. Electrochemical conditions as described in the text.

(intraday precision) was evaluated by assaying (AdSV) during the same day 6 samples containing 30 ng L^{-1} of LSD and the reproducibility (interday precision) in the same number of samples in two different days. Recovery, average value of 3 replicates, was carried out by addition of known amounts of standard drug solution in DMF (1, 3, 10, 30 ng L^{-1}) and ranged from 94% to 108%. In Table 1 are listed the figures of merits obtained that show the comparability with other already existing methods [11].

3.5. Analysis in urine samples, plasma, toons and hair

The method was applied to the analysis of LSD in biological matrices and toons, before and after spiking with known amounts of LSD (see Fig. S4 in Supplementary information for typical voltammograms obtained). Undiluted aliquots of urine were spiked with LSD (1–30 μg L^{-1}) and extracted by adapting a procedure reported in the literature (see Section 2.6) [12]. A typical calibration curve obtained by the standard additions method was $i(\mu A)=0.0063$ (C, ngL^{-1})+0.119, $r^2=0.9917$, and the concentration of LSD in the sample was calculated. Recovery was quantitative with a single extraction obtaining yield in the range 84–122%.

Plasma samples, spiked with LSD to obtain solutions at concentrations in the range 1–10 μg L^{-1}, were extracted and analyzed following the same procedure (see Section 2.6). A typical calibration curve obtained by the standard additions method was $i(\mu A)=0.0223$ (C, ngL^{-1})+0.4303 with $r^2=0.999$. Recoveries were in the range 83.5–110%.

Concerning the hair, a proper amount of LSD standard solution were added to 0.5 g of samples, obtaining concentrations between 1 and 10 ng g^{-1}; 50 mg were sampled and extracted as illustrated in Section 2.6. A second extraction demonstrated that the recovery was quantitative. The equation of the calibration curve was $i(\mu A)=0.0145$ (C, ng L^{-1})+0.4055, $r^2=0.9976$ and recovery between 65% and 135%.

The application of the method on biological samples enables the determination of LSD at a concentration that can be reasonably found in plasma, urine [12] and hairs [26] of drug abuser.

Toons containing LSD between 50 and 100 μg were obtained depositing known amounts of the drug on filter paper cards, size 2×3 cm^2. For the extraction, the sample was suspended in 15 mL of DMF and sonicated for 10 min.

A blank extraction of a card of the same size not containing LSD demonstrated the absence of electroactive or interfering substances. Quantitative analysis with recovery between 91.5% and 103% was performed by the standard additions method, and a typical equation of calibration curve was $i(\mu A)=0.0142$ (C, ng L^{-1})+0.3967, $r^2=0.9945$.

Results are shown in Table 2.

To better understand the possible interference of amphetamine, bromazepam, caffeine and mescaline, these substances were added to the biological matrices (plasma and urine) at up to 50 times the concentration of the LSD, before the extraction procedure.

1-Chlorobutane resulted to be quite selective for the extraction of LSD, while amphetamine, caffeine and bromazepam are poorly extracted, as LSD partition coefficient (log $P=2.95$ [27]) is greater with respect to the other drugs' one (caffeine log $P=-0.07$ [27a], bromazepam log $P=2.05$ [27b], amphetamine log $P=1.76$ [27c], mescaline log $P=0.78$ [27d]). Thus, LSD can be accurately determined by following this approach.

Table 1
Figures of merit obtained for LSD. Electrochemical conditions as described in the text. The uncertainty on the last digit has been reported in brackets when appropriate.

Parameters	AdSV
Concentration range	5–90 ng L^{-1}
Slope ± standard error	0.0308(4)
Intercept ± standard error	−0.0815(6)
Correlation coefficient (r^2)	0.9998
LOD	1.4 ng L^{-1}
LOQ	4.3 ng L^{-1}
Intraday precisions (%)	9.08
Interday precisions (%)	7.4
Recovery (%)	84–117

Table 2
Measured concentrations (and relative confidence interval, calculated at the 95% level, $p=0.05$) of LSD in various matrices spiked with LSD. n=number of samples analyzed.

Sample	Concentration of LSD spiked	Measured concentration and confidence intervals
Urine	30 μg L^{-1}	27.47 μg L^{-1} ± 1.67 $n=5$, $p=0.05$
	10 μg L^{-1}	10.67 μg L^{-1} ± 1.20 $n=8$, $p=0.05$
	3 μg L^{-1}	3.02 μg L^{-1} ± 0.57 $n=5$, $p=0.05$
	1 μg L^{-1}	1.01 μg L^{-1} ± 0.16 $n=5$, $p=0.05$
Plasma	10 μg L^{-1}	9.5 μg L^{-1} ± 3.4 $n=3$, $p=0.05$
	3 μg L^{-1}	3.04 μg L^{-1} ± 0.17 $n=12$, $p=0.05$
	1 μg L^{-1}	1.02 μg L^{-1} ± 0.11 $n=5$, $p=0.05$
Hair	10 ng g^{-1}	9.2 ng g^{-1} ± 1.53 $n=14$, $p=0.05$
	5 ng g^{-1}	5.5 ng g^{-1} ± 1.95 $n=4$, $p=0.05$
Toons	100 μg	100.78 μg ± 2.53 $n=7$, $p=0.05$
	50 μg	47.45 μg ± 3.18 $n=5$, $p=0.05$

4. Conclusions

A rapid, sensitive and specific adsorptive stripping voltammetric method at glassy carbon electrode for the determination of LSD has been developed and optimized after the investigation of

the electrochemistry of the drug. It is alternative to the LC–MS, less expensive and with comparable sensitivity. The method can be applied to different matrices, from toons to body fluids such as urine, plasma, and hairs, and shows good reproducibility and recovery rate at realistic LSD concentration. Excipients and drugs that can commonly be administered together with LSD do not interfere in its analytical determination even at up to a 50 times the LSD concentration.

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Appendix A. Supplementary informations

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.talanta.2014.07.037.

References

[1] T. Passie, J.H. Halpern, D.O. Stichtenoth, H.M. Emrich, A. Hintzen, CNS Neurosci. Ther. 14 (2008) 295–314.
[2] S.A. Reuschel, S.E. Percey, S. Liu, D.M. Eades, R.L. Foltz, J. Anal. Toxicol. 23 (1999) 306–312.
[3] O.H. Drummer, J. Chromatogr. B 733 (1999) 27–45 (and reference therein).
[4] J. Canezin, A. Cailleux, A. Turcant, A. Le Bouil, P. Harry, P. Allain, J. Chromatogr. B 765 (1) (2001) 15–27.
[5] J. Inczeffy, Z.B. Somodi, Z. Pap-Sziklay, G. Farsang, J. Pharm. Biomed. Anal. 11 (3) (1993) 191–196.
[6] A. Shulgin, A. Shulgin, TiHKAL—The Continuation, Transform Press, Berkeley, CA (1997) 490–491.
[7] D. Merli, L. Pretali, E. Fasani, A. Albini, A. Profumo, Electroanalysis 23 (10) (2011) 2364–2372.
[8] D. Merli, F. Zavarise, I. Tredici, M. Pesavento, A. Profumo, Electroanalysis 24 (4) (2012) 825–832.
[9] F. Zavarise, D. Merli, A. Profumo, Anal. Chim. Acta 668 (2010) 177–181.
[10] F. Scholz, Electroanalytical Methods, 78, Springer-Verlag, Berlin (2002) 319.
[11] ⟨http://www.chem.agilent.com/Library/applications/5968-4920.PDF⟩.
[12] J. Pietsch, K. Schulz, B. Korner, H. Trauer, J. Dressler, M. Gey, Chromatographia 60 (2004) 89–92.
[13] T. Dankházi, E. Fekete, K. Paál, G. Farsang, Anal. Chim. Acta 282 (2) (1993) 289–296.
[14] D. Merli, D. Dondi, D. Ravelli, D. Tacchini, A. Profumo, J. Electroanal. Chem. 711 (2013) 1–7.
[15] F. Scholz, Electroanalytical Methods, Springer-Verlag, Berlin (2002) 64–65.
[16] S.A. Ozkan, B. Dogan, B. Uslu, Microchim. Acta 153 (2006) 27–35.
[17] R.N. Hedge, B.E. Kumara Swamy, B.S. Sherigara, S.T. Nandibewoor, Int. J. Electrochem. Sci. 3 (2008) 302–314.
[18] E. Laviron, L. Roullier, C. Degrand, J. Electroanal. Chem. 112 (1980) 11–23.
[19] J. Wang, P. Tuzhi, M.-S. Lin, T. Tapia, Talanta 33 (9) (1986) 702–712.
[20] R.N. Goyal, V.K. Gupta, M. Oyama, N. Bachheti, Electrochem. Commun. 8 (1) (2006) 65–70.
[21] G. Zotti, S. Zecchin, G. Schiavon, R. Seraglia, A. Berlin, A. Canavesi, Chem. Mater. 6 (1994) 1742–1748.
[22] T. Hu, G. Dryhurst, J. Electroanal. Chem. 362 (1–2) (1993) 237–248.
[23] T.R. Copeland, J.H. Christie, R.K. Skogerboe, R.A. Osteryoung, Anal. Chem. 45 (6)) (1973) 995–996.
[24] Z. Guo, F. Feng, X. Hou, N. Jaffrezic-Renault, Talanta 65 (2005) 1052–1055.
[25] (a) ICH Q2A, Validation of Analytical Procedures: Definitions and Terminology, Geneva, 1995, in 2005 incorporated in Q2(R1); (b) ICH Q2B, Validation of Analytical Procedures: Methodology, adopted in 1996, Geneva Q2B, in 2005 incorporated in Q2(R1).
[26] J. Röhrich, S. Zörntlein, J. Becker, Forensic Sci. Int. 107 (2000) 181–190.
[27] ⟨http://www.drugbank.ca/drugs/DB04829⟩;
(a) ⟨http://www.drugbank.ca/drugs/DB00201⟩;
(b) ⟨http://www.drugbank.ca/drugs/DB01558⟩;
(c) ⟨http://www.drugbank.ca/drugs/DB00182⟩;
(d) ⟨http://pubchem.ncbi.nlm.nih.gov/rest/chemical/mescaline#x27⟩.