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Determination of Drugs of Abuse in Airborne Particles by Pressurized Liquid Extraction and Liquid Chromatography-Electrospray-Tandem Mass Spectrometry

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This work describes the first analytical method specifically developed for the multianalyte determination of several drugs of abuse and their metabolites in air. The methodology is based on pressurized liquid extraction (PLE) of atmospheric particles collected by means of high volume sampler equipped with quartz microfiber filters and subsequent analysis of the extracts by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Up to 17 different compounds belonging to five different chemical classes (cocainics, amphetamine-like compounds, opioids, cannabinoids, and lysergic compounds) are determined by means of this methodology. Acquisition is performed in the selected reaction monitoring (SRM) mode recording two transitions per compound (except for amphetamine). Quantitation by the internal standard method is based on the use of surrogated deuterated standards. The method has been validated in terms of linearity, accuracy, repeatability and sensitivity with satisfactory results. Absolute recoveries were above 50% for most investigated compounds. Method precision showed relative standard deviations (RSD) below 13% for all compounds, except for cannabinoids. The method limits of determination ranged from 0.35 pg/m^3 (for 2-oxo-3-hydroxy-LSD) to 22.55 pg/m^3 (for 11-nor-9 carboxy THC). Finally, as a part of the method validation, the optimized procedure was applied to the analysis of ambient air samples (fine grain-size particulates, $PM_{2.5}$) collected at two urban background sites in Barcelona and Madrid (Spain). Results evidenced the presence of cocaine, benzoilecgonine, tetrahydrocannabinol, ecstasy, amphetamine, methamphetamine, and heroin in some or all of the samples investigated. The highest mean daily levels corresponded to cocaine (850 pg/m^3) followed by heroin (143 pg/m^3).

In the last years several analytical methodologies have been proposed to determine drugs of abuse and metabolites in sewage and surface river water as a means to estimate drug consumption by the population at the community level.[1−11] Contrary to the methods based on population surveys and social, medical, and criminal statistics that have traditionally been used to estimate drug consumption, this approach provides information in an anonymous, fast, and relatively economic way.

Recently, Cecinato et al.[12] have also proposed the use of atmospheric airborne particles as a potentially useful matrix to investigate drug consumption patterns. Because of their physicochemical properties (low vapor pressures, high and medium polarity, weak alkalinity, molecular weights reaching 300 uma), drugs of abuse, and metabolites present in the atmosphere are expected to be associated primarily with particulates.

So far, only a few papers have reported the measurement of drugs of abuse in air. In 1993, Zaromb et al.[13] developed a high-throughput liquid-absorption preconcentration system for sampling and further analysis of airborne cocaine and heroin by LC-electrochemical detection, a system that could also be applied to the detection and monitoring of other compounds.

In 1998 Hannigan et al.[14] detected the presence of cocaine at measurable concentrations in outdoor air from Los Angeles in the course of a study conducted to identify mutagenic compounds through a bioassay-directed chemical analysis based on the use of a human cell mutagenicity assay and gas chromatography−mass spectrometry (GC/MS) analysis.

Within the framework of an intensive program of field measurements of air pollution in Rome (Italy), Cecinato et al.[12] also put into evidence the presence of cocaine in the air of Rome and Taranto. Analysis of cocaine in carbonaceous aerosol samples was performed by Soxhlet extraction with a mixture of dichloromethane and acetone (80:20), cleanup by column chromatography through basic alumina, and analysis by high-resolution GC/MS. Cocaine concentrations seemed to be in agreement with the amounts consumed or destroyed in Italy. Levels measured

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exceeded sometimes 100 pg/m^3 but were on average similar to those of other toxic pollutants like polychlorobiphenyls or nitrated polynuclear aromatic hydrocarbons and higher than those of polychlorodibenzo-*p*-dioxins/polychlorodibenzofurans.

Finally, Lai et al. [15] described a quick, noninvasive method for screening of cocaine, methylenedioxymethylamphetamine (MDMA) and marijuana in cargo containers based on solid phase microextraction (SPME) followed by ion mobility spectrometry (IMS) detection of their volatile markers methyl benzoate, piperonal, and terpenes, respectively.

In this context, the main objectives of the present work were (i) to develop the first analytical methodology, based on pressurized liquid extraction (PLE) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis, for the multianalyte determination of different drugs of abuse and metabolites in atmospheric airborne particles, and (ii) to apply this method to the analysis of real urban air quality samples to validate the method, check the usefulness of such an approach, and obtain a first general picture on the occurrence of these substances in the air in urban areas in Spain.

EXPERIMENTAL SECTION

Chemicals. A total of 17 compounds, belonging to 5 different classes, were investigated: 3 cocainics (cocaine (CO), its metabolite benzoylecgonine (BE), and the transesterification product cocaethylene (CE) formed when cocaine is taken together with ethanol), 5 amphetamine-like compounds (amphetamine (AM), methamphetamine (MA), 3,4-methylenedioxymethamphetamine (MDMA or ecstasy), (*R*,*R*)(-)-pseudoephedrine (PS-EPH), and (1*S*,2*R*)(+)-ephedrine hydrochloride (EPH-HCl), the last two measured together as total ephedrine (EPH)), 3 opiates (heroin (HER), morphine (MOR), and the hydrolyzed product of heroin 6-acetylmorphine (6ACM)), 3 cannabinoids (Δ^9-tetrahydrocannabinol (THC) and its metabolites 11-nor-9-carboxy-THC (nor-THC) and 11-hydroxy-THC (OH-THC)), and lysergic acid diethylamide (LSD) and its metabolites nor-LSD and nor-iso LSD (nor-LSD), and 2-oxo-3-hydroxy-LSD (O-H-LSD).

High purity (>97%) standard solutions of the target compounds were obtained from Cerilliant (Round Rock, TX, U.S.A.) as solutions in methanol or acetonitrile. CO, BE, CE, MA, MDMA, PS-EPH, EPH-HCl, HER, MOR, 6ACM, THC, and LSD were provided at a concentration of 1 mg/mL; AM, nor-THC, OH-THC, O-H-LSD, and nor-LSD were supplied at a concentration of 100 μg/mL.

Several deuterated compounds, also purchased from Cerilliant as solutions in methanol or acetonitrile at a concentration of 1 or 0.1 mg/mL, were used as surrogate standards (SS) for quantitation: benzoylecgonine-d_8 (BE-d_8), cocaine-d_3 (CO-d_3), cocaethylene-d_3 (CE-d_3), LSD-d_3, amphetamine-d_5 (AM-d_5), methamphetamine-d_{14} (MA-d_{14}), MDMA-d_5, 1*S*,2*R*-ephedrine-d_3-hydrochloride (EPH-d_3), heroin-d_9 (HER-d_9), morphine-d_3 (MOR-d_3), and Δ^9-THC-d_3 (THC-d_3).

Individual stock solutions at 1 μg/mL and working standard mixtures at concentrations ranging from 0.1 ng/mL to 1 μg/mL were prepared by appropriate dilution of the standards in methanol (concentration of internal standards 20 ng/mL). All solutions were stored at −20 °C in the dark. The standard mixtures were used for calibration and as spiking solutions for recovery studies.

All solvents used, HPLC-grade methanol, acetone, acetonitrile, and water, were acquired from Merck (Darmstadt, Germany). High quality nitrogen, used to evaporate extracts, was obtained with a nitrogen generator supplied by Centralair (San Sebastián, Spain).

Analytical instrumentation. Extraction of the target analytes from the filters was performed by PLE using an accelerated solvent extraction system ASE 200 (Dionex, Sunnyvale, CA, U.S.A.).

LC-MS/MS analyses were carried out in a system consisting of an Agilent HP 1100 pump (Agilent Technologies, Palo Alto, CA, U.S.A.) equipped with an autosampler and connected in series with a 4000QTRAP hybrid triple quadrupole-linear ion trap (QqLIT) mass spectrometer equipped with a Turbo Ion Spray source (Applied Biosystems-Sciex, Foster City, CA, U.S.A.).

Sample Collection. Airborne particles with an aerodynamic diameter equal or lower than 2.5 μm ($PM_{2.5}$) were collected on 15 cm diameter quartz microfiber filters QF20 (Schleicher and Schuell, Dassel, Germany) at a flow rate of 30 m^3/hour during 24 h by means of MCV CAV/A high-volume samplers with $PM_{2.5}$ cutoff inlets (MCV, Barcelona, Spain). One set of samples, consisting of 12 filters, was collected at an urban background air quality monitoring site at one of the university campuses of Barcelona from September to November 2007. A second set of samples, 7 filters in total, was collected at another similar urban background air quality monitoring site located in one of the university campuses of Madrid from November 2007 to January 2008. Samples were collected on different days of the week, including on weekends in Barcelona but not in Madrid. Compared to the Madrid site, the Barcelona monitoring station is characterized by a larger influence of traffic emissions because of its proximity to one of the city's main traffic avenues and recreational areas. On the other hand, the monitoring site in Madrid is characterized by a denser student transit on weekdays, and the absence of it during weekends.

After collection, samples were folded and wrapped in aluminum foil, sealed, and stored in the dark at −20 °C until analysis.

Sample Extraction. In the optimized approach, half of the collection substrate was placed in 11 mL pressure resistant stainless steel PLE cells. Once the filter was placed in the cell, a known amount of internal standard was spiked on it for quantitation purposes and left overnight at 4 °C. The extraction cells

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were sealed at both ends with glass-fiber filters (Ø 19.8 mm; Dionex, Sunnyvale, CA, U.S.A.) and void volumes in the cell were filled up with hydromatrix bulk sorbent (Varian, Palo Alto, CA, U.S.A.).

PLE of the analytes from the samples was performed with two extraction cycles: methanol (100%) was used as extraction solvent in the first one, and a mixture of methanol-acetone (50:50, v/v) was used in the following one. The extraction conditions were similar in both cycles: pressure, 1250 psi; temperature, 90 °C; preheat time, static time, and heat time, 5 min each; flush volume, 60%; and purge time, 60 s.

The PLE extracts were reduced almost to dryness under a gentle stream of N_2 in a Turbo Vap LV evaporator (Zymark, Hopkinton, MA, U.S.A.). The walls of the PLE vials were washed out with 1.5 mL of methanol and the so-obtained concentrated extracts were transferred to small LC vials to be further evaporated to dryness in a Pierce-Reacti-Vap III evaporator (Rockford, IL, U.S.A.). Final reconstitution of the extracts was done with 500 μL of methanol.

LC-MS/MS Analysis. The presence of drugs of abuse and metabolites in the reconstituted extracts was analyzed following the LC-MS/MS protocol previously described by Postigo et al. for the determination of these substances in sewage water.[9] Chromatographic separation was performed with a Purospher Star RP-18 endcapped column (125 mm × 2.0 mm, particle size 5 μm) preceded by a guard column (4 × 4 mm, 5 μm) of the same packing material, both from Merck, and a mobile phase consisting of gradient acetonitrile/water at a constant flow rate of 300 μL/min. Injection volume was 5 μL. LC-MS/MS analysis of cannabinoids was performed in the negative ionization (NI) mode and the analysis of the remaining compounds was performed in the positive ionization (PI) mode with an electrospray (ESI) interface. For quantitative analysis and to get enough identification points to achieve analyte confirmation, data acquisition was performed in the SRM mode, recording the transitions between the precursor ion and the two most abundant product ions for each target analyte. Optimum experimental conditions for the spectrometric determination of the target analytes are described in detail elsewhere.[9]

RESULTS AND DISCUSSION

Optimization of the PLE Procedure. In the optimization of the PLE procedure the following main parameters affecting extraction were tested: extraction solvent, pressure, temperature, and number of extraction cycles.

To select the best solvent combination, spiked 1/2 sections of the filters containing 25 ng of the target analytes were extracted sequentially with a series of decreasing polarity solvents and solvent mixtures: methanol, methanol/acetone (50:50, v/v), acetone, hexane/acetone (50:50, v/v), dichloromethane, and hexane. In this experiment the bulk of the analytes was shown to be extracted in the first two steps, corresponding to a solvent cycle with methanol followed by another one with a mixture of methanol/acetone (50:50, v/v). Subsequent extraction of the disks with more apolar solvents was not shown to improve analyte recoveries and would have increased matrix interferences in the extracts.

Further optimization of the number of extraction cycles was carried out in a second set of experiments in which a sample filter was divided into two equal sections, and each section was placed in a PLE extraction cell and spiked with 100 ng of the target analytes. One of the PLE cells was extracted with three methanol cycles, and the extract resulting from each cycle was collected in an independent vial. The same was done with the other PLE cell, but each of the three extracts collected was the result of two consecutive extraction cycles using methanol in the first cycle and methanol/acetone (50:50, v/v) in the second one. The best results were obtained when applying sequential extraction with methanol followed by methanol/acetone 1:1. The performance of various extraction cycles with methanol, as well as the iteration of the extraction sequence methanol and methanol/acetone (50:50, v/v) did not result in comparatively higher absolute recoveries; therefore, the extraction sequence consisting of one cycle with methanol followed by one cycle with methanol/acetone (50:50, v/v) was finally selected.

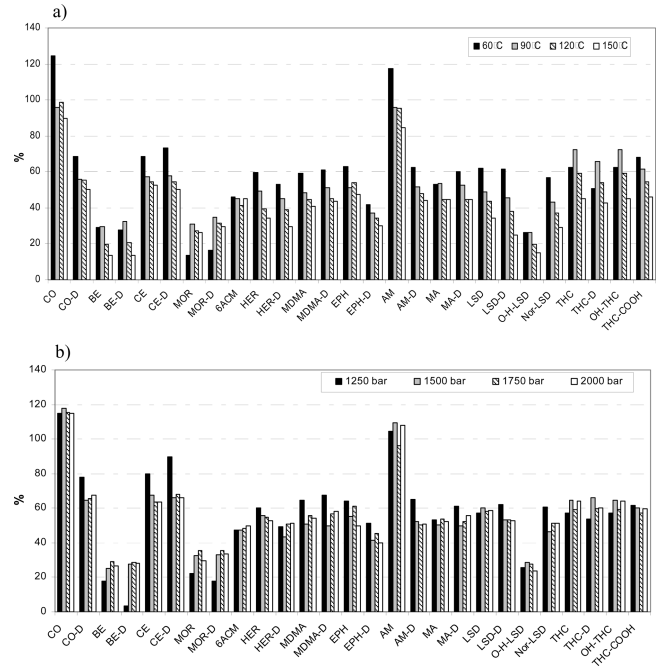

Figure 1. Efficiency of extraction (absolute recoveries) of the target analytes from filters spiked with 50 ng under different (a) temperature and (b) pressure values.

In the optimization of the PLE procedure, four different temperatures (60, 90, 120, and 150 °C) and pressure values (1250, 1500, 1750, and 2000 bar) were also tested. As it can be observed in Figure 1, the optimum conditions for extraction of the investigated analytes varied from one to another; therefore, final selection was done taking into account the extent of the deviation of the analyte recoveries from 100%, evaluating both the sum and the average of the standard deviations obtained under each tested condition. Overall, the best results (lowest standard deviations) were obtained for a pressure of 1250 bar and a temperature of 60 °C; however, 90 °C was finally selected because for the compounds showing the lowest recoveries (morphine and benzoylecgonine) extraction was more efficient at this temperature.

Method Performance. The performance of the method was evaluated through determination of the linearity, sensitivity, repeatability, recovery, and matrix effects of the method. Results obtained are summed up in Table 1.

Table 1. Quality Control Parameters of the Analytical Method: Linear Correlation Coefficients (r^2), Limits of Detection, Limits of Determination, Repeatability and Absolute and Relative Recoveries in Extracted Air Sampling Filters

	linearity r^2 [a]	limits of detection[b] (LOD) [pg/m3]	limits of determination[b] (LODet) [pg/m3]	repeatability[c] RSD %	absolute recovery[d] (AR) %	relative recovery[e] (RR) %
EPH	0.9950	0.64	1.73	12.7	43.4	103.0
EPH-d_3					42.1	
AM	0.9956[f]	0.39[f]	1.05[f]	5.8[f]	54.3[f]	98.5[f]
AM-d_5					55.1	
MDMA	1.0000	0.34	1.26	5.7	54.7	98.7
MDMA-d_5 (IS)					55.4	
MA	1.0000	1.02	2.73	7.3	59.6	98.0
MA-d_{14} (IS)					60.9	
BE	0.9986	0.34	2.49	9.3	16.6	96.3
BE-d_8 (IS)					17.2	
CO	0.9988	0.11	3.10	7.6	62.0	97.7
CO-d_3 (IS)					63.4	
CE	0.9946	0.07	1.21	6.6	66.4	97.3
CE-d_3 (IS)					68.3	
O-H-LSD	0.9902	0.13	0.35	5.2	25.8	57.7
nor-LSD	0.9996	0.27	0.73	8.9	52.5	117.2
LSD	0.9996	0.26	0.70	7.0	52.6	117.5
LSD-d_3 (IS)					44.8	
6ACM	0.9996	2.76	7.36	8.2	43.4	158.5
MOR	0.9992	6.33	16.87	11.7	24.3	88.5
MOR-d_3 (IS)					27.4	
HER	0.9998	2.42	9.03	6.8	60.3	98.7
HER-d_9 (IS)					61.1	
nor-THC	0.9958	8.46	22.55	15.0	50.2	100.2
OH-THC	0.9904	1.08	5.30	22.2	48.1	95.9
THC	1.0000	1.96	5.23	23.1	43.4	86.5
THC-d_3 (IS)					50.1	

[a] Linearity. Calibration range 0.1−1000 ng/mL (equivalent to 0.14–1400 pg/m^3). [b] Limit of determination: minimum concentration that can be quantified (>LOQ, SRM1) and confirmed (>LOD, SRM2). [c] Relative standard deviation, spiking concentration: 50 ng ($n = 5$). [d] Average recovery of the investigated analytes after extraction of spiked disks (50 ng, $n = 5$). [e] Relative to the associated deuterated surrogate standard. [f] Values corresponding to the SRM2 of AM (SRM1 was affected by matrix interferences that increase its signal up to 3 times, but not the signal of the deuterated analogue).

Quantitation, based on peak areas, was performed by the internal standard (IS) method using deuterated analogues of the compounds (and in the absence of them the most similar in terms of structure) as surrogate standards. The linearity of the method was evaluated by constructing eight-point calibration curves with concentrations ranging from 0.1 ng/mL (or the limit of quantitation if higher) to 1000 ng/mL (equivalent to 0.14 and 1400 pg/m^3, respectively). The concentration of the internal standard along the calibration curve was maintained constant at 20 ng/mL (equivalent to 28 pg/m^3). Correlation coefficients (r^2) for both monitored transitions SRM1 and SRM2 were always higher than 0.99 (see Table 1).

The limits of detection (LOD) and quantification (LOQ) were experimentally estimated from the analysis of real samples as the concentration of analyte giving a signal-to-noise ratio of 3 and 8, respectively. Because the LODs and LOQs vary considerably from sample to sample, these limits correspond to the average of the LODs and LOQs, respectively, calculated for the various real samples investigated. In the case of undetected compounds (CE, MOR, PS-EPH, EPH-HCl, LSD, O-H-LSD, nor-LSD, OH-THC, and nor-THC), these limits were calculated from extracted blank filters (used in the recovery study) spiked with the target analytes at a concentration of 50 ng.

As it is shown in Table 1, the method LODs and limits of determination (minimum concentration of a compound that can be quantified (>LOQ, SRM1) and confirmed (>LOD, SRM2)) were below 8 and 23 pg/m^3, respectively.

The overall method repeatability, calculated as the relative standard deviation (RSD) of the analysis of five replicates of spiked filters (50 ng), was satisfactory, with RSD values ranging from 5 to 13% for all target analytes except for the group of the cannabinoids (15 to 23%).

Method absolute recoveries were calculated from the peak areas obtained for each analyte in the analysis of spiked (50 ng) air filters as percentages of the peak areas obtained from direct chromatographic injection (5 μL) of equivalent amounts of the standards in methanol. Relative recoveries were determined from the absolute recoveries for each compound as percentages of the absolute recoveries of the associated surrogates. As it can be observed in Table 1, absolute recoveries were between 43 and 66% for all analytes but BE and MOR, compounds that presented considerably poor recoveries (17 and 24%, respectively). Absolute recoveries of the deuterated compounds were fairly similar to those provided by the non-deuterated analogues. Relative recoveries achieved were equal to 99.6 ± 8.7% for all compounds except O-H-LSD (58%) and 6ACM (159%). In the absence of the corre-

sponding deuterated analogues, these two compounds were quantified using as surrogate standards the structurally related compounds LSD-d3 and MOR-d3, respectively.

Processing of the data originated in the recovery experiments showed that the SRM transition initially selected for quantification of amphetamine from the analysis of standard solutions (136.2 > 91) was affected by a matrix interference that increased the signal of this transition in the samples (as compared to the standard) and raised the SRM1/SRM2 ratio characteristic of the amphetamine standard 2 to 3 times; therefore, all data provided for amphetamine (including method performance values and samples levels) correspond to the SRM transition initially selected for confirmation (136.2 > 119). The SRM transition selected for determination of the AM deuterated analogue (141.2 > 96) was not affected by this phenomenon. The availability of just one SRM transition to monitor AM presence does not allow to confirm the obtained results; however, this analyte was kept in the analytical method, as it has been reported to be very volatile, and therefore likely to be found in the airborne particles.[16,17]

Matrix Effects. The low absolute recoveries obtained for the target analytes in the analysis of spiked samples could be attributed to a decrease of the analyte MS signals because of coeluting matrix components. LC-MS/MS methodologies using electrospray as ionization source are known to be prone to matrix ionization suppression effects that result in a decrease of the method sensitivity and repeatability.[18,19] To evaluate this phenomenon, three 100 μL aliquots of a reconstituted extract obtained after extraction of a spiked (50 ng) filter were diluted 1:10 (aliquot 1), diluted 1:2 (aliquot 2), and evaporated to dryness and reconstituted with 100 μL of a standard mixture of the analytes at a concentration of 100 ng/mL (aliquot 3) to obtain theoretical final concentrations in the vials of 10 ng/mL, 50 ng/mL and 200 ng/mL, respectively. In the absence of matrix effects the analytes peak areas should provide a signal proportional to their concentration, whereas in the presence of matrix effects the signals obtained would be higher or lower depending on whether there is signal enhancement or suppression. Contrary to the authors' expectations, the results obtained, depicted in Figure 2, showed that the compounds are not affected by matrix ionization suppression or enhancement effects, as the observed deviations from the expected concentration were not relevant. On the other hand, deuterated compounds showed a similar behavior as their non-deuterated analogues. In the light of these results the use of deuterated surrogate standards would not be critical in this case, although it is still recommended to correct for potential losses of the target analytes during sample treatment and prevent potential matrix effects in other samples eventually more contaminated than the ones investigated in this study. On the basis of these results, further cleanup of the PLE extracts by, for instance, solid phase extraction, was deemed unnecessary.

Levels of Drugs of Abuse Levels in Airborne Particles. The validated methodology was applied to 12 and 7 daily samples of atmospheric particulate matter ($PM^{2.5}$) collected at two air quality monitoring stations located in Barcelona and Madrid, respectively. Table 2 shows the number of positive samples and the average and standard deviations of the concentrations of drugs determined in the air samples collected in each area. Figure 3 shows, as an example, the reconstructed SRM chromatograms resulting from the analysis of two positive real samples.

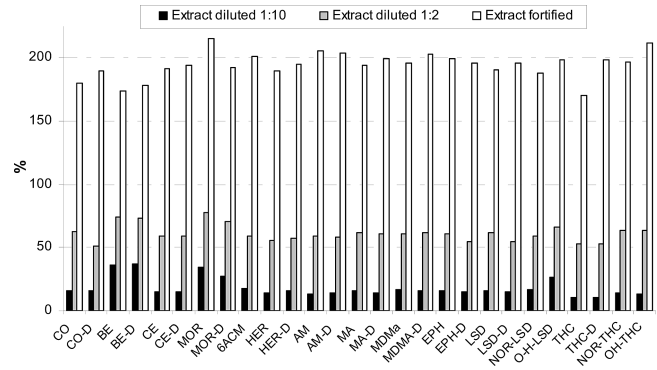

Figure 2. Evaluation of matrix effects. Relative signals obtained after dilution 1:10 and 1:2 and fortification 1:2 of a spiked (50 ng) sample extract. The peak areas have been normalized to the analyte peak areas obtained in the original extract.

Identification of the target analytes in the samples is accomplished by comparing the retention time and the relative abundance of the two SRM transitions selected for their determination with those of standards analyzed under the same conditions. Whenever the SRM1/SRM2 ratio surpasses the limits set by the European legislation regarding analytical performance and data interpretation, the result is considered negative.[9,20]

Some of the investigated compounds, namely, CE, MOR, PS-EPH, EPH-HCl, LSD and its two metabolites O-H-LSD and nor-LSD, and the two THC metabolites OH-THC and nor-THC, were not detected in any of the samples analyzed. HER and its metabolite 6ACM were found only in some of the samples collected in Madrid; however, the frequency of detection of the metabolite (2 out of 7 samples) was very low compared to that of the parent drug (7 out of 7 samples). MDMA was determined in only one sample collected in Barcelona, and MA was present in one sample from each investigated area. The most abundant amphetamine-like compound determined in the collected samples was AM; however, amphetamine results are not confirmed because of the presence of an interference in one the two SRM transitions selected for its determination.

The most ubiquitous analytes were CO, BE, and THC, found at detectables levels in all samples analyzed. Regarding abundance, CO presents the highest concentrations of all investigated compounds. CO levels, ranging from 29 to 850 pg/m^3, were in most cases 1 order of magnitude higher than those determined for other compounds in this study and exceeded by far the CO levels measured by Cecinato et al. in Rome and Taranto (<5−98 ± 13 pg/m^3).[12] HER is the second most abundant compound detected in Madrid, but not in Barcelona, with an average concentration in airborne particles of 84 pg/m^3. THC, BE, and 6ACM present similar average levels that range from 23 pg/m^3 (BE and 6ACM) to 33 pg/m^3 (THC), and amphetamine-like compounds were detected in all cases below 5 pg/m^3.

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Table 2. Number of Positive Samples (Freq.) and Average and Standard Deviation of the Concentrations of Drugs of Abuse Determined in the Air Samples Investigated in Barcelona and Madrid[a]

	Barcelona		Madrid		total	
	freq	average conc. ± std dev [pg/m^3]	freq	average conc. ± std dev [pg/m^3]	freq	average conc. ± std dev [pg/m^3]
CO	12/12	204.03 ± 172.27	7/7	479.74 ± 275.68	19/19	305.61 ± 249.28
BE	12/12	29.07 ± 23.89	7/7	13.95 ± 6.09	19/19	23.50 ± 20.43
HER	0/12	n.d.	7/7	83.72 ± 52.74	7/19	83.72 ± 52.74
6ACM	0/12	n.d.	2/7	22.80 ± 11.40	2/19	22.80 ± 11.40
MDMA	1/12	2.90	0/7	n.d.	1/19	2.90
MA	1/12	<LODet	1/7	3.49	2/19	3.49
AM	9/12	2.28 ± 1.18	4/7	1.42 ± 0.91	13/19	2.02 ± 1.14
THC	12/12	27.12 ± 42.38	7/7	43.70 ± 34.73	19/19	33.23 ± 39.59

[a] CO, cocaine; BE, benzoylecgonine; HER, heroin; 6ACM, 6-acetylmorphine; MDMA, ecstasy; MA, methamphetamine; AM, amphetamine; THC, Δ^9-tetrahydrocannabinol; LODet, limit of determination.

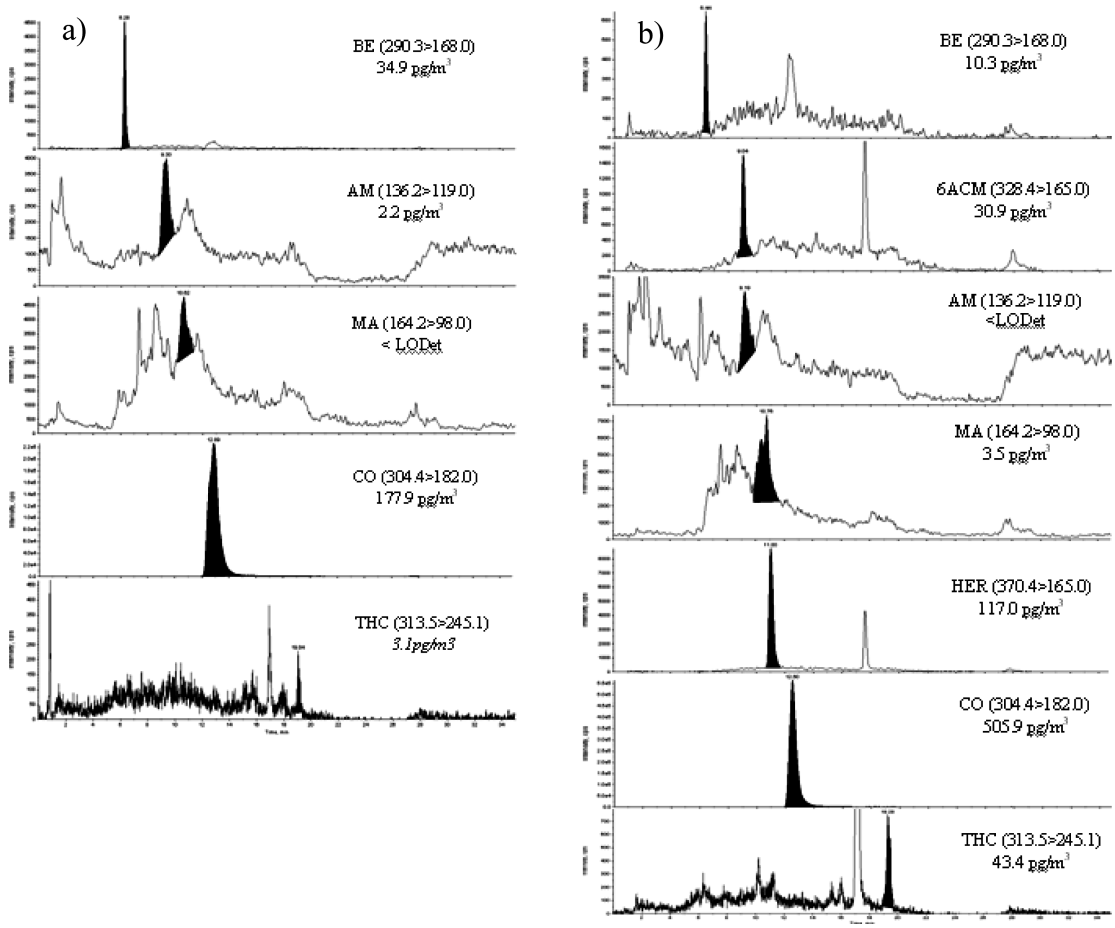

Figure 3. SRM chromatograms resulting from the analysis of a positive sample collected in (a) Barcelona, 19/10/2007, and (b) Madrid, 12/12/2007. Only analytes positively identified in these samples are shown. Levels written in italics are above the sample limit of determination but below the average method limit of determination calculated for that analyte.

Overall, concentrations of drugs of abuse and metabolites determined in the airborne particles of Madrid were higher than those detected in the airborne particles of Barcelona, except for BE, AM, and MDMA (see Figure 4). HER was present in all samples collected in Madrid; on the contrary, this drug was absent in the samples taken in Barcelona. This could be due to the location of the monitoring site in Madrid, in relative proximity of a potentially drug-dealing suburb. On the other hand, these results are in agreement with a study carried out in three Spanish cities (Madrid, Barcelona, and Sevilla) regarding heroin consumption habits. This study states that injected heroin is rather extended in Barcelona, whereas in Madrid and Sevilla, heroin is preferentially smoked; consumption habit that may favor heroin transfer into airborne particles.[21]

As shown in Figure 4, in Barcelona the highest values of the investigated analytes were observed on the weekends, especially in the case of cocaine. This is in line with the already reported higher consumption of this drug during weekends as compared to working days, a trend that has been observed both in

(21) De la Fuente de Hoz, L.; Brugal Puig, M. T.; Ballesta Gómez, R.; Bravo Portela, M. J.; Barrio Anta, G.; Domingo Salvany, A.; Silva do Rosario, T.; Ambrós Hortensi, M. *Rev. Esp. Salud Pública* **2005**, *79*, 475–491.

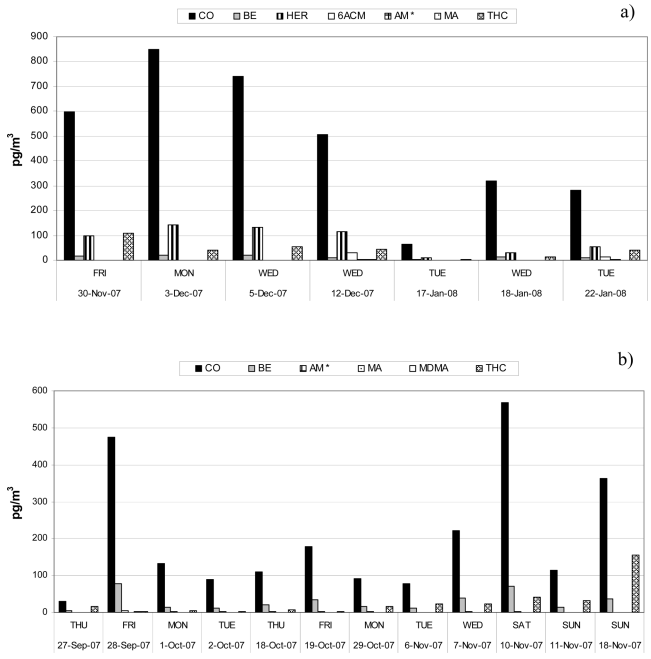

Figure 4. Levels of drugs of abuse and metabolites in the various samples collected in (a) Madrid and (b) Barcelona. *Amphetamine (AM) results are not confirmed by a second SRM transition. CO, cocaine; BE, benzoylecgonine; HER, heroin; 6ACM, 6-acetylmorphine; AM, amphetamine; MA, methamphetamine; THC, Δ^9-tetrahydrocannabinol; MDMA, ecstasy.

Barcelona[9] and in other areas.[22,23] In Madrid, all samples were taken during working days. Therefore, it is not possible to derive any temporal trend. Finally, this methodology aims to become an indicator to be potentially used by public health authorities to assess drug consumption and abuse. This indicator would be an additional tool to surveys, statistics on hospital admissions, police records, and so forth, which are currently used to evaluate and quantify drug consumption by the population. A priori, the main advantages of this methodology over the usual indicators are fast information, anonymity, and cost. Traditional methods to estimate drug abuse are generally less precise, more time-consuming, and costly, and they invade the privacy of individuals. In addition, the determination of drugs in airborne particulates allows for the detection of activities such as drug handling and dealing, which are related to consumption but undetected by indicators such as population health statistics.

(22) Zuccato, E.; Chiabrando, C.; Castiglioni, S.; Bagnati, R.; Fanelli, R. *Environ. Health Perspect.* **2008**, *116*, 1027–1032.

(23) Huerta-Fontela, M.; Galceran, M. T.; Martin-Alonso, J.; Ventura, F. *Sci. Total Environ.* **2008**, *397*, 31–40.

CONCLUSIONS

A novel analytical method has been successfully developed for the multianalyte determination of several drugs of abuse and their metabolites in airborne particles. The methodology is based on PLE of the target compounds from atmospheric particulates deposited on quartz fiber filters and analysis of the extracts by LC-MS/MS.

Application of the method to several samples collected in two urban air quality monitoring sites sampling stations located in university areas of Barcelona and Madrid (Spain) has shown the presence of CO, BE, THC, MDMA, AM, MA, and HER. CO, BE, and THC have been found in all samples collected. CO has been the drug determined at the highest levels (850 pg/m^3) in both investigated areas. Cocaine concentrations are about 1 order of magnitude above those registered in Italian cities by Cecinato et al.[12] and are also considerably higher than those determined in this study for the other drugs.

Further research is underway to identify potential temporal and spatial variations of the compounds analyzed in the investigated urban environments, as well as occurrence in other areas, and to give proof of correlation of the environmental data with drug related activities. On the assumption that such a correlation were proved, this approach could constitute a useful tool for the authorities fighting drug abuse to identify drug-dealing areas and high consumption zones, as well as geographical and temporal variations.

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