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A ROBUST SPME-GC-MS METHOD FOR QUANTIFYING CLUB DRUGS IN HUMAN URINE

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Abstract

A solid-phase microextraction-gas chromatographic–mass spectrometric (SPME-GC–MS) method has been developed and validated to measure four common club drugs: γ-hydroxybutyric acid (GHB), methamphetamine (MET), Methylenedioxymethamphetamine (MDMA) and 3,4-Methylenedioxyamphetamine (MDA) in human urine samples. These substances are frequently associated with parties and raves, that's why they are categorized as 'club drugs.' Deuterium-labeled internal standards were employed for each of the four drugs to enhance quantitation accuracy. The drugs were spiked into urine samples and derivatized with N-methyl-N-trimethylsilyl trifluoroacetamide (MSTFA) to prepare them for GC–MS analysis. The SPME conditions, including extraction time and temperature, as well as desorption time and temperature, were optimized to maximize the peak area for each drug. The final SPME parameters were a 90 °C extraction for 20 minutes, followed by a 1-minute desorption in the GC injector at 225 °C using split-less injection. A 100 µm PDMS fiber from Supelco was used for all SPME procedures. The GC separation was performed on a VF-5ht column (30 m, 0.25 mm i.d., 0.10 µm film thickness) from Varian, using a temperature program ranging from 150 °C to 270 °C at a rate of 10 °C/min. The instrumentation included a ThermoFinnigan Trace GC-Polaris Q, interfaced with a LEAP CombiPal autosampler. Data collection involved using extracted ion chromatograms of specific marker m/z values for each drug from the total ion chromatograms (TIC) in full scan mode. Calibration curves with R^2 values greater than 0.99 were generated daily, based on the peak area ratios (drug peak area/internal standard peak area) against concentration. The validated method demonstrated intra-day and inter-day precision (% RSD) below 15% and a % error below 15% for four concentrations within the ranges of 0.05–20 µg/mL for MET and 0.10–20 µg/mL for GHB, MDMA, and MDA. This method offers simple sample preparation with acceptable accuracy and

precision for the simultaneous quantification of these four drugs of abuse, and it shows no interference from the urine matrix.

Keywords: Club drugs, Recreational drugs, Ecstasy, Ice, SPME, GCMS

1. Introduction

The category of recreational drugs known as 'club drugs' has been rapidly expanding in popularity. These substances are frequently associated with all-night events, such as raves and nightclubs, and are particularly prevalent among younger populations [1]. The drugs typically classified under this category include Methamphetamine (MET, commonly known as Ice), 3,4-methylenedioxy methamphetamine (MDMA, commonly known as Ecstasy), gamma-hydroxybutyrate (GHB), and Methylenedioxyamphetamine (MDA) (Fig. 1) [2]. A survey conducted among college students revealed that 42% had experimented with club drugs at some point in their lives, and 22.6% admitted to using these substances between 7 and 12 times per year [3]. The issue of club drug abuse is not confined to any single region; it has become a global concern. For example, a recent study in Taiwan found that 42.9% of a group of police detainees tested positive for amphetamines [4].

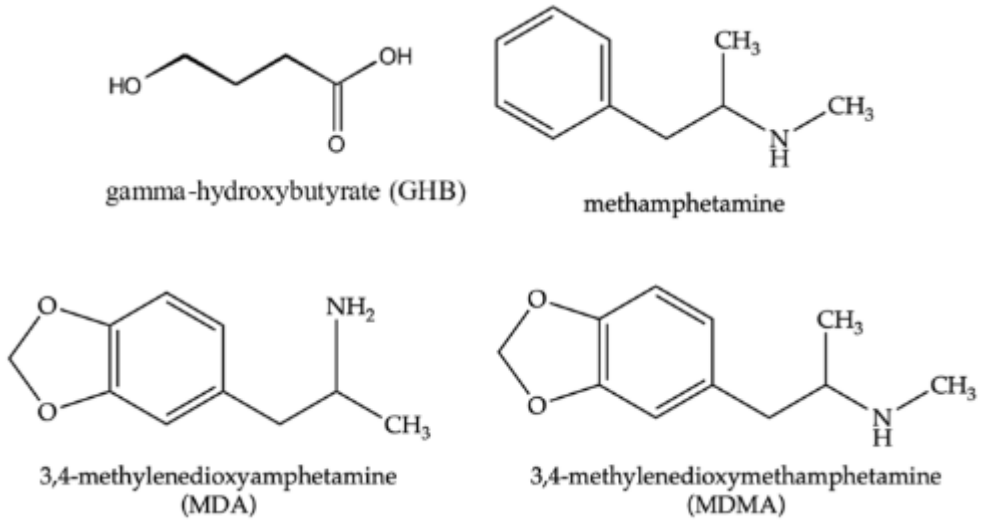


Fig. 1. Structure of four club drugs

Solid-phase microextraction (SPME) is a highly effective sample preparation technique that has gained traction in various fields, including forensic science. SPME utilizes a fiber that is coated with a gas chromatography (GC) packing material to extract sample molecules from their matrix [5]. These molecules are adsorbed onto the fiber and later desorbed into the GC injection port for analysis. One of the major advantages of SPME is that it does not destroy the sample, making it particularly useful in forensic investigations where preserving the integrity of the evidence is crucial. Furthermore, SPME can concentrate the sample molecules, thereby lowering the detection limit for the analytes of interest. Unlike other common sample preparation methods, such as solid-phase extraction and liquid–liquid extraction, SPME is considered environmentally friendly because it does not require the use of organic solvents.

Initially, SPME was thought to be suitable only for the extraction of volatile analytes. However, recent advancements in sample derivatization techniques have broadened its applicability to include non-volatile compounds as well [6]. Today, SPME is most commonly used in conjunction with gas chromatography-mass spectrometry (GC–MS), a powerful analytical technique widely employed in both federal and state crime laboratories. This combination of SPME with GC–MS allows for precise and accurate detection and quantification of a wide range of substances, making it an indispensable tool in modern forensic science.

Given that all four drugs targeted in this assay—gamma-hydroxybutyrate (GHB), methamphe

tamine, methylenedioxy methamphetamine (MDMA) and 3,4-methylenedioxyamphe tamine (MDA)are semi-volatile, derivatization prior to gas chromatography-mass spectrometry (GC–MS) analysis is essential to achieve maximum sensitivity. To streamline the process and minimize potential damage to the column head, in situ derivatization within the solid-phase microextraction (SPME) vial was selected. This approach reduces the number of sample preparation steps while enhancing the overall efficiency of the assay.

Various derivatizing agents have been employed for the analysis of amphetamines, including alkyl chloroformates [7–9], heptafluoro-n-butyryl chloride [10,11], pentafluorobenzoyl chloride [12], propionic anhydride [13], heptafluorobutyric anhydride [14,15], and N-methyl-bis(trifluoroacety lamide) [16]. When it comes to GHB analysis from biological fluids, many methods involve initially converting GHB into gamma-butyrolactone (GBL) under acidic conditions to boost assay sensitivity [17–20]. However, this conversion process was excluded from the development of this assay because it involves acidic conditions that could potentially interfere with the basic nature of the other analytes—amphetamines—being analyzed.

Other studies have opted to analyze GHB directly, without converting it to GBL, using derivatization agents like hexyl-chloroformate [21] or bis(trimethylsilyl)trifluoroacetamide (BSTFA) in combination with trimethylchlorosilane (TMCS) [1,22–25].

The validation of bioanalytical methods, particularly those dealing with biological matrices, is an area of ongoing research, with updates periodically introduced by experts in the field [27]. For this specific method, urine was identified as the most appropriate biological matrix. Urine is particularly advantageous for detecting GHB because it offers a longer detection window, which is crucial in cases involving drug-facilitated sexual assault [28,29]. Additionally, MET, MDMA and MDA are known to be excreted unchanged in the urine, making it a reliable matrix for analysis [30]. The simultaneous quantification of GHB, methamphetamine, MDMA and MDA in urine represents a significant advancement, filling a gap in the existing methodologies for detecting these substances.

2. Experimental

2.1 Reagents

Solid samples of GHB, MET, MDMA and MDA were procured from Sigma-Aldrich (Milwaukee, WI). The derivatizing agentN-methyl-N-trimethylsilyl trifluoroacetamide (MSTFA)was sourced from Sigma-Aldrich and Fisher Scientific (Pittsburgh, PA), respectively. Drug-free human urine samples (pooled from mixed male and female donors) were obtained from Bioreclamation, Inc. (Hicksville, NY). Deuterium-labeled internal standards for MET, MDMA, MDA, and GHB were acquired from Cerilliant Chemical Products (Round Rock, TX).

2.2 Instrumentation and equipment

All experiments were conducted using a ThermoFinnigan Trace gas chromatograph coupled with a Polaris Q mass spectrometer, both from Thermo Electron Corporation (Waltham, MA). The chromatographic separation was carried out using a VF-5ht column, which measured 30 meters in length, with an internal diameter of 0.25 mm and a film thickness of 0.10 mm (Varian, Lake Forest, CA). Automated sample handling was facilitated by the LEAP CombiPAL autosampler, provided by LEAP Technologies (Carrboro, NC). Solid-phase microextraction (SPME) fibers, made of 100 µm polydimethylsiloxane (PDMS), were obtained from Supelco (Milwaukee, WI) and were used for approximately 200 injections before replacement. Gas-tight autosampler vials with a capacity of 20 mL were supplied by Microliter Analytical (Suwanee, GA). This setup allowed for precise and reproducible analysis of the target compounds, ensuring consistent results across all experiments.

2.3 Preparation of stock and calibration standards

To prepare the necessary solutions for the experiment, precise quantities of each drug were weighed and dissolved in deionized water to create initial stock solutions with a concentration of 10 mg/mL. Subsequently, individual stock solutions with concentrations of 1 mg/mL were prepared for each drug. These individual stock solutions were then combined to create mixed working solutions

containing all four drugs at concentrations of 1 mg/mL, 100 µg/mL, and 10 µg/mL.These mixed working solutions were utilized to generate calibration curves by spiking them into drug-free urine, resulting in final drug concentrations of 0.05, 0.1, 0.2, 1, 2, 5, 10, and 20 µg/mL. The same mixed working solutions (1 mg/mL, 100 µg/mL, and 10 µg/mL) were also employed to prepare samples for method validation purposes. All stock and working solutions were stored at a refrigerated temperature of 4°C when not in use to maintain their stability and were replaced as necessary.Internal standards were obtained in methanol, with concentrations of 100 µg/mL for d5-MET, d5-MDMA, d3-MDAand 1 mg/mL for d6-GHB. These internal standards were crucial for ensuring accurate quantitation during the analysis. The careful preparation and maintenance of these solutions were essential for the reliability and precision of the experimental results.

2.4 Instrumental conditions

Chromatographic separations were conducted using a temperature gradient that ranged from 150°C to 270°C, with a ramp rate of 10°C per minute. The extraction of the target drugs was performed using a 100 µm polydimethylsiloxane (PDMS) fiber. During the extraction process, the sample was exposed to the headspace for 20 minutes at an elevated temperature of 90°C, with agitation to enhance the efficiency of the analyte transfer onto the fiber. Following extraction; the analytes were desorbed into the gas chromatograph's split-less injection port at a temperature of 225°C for duration of one minute. This process ensured the complete transfer of the analytes into the gas chromatography system for subsequent analysis. For detection, the mass spectrometer utilized electron ionization (EI) with the ion source maintained at 200°C. The mass spectrometer was operated in full scan mode, covering a mass-to-charge ratio (m/z) range of 50 to 450. This broad scan range allowed for the detection and identification of the analytes and their corresponding internal standards. Quantitation was performed by analyzing the extracted ion chromatograms, which were derived from the total ion chromatogram (TIC). The peak areas of the analytes and internal standards were used for accurate quantification. This method provided a robust and sensitive approach to detecting and quantifying the drugs of interest in the samples.

2.5 Sample preparation

Calibration and validation samples were meticulously prepared in 1.5 mL centrifuge tubes using the mixed stock solutions of the four target drugs at concentrations of 1 mg/mL, 100 µg/mL, and 10 µg/mL. To each tube, internal standard solutions were added to achieve final concentrations of 1 µg/mL for d5-MET, d5-MDMA, d3-MDAand 10 µg/mL for d6-GHB. These internal standards were critical for ensuring the accuracy and precision of the quantification process.Next, appropriate volumes of drug-free human urine were introduced into each calibration sample to bring the total sample volume up to 1 mL. To initiate the derivatization process, 10 µL of MSTFA (derivatizing agent) were added to each sample. The samples were then vortexed thoroughly to ensure complete mixing of the reagents and the sample matrix. Following vortexing, the samples underwent sonication for 5 minutes at room temperature to further ensure homogeneity and to aid in the derivatization reaction. After sonication, the prepared samples were transferred to autosampler vials for analysis. Each autosampler vial was pre-filled with 1 mL of deionized water, and 500 µL of the sample solution was added to it. To ensure that the samples could be reanalyzed, if necessary, the remaining 500 µL of each sample solution was stored in a freezer at -4°C. This careful preparation and storage protocol ensured the reliability and reproducibility of the calibration and validation process, while also providing a backup in case reanalysis was required.

2.6 Method optimization and validation

Before finalizing the use of MSTFAfor the derivatization process, several other derivatizing agents were tested, including propyl-chloroformate, heptafluoro-n-butyryl chloride, pentafluoro-benzoyl chloride, propionic anhydride, heptafluorobutyric anhydride, N-methyl-bis(trifluoroacetylamide), and trimethylchlorosilane. Unfortunately, none of these alternatives provided adequate derivatization of all four drugs to enable accurate quantification. Additionally, attempts to analyze

the drugs in their underivatized form yielded unsatisfactory results, further highlighting the necessity for effective derivatization. The optimization of MSTFA involved testing its various concentrations. Different concentrations were evaluated by preparing triplicate samples containing 10 µg/mL of each drug and measuring the resulting peak areas in the chromatograms. After comprehensive testing, the optimal concentration was selected based on the peak area responses, ensuring maximal derivatization efficiency for all four drugs. Simultaneously, the solid-phase micro-extraction (SPME) conditions were meticulously optimized. These included fine-tuning parameters such as incubation time, incubation temperature, desorption time, and desorption temperature. To achieve optimal conditions, triplicate samples containing 10 µg/mL of each drug were analyzed under various SPME settings, with the aim of maximizing the peak areas. These adjustments ensured that the method provided consistent and robust results. The final method was validated over a three-day period, using four different concentrations for each drug within their respective calibration ranges. For each concentration and for each day, five replicates were analyzed. The validation process focused on evaluating accuracy (expressed as percent error) and precision, both within a single day (intra-day precision) and across the three days (inter-day precision). On each validation day, a calibration curve was generated for each drug. For gamma-hydroxybutyrate (GHB), methylenedioxyamphetamine (MDA) and methylenedioxymetham phetamine (MDMA), the calibration curves consisted of eight concentration points: 0.1, 0.2, 0.5, 1.0, 2.0, 5.0, 10, and 20 µg/mL. For methamphetamine (MET), the calibration curve included an additional lower concentration point, covering nine levels: 0.05, 0.1, 0.2, 0.5, 1.0, 2.0, 5.0, 10, and 20 µg/mL. Method precision and accuracy were thoroughly assessed for GHB, MDA and MDMA at the 0.5, 1, 5, and 15 µg/mL levels. For MET, these validation parameters were measured at 0.1, 0.2, 2, and 15 µg/mL. This rigorous validation process confirmed the reliability of the method for quantifying these drugs across a range of concentrations.

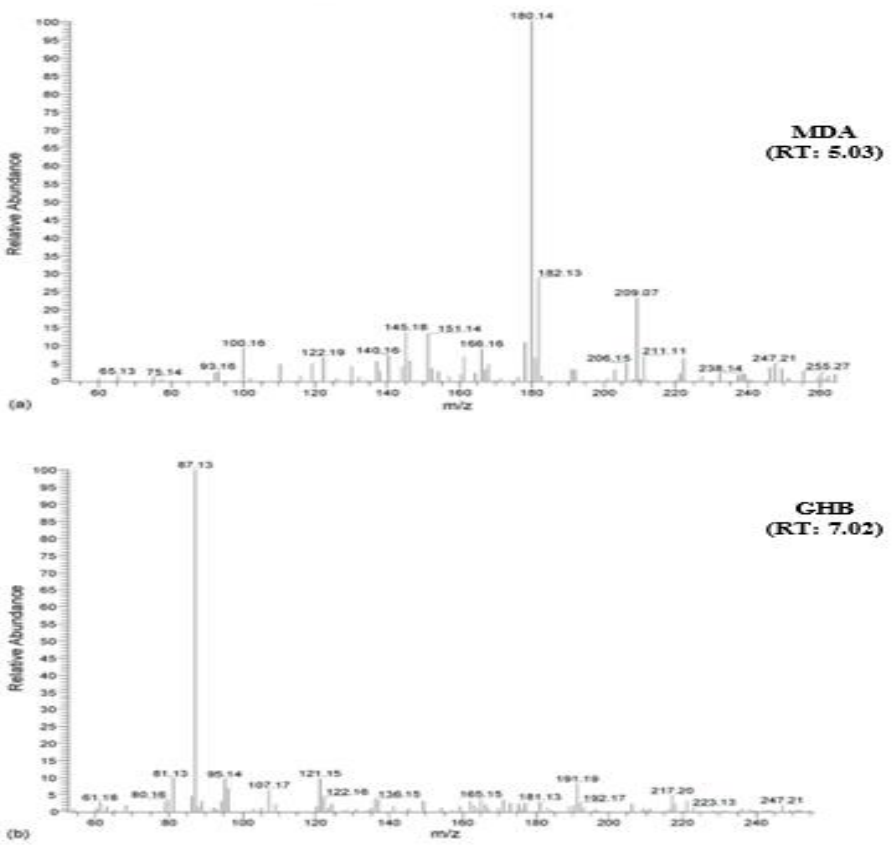
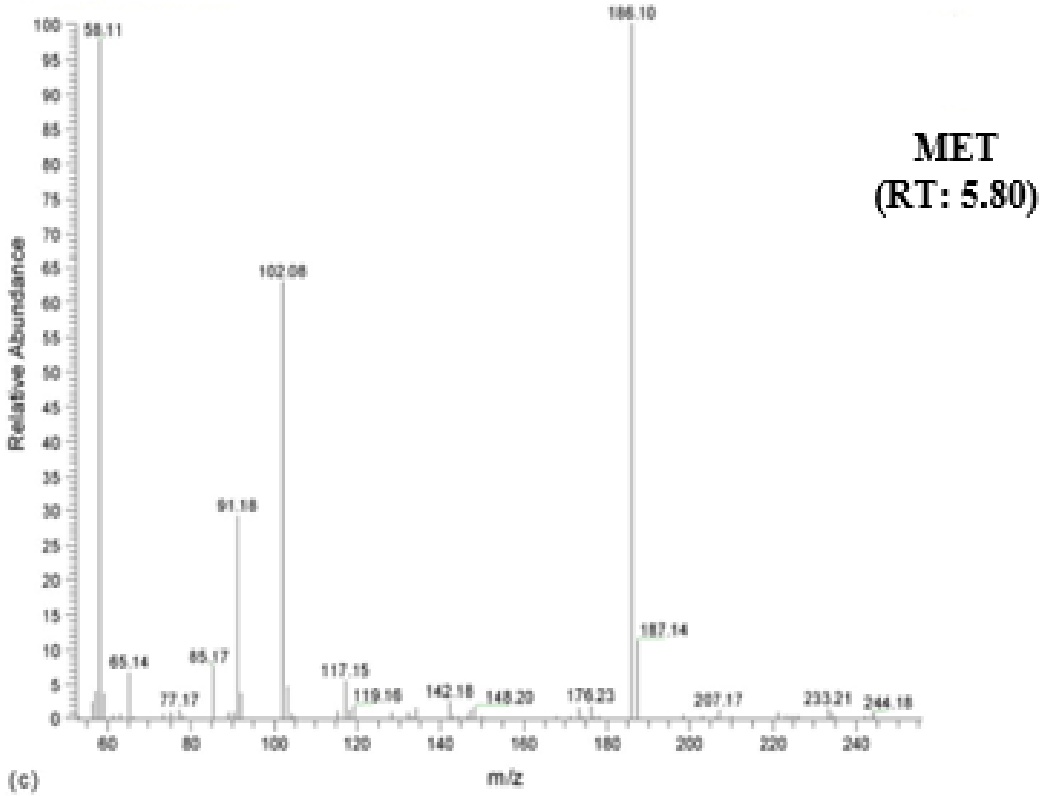


Fig.2. Mass spectra of four club drugs showing the transitions monitored for extracted ion chromatograms (a) MDA(m/z180), (b)GHB(m/z87), (c)MET(m/z102,186), and (d) MDMA (m/z 102, 186).



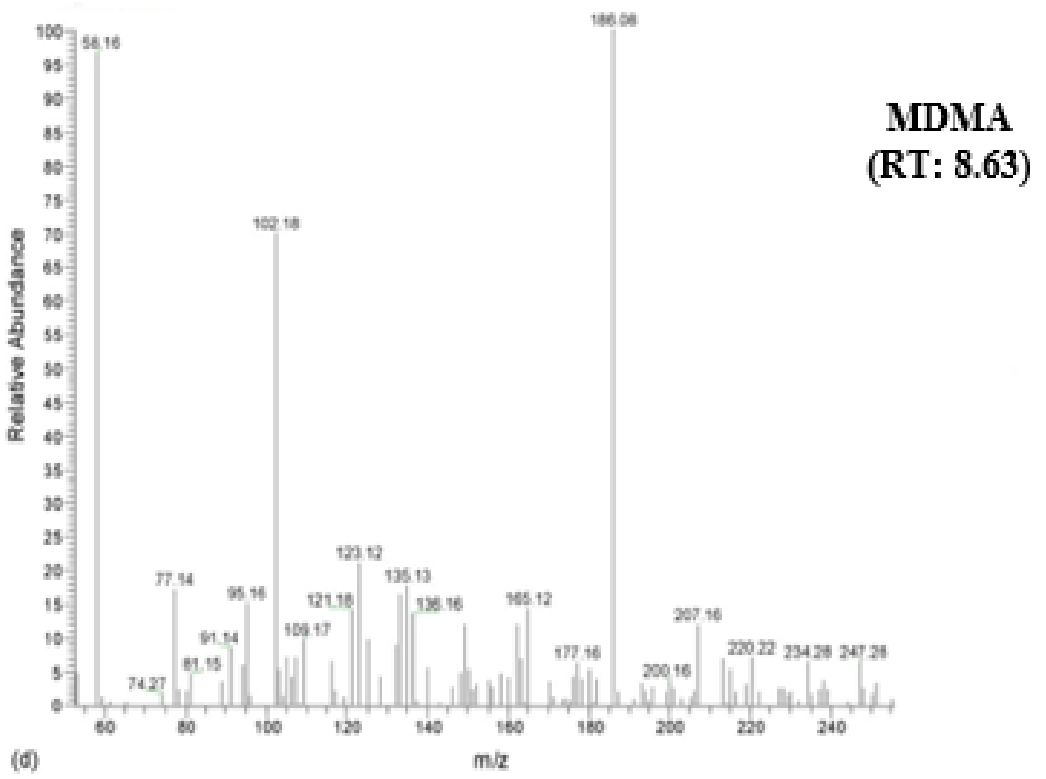


Fig.2. (Continued).

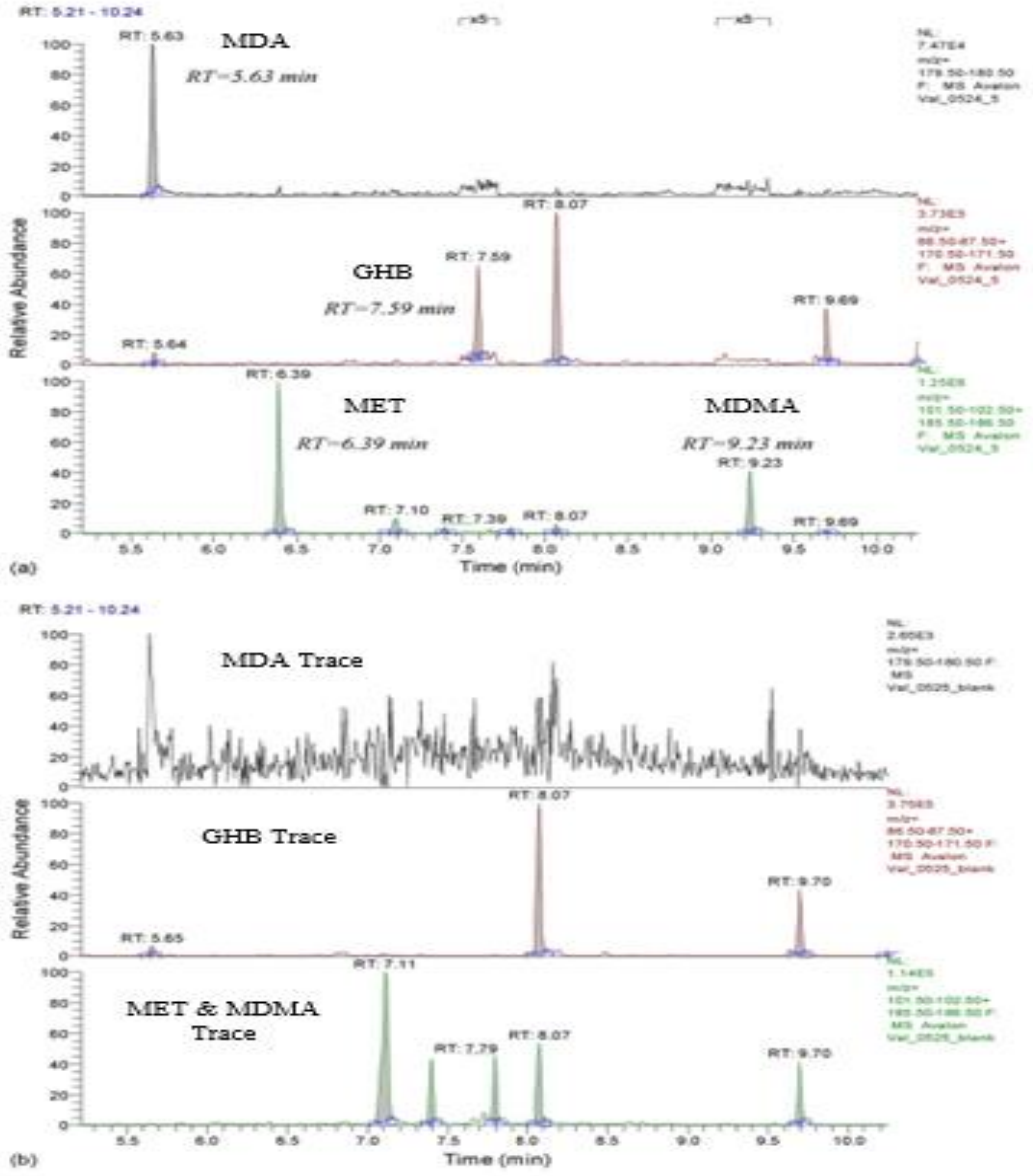


Fig. 3. Extracted ion chromatograms of (a) four club drugs (2 mg/mL each) and (b) blank urine.

3. Results and discussion

Figure 1 illustrates the structures of the four drugs analyzed in this assay. While the three amphetamine derivatives each feature secondary amines, GHB is characterized by a hydroxyl group and a carboxylic acid. This structural distinction posed challenges in using derivatizing agents suited for secondary amines. Initial efforts to identify a universal derivatizing agent for all four drugs were unsuccessful. However, literature reviews identified pyridine and hexyl-chloroformate as effective for GHB derivatization in GC-MS analysis [21]. Testing various ratios of these chemicals, an optimized combination of 10 mL hexyl-chloroformate and 40 mL pyridine was found to maximize peak areas for all four drugs. Although a 25/40 mL ratio also performed well, reducing hexyl-chloroformate to 10 mL did not significantly alter peak areas.

During method development, specific mass spectral fragments of each drug were identified for use in extracted ion chromatograms. Unlike selected ion monitoring (SIM), which isolates peaks during data acquisition, extracted ion chromatograms isolate peaks during data processing. Figure 2 shows these characteristic fragments. MET and MDMA both have major fragments at m/z 186 and 102, but they can be differentiated by their retention times—MDMA elutes later than MET. Both drugs undergo derivatization at the secondary amine, but their primary fragments still retain the ester and

alkyl chain from the hexyl-chloroformate. GHB is derivatized at its hydroxyl group, and the major fragment observed is m/z 87, formed by cleavage of the ester bond opposite the carbonyl group.

Although all samples were analyzed in full scan mode, utilizing extracted ion chromatograms improved sensitivity and reduced background noise, crucial for accurate quantification. This technique is particularly valuable when using deuterium-labeled internal standards, as these labeled versions cannot be chromatographically separated from their non-labeled counterparts. Extracted ion chromatograms also facilitate positive drug identification, which is especially useful in qualitative assays.

Figure 3 illustrates the chromatographic separation of the four drugs from each other and from significant interfering peaks. These interfering peaks arise from reactions between endogenous urinary substances and the derivatizing agents, and are not present in unmodified urine or in samples containing only deionized water and the derivatization reagents (pyridine and hexyl-chloroformate). The chromatographic separation achieved within 10 minutes, with MDA eluting first at 5.63 minutes and MDMA eluting last at 9.23 minutes.

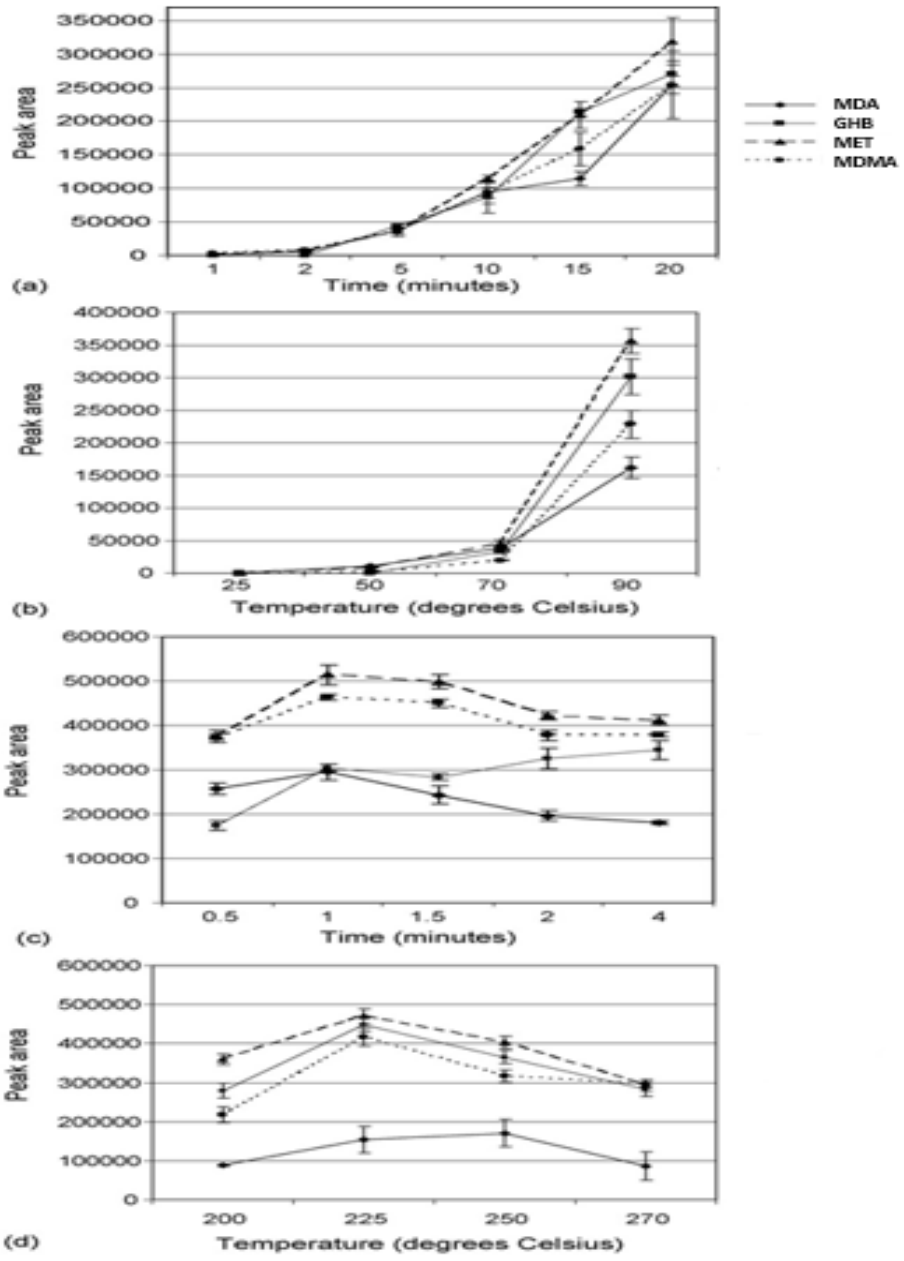


Fig. 4. Data showing the optimized SPME parameters (a) incubation time (b) incubation temperature (c) desorption time and (d) desorption temperature for the four club drugs (n = 3 at each data point).

Figure 4 details the optimization of solid-phase microextraction (SPME) conditions. The incubation time, which refers to how long the fiber is exposed to the headspace of the sample, was tested at 1, 2, 5, 10, 15, and 20 minutes. The peak areas for all four drugs were maximized at an incubation time of 20 minutes. Incubation temperature, which is the temperature of the extraction environment, was evaluated at 25°C, 50°C, 70°C, and 90°C. To avoid excessive pressure build-up from water vapor in the gas-tight vial, temperatures above 90°C were avoided. The highest peak areas for all drugs were obtained at 90°C.

Desorption time, which is the period the fiber is exposed in the injection port before the chromatographic analysis begins, was tested at 0.5, 1, 1.5, 2, and 4 minutes. Optimal desorption times for three of the four drugs (excluding GHB) were found to be 1 minute. Although GHB exhibited a higher peak area at a 4-minute desorption time, the peak shape was compromised. Desorption temperature, or the temperature of the injection port during desorption, was optimized at 200°C, 225°C, 250°C, and 270°C. The SPME fiber used in this assay had a maximum temperature capability of 300°C, beyond which degradation would occur. For three drugs, the peak area was maximized at 225°C, while MDA showed a peak area maximized at 250°C. However, the peak area for MDA at 250°C was not statistically different from that at 225°C when considering the standard deviation (n = 3).

The method was validated over a three-day period with four different concentrations along the calibration curves for each drug. Calibration curves for GHB, MDA, and MDMA ranged from 0.1 to 20 mg/mL, with validation conducted at 0.5, 1, 5, and 15 mg/mL. Each day's calibration curve had a correlation coefficient (R^2) greater than 0.99. The limit of detection (LOD) for GHB, MDA, and MDMA was determined to be 0.1 mg/mL, using a signal-to-noise (S/N) ratio of 3:1. The lowest validation concentration (0.5 mg/mL) was used to establish the limit of quantitation (LOQ) with an S/N ratio of 10:1. MET, being slightly more sensitive, had a calibration curve extending down to 0.05 mg/mL, with validation at 0.1, 0.2, 2, and 15 mg/mL levels. The LOD for MET was 0.05 mg/mL, and the LOQ was 0.1 mg/mL.

Table 1 The inter-day precision (% relative standard deviation) and accuracy (% error) for four club drugs from human urine

Drug	Concentration added (mg/mL)	Concentration found (mg/mL)	Average % error (*n* = 15)	% RSD (*n* = 15)
MDA	15	13.7 ±1.8	10.4	12.4
	5.0	3.95 ± 0.59	9.87	12.2
	1.0	1.01 ± 0.11	9.84	11.3
	0.5	0.47 ± 0.06	11.4	12.6
GHB	15	13.3 ± 0.99	6.25	6.42
	5.0	4.00 ± 0.36	5.32	7.28
	1.0	1.01 ± 0.076	6.31	7.44
	0.5	0.41 ± 0.04	7.92	9.13
Methamphetamine	15	13.2 ± 1.65	10.2	11.4
	2.0	1.75 ± 0.18	9.77	9.72
	0.2	0.19 ± 0.02	9.41	11.2
	0.1	0.08 ± 0.01	8.90	11.2
MDMA	15	13.4 ± 1.82	11.2	12.5
	5.0	4.90 ± 0.63	11.3	12.7
	1.0	1.02 ± 0.08	7.85	7.93
	0.5	0.45 ± 0.05	9.64	9.70

Table 2 The intra-day precision (% relative standard deviation) and accuracy (% error) for MDA from human urine

MDA	Concentration added (mg/mL)	Concentration found (mg/mL)	Average % error (*n* = 5)	% RSD (*n* = 5)
Day 1	15	12.5 ± 0.92	9.84	7.78
	5.0	3.74 ± 0.32	4.89	6.59
	1.0	0.89 ± 0.12	9.53	10.8
	0.5	0.37 ± 0.04	7.66	9.03
Day 2	15	12.7 ±0.89	8.22	6.36
	5.0	3.34 ± 0.32	10.49	7.25
	1.0	0.82 ± 0.02	5.25	3.06
	0.5	0.32 ±0.01	12.3	3.53
Day 3	15	15.8 ±1.16	11.5	6.45
	5.0	4.50 ± 0.36	11.5	6.42
	1.0	0.08 ± 0.13	12.6	12.2
	0.5	0.42 ± 0.07	13.3	14.8

Table 3 The intra-day precision (% relative standard deviation) and accuracy (% error) for GHB from human urine

GHB	Concentration added (mg/mL)	Concentration found (mg/mL)	Average % error (*n* = 5)	% RSD (*n* = 5)
Day 1	15	13.4±0.77	5.07	4.31
	5.0	3.66 ± 0.36	6.75	6.65
	1.0	0.89 ± 0.09	6.34	8.32
	0.5	0.39 ± 0.04	7.28	8.21
Day 2	15	14.7 ± 0.88	6.27	4.57
	5.0	4.05 ±0.23	3.42	3.54
	1.0	0.89 ± 0.03	2.63	2.02
	0.5	0.37 ± 0.03	4.80	5.15
Day 3	15	15.2 ± 0.55	6.24	3.34
	5.0	4.27 ±0.20	4.55	3.71
	1.0	1.02 ± 0.02	8.72	2.44
	0.5	0.44 ± 0.03	10.1	6.31

Table 4 The intra-day precision (% relative standard deviation) and accuracy (% error) for methamphetamine from human urine

Methamphetamine	Concentration added (mg/mL)	Concentration found (mg/mL)	Average % error (*n* = 5)	% RSD(*n* = 5)
Day 1	15	15.1 ± 1.28	10.5	7.91
	2.0	1.89 ± 0.13	4.23	6.64
	0.2	0.17 ± 0.01	8.08	6.97
	0.1	0.11 ± 0.07	9.45	6.72
Day 2	15	13.2 ±0.70	11.3	5.23
	2.0	1.832± 0.20	11.1	10.6
	0.2	0.198± 0.06	6.36	5.48
	0.1	0.11±0.04	2.96	3.52
Day 3	15	13.54±1.02	10.2	7.57
	2.0	1.721±0.11	14.1	6.31
	0.2	0.221± 0.05	13.7	2.38
	0.1	0.084± 0.02	14.4	2.31

Table 5 The intra-day precision (% relative standard deviation) and accuracy (% error) for MDMA from human urine

MDMA	Concentration added (mg/mL)	Concentration found (mg/mL)	Average % error (*n* = 5)	% RSD (*n* = 5)
Day 1	15	15.7 ± 0.36	11.8	2.18
	5.0	4.26 ± 0.39	8.67	7.22
	1.0	1.02 ± 0.09	6.14	8.66
	0.5	0.40 ± 0.04	6.72	8.41
Day 2	15	12.4 ±0.90	11.3	6.68
	5.0	4.33 ± 0.12	12.2	2.82
	1.0	1.04 ± 0.06	5.42	7.26
	0.5	0.55 ± 0.07	12.4	2.89
Day 3	15	13.4 ± 1.07	11.3	8.09
	5.0	5.01 ± 0.72	11.4	14.4
	1.0	1.06 ± 0.09	11.1	9.09
	0.5	0.10 ±0.06	8.5	12.0

Table 1 provides cumulative data on precision and accuracy (n = 15) for each drug at various validation levels, showing that all drugs had a percentage error of less than 12% over the three-day period and a relative standard deviation (R.S.D.) of less than 13%. Tables 2–5 present intra-day validation data (n = 5), confirming that no individual point exceeded 15% for either percentage error or R.S.D.

4. Conclusions

This study introduces a validated GC-MS method designed for the simultaneous quantification of four club drugs: GHB, MET, MDMA and MDA. Leveraging the rapidly advancing technology of solid-phase microextraction (SPME), the method has been fine-tuned to optimize the extraction of these analytes using this efficient and environmentally friendly technique. Sample preparation is streamlined and straightforward, requiring only the addition of minimal amounts of derivatizing agents to produce the volatile compounds necessary for GC-MS analysis.

The method demonstrates high precision and accuracy, with errors and relative standard deviations (RSD) consistently below 15% over a three-day validation period. It effectively detects low concentrations of each drug in urine samples. Urine is an ideal matrix for this analysis due to its non-invasive collection process and the fact that each drug of interest is excreted in a detectable form. This makes the method particularly valuable for drug testing and monitoring.

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