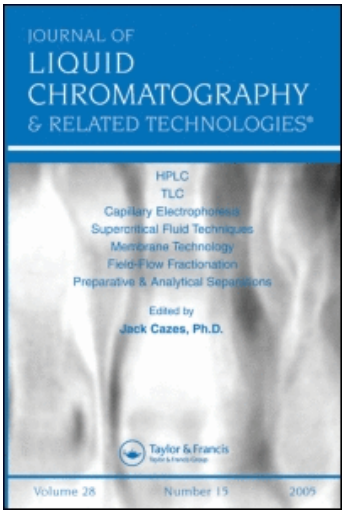

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Application of Carbon Adsorbents for Extraction of MDMA Impurities in TLC Drug Profiling

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Abstract: The efficiency of carbon adsorbents in the extraction of impurities from 1-phenylethylamine (a model substance) and MDMA (3,4-methylenedioxymethamphetamine), the main psychoactive component of 'ecstasy' tablets, was investigated. MDMA was synthesized according to two different ways in which piperonal and isosafrole were used as precursors. Three types of carbon absorbents were tested: Envicarb (surf. area 98 m^2/g, Supelco), Carboprep (surf. area 400 m^2/g, Restek Corporation), and Hypercarb (surf. area 94 m^2/g, Thermo Electron Corporation UK). The efficiency of extraction was studied by thin layer chromatography (TLC) with UV detection (254 and 366 nm). The separation of impurities was carried out on silica gel plates with fluorescent indicator F_{254} and the mixture of chloroform:methanol:acetonitrile (5:2:3 v/v/v) was used as TLC eluent. The elaborated profiling procedure enables distinction between samples of MDMA obtained according to different synthesis methods.

Keywords: Carbon adsorbents, SPE/TLC, Profiling, Drug impurities, MDMA

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INTRODUCTION

According to the last report of United Nation Office on Drugs and Crime,[1] a steady increase of ATS (amphetamine type stimulants) abuse all over the world has been observed. MDMA (3,4-methylenedioxymethamphetamine), a main psychoactive component of illicit tablets called 'ecstasy', is becoming one of the most popular synthetic drugs. To control the drug market and abuse of the drug, it is necessary to develop analytical procedures, which provide valuable information for police and law enforcement purposes.

Samples of the illegally produced drug contain impurities which the composition depends on the method of synthesis, substrates used, intermediate products, and purification process. Composition of impurities in a drug, expressed, for example, as a chromatogram, makes a so called profile of impurities. The main purpose of profiling of drug impurities is determination of chemical similarity between seized samples of the drug. Consequently, profiling supplies information relating to the method of synthesis, connection between drug samples, and illicit laboratory distribution routes, and dealers.

Separation of characteristic impurities from the drug matrix is one of the most important stages in the profiling procedure. Liquid-liquid extraction (LLE) is usually applied in the separation of characteristic impurities from MDMA matrix.[2–8] Solid phase extraction of characteristic drug impurities was usually performed on C_8 or C_{18} columns.[9–13] Rashed et al.[9] applied SPE in profiling of ecstasy tablets, and compared its efficiency to LLE. In our studies, we successfully used SPE for separation of impurities from amphetamine type substances.[10–13] However, recently Tomaszewski et al.[14] presented a comparative investigation of adsorption-desorption of N-alkyl substituted amphetamines on a variety of adsorbents (five carbons and one polymeric). They demonstrated, among other things, weak adsorption of polar amphetamine and its mono alkyl substituted derivatives on graphitized carbons.

Based on the results,[14] the assumption was undertaken that such adsorbents might be however useful for concentration of less polar impurities of ATS. In the present work, graphitized carbon adsorbents were used in extraction of impurities from selected derivatives of amphetamine: 1-phenylethylamine (1-FEA, a model substance) and MDMA. Actually, 1-phenylethylamine was used in the elaboration and optimization of the SPE/TLC procedure. MDMA was synthesized according to two different ways in which piperonal and isosafrole were used as precursors. Three types of carbon absorbents in SPE were tested: Envicarb, Carboprep, and Hypercarb. Octadecyl (C_{18}) silica adsorbents and polymeric Lichrolut EN were used in comparative studies. A solid sample was dissolved in a buffer of pH 7, 8, or 9. Tetrahydrofuran (THF), N,N-dimethylformamide (DMF), chloroform, and methanol were tested as washing solvents in SPE. The efficiency of extraction was

studied by thin layer chromatography (TLC) with UV detection (254 and 366 nm).

EXPERIMENTAL

Apparatus and Accessories

Centrifugation of the drug solution before the extraction process was conducted with a MPW-250 centrifuge (MPW Med. Instruments, Poland); Vac Elut (Varian, USA) and extraction columns: Envicarb (surf. area 98 m^2/g, 100 mg, Supelco), Carboprep (surf. area 400 m^2/g, 100 mg, Restek Corporation), Hypercarb (surf. area 94 m^2/g, 100 mg, Thermo Electron Corporation UK), C_{18} (100 mg, Varian), Lichrolut EN (crossed-linked styrenedivinylbenzene copolymer, surf. area 1500 m^2/g, 100 mg, Merck) were used in solid phase extraction of impurities from the drug matrix. A concentration set from Cobrabid (Poland) was used in evaporation of extract under stream of nitrogen; Nanomat IV (Camag, Switzerland) was employed for application of concentrated extract onto silica gel plates with fluorescent indicator F_{254} (Merck). The UV lamp (Cobrabid, Poland) was used for detection of spots at $\lambda_{ext} = 254$ and 366 nm.

Reagents

1-Phenylethylamine (1-FEA) was synthesized according to the Leuckart procedure. MDMA was synthesized from piperonal (MDMA-1) and isosafrole (MDMA-2). Acetonitrile, acetone, chloroform, methanol, tetrahydrofuran (THF), ethyl acetate, hexane, dimethylformamide (DMF), all gradient grade were from Merck. Buffer solutions: phosphate, pH = 7 from POCh (Poland); borate, pH = 8 and 9 were from Sigma-Aldrich; gas nitrogen (99.99% purity).

Preparations of Samples. SPE/TLC Profiling of Impurities

A proper amount of the drug sample was dissolved in buffer solution and centrifuged, if necessary. A required volume of solution was taken for the extraction process. SPE columns were conditioned before extraction. The impurities were washed out and concentrated in a stream of nitrogen, if necessary. A proper volume of the extract was put onto TLC plates. After development, the TLC plates were dried for a few minutes in 100°C and the separated spots were visualized under UV light. The details of the procedures are presented in Table 1.

Table 1. Studies procedures for SPE/TLC profiling of drug impurities

	Extraction				TLC Separation		
Sample preparation	Conditioning of extraction columns	Elution of matrix	Drying up of adsorbent	Washing out of impurities	Volume of extract putting on TLC plate	Composition of mobile phase	Detection
Procedure 1[a]							
Dissolution: 150 mg 1-FEA in 1.2 mL buffer solution (pH 7)	C18: Methanol, distillated water (2 × 3 mL of each solvent)	Distillated water 2 × 3 mL	15 min Under a stream of air	Methanol 7 × 100 μL	10 μL	Chloroform: Methanol: Acetonitrile (5:2:3 v/v/v)	Under UV light at 254 and 366 nm (after drying TLC plate in 110°C for 15 minutes)
Procedure 2							
Dissolution: 50 mg 1-FEA in 25 mL buffer solution (pH 7)	Carbon columns: DMF acetone, distillated water (2 × 3 mL of each solvent)	—	15 min Under a stream of air	Chloroform 1 × 500 μL 3 × 100 μL	10 μL	Chloroform: Methanol: Acetonitrile (5:2:3 v/v/v)	Under UV light at 254 and 366 nm (after drying TLC plate in 110°C for 15 minutes)
Procedure 3							
Dissolution: 75 mg MDMA in 1.2 mL buffer solution (pH 7); centrifugation, dilution of 1 mL of supernatant to 25 mL with buffer solution	C18, carbon columns: DMF acetone, distillated water (2 × 3 mL of each solvent)	—	15 min Under a stream of air	Chloroform 2 × 500 μL 5 × 100 μL; Removal of water layer (traces) from over chloroform layer	5 μL (After evaporation of extract to dryness under a steam of nitrogen and dissolution of dry residue in 100 μL of chloroform)	Chloroform: Methanol: Acetonitrile (5:2:3 v/v/v)	Under UV light at 254 and 366 nm (after drying TLC plate in 110°C for 15 minutes)

[a]Based on our earlier experiments [13].

RESULTS AND DISCUSSION

Development of Extraction and Profiling Procedures

Extraction of Impurities of 1-FEA. Elaboration of Separation Procedure

TLC profiles of 1-FEA impurities were obtained according to Procedure 1 (see Table 1). However, application of this procedure to carbon adsorbents did not give satisfactory results; only a few faint fluorescing spots were revealed on the TLC plate. In order to increase the efficiency and repeatability of the extraction, the sample solution was diluted with buffer solution to 25 mL. For elution of adsorbed impurities the solvent of larger elution strength, DMF, was used. However, extraction still appeared unrepeatable. Then, instead of matrix elution, the following solvents were tested as eluents of impurities: n-hexane, ethyl acetate, and chloroform. Finally, chloroform was chosen. These modifications, given in Procedure 2, significantly improved efficiency and repeatability of extraction on carbon columns. Additionally, the required mass of sample could be reduced twice, to 50 mg (for 1-FEA). This procedure also proved to give satisfactory results for modified silica adsorbents.

Also, it was observed that the buffer sample solution loaded on the SPE column made complete drying of adsorbent before elution of analytes impossible. When an eluent which was mixed with water was used in the elution of impurities, difficulties in TLC plate development appeared and changes of R_f values of separated spots and retention of some substances at the start were observed. It seems likely that this phenomenon is related to the presence of inorganic substances (phosphates) in the extract. The solution to this problem was application of a solvent immiscible with water, e.g., chloroform. Then the extract consisted of two layers: aqueous and organic. For TLC separation the organic layer should be taken; the aqueous layer can be easily removed with a micropipette. The volume of retained water depended on the type of adsorbent: the largest was observed for Envicarb, and the smallest for octadecyl (C_{18}) adsorbent. Solvents like THF or DMF, in spite of their large elution strength, should not be used because of their perfect miscibility with water.

Extraction of MDMA Impurities

Procedure 2 was modified for extraction of impurities from MDMA-1. First of all, centrifugation of the MDMA suspension proved to be necessary. Then, the volume of chloroform used for the washing out of analytes was increased to 1500 μL. Furthermore, the extract was concentrated 15 times and for TLC separation only 5 μL of concentrated extract was taken. These final changes resulted in Procedure 3.

Next, the effect of pH of buffer solution (pH = 7, 8, and 9) used for dissolution of MDMA sample was examined. The buffer solution of pH 7

appeared to be the best. Higher pH resulted in the decrease of the number of revealed spots, their fluorescence intensities, and R_f's. Moreover, the MDMA spot was significantly extended and tailing.

Repeatability of SPE/TLC Profiling of MDMA Impurities

The repeatability of profiling of MDMA–1 impurities (according to Procedure 3) with the use of the tested SPE columns (carbon and C_{18}) was examined. Three TLC separations of the same extract showed R_f values of separated spots which were changed at the most 0.02. The repeatability between three extractions was worse: R_f values varied in the range 0.04–0.08, which was probably related to different concentration of impurities in the extract. However, shape and colour of spots indicated that separated impurities originated from the same MDMA sample. In a few cases, one or two spots disappeared; this could be a result of low concentration of the corresponding impurities in the extract (faint fluorescence observed in other chromatograms).

Comparison of SPE/TLC Profile Obtained for Different Extraction Columns

A comparison of TLC profiles (R_f values of separated spots) obtained for MDMA–1 impurities extracted with the use of different adsorbents according to Procedure 3 was carried out and the results are presented in Table 2. It is seen that the best profiles were received for Hypercarb, Envicarb, and C_{18} extraction columns. For Carboprep and Lichrolut EN, the lack of two spots was observed at 366 nm. This could be due to the large surface area of these adsorbents, 400 and 1500 m^2/g for Carboprep and Lichrolut EN, respectively. Probably, the volume of the washing agent

Table 2. Comparison of TLC profiles of MDMA-1 impurities obtained for different SPE adsorbents

Hypercarb (R_f)		Envicarb (R_f)		Carboprep (R_f)		C_{18} (R_f)		Lichrolut EN (R_f)	
254 nm	366 nm	254 nm	366 nm	254 nm	366 nm	254 nm	366 nm	254 nm	366 nm
	0,00	0,27	0,00	0,28	0,00	0,35	0,00	0,39	0,00
0,25	0,25	0,78	0,27	0,77	0,29	0,77	0,35	0,77	0,39
0,79	0,30	0,82	0,31	0,82	—	0,82	0,38	0,82	—
0,83	0,37	0,83	0,37	0,88	—	0,86	0,41	0,88	—
0,88	0,40		0,40		0,45		0,45		0,45
	0,59		0,60		0,58		0,59		0,58
	0,67		0,66		0,64		0,65		0,64

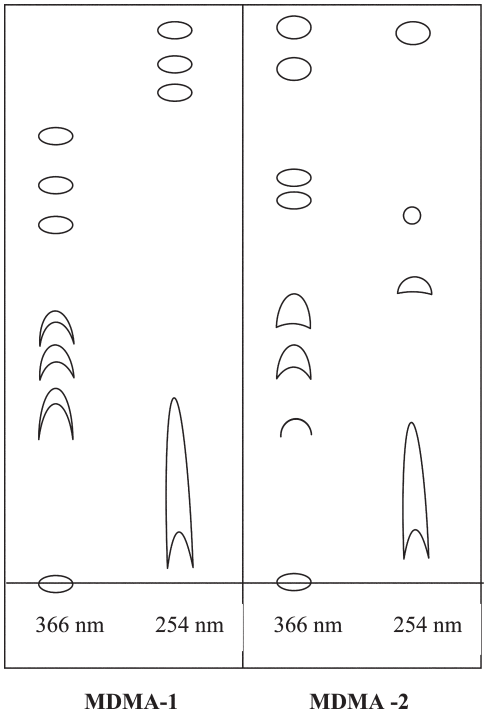

Figure 1. TLC profiles of MDMA-1 and MDMA-2 impurities; extraction of analytes: Hypercarb column.

(1500μL of chloroform) was, in that case, not sufficient for complete removal of impurities from the adsorbent surface.

Possibility of the Distinction of Drugs Synthesized According to Different Methods on the Basis of SPE/TLC Profile

In order to check if the SPE/TLC profiles of impurities make possible the distinction between drugs synthesized according to different methods, chromatograms of MDMA-1 and MDMA-2 impurities concentrated on Hypercarb, were compared. They are shown in Figure 1. It is seen that obtained profiles significantly differ; the number of spots and their shape depended on the synthesis method.

CONCLUSIONS

The presented studies proved that carbon adsorbents can be very useful in SPE/TLC screening and profiling of drug impurities. The obtained profiles

appeared as well shaped and separated spots. The final procedure of extraction proved to be suitable not only for carbon adsorbents (Envicarb, Carboprep, Hypercarb), but also for modified silica (octadecyl) and polymeric (Lichrolut EN) adsorbents. The described procedure enables distinction of amphetamine derivates, and also differentiation of drug profiles can be noticed if drugs are synthesized in different ways of synthesis.

The method proposed seems to be attractive for forensic laboratories as a screening procedure before application of more advanced and expensive methods (GC/MS, HPLC) appear necessary.

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