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Identification of LSD by AccuTOF™ LC/Time-of-Flight Mass Spectrometry

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1. INTRODUCTION

Lysergic acid diethylamide (LSD) is a psychoactive drug with a long history of abuse. It is one of the most difficult drugs of abuse to detect in urine since the parent drug is excreted at very low concentration. Less than 1% of the ingested LSD dose is eliminated unchanged [1]. Analysis is further complicated because the isomeric compound iso-LSD, N-n-propylamide (LAMPA), which is itself a controlled drug, has a virtually identical mass spectrum [2]. Several GC/MS or GC/MS/MS methods have been developed for confirmation of LSD in urine, but a tedious and unstable derivatization procedure is required. The use of LC/MS for the analysis of LSD does not require derivatization of the analytes, thus simplifying the procedure. This application note demonstrates the feasibility by using the AccuTOF™ LC/MS for identification of LSD and related compounds. Additional method development and validation may be required for routine analysis.

2. EXPERIMENTAL

The system included a JEOL AccuTOF™ time-of-flight mass spectrometry system and an Agilent 1100 HPLC. All instruments were controlled by a JEOL MassCenter™. All solvents used were of HPLC grade. The standard solutions were purchased from Cerilliant (Round Rock, TX) and further diluted with mobile phase A. The HPLC and MS conditions are listed in Table 1.

Table 1. LC/MS Conditions

Column:	**Luna CN 150 x 2.0 mm, 3µm**
Mobile Phase:	**A = 0.1% Formic Acid B = acetonitrile**
Gradient:	**started from 20% B to 65% B in 10 min**
Flow rate:	**0.2 mL/min**
Injection volume:	**10 µL**
Ion source:	**positive ESI**
Needle voltage:	**1000 V**
Orifice 1 voltage:	**45 V**
Orifice 2 voltage:	**4 V**
Ring lens voltage:	**7 V**
Peak voltage:	**1500 V**
MCP voltage:	**2400 V**
Orifice 1 temp:	**80 °C**
Desolvating temp:	**250 °C**
Nebulizing gas:	**2 L/min**
Desolvating gas:	**3 L/min**

3. RESULTS

Figure 1 shows the mass chromatogram for LSD and related compounds. All components including the isomers were well separated under current HPLC conditions.

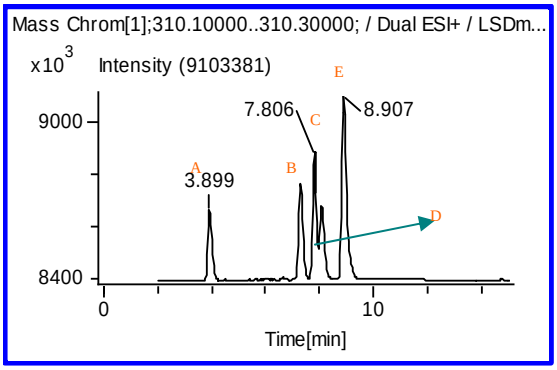

Figure 1. Mass chromatogram of LSD and related compounds. Peaks: A=2-oxo-3-hydroxy-LSD; B=nor-LSD; C=LSD; D=LAMPA; and E= iso-LSD.

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Figure 2 shows the mass chromatogram for LSD with an injection amount of only 2.5 pg. A s/n ratio of 18.9 has been achieved. If we assume that 1 mL of urine sample was used and the extraction recovery was 80%, and the final reconstitution volume was 50µL, this amount is equivalent to the concentration of 15.6 pg/mL in the urine sample, indicating a very high sensitivity.

Figure 3 shows the mass spectrum of LSD and related compounds in Figure 1. The protonated ion for each compound was clearly observed. The accurate mass was obtained with an error smaller than 3 ppm by using the "lock mass" drift compensation. The results were shown in Table 2.

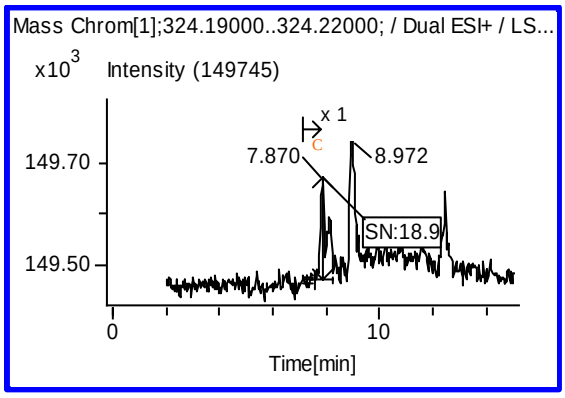

Figure 2. Mass chromatogram for LSD with an injection amount of 2.5 pg. An s/n ratio of 18.9 was achieved. Peak: C=LSD.

Table 2. Results of accurate mass measurements for LSD and related compounds

Compound name	Measured mass	Calculated mass	Mass difference (mmu)	Mass difference (ppm)	Possible formula
2-oxo-3-hydroxy-LSD	356.19693	356.19742	0.49	1.38	$C_{20}H_{26}N_3O_3$
Nor-LSD	310.19176	310.19194	0.18	0.58	$C_{19}H_{24}N_3O_1$
LSD	324.20699	324.20759	0.6	1.85	$C_{20}H_{26}N_3O_1$
LAMPA	324.2076	324.20759	-0.01	-0.03	$C_{20}H_{26}N_3O_1$
Iso-LSD	324.20668	324.20759	0.91	2.81	$C_{20}H_{26}N_3O_1$

4. CONCLUSION

The AccuTOF™ LC/time-of-flight mass spectrometry system provides a high sensitivity and a high selectivity which allow the analysis of LSD and related compounds. In combination with accurate mass measurement and HPLC separation obtained from AccuTOF™, this makes possible a rapid, sensitive and unambiguous identification of LSD in biological samples.

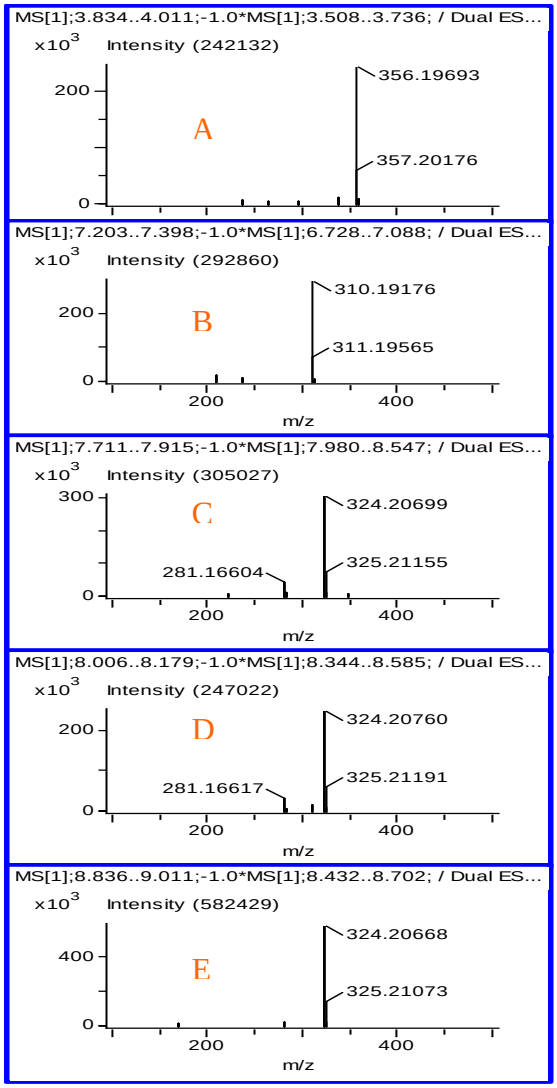

Figure 3. Mass spectrum for LSD and related compounds. Spectra: A=2-oxo-3-hydroxy-LSD; B=nor-LSD; C=LSD; D=LAMPA; and E=iso-LSD.

5. REFERENCES

[1] G. K. Poch *et al*. J. Chromatogr. B 724 (1999) 23-33.

[2] S.A. White *et al*. J. Chromatogr. B 689(1997) 335-340.