

II.2.6 Lysergic acid diethylamide (LSD)

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Introduction

Lysergic acid diethylamide (LSD, lysergide) is known as one of the most powerful hallucinogenic drugs of abuse. LSD was explosively abused in U.S.A. in the latter half of the 1960s. In Japan, the amount of seizure of LSD is much smaller than that of methamphetamine. However, in recent years, it has been increasing markedly; 3,500 tablets of LSD were seized in 1996, while 53,043 tablets in 2000 (about 15-fold increase), arousing a serious concern about the phenomenon.

LSD is a compound chemically modified from ergot alkaloid produced by a bacterium *Claviceps purpurea*. LSD is one of the compounds synthesized by the reactions of lysergic acid isolated from the ergot with various amines at the Rockefeller Institute in the 1930s; LSD was synthesized as the 25th compound and thus called LSD-25. The strong hallucinogenic activity of LSD was confirmed by Albert Hofmann who did synthesize the compound; the pharmacological activity can be obtained by oral administration of as small as 20–75 µg of LSD. The absorption of LSD from the digestive tract is rapid and distinct visual hallucination takes place 45 min–1 h after oral intake of about 20 µg of LSD [1]. The hallucination becomes most marked 2–3 h after the intake and lasts for 8–12 h.

In this chapter, a detection method by TLC and confirmatory analysis by GC/MS for LSD are presented.

Reagents and their preparation

- LSD can be obtained from each local bureau of drug enforcement officers under an official transfer process.
- *p*-Dimethylbenzaldehyde reagent: a 0.125-g aliquot of *p*-dimethylaminobenzaldehyde (Wako Pure Chemical Industries, Ltd., Osaka, Japan and other manufacturers) is dissolved in 100 mL of 65 % sulfuric acid solution, followed by the addition of 0.1 mL of 5 % ferric chloride aqueous solution.
- Dragendorff reagent [2]: there are various modifications of its preparation; the most typical method is described here. A 0.85-g aliquot of bismuth subnitrate is dissolved in a mixture of 40 mL distilled water and 10 mL acetic acid to prepare “A” solution. A 8-g aliquot of potassium iodide is dissolved in 20 mL distilled water to prepare “B” solution. Then, a mixture of A/B/acetic acid/distilled water (1:1:4:20, v/v) is prepared.
- Iodoplatinate reagent [2]: A 1-mL aliquot of 10 % platinum chloride solution is mixed with 25 mL of 4 % potassium iodide solution and 24 mL distilled water.

Pretreatments

LSD is seized in the forms of tablets, capsules and paper sheets. The latter is most popular; a paper sheet which had absorbed LSD can be cut into pieces along perforation lines. One of the pieces is put in the mouth and sucked.

LSD shows strong bluish fluorescence; therefore, LSD can be easily located on a TLC plate, and the LSD fraction can be obtained for purification by LC under an ultraviolet light.

For a piece of paper, which is suspected to contain LSD, the drug is extracted by adding 1 % tartaric acid aqueous solution and by shaking it for 5 min. This procedure is repeated six times and the tartarate extract solutions are combined. After the pH of the solution is adjusted to 8.5, the solution is extracted with an appropriate amount of chloroform four times. The combined chloroform extract is evaporated to dryness; the residue is dissolved in a small amount of methanol to be subjected to further analysis.

TLC analysis

Analytical conditions

TLC plate: a usual silica gel plate, for example, Kieselgel (0.25 μm thickness, Merck, Darmstadt, Germany and other manufacturers).

Developing solvents: (A) acetone/chloroform (4:1, v/v); (B) chloroform/methanol/*n*-hexane (4:2:1, v/v).

Assessment of the method

The R_f values of LSD were 0.29 with the (A) solvent system and 0.55 with the (B) system. The colors of the spot of LSD are blue-purple with the *p*-dimethylaminobenzaldehyde reagent, orange with the Dragendorff reagent and purple with the iodoplatinate reagent.

MS by the direct inlet method

Under the ultraviolet light at 365 nm, the fraction showing strong fluorescence is obtained by TLC or LC, and extracted with chloroform. The resulting residue is subjected to analysis by the direct inlet method of EI-MS.

Analytical conditions

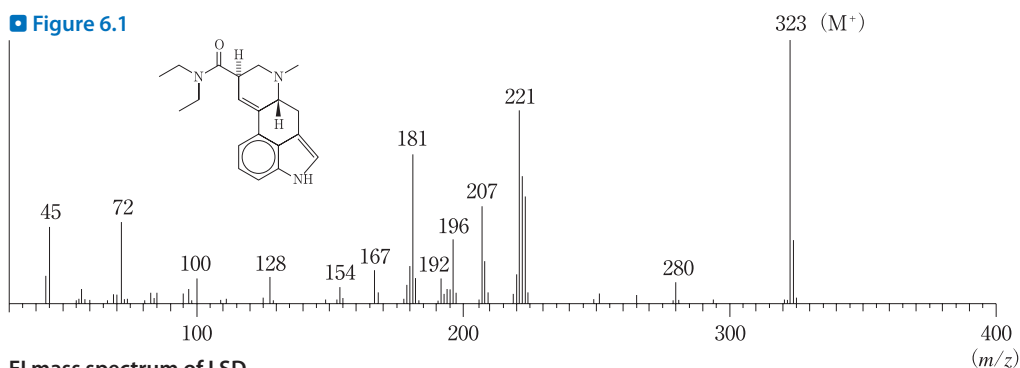
Any type of an MS instrument can be used; electron energy: 20 eV; ionization current: 110 μA ; measurements: full-scan mode.

Assessment and some comments on the method

An EI mass spectrum of LSD is shown in [▶ Fig. 6.1](#). The molecular ion appears as the base peak. Fragment peaks can be observed at m/z 221, 207, 181 and 167. The fragmentation pathways are shown in [▶ Fig. 6.2](#). The confirmation of LSD should be made with each mass spectrum.

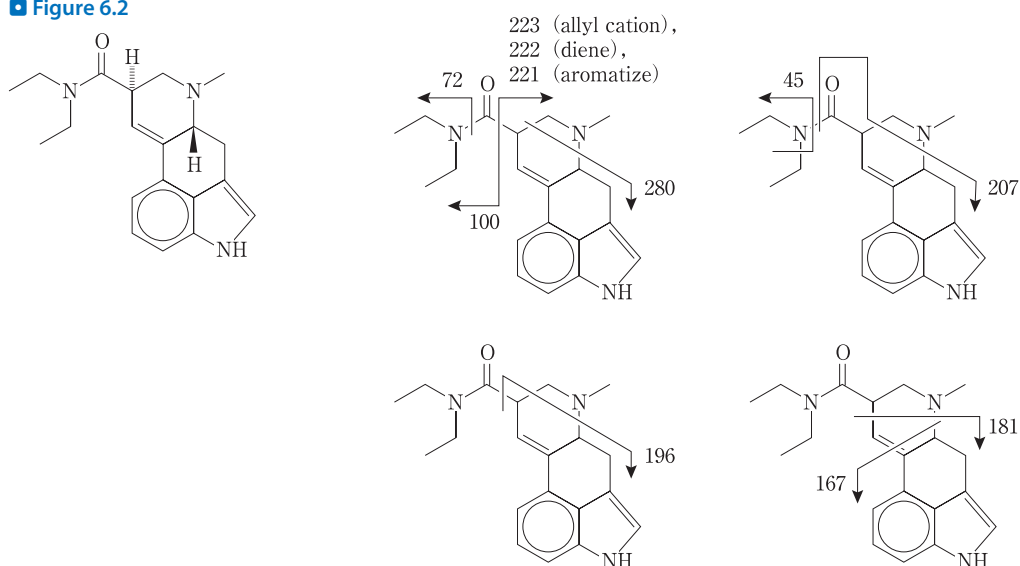
LSD is easily decomposed by light; all procedure is preferably made under shading from light.

■ **Figure 6.1**



EI mass spectrum of LSD.

■ **Figure 6.2**



Fragmentation pathways for ions observable in the EI mass spectrum of LSD.

Toxicity, and concentrations in blood and urine

The acute toxicity of LSD is generally low; it does almost not cause death.

In this chapter, detection and identification methods have been described for seized items, and not for human specimens. It is actually not easy to detect LSD from blood and urine, because its amount to be ingested is as small as about 10 µg and LSD is rapidly metabolized in human bodies. As metabolites of LSD, 2-oxo-LSD, 3-, 13- and 14-hydroxy-LSDs and an *N*-de-ethyl-LSD are known [3]. After oral ingestion of 160 µg LSD, the maximum blood concentration of LSD was 9 ng/mL and its half-life is said to be about 2 h. The concentrations of LSD of LSD-abusing patients, who had been brought to a critical care medical center were 0.5–1.9 ng/mL in blood and 0.2–7.7 ng/mL in urine [4].

References

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- 3) Cody JT (2000) Hallucinogens. In: Bogusz MJ (ed) Handbook of Analytical Separations, Vol. 2, Forensic Science. Elsevier, Amsterdam, pp 143–162
- 4) Karch SB (1996) The Pathology of Drug Abuse, 2nd edn. CRC Press, Boca Raton, pp 267–270