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## Trace Elemental Analysis of Drugs of Abuse Using Synchrotron Radiation Total Reflection X-Ray Fluorescence Analysis (SR-TXRF)

**ABSTRACT:** Synchrotron radiation total reflection X-ray fluorescence spectroscopy (SR-TXRF) was utilized to analyze various trace elements in small amounts of drugs of abuse. Sample amounts of 1  $\mu\text{L}$  solutions containing 10  $\mu\text{g}$  of drugs (methamphetamine, amphetamine, 3,4-methylenedioxymethamphetamine, cocaine, and heroin) were spotted on silicon wafers for direct analysis. In addition, a leaflet of marijuana was set directly on a silicon wafer, and opium in the form of a soft lump was smeared on another silicon wafer for analysis. In these experiments, about 10 pg of contaminant elements could be detected. For example, in a seized methamphetamine sample, iodine was found, which could be indicative of synthetic route. In seized 3,4-methylenedioxymethamphetamine samples, variable amounts of phosphorus, calcium, sulfur, and potassium were found, which could not be detected in a control 3,4-methylenedioxymethamphetamine sample. For marijuana and opium, two spectral patterns were obtained that were far different from each other and could be easily discriminated. Using SR-TXRF, pg amounts of each trace element in 10  $\mu\text{g}$  of various drugs can be easily detected, which is not the case either for a standard TXRF experimental system or for other elemental analysis techniques.

**KEYWORDS:** forensic science, total reflection X-ray fluorescence analysis, synchrotron radiation, drugs of abuse, inorganic impurity, trace elemental analysis, impurity profiling

Total reflection X-ray fluorescence analysis (TXRF) was first presented by Yoneda and Horiuchi as a trace elemental analytical technique for high sensible X-ray fluorescence analysis (1). TXRF is also a very useful technique for trace forensic samples because it is nondestructive and has high sensitivity for trace elements. A number of studies have applied this technique to various forensic samples (2–15). Prange et al. reported the characterization of single fibers (16), and Duwel et al. reported quantitative elemental microanalysis of thermoplastic remains (17).

Drug abuse is currently one of the more serious worldwide problems in society. Impurity profiling analysis has been extensively utilized for the characterization and classification of illicit drugs. Trace organic ingredient analyses of methamphetamine or amphetamine salts have been studied and reported by Verweij (18), Inoue (19), and other authors (20–26). Inorganic ingredient analyses of methamphetamine or amphetamine salts by neutron activation analysis (27,28), ICP-MS analysis (29–31), and ion chromatography (30) have also been reported. However, those methods used sample amounts of 2 to 50 mg, 10 to 100 mg, and so on, and detected ppm level of each trace element. Furthermore, the methods require some complicated pretreatments of samples and are often destructive.

The authors have previously applied TXRF analysis to methamphetamine salts, and reported ng order detection of each trace element in 1 mg of sample (15). However, it was impossible to detect pg levels of trace elements in methamphetamine salts using TXRF.

Synchrotron radiation is an excellent X-ray source for forensic elemental analysis. The authors recently reported an application of synchrotron radiation analysis for fingerprint mapping (32). We expected that the detection limit of this system would be lower than TXRF by a factor of between 100 and 1000. Herein, we report ultratrace elemental analysis of drugs of abuse using SR-TXRF.

### Experimental

The soluble drugs methamphetamine, amphetamine, 3,4-methylenedioxy-methamphetamine (MDMA), cocaine, and heroin were used all as salt forms. A sample size of 1  $\mu\text{L}$  of an aqueous solution containing 10  $\mu\text{g}$  of each drug was spotted on a clean silicon single crystal wafer (40 by 40 by 0.6 mm) and dried under atmospheric conditions prior to analysis. The marijuana leaflet was put directly on a clean silicon wafer surface, and a sample of black opium was smeared on another clean silicon wafer surface. As exciting X-rays, undulator radiation from the Hyogo-BL (BL24XU) of SPring-8 (X-ray energy was tuned to be 10 keV) was used, the X-ray incident angle was set at  $0.005^\circ$ . A Si(Li) detector from Oxford Inc. (efficient area of Si(Li) was 80  $\text{mm}^2$  in size) was used, and accumulation times were set at 500 s.

To establish a calibration curve, 1  $\mu\text{L}$  samples of each aqueous solution containing Sc, Cr, Co, and Zn (each metal concentration was adjusted to 1, 0.1, and 0.01 ppm) were spotted on clean silicon wafer surfaces using an Eppendorf pipette. After being dried under atmospheric conditions, each sample was measured as described above.

### Results and Discussion

#### *Methamphetamine*

Figures 1a and 1b represent the SR-TXRF spectra of a control methamphetamine HCl and a seized sample, respectively. In Fig.

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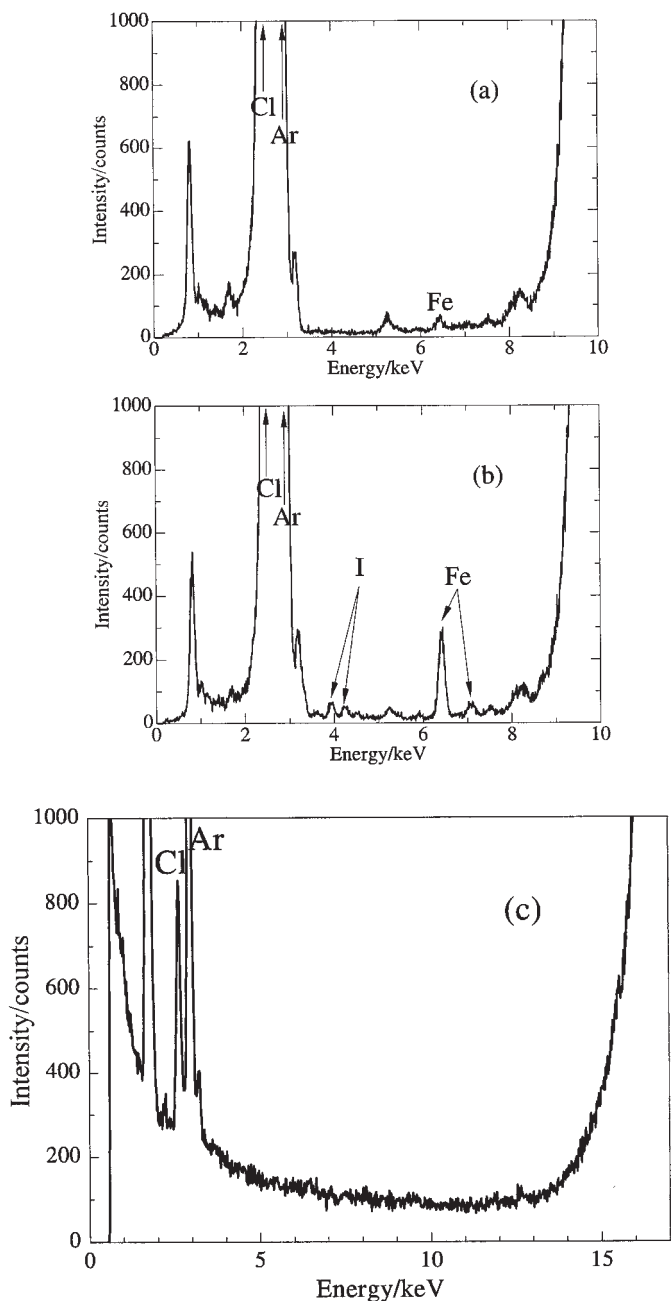


FIG. 1—Two SR-TXRF spectra (a), (b), and a conventional TXRF spectrum (c) of methamphetamine: (a) a control methamphetamine HCl; (b) a seized methamphetamine HCl; (c) the same seized methamphetamine HCl (b).

In Fig. 1a, a strong peak for Cl K $\alpha$  at 2.6 keV and a weak peak for Fe K $\alpha$  at 6.4 keV were observed. An Ar K $\alpha$  peak (derived from atmospheric contamination) was also observed at 3.0 keV, overlapping the Cl K $\alpha$  peak. In Fig. 1b, two characteristic weak peaks for iodine at 3.9 keV (I L $\alpha$ ) and 4.2 keV (I L $\beta$ ) were observed. In addition, the peak for Fe K $\alpha$  at 6.4 keV was far stronger than the control sample. The strong peak for Cl K $\alpha$  at 2.6 keV was also present.

From the above results, iodine (HI or I<sub>2</sub>) may have been used as a synthetic reagent for the manufacture of the seized methamphetamine sample. The fairly strong Fe K $\alpha$  peak at Fig. 1b is possibly from contamination with iron compounds either during the synthetic or smuggling processes.

Figure 1c represents the conventional TXRF spectrum (1000 s measurement) of the same seized methamphetamine sample. No peaks for iodine or iron could be detected. This demonstrates the superiority of SR-TXRF versus conventional TXRF for the detection of trace elements.

#### Amphetamine

The SR-TXRF spectra of a control amphetamine sulfate and a seized tablet sample are shown in Figs. 2a and 2b, respectively. In Fig. 2a, a strong peak for S K $\alpha$  at 2.3 keV was observed. No other remarkable elements were observed in the range of 3 to 10 keV, except the standard peaks for Ar atmospheric near at 3.0 keV. The sulfur peak is due to the sulfate salt of amphetamine. For the seized tablet, the peak for S K $\alpha$  at 2.3 keV was weak, and a peak for Ca K $\alpha$  at 3.7 keV appeared clearly. A peak for Zn K $\alpha$  at 8.6 keV also appeared weakly. It is possible that the calcium peak is due to pharmacologically inert excipients or diluents.

#### 3,4-Methylenedioxyamphetamine (MDMA)

The SR-TXRF spectra of a control MDMA HCl crystal and seized MDMA No. 1 are shown in Figs. 3a and 3b, respectively. In Fig. 3a, a strong peak for Cl K $\alpha$  was observed at 2.6 keV, and no

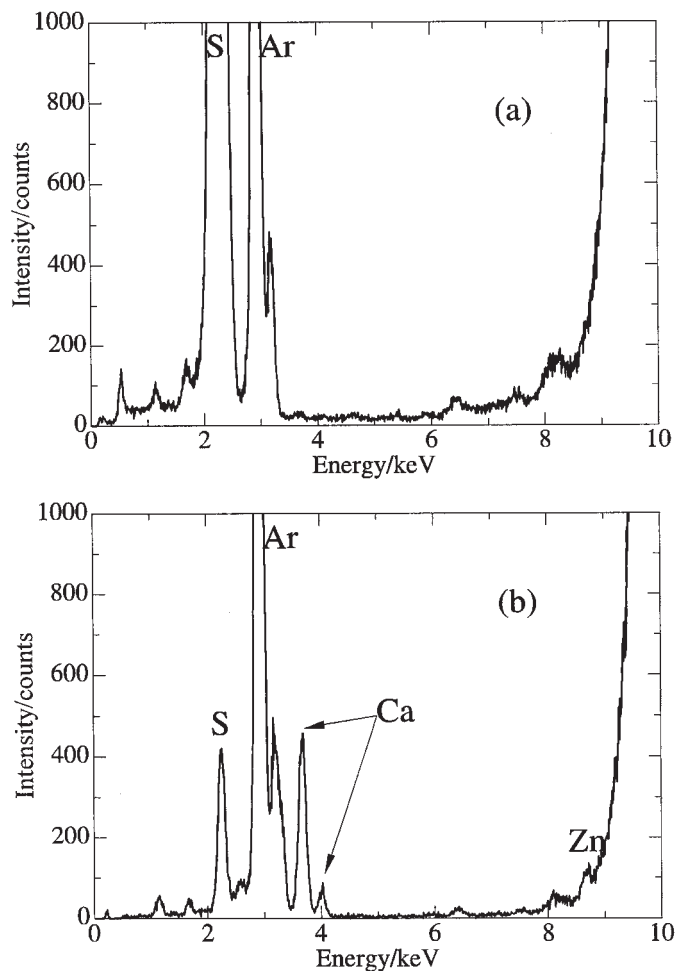


FIG. 2—Two SR-TXRF spectra of amphetamine: (a) a control amphetamine sulfate; (b) a seized amphetamine tablet.

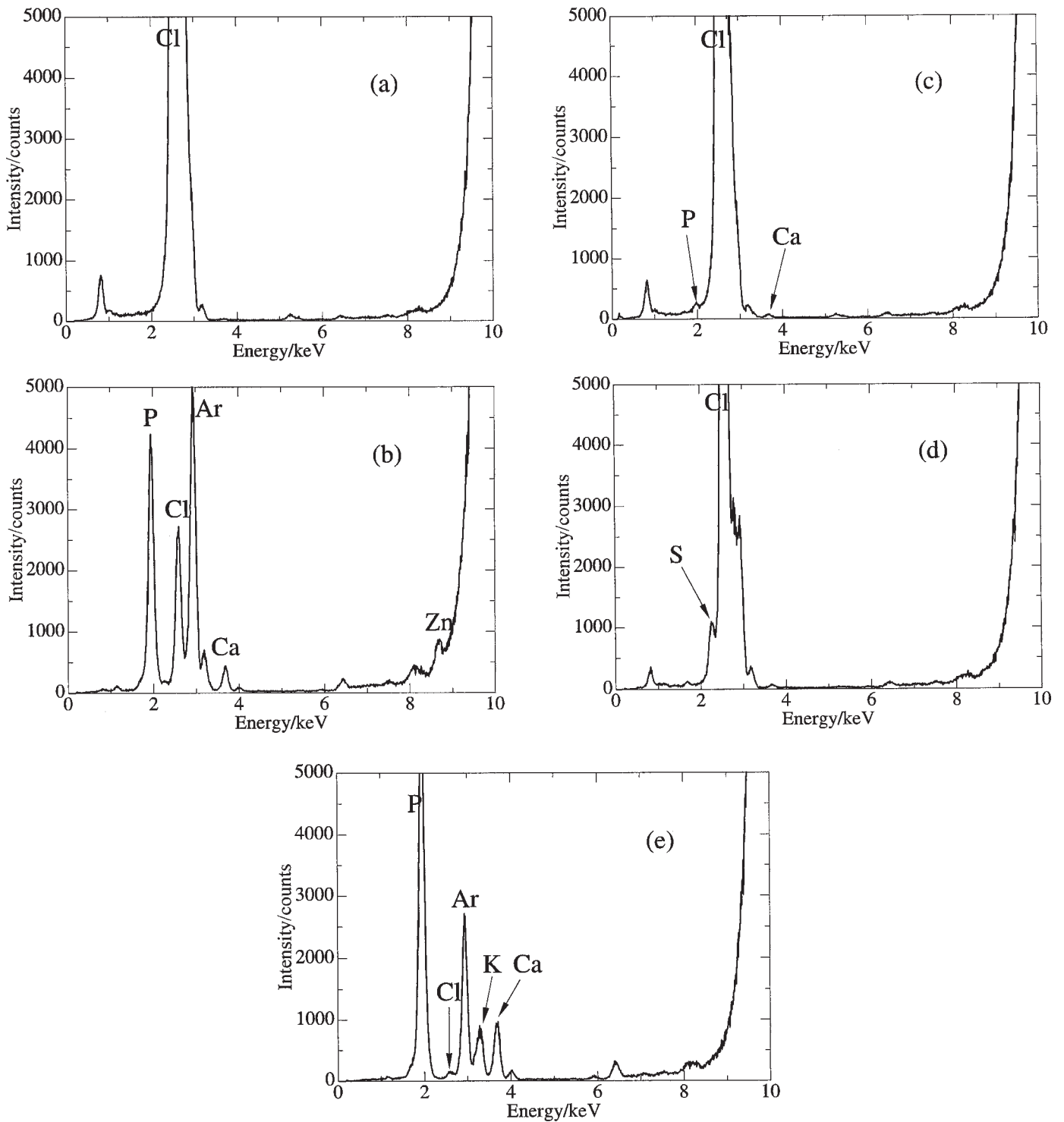


FIG. 3—Five SR-TXRF spectra of MDMA: (a) a control MDMA HCl; (b) seized MDMA tablet No. 1; (c) seized MDMA tablet No. 2; (d) seized MDMA tablet No. 3; (e) seized MDMA tablet No. 4.

other noticeable peaks could be observed. Then, it is clarified that the control MDMA HCl, which is used as a chemical standard for FT-IR analysis, contains no contaminants. For MDMA No. 1, peaks for P K $\alpha$  at 2.0 keV and for Cl K $\alpha$  at 2.6 keV were observed. In addition, weak peaks for Ca K $\alpha$  at 3.7 keV and Zn K $\alpha$  at 8.6 keV were observed. From those results, it was postulated that MDMA No. 1 might contain both the hydrochloride and phosphate salts, and that calcium might be attributed to excipients.

The SR-TXRF spectra of seized MDMA No. 2 and No. 3 are shown in Figs. 3c and 3d, respectively. MDMA No. 2 is very similar to that of the control MDMA HCl, except for a weak peak for P K $\alpha$  at 2.0 keV and a weak peak for Ca K $\alpha$  at 3.7 keV. For MDMA No. 3, a strong peak for Cl K $\alpha$  at 2.6 keV and a weak peak for S K $\alpha$  at 2.3 keV were observed. The spectral pattern for MDMA No. 3 was far different from the control MDMA HCl. Sulfur was attributed to the sulfate anion, also seen in MDMA No. 3. Amphetamine sulfate was isolated from the MDMA HCl mixture and identified by GC-MS and FT-IR analysis. From those results, MDMA No. 2 was hypothesized to be more pure in comparison with MDMA No. 1 or No. 3.

The SR-TXRF spectrum of MDMA No. 4 is shown in Fig. 3e. In this spectrum, a very strong peak for P K $\alpha$  at 2.0 keV was observed, a peak for Cl K $\alpha$  at 2.6 keV was hardly observed, while both a strong peak for P K $\alpha$  at 2.0 keV and a peak for Cl K $\alpha$  at 2.6 keV were found in the spectrum of MDMA No. 1. Moreover, a peak for K K $\alpha$  at 3.3 keV, which could not be observed in the spectrum of MDMA No. 1, was observed. The spectra from all five MDMA samples could be discriminated using SR-TXRF analysis.

#### Cocaine

The SR-TXRF spectra of a control cocaine HCl crystal and a seized sample are shown in Figs. 4a and 4b, respectively. In comparison with the control sample, two peaks for Ca at 3.7 keV (K $\alpha$ ) and 4.0 keV (K $\beta$ ) were observed in the seized sample. Peaks for Zn K $\alpha$  at 8.6 keV and for Cl K $\alpha$  at 2.6 keV were common in both spectra.

The calcium found in the seized sample is probably due to adulterants or contaminants in the cocaine. Zinc found in both samples is possibly due to contamination during the extraction procedure.

#### Heroin

The SR-TXRF spectra of three seized heroin samples are shown in Figs. 5a, 5b, and 5c, respectively. In Fig. 5a, a weak peak for Ca K $\alpha$  at 3.7 keV and a peak for Zn K $\alpha$  at 8.6 keV were observed. In Fig. 5b, two peaks for Ca K $\alpha$  and K $\beta$  were moderately stronger than the corresponding peaks in Fig. 5a. In Fig. 5c, characteristic peaks for iodine were observed at 3.9 keV (L $\alpha$ ), 4.2 keV (L $\beta$ 1), 4.5 keV (L $\beta$ 2), and 4.8 keV (L $\gamma$ 1). The spectral pattern for heroin sample No. 3 was far different from heroin samples No. 1 and No. 2.

Infante et al. reported metal contamination in illicit heroin samples and also reported that calcium was encountered in most of the samples (33). However, they did not report iodine in illicit heroin samples. The origin of iodine in this sample shown in Fig. 5c is unclear.

#### Marijuana and Opium

Marijuana and opium are botanical samples and represent unusual substrates for SR-TXRF analysis. The SR-TXRF spectrum of

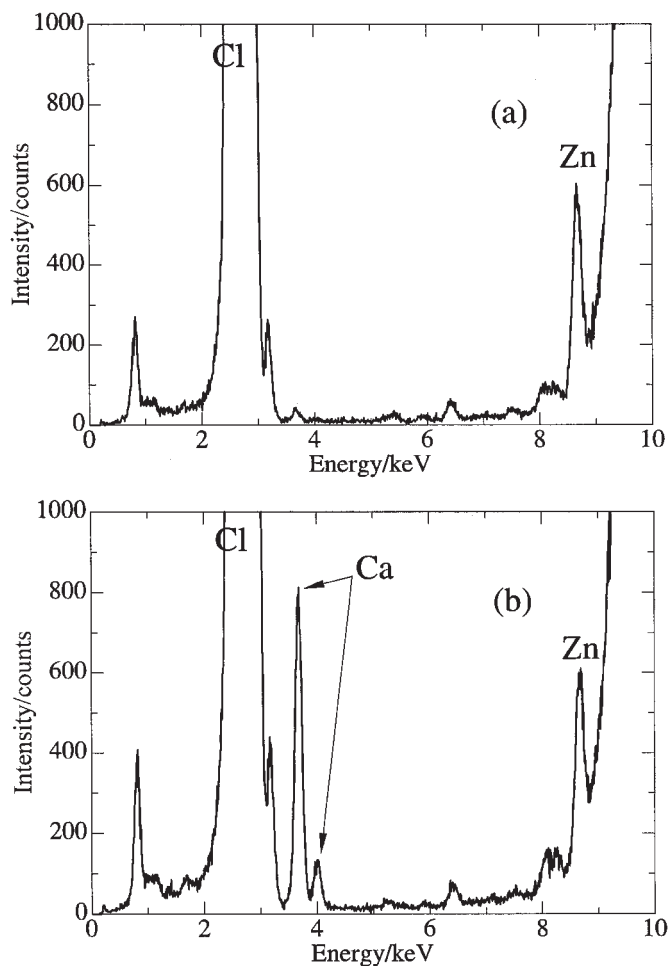


FIG. 4—Two SR-TXRF spectra of cocaine: (a) a control cocaine HCl; (b) a seized cocaine HCl.

a chip of marijuana leaflet is shown in Fig. 6a, while the SR-TXRF spectrum of a smear of black opium is shown in Fig. 6b. The marijuana displayed peaks for Ca at 3.7 keV (K $\alpha$ ) and 4.0 keV (K $\beta$ ), a peak for Fe K $\alpha$  at 6.4 keV, a peak for Zn K $\alpha$  at 8.6 keV, a peak for Ti K $\alpha$  at 4.5 keV, a peak for Cl K $\alpha$  at 2.6 keV, and a small peak for S K $\alpha$  at 2.3 keV. The opium displayed a peak for K K $\alpha$  at 3.3 keV and a moderately large peak for S K $\alpha$  at 2.3 keV. No peaks for Ti, Fe, or Zn were observed.

From the above results, even small amounts of botanical samples can be differentiated by SR-TXRF. This is potentially very valuable for trace, black, resin-like compounds that cannot be easily discriminated by physical appearance. The SR-TXRF impurity profiling of many additional marijuana and opium samples is planned. The SR-TXRF can also be applied to discriminate between other botanical samples.

#### Calibration Curve

Calibration curves for Sc, Cr, Co, and Zn (total amounts: 0.01 to 1 ng) are shown in Fig. 7. In the range of 0.01 to 1 ng, calibration curves were nearly straight, and 10 pg amounts of each trace element were detectable using this experimental system.

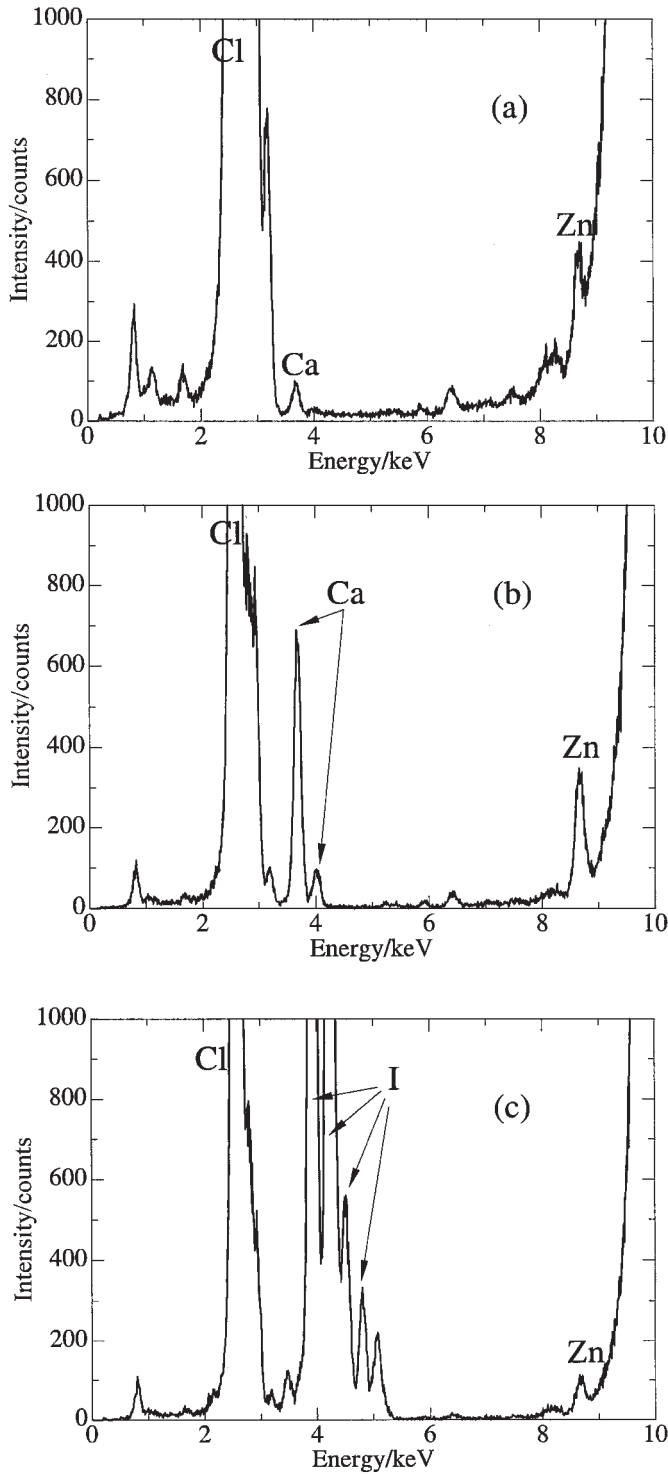


FIG. 5—Three SR-TXRF spectra of heroin: (a) seized heroin No. 1; (b) seized heroin No. 2; (c) seized heroin No. 3.

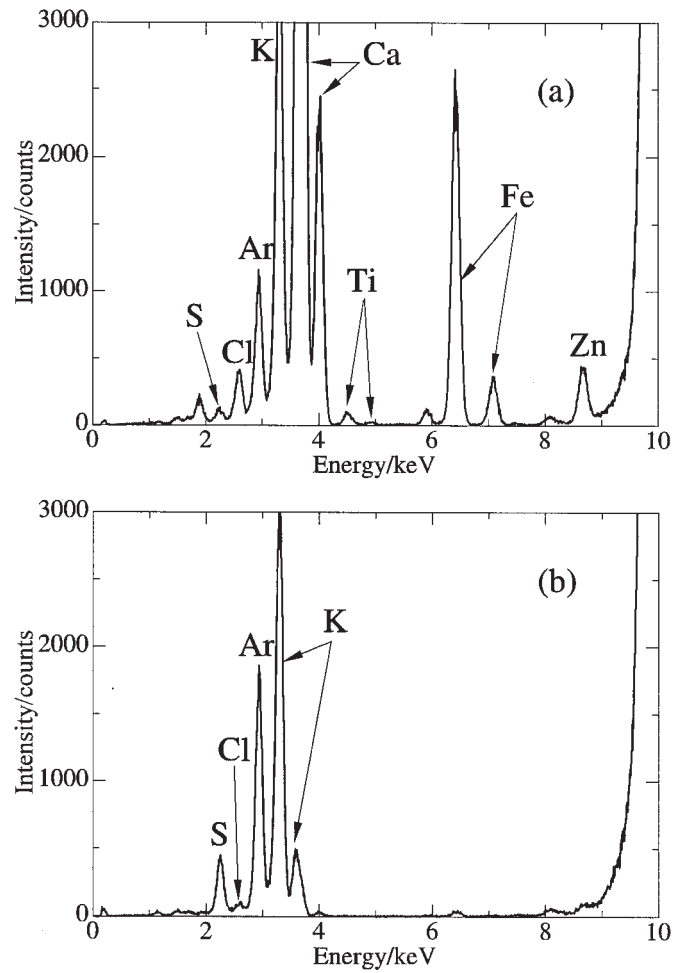


FIG. 6—SR-TXRF spectra of marijuana (a) and opium (b).

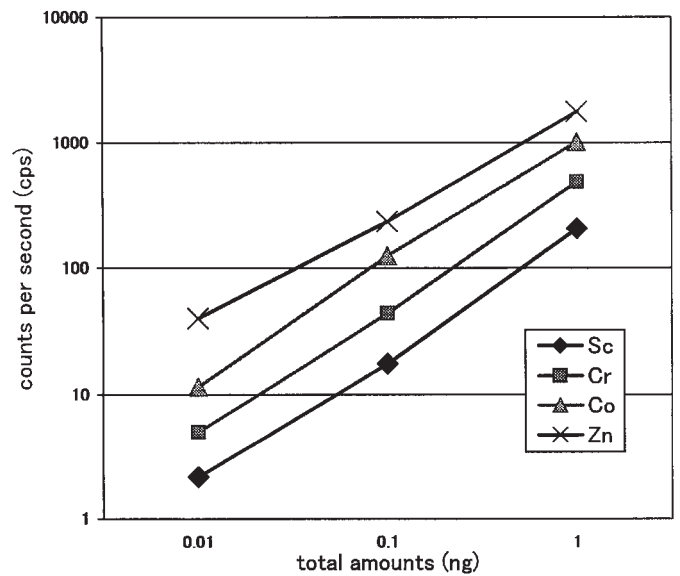


FIG. 7—Calibration curves of Sc, Cr, Co, and Zn (total amounts: 0.01 to 1 ng).

## Conclusions

Ultratrace elements in small amounts of various drugs of abuse can be easily detected using SR-TXRF analysis. This is in contrast to other elemental analysis techniques such as atomic absorption analysis or ICP-MS. With SR-TXRF, pg amounts of each trace element in 10 µg drug samples were easily detectable. The detection limit of this system was lower than standard TXRF by a factor of between 100 and 1000. The technique can be a very useful discrimination method for impurity profiling of drugs of abuse.

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