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## Chemical Profiling of 3,4-Methylenedioxymethamphetamine (MDMA) Tablets Seized in Hong Kong\*

**ABSTRACT:** During 2000–2001, the Government Laboratory of Hong Kong received over 600,000 ecstasy tablets in more than 2,600 cases. Using GC-MS or FTIR, the major amphetamine-type stimulants were identified, and the samples were categorized into four groups containing: (1) 3,4-methylenedioxymethamphetamine (MDMA), (2) methamphetamine (MA), (3) 3,4-methylenedioxyamphetamine (MDA), or (4) amphetamine. Our study revealed that in Hong Kong MDMA tablets have made up 98 and 71% of the total ecstasy tablets examined in 2000 and 2001, respectively. Among the MDMA cases, 613 cases involving a total of 123,776 tablets in 2001 were randomly selected, and their active ingredients, minor ingredients, and/or impurities were studied using GC-MS and HPLC. Based on the chemical profiles, and irrespective of their different physical characteristics, tablets obtained in different seizures could be determined as to whether or not they could have come from a common origin. The impurities detected in the MDMA tablets also served as excellent chemical markers from which plausible synthetic route(s) of the MDMA were inferred. Our study revealed that 3,4-methylenedioxyphenyl-2-propanone (MDP2P), 3,4-methylenedioxyphenyl-2-propanol (MDP), 3,4-methylenedioxy-N-methylbenzylamine (MDB), piperonal and N-formyl-3,4-methylenedioxymethamphetamine (N-formyl-MDMA) were the most common impurities detected in MDMA tablets seized in Hong Kong. The finding of the phosphate salt of MDMA is intriguing. Based on a presumptive color test, spectroscopic data (FTIR/ESI-MS) and the percentage of MDMA content in a purified phosphate salt of MDMA, the ratio of the phosphate to MDMA was determined to be 1:1, suggesting that the compound is a dihydrogen phosphate salt [i.e. (HMDMA)H<sub>2</sub>PO<sub>4</sub>].

**KEYWORDS:** forensic science, ecstasy, 3,4-methylenedioxymethamphetamine, impurity profiling

In Hong Kong, there has been growing popularity in recent years in the abuse of “club drugs” among the youngster generation. Club drugs refer to those drugs being used by young people at all-night dance parties commonly known as “raves.” One of the most common club drugs encountered in Hong Kong is ecstasy, usually in tablet form. Ecstasy is a street name originally designated for 3,4-methylenedioxymethamphetamine (MDMA), but ecstasy is currently used more generally so that what are being sold as ecstasy tablets may not necessarily contain MDMA but rather a mixture of MDMA and one or more amphetamine-type drug(s) and other substances (e.g., caffeine, ketamine, diazepam, etc.). In many cases, there may be no MDMA in ecstasy tablets or exhibits.

For illicit heroin (1–4), methamphetamine (5–9), amphetamine (10–12), and cocaine (13–15), chemical profiling has been widely employed as a tool for intelligence purposes such as establishing geographic origins, synthetic routes, and distribution routes. In the past decades, the global increase in the abuses of ecstasy prompted many scientists to look into different methodologies in achieving similar profiling studies (16–21). One common method of gathering useful information on the source of illicitly-made tablets is by comparison of their physical appearances, e.g., mark-

ings, colors, sizes, and shapes. Nevertheless, tablets having the same physical characteristics are not necessarily associated with the same chemical compositions, since tablets with different chemical compositions could be manufactured with the same die. Indeed, evidence has emerged that in some clandestine laboratories various combinations of metal taps and dyes are often used to produce tablets of different physical appearances (e.g., color, size, shapes) but having the same chemical contents. In this regard, drug intelligence based solely on physical appearance of the tablets may be misleading. It is also not inconceivable that drug syndicates would exploit the diversity of physical appearance of the tablets to divert attention of law enforcement agencies that are tracing drug distribution routes.

Therefore, in addition to physical characterization of ecstasy tablets, profiling of chemical compositions with respect to active ingredient(s), other drugs, and/or the impurities present and the salt of crystallization associated with the active ingredient could yield valuable information for drug intelligence. As a forensic drug laboratory in Hong Kong, we play a role in developing a sound protocol for gathering essential information to assist law enforcement agencies in elucidating the origin and the plausible synthetic routes of seized ecstasy tablets. An account of the current situation with ecstasy abuse in Hong Kong and the endeavor to establish a protocol for chemical profiling of MDMA tablets are presented in this paper. In this study, we study the (i) chemical compositions (active ingredients and their dosages, and/or other drugs ingredients); (ii) impurities; and (iii) salts of crystallization of MDMA. The data derived from these studies form the basis for intelligence relating to the origins and plausible synthetic routes of the illicit drugs.

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## Experimental Section

### Reagents and Standards

Authentic standards of MDMA, ketamine, and methoxyphenamine were purchased from Sigma Chemical Co. HPLC grade acetonitrile (Lab-scan Analytical Sciences), absolute ethanol (CSR Ltd.), methanol (Lab-scan Analytical Sciences), diethyl ether (Lab-scan Analytical Sciences), and KBr (spectroscopic grade, BDH Laboratory Supplies) were obtained commercially and used as received. Deionized water from a Millipore Milli-Q System was used. Ammonium molybdate solution (7% w/v) used for the phosphate test was prepared by dissolving 7 g of ammonium molybdate (Merck) in 70 mL of deionized water and 30 mL of concentrated nitric acid (Lab-scan Analytical Sciences).

### Infrared Spectroscopy

Solid-phase infrared spectra were obtained on a Perkin-Elmer Spectrum One FTIR as KBr pellets.

### High-Performance Liquid Chromatography (HPLC)

The concentrations of MDMA and ketamine were determined by a Shimadzu model LC-10AD high-performance liquid chromatograph (HPLC) interfaced with Shimadzu model SPD-M10AVP diode array detector (DAD), using an Alltima C18 column (5  $\mu\text{m}$ , 150 by 4.6 mm) (Alltech Associates Inc.) with a  $\text{CH}_3\text{CN}:\text{H}_2\text{O}$  mixture (1:3 v/v) as the mobile phase. The absorbance of MDMA and ketamine was measured at 218 nm with methoxyphenamine as the internal standard.

### Gas Chromatograph/Mass Spectrometry (GC-MS)

GC-MS analyses were performed using a Hewlett-Packard (HP) series 6890 GC interfaced to a HP 5972 series mass selective detector (MSD). A cross-linked phenylmethyl siloxane capillary column was used (Hewlett-Packard HP-1MS, 0.25 mm by 30 m, 0.25  $\mu\text{m}$  in thickness) with ultra-high-purity-grade helium gas as the carrier gas (constant flow rate, 1.0 mL/min). The typical temperature settings were as follows: injector port, 260°C; initial column temperature, 70°C; hold time, 1 min; temperature ramp, 30°C/min to 180°C; then 7°C/min to 300°C and final temperature, 300°C; hold time, 10 min. The mass spectra were compared with a commercially available NIST library.

### Electrospray Ionization-Mass Spectrometry (ESI-MS)

ESI-MS analyses were performed on a Bruker ESQUIRE-LC Ion-trap LC/MS<sup>(n)</sup> system equipped with an electrospray ionization source. The spectrometer was comprised of an octapole and ion trap mass analyzer with nitrogen as drying gas. The temperature of the drying gas was 300°C and the flow rate was 4 L/min. Nitrogen was also applied as the sheath (nebulizing) gas. The sample was dissolved in a mixture of MeOH and water (1:1 v/v), and the sample flow was set at 4  $\mu\text{L}/\text{min}$ . The electrospray voltage was set at 4 kV for the capillary, and  $-400$  V for the end plate. The multiplier voltage was 1.6 kV and the dynode at 7 kV. To obtain good peak intensities for the lens system, the capillary exit was maintained at 45 V, the Skimmer 1 at 15 V, the capillary exit offset at 30 V, and the two exit lenses at  $-5$  and  $-60$  V, respectively. The direct current (dc) offset of the octapole was set at 2 V, and the radio frequency amplitude at 120 V.

### Sample Preparations

HPLC quantitations of MDMA and ketamine were based on three-point calibration curves established using authentic standards of MDMA·HCl (0.2 to 1.6 mg/mL) and ketamine·HCl (1 to 15 mg/mL), respectively, in the presence of methoxyphenamine (2 mg/mL) dissolved in a  $\text{CH}_3\text{CN}:\text{H}_2\text{O}$  mixture (1:3 v/v) (mobile phase).

The tablets were ground into powder. About 20 mg of powder was accurately weighed into a 10-mL volumetric flask followed by the addition of 1.0 mL of methoxyphenamine·HCl (2 mg/mL) in the mobile phase and was made up to mark using the mobile phase. The mixture was sonicated for about 30 min, filtered through a 0.45- $\mu\text{m}$  pore-size nylon membrane, and diluted five times using the mobile phase into an LC vial before injection.

For GC-MS analyses, the tablets were ground into powder, and about 5 mg of the homogenous powder were extracted with 1 mL of absolute ethanol and were filtered through a 0.45- $\mu\text{m}$  pore-size nylon membrane into a GC vial.


## Results and Discussion

In most of the cases received by our laboratory, the tablets were embossed with logos (e.g., Diamond, Mitsubishi) or alphanumeric characters (e.g., P, CK, CC, HQ, 88, B29) and were also dyed with various colors. Before 2000, most of the seized ecstasy tablets were found to contain only a single active ingredient such as MDMA, 3,4-methylenedioxyamphetamine (MDA), 1-(1,3-benzodioxol-5-yl)-2-butanamine (MBDB), or 3,4-methylenedioxyethylamphetamine (MDEA), and tablets containing a mixture of MDMA and MDEA were found only occasionally. However, since 2000 the composition of the ecstasy tablets has undergone drastic changes, with tablets now often containing complex chemical compositions. Of note, increasing numbers of ecstasy tablets were found to contain nonamphetamine-type ingredients such as ketamine and caffeine. In some tablets, MDMA was not present, but methamphetamine (MA) was instead used as the principal ingredient. In addition, for these MA tablets, different combinations of other drug ingredients such as ketamine, caffeine, diazepam, phenobarbital, chlorpromazine, and imipramine were commonly encountered.

The more than 600,000 tablets received in our laboratory in the years 2000 and 2001 were categorized into 212 types according to their physical appearances and the types of amphetamines found. Chemical analysis of these tablets indicated that some with similar physical appearances had different chemical compositions. A typical example is illustrated in Table 1, showing a relationship between analytical profiles and the commonly encountered rectangular tablets with the "CC" marking. For the samples having a similar orange color and physical dimensions (Entries 1, 2, and 3), either MDMA (Entry 1) or MA (Entries 2 and 3) were found as the active ingredient. In addition, even for similar orange "CC" tablets containing MA as the active ingredient, different combinations with other nonamphetamine components such as diazepam and phenobarbital (Entry 2) and ketamine and caffeine (Entry 3) were detected. On the other hand, different-colored tablets bearing similar markings may contain similar chemical ingredients (e.g., compare Entries 1 and 7, Entries 3 and 5).




In some cases, ecstasy tablets with different physical characteristics contained similar constituents. Typical examples are the MDMA tablets with markings "CC," "88," and "P," shown in Table 2. Although they have different logos/markings, sizes, shapes, and/or colors, all of them were found to have similar MDMA contents (about 50%). Furthermore, ketamine was de-

TABLE 1—Chemical profiles of rectangular tablets with logo C/C in various colors: c = caffeine, ch = chlorpromazine, d = diazepam, k = ketamine, p = phenobarbital.

|  | Orange |      |      | Blue | Violet | Green | Yellow |
|---|--------|------|------|------|--------|-------|--------|
| Entry no.   | 1      | 2    | 3    | 4    | 5      | 6     | 7      |
| Amphetamines  | MDMA   | MA   | MA   | MDMA | MA     | MA    | MDMA   |
| Purity (%)  | 55     | 20   | 4.7  | 55   | 4.9    | 3.5   | 56     |
| Additives*  | k      | d, p | k, c | k, c | k, c   | k, ch | k      |

\*k: ketamine, d: diazepam, c: caffeine, p: phenobarbital, ch: chlorpromazine

TABLE 2—Three types of tablets in different physical forms having similar chemical compositions.

| Marking   | No. of cases encountered (no. of tablets) | MDMA (%) | Additive(s) |
|---|---|----------|-------------|
|   | 137 (1893)                                | 45-51    | ketamine    |
|  | 78 (530)                                  | 46-48    | ketamine    |
|  | 2 (5)                                     | 51       | ketamine    |

ected in all of these tablets. Thus, general physical characteristics of the tablets do not bear a direct relationship with their inherent chemical compositions. In fact, the uses of several dyes (e.g., yellow, blue, and red) and metal dies with different shapes, logos, or letters (e.g., rectangular CC, circular 88, and AP) were found at a local ecstasy tablet-manufacturing scene. This indicates that different combinations of dyes and metal tablet dies are likely to be employed for ecstasy manufacturing even at a single site (personal communication). In order to collect systematic information for drug intelligence, we set forth to establish a protocol for chemical profiling of the ecstasy seizures.

To begin our study, the ecstasy tablets were first classified into the four groups according to their principal ingredient: (1) MDMA, (2) MA (methamphetamine), (3) MDA, or (4) amphetamine. As noted earlier, there were a total of 212 different types of ecstasy tablets. According to Fig. 1, the relative abundance of MDMA, MA, MDA, and amphetamine in the 212 types of ecstasy tablets can be arranged in a descending order: MDMA(55%) > MA(40%) >> MDA ≈ amphetamine (5%). Based on the percentage of the number of ecstasy tablets received in 2000 and 2001 (Fig. 2), MDMA tablets were the most commonly encountered. Yet the abundance of MDMA tablets decreased from 98% in 2000 to 71% in 2001. By contrast, there was a significant increase in MA and MDA tablets in 2000–2001: from 2 to 22% (MA) and from <1 to 6% (MDA). Tablets containing amphetamine contributed less than 1% of the total number of tablets being examined. However, on the

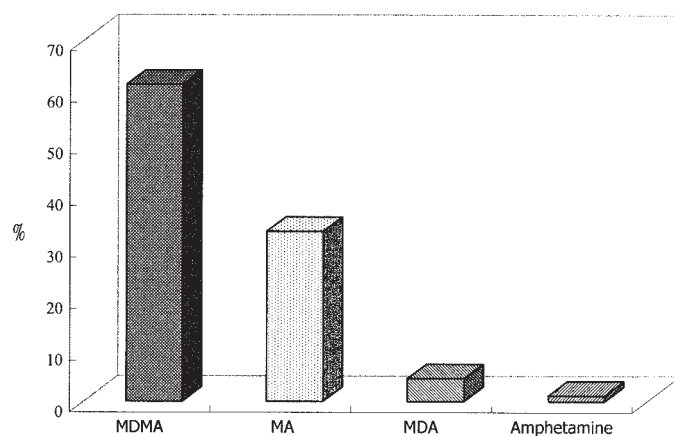


FIG. 1—Percentage distribution of 212 types of ecstasy tablets based on physical features according to the amphetamines found: (1) MDMA; (2) MA; (3) MDA; (4) amphetamine.

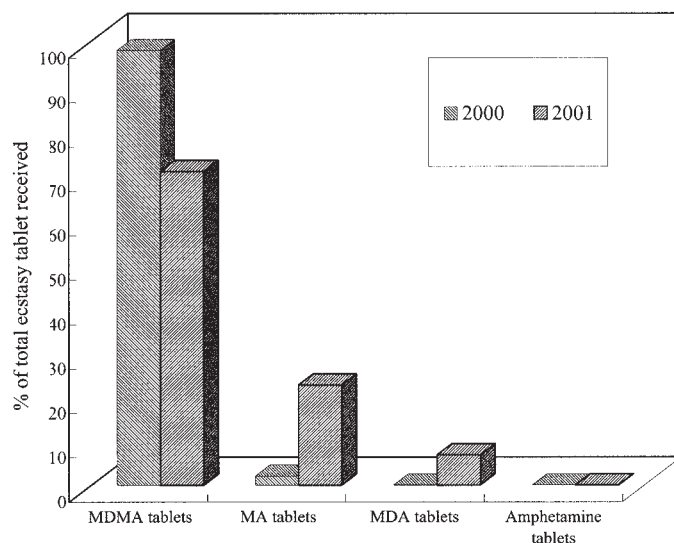


FIG. 2—Percentage distribution of the same four groups of amphetamines in Fig. 1 in terms of the total number of tablets received in the years 2000 and 2001.



basis of these relative abundances, MDMA constituted the major drug type for ecstasy abuse in Hong Kong, and hence our study focused on the chemical profiling of MDMA tablets.

#### Chemical Profiling

Although a majority of the ecstasy samples seized in Hong Kong were MDMA-only tablets, the number of tablets containing ketamine in addition to MDMA rose. In 2000, around 12% of the total MDMA cases were found to contain ketamine in addition to MDMA (i.e., 125 cases out of a total of 1,023 cases). However, the figure rose significantly to 42% in 2001 (i.e., 413 cases out of 973 cases). A similar trend (ca. three-fold increase) was also observed for MA tablets: MA tablets also containing ketamine rose from 23% (i.e., 59 cases out of 255 cases) in 2000 to 83% (i.e., 653 cases out of 780 cases) in 2001.

For the MDMA tablets seized in 2001, those containing ketamine were found to have a comparable percentage of MDMA content to that of the MDMA-only tablets. For instance, examination of 137 cases (with a total of 1893 tablets) of the orange rectangular tablets with the same "CC" logo indicated that the tablets contained 45 to 51% (weight by weight) of MDMA and 7 to 13% (weight by weight) of ketamine. The percent MDMA is close to the average MDMA content of 46% found in the MDMA-only tablets. The average MDMA content was determined from a population of 31,508 tablets MDMA-only tablet obtained in 333 cases during the year 2001. This similarity in the percent MDMA content suggested that similar amounts of MDMA were used to make up a tablet with similar size and weight irrespective of whether or not ketamine is added. Therefore, the addition of ketamine in such tablets may not only be used to replace part of excipients or inert substances but also be used as an adulterant probably to enhance the drug effects of MDMA.

#### Impurities Profiling

Upon close scrutiny of the chemical compositions of MDMA tablets, we detected, in some cases, trace impurities that were ei-

ther structurally related to MDMA or its precursors. These trace impurities, which were either starting materials, intermediates, or manufacturing by-products, can serve as markers characterizing the synthetic route(s) employed for MDMA production. Collection of the impurity profiles could generate useful intelligence information to trace the origin of the tablets and possibly the synthetic route(s) of MDMA currently found in the blackmarket.

As an example, the GC-MS result of an MDMA tablet is depicted in Fig. 3. The total ion chromatogram showed two prominent peaks at  $R_t = 6.3$  and 8.8 min, assignable to MDMA and caffeine, respectively. There are two partially overlapping peaks at  $R_t = \text{ca. } 5.9$  min; their mass spectra correspond to 1-(3,4-methylenedioxyphenyl)-2-propanone (MDP2P) and 1-(3,4-methylenedioxyphenyl)-2-propanol (MDP), respectively. Furthermore, another peak at  $R_t = 5.5$  min was confirmed to be 3,4-methylenedioxy-*N*-methylbenzylamine (MDB).

Several methods are known in the literature for the synthesis of MDMA (22,23), and those methods that use MDP2P as the key precursor are (i) Leuckart's reaction (24,25) and (ii) reductive amination (26) (Fig. 4). It is likely that the MDP detected in the MDMA tablets is a side product resulting from direct reduction of MDP2P with excess reductant (e.g., sodium cyanoborohydride) consistent with a typical reductive amination route being employed for the MDMA production. However, an alternative two-step reaction method has been identified by Liang (27). This method involves the reaction of *N*-methylbenzylamine (as a substitute source for methylamine) with sodium cyanoborohydride and MDP2P to give *N*-benzyl-3,4-methylenedioxymethamphetamine, followed by reduction with hydrogen in the presence of palladium/carbon (by cleaving the benzyl group). In this case, production of a significant amount of the MDP as a side product was also reported.

The presence of MDB in the sample implies that piperonal was the precursor for making the MDMA via reductive amination of MDP2P (Eq 3, Fig. 4) (16). It is known that MDP2P can also be

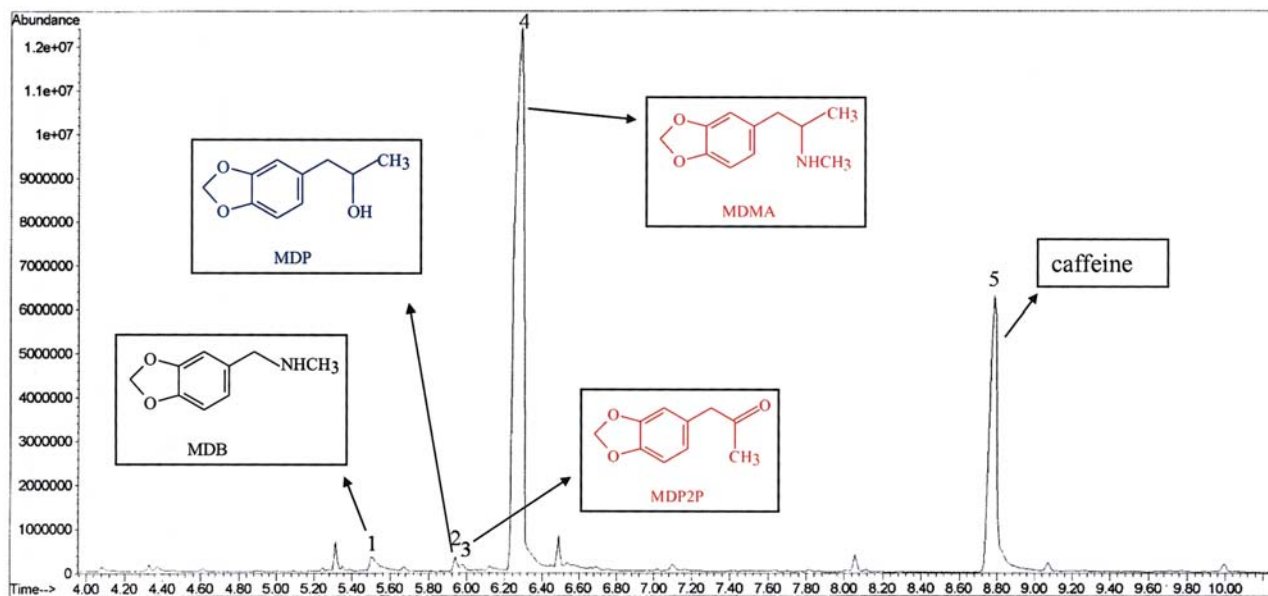


FIG. 3—Typical total ion chromatogram of MDMA tablets that contain impurities and other drugs: (1) 3,4-methylenedioxy-*N*-methylbenzylamine (MDB), (2) 1-(3,4-methylenedioxyphenyl)-2-propanol (MDP), (3) 3,4-methylenedioxyphenyl-2-propanone (MDP2P), (4) MDMA, (5) caffeine.

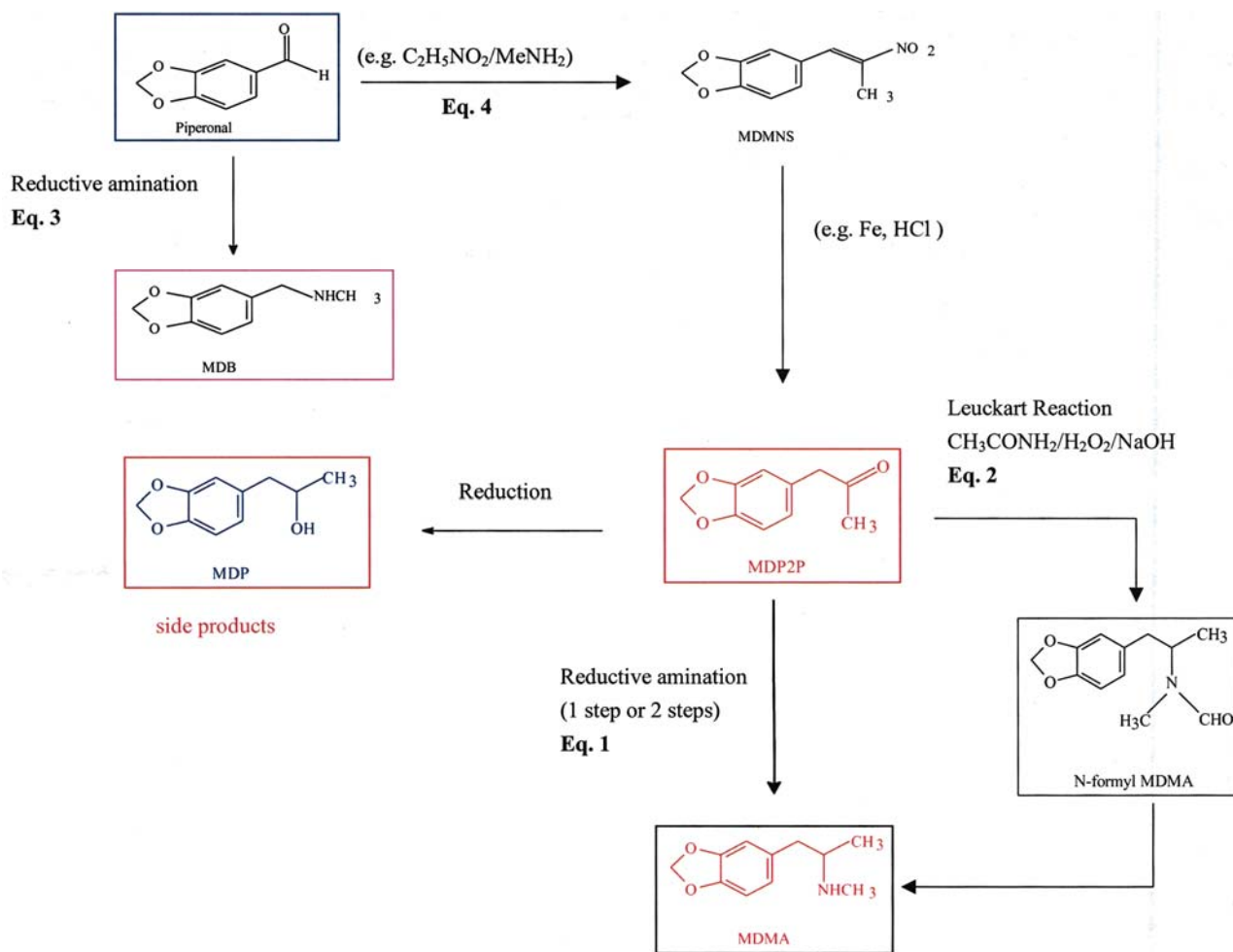


FIG. 4—Typical synthetic routes of MDMA.

prepared by oxidation of isosafrole (ISOSAF) (23,25), 3,4-methylenedioxy-methyl-nitrostyrene (MDMNS) (28–30) or  $\beta$ -3,4-methylenedioxyphenyl- $\alpha$ -methyl glycidic ester (31). Dal Cason has described how piperonal can serve as primary precursor for MDMNS (Eq 4, Fig. 4) (23). Therefore, the co-existence of MDP and MDB together implies that the MDMA was derived from piperonal via MDMNS as intermediate to produce MDP2P. Subsequent reductive amination of MDP2P, via either a one-step (e.g.,  $Na(CN)BH_4$ /methylamine) or two-step reaction (27), produces MDMA.

Among the 613 cases (with a total of 123,776 tablets) randomly taken for study in 2001, there were a total of 416 cases having been taken for GC-MS analyses. As laboratory policy, no GC-MS analysis was performed if a definitive FTIR matching of MDMA for a particular case was accomplished. Of the 416 cases taken for GC-MS analyses, a total of 341 cases were found to contain traces amounts of impurities such as 3,4-methylenedioxyphenyl-2-propanone (MDP2P), 3,4-methylenedioxyphenyl-2-propanol (MDP), 3,4-methylenedioxybenzylamine (MDB) and/or piperonal. The presence of these impurities strongly suggested that the MDMA found in Hong Kong in 2001 was predominantly synthesized via the key intermediate, MDP2P, which in turn was prepared from piperonal.

The comparison of the chemical profiles to link different cases is governed by two factors: (1) the resemblance of the correlation of

TABLE 3—Three groups of orange rectangular MDMA tablets with logo C/C found to contain MDMA and ketamine according to the difference in MDMA and ketamine contents.

| Batch No. | No. of cases | No. of tablets | % of MDMA | % of Ketamine | Date of first encountered |
|-----------|--------------|----------------|-----------|---------------|---------------------------|
| 1         | 53           | 940            | 49-51     | 7-8           | Nov, 2000                 |
| 2         | 55           | 555            | 45-47     | 8-10          | Jan, 2001                 |
| 3         | 29           | 398            | 46-47     | 12-13         | Mar, 2001                 |

two or more impurities/additives profiles, and (2) the frequency of particular profiles. As shown in Table 2, there were a total of 1893 orange rectangular MDMA tablets marked “CC” from 137 cases. These tablets were first encountered in November 2000, and all of them were found to contain ketamine with impurities such as MDP2P, MDP, and piperonal frequently detected. Yet, irrespective of the physical and chemical similarities, these tablets could be further classified into three different groups according to their MDMA and ketamine contents (Table 3). The total ion-chromatograms (TIC) of these three groups are depicted in Fig. 5. In addition to the detection of the above-mentioned known impurities, a full

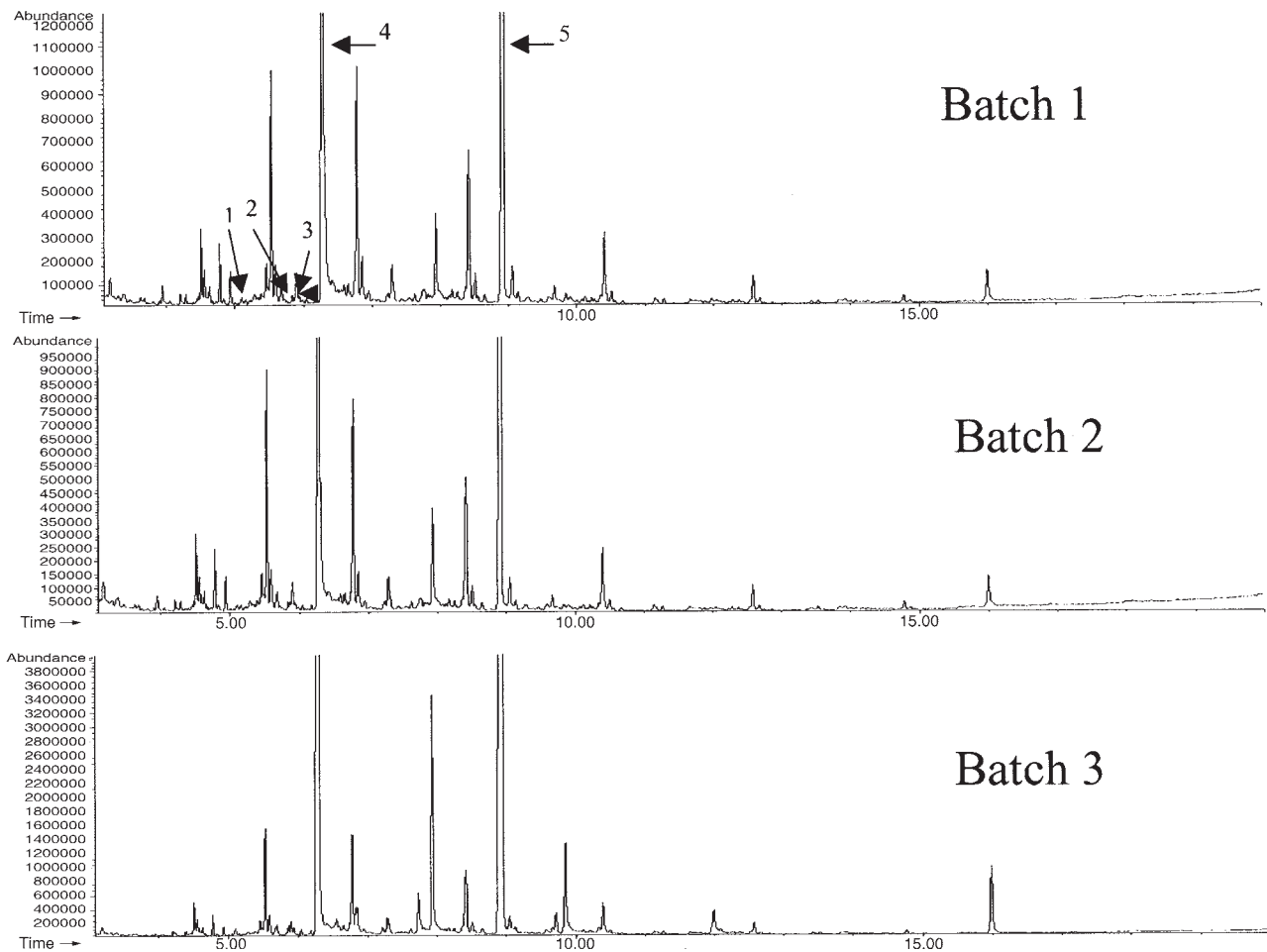





FIG. 5—Representative total ion chromatogram profiles for the three batches of rectangular tablets with logo C/C: (1) piperonal, (2) MDP, (3) MDP2P, (4) MDMA, (5) ketamine.

TABLE 4—Summary of results of three types of physically different tablets having similar chemical profiles.

| Marking   | Total no. of cases studied | MDMA (%) | Ketamine (%) | MDP (No. of cases encountered) | MDP2P (No. of cases encountered) | Piperonal (No. of cases encountered) |
|---|----------------------------|----------|--------------|--------------------------------|----------------------------------|--------------------------------------|
|  | 137                        | 45-51    | 7-13         | 96                             | 97                               | 21                                   |
|  | 78                         | 46-48    | 8-9          | 50                             | 49                               | 6                                    |
|  | 2                          | 51       | 9            | 1                              | 1                                | 1                                    |

comparison of the TIC profiles also showed high degrees of similarity among these three groups of MDMA tablets. These results collectively provided substantial evidence to suggest that even though these three groups of tablets could have associated with a common origin, they were probably produced at different times. Indeed, the cases involving these three batches of tablets were first received by our laboratory at different times [Nov. 2000 (Entry 1), Jan. 2001 (Entry 2), and March 2001 (Entry 3)].

As shown in Table 4, orange circular tablets with an impressed logos "88" or "P" that were obtained from a total of 78 cases and 2 cases, respectively, were compared with the above-mentioned

orange "CC" tablets. It is striking that they all contained the same major ingredients (i.e., MDMA and ketamine). Furthermore, impurities like MDP2P, MDP, and piperonal were also frequently detected. Added to this, the representative TIC profiles for tablets of "CC" and "88" also showed great resemblance (see Fig. 6). Apart from the above findings, the MDMA and ketamine contents (46 to 48% of MDMA and 8 to 9% of ketamine for "88" tablets, and 51% of MDMA and 9% of ketamine for "P" tablets) were similar to one group of the "CC" tablets (Entry 2, Table 3). Therefore, the similarity in the analytical profiles of these three different types of tablets, namely the tablets of orange rectangular "CC" and orange circular

“88” and “P,” suggested a reasonable linkage that they are likely to have associated with a common origin regardless of having different physical characteristics and being from different cases.

In another type of tablet with the impressed logo “HQ” on both sides and occurring in various colors, GC-MS analysis (Fig. 7) confirmed the presence of MDMA with a prominent peak at  $R_t =$  ca. 6.0 min. In addition to MDP at  $R_t =$  ca. 5.7 min, another small peak at  $R_t = 9.2$  min was confirmed to be *N*-formyl-3,4-methylenedioxymethamphetamine (*N*-formyl-MDMA) by matching its mass

spectrum with an authentic spectrum obtained from a NIST mass spectral library. *N*-Formyl-MDMA has been reported as a marker for the conversion of MDP2P to MDMA via the Leuckart reaction, which proceeds by reacting MDP2P with *N*-methylformamide and formic acid (Eq 2, Fig. 4) (26).

In the past, MDMA found in the tablets was solely in the form of hydrochloride salt; however, a preliminary anion test for chloride on the above-referenced “HQ” tablets gave a negative result. Instead, a presumptive ion test for phosphate using a solution of am-

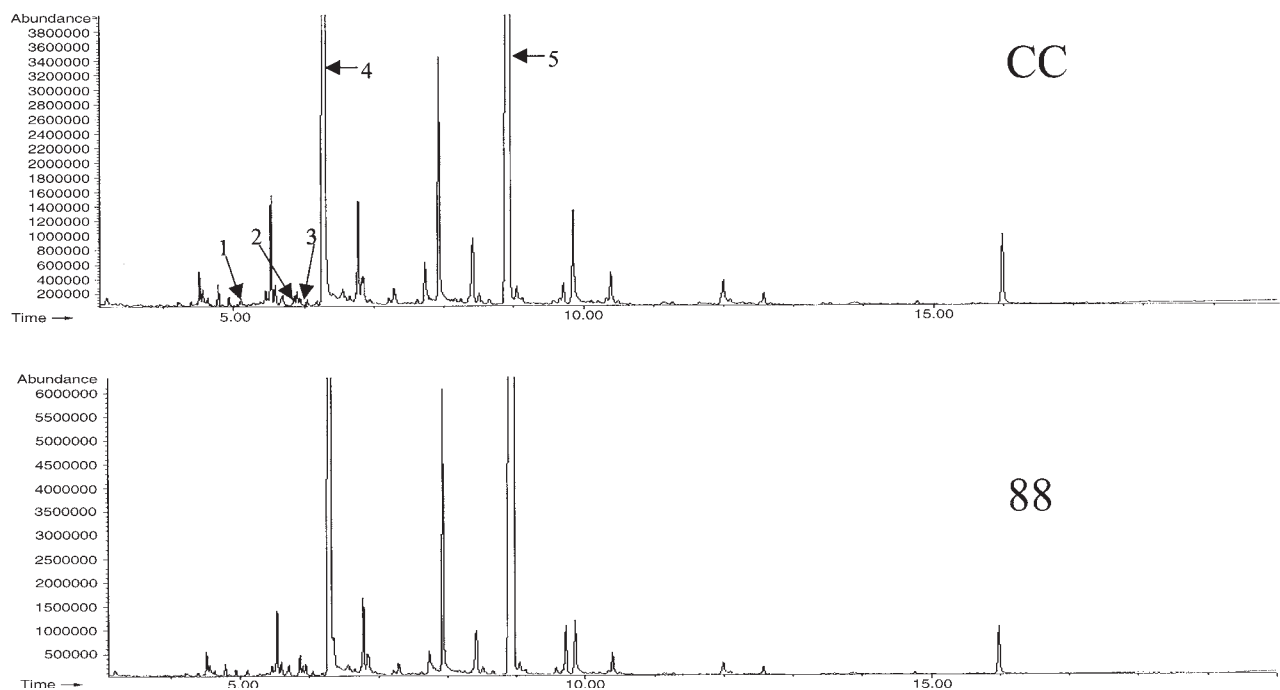


FIG. 6—Representative total ion chromatogram profiles for: (i) rectangular tablets with logo CC; and (ii) circular tablets with logo 88: (1) piperonal, (2) MDP, (3) MDP2P, (4) MDMA, (5) ketamine.

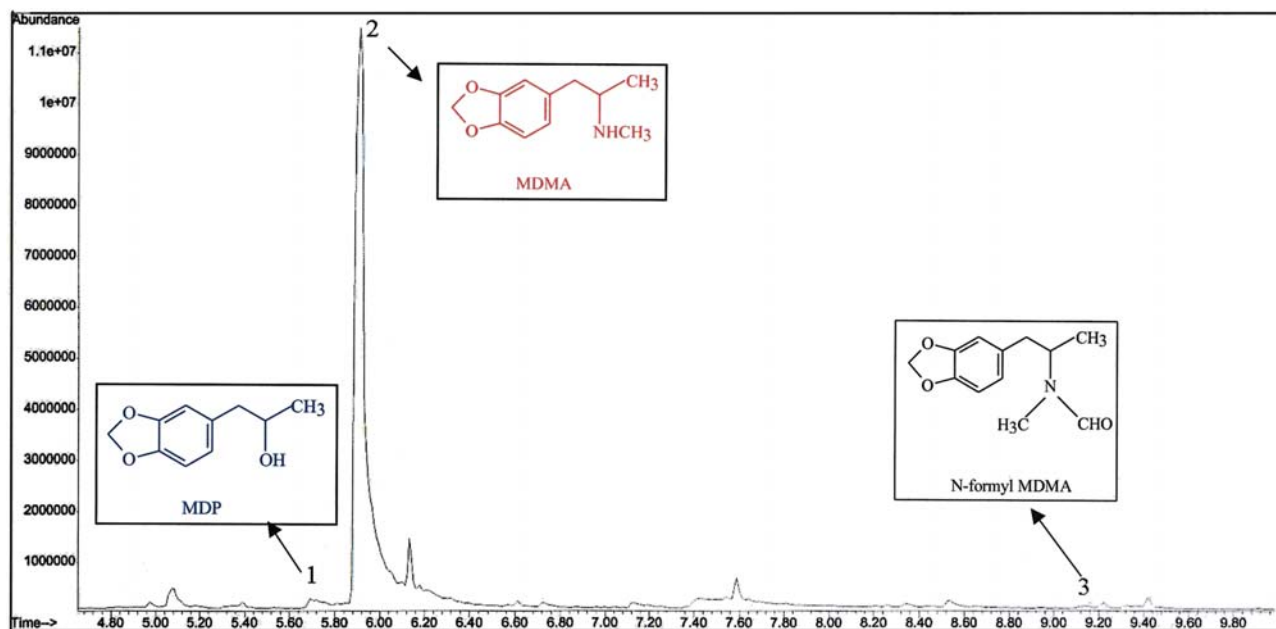


FIG. 7—Typical total ion chromatogram of MDMA tablets with logo “HQ” on both sides that contain impurities: (1) MDP, MD2P (2) MDMA, (3) *N*-formyl-3,4-methylenedioxymethamphetamine (*N*-formyl-MDMA).

monium molybdate gave a yellow precipitate. With this information, we expanded our studies to elucidate the chemical structure of the suspected phosphate salt of MDMA.

#### MDMA Phosphate—An Unusual Salt of Illicit MDMA

After extracting the tablets with chloroform and evaporating the extracts to dryness over a steam bath, the sample was subjected to FTIR analyses. Detailed examination of the IR spectrum (Fig. 8) showed that the sample possessed virtually all the characteristic peaks of MDMA hydrochloride; however, all peaks in the range of 1300 to 850  $\text{cm}^{-1}$  (attributed to the vibrational absorption of MDMA) were overlapped with some broad peaks. Comparing this region with the IR spectrum of disodium hydrogen phosphate

(same region), these broad peaks appeared to be the stretching vibrations of ( $P = O$ ) and ( $P - O$ ).

To confirm phosphate as being the salt of crystallization, the MDMA sample (MeOH/H<sub>2</sub>O = 1:1) was analyzed by electrospray mass spectrometry. The mass spectrum (Fig. 9) showed two intense peaks at  $m/z = 485$  and 194. The former peak was assigned as  $[(\text{HMDMA})_2(\text{H}_2\text{PO}_4)]^+$  (**1**), while the latter was assigned to  $\text{HMDMA}^+$ . The MS/MS analysis of the peak at  $m/z = 485$  is shown as an inset in Fig. 9; the peak at  $m/z = 387$  is consistent with the formulation of  $[(\text{HMDMA})(\text{MDMA})]^+$ , arising from the loss of a  $\text{H}_3\text{PO}_4$  from **1**.

Figure 10 showed the electrospray ion mass spectrum of the sample in negative polarity; the peak at  $m/z = 97$  corresponds to the  $\text{H}_2\text{PO}_4^-$  anion.

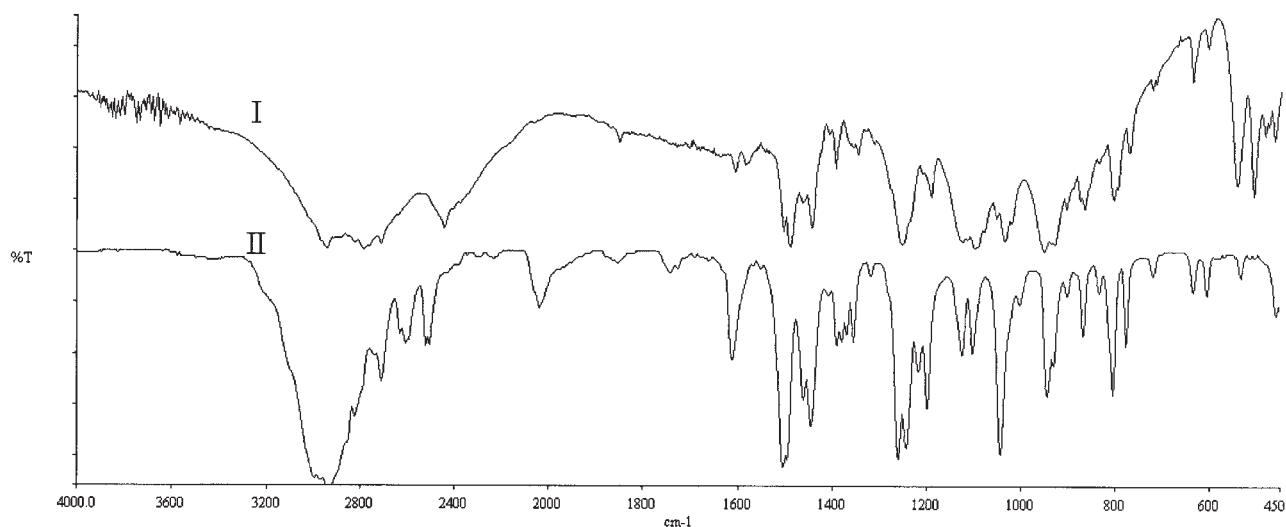


FIG. 8—FTIR spectra of (I) a sample suspected to contain phosphate salt of MDMA; (II) standard MDMA.HCl.

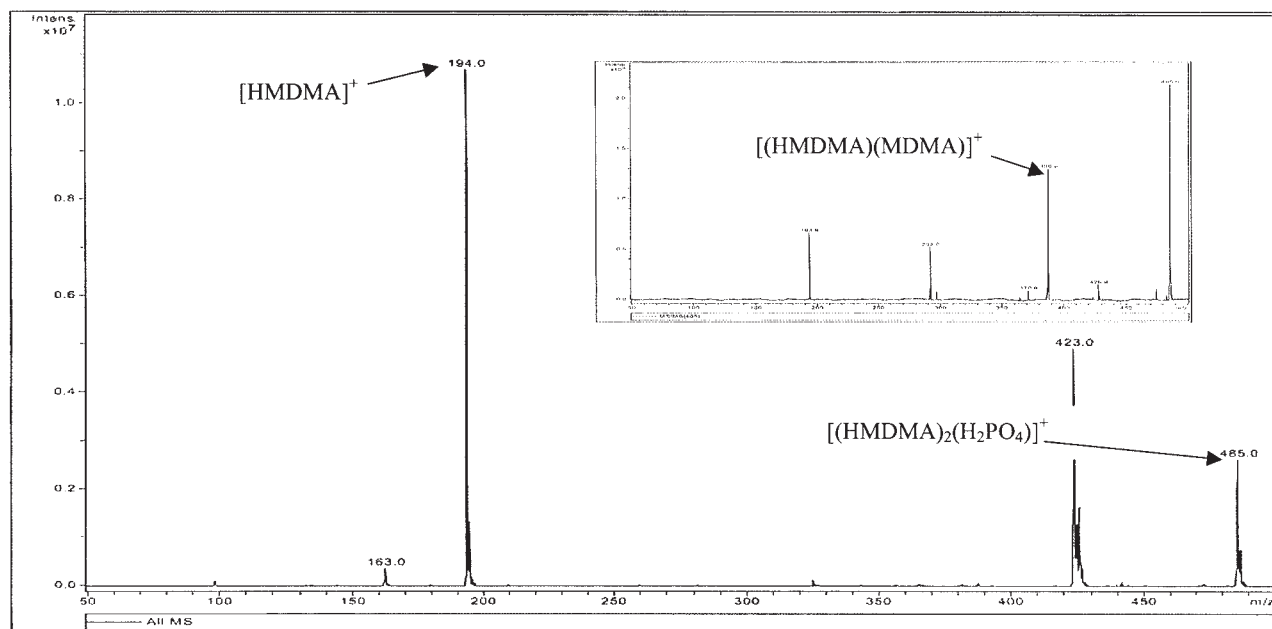


FIG. 9—Electrospray ion mass spectrum of the sample that contained phosphate salt of MDMA operated in positive mode. Inset shows the MS/MS spectrum at  $m/z = 485.0$ .



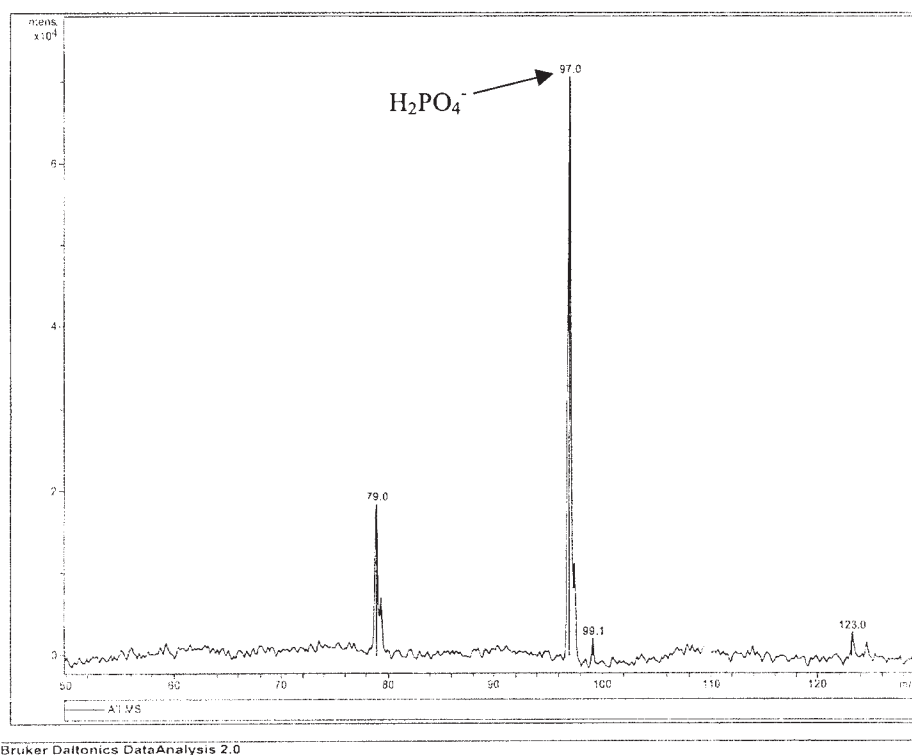



FIG. 10—Electrospray ion mass spectrum of the same sample as in Fig. 9 operated in negative mode.

Unlike MDMA hydrochloride, which has only one formulation (i.e., [HMDMA]Cl), a triple-charged phosphate anion can exist in three ionization forms, namely  $\text{PO}_4^{3-}$ ,  $\text{HPO}_4^{2-}$ , or  $\text{H}_2\text{PO}_4^-$ . Thus, three phosphate salt formulations of MDMA:  $(\text{HMDMA})_3\text{PO}_4$  (**2**),  $(\text{HMDMA})_2\text{HPO}_4$  (**3**), and  $(\text{HMDMA})\text{H}_2\text{PO}_4$  (**4**) are possible. One way to ascertain the most plausible formulation is to determine the MDMA content of a purified phosphate salt obtained from the tablets. Assuming 100% chemical purity, the expected MDMA content in **2**, **3**, and **4** are 85.6, 79.8, and 66.3%, respectively. Prior to LC analysis, the samples were purified by extraction with MeOH, followed by slow recrystallization through slow diffusion of diethyl ether into a saturated MDMA solution in MeOH. The crystalline samples obtained were analyzed by HPLC and the MDMA content found to be 66.2%. This value was consistent with the expected value of **4** (66.3%), i.e., the phosphate anion and MDMA were in a ratio of 1:1. The formulation of MDMA found in those tablets was therefore assigned to  $(\text{HMDMA})(\text{H}_2\text{PO}_4)$ , the dihydrogen phosphate salt of MDMA.

Of the cases being studied in 2001, there were a total of 31 cases containing 292 tablets in red, green, or blue and bearing the same impressed logo of “HQ” on both sides. They were found to contain only MDMA dihydrogen phosphate **4** as the principal drug based on GC-MS analysis. In these cases, it was found that the MDMA content was within the 36 to 43% range (see Table 5). Again, the TIC profiles for all three colored “HQ” tablets displayed similar patterns as shown in Fig. 11. Hence, regardless of the difference in color, the similar chemical profiles (phosphate salt as a counter anion of crystallization, detection of MDP and *N*-formyl-MDMA, and similar TIC profiles based on GC-MS analysis) of all these tablets suggested that they could have associated with a common origin. The unusual occurrence of **4** and the detection of these synthetic impurities further suggested that in these tablets MDMA

TABLE 5—Summary of results of circular MDMA phosphate tablets with logo HQ in different colors.

|  | No. of cases (no. of tablets) | MDMA (%) |
|--|-------------------------------|----------|
| Red  | 27 (284)                      | 36-40    |
| Green  | 3 (6)                         | 39       |
| Blue   | 1 (2)                         | 43       |

could have been produced by a common synthetic route using MDP2P to produce MDMA via the Leuckart reaction.

## Conclusions

Intelligence studies solely based on physical appearance of ecstasy tablets are insufficient. The present work demonstrated the use of chemical profiling, collectively using the active ingredient(s) found, quantitative data; other drugs present; the synthetic impurities; and the salts of crystallization of MDMA (e.g., phosphate salt of MDMA) in correlating tablets with similar chemical profiles, whether or not they bear the similar physical appearances. It can also provide such information as different consignments of tablets produced, and plausible synthetic routes. While extensive correlation of all the cases received by this laboratory using chemical profiling is beyond the scope of the present work, the latter

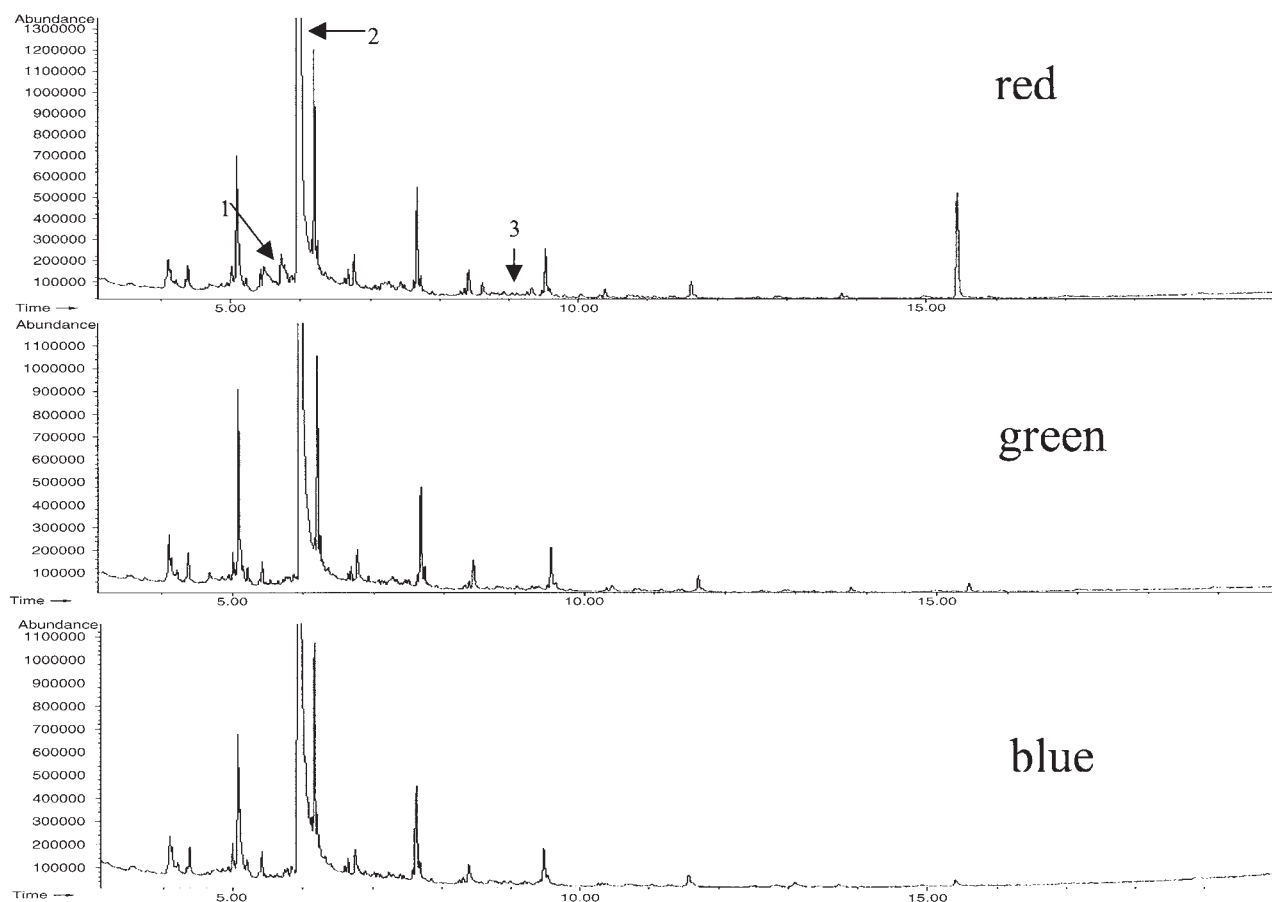


FIG. 11—Representative total ion chromatogram profiles for the three different colored tablets with logo HQ: (1) MDP, MD2P, (2) MDMA, (3) *N*-formyl-MDMA.

nevertheless forms the basis of analytical profiling of illicit drugs. We envision that chemical profiling will be beneficial to the law enforcement agencies for intelligence purpose in tracing the source of ecstasy tablets. Similar studies on MA tablets are currently in progress.

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