

Detection of Methamphetamine in Urine Stains

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ABSTRACT

Objective: The aim of this study is to determine the stability of methamphetamine in urine stains on two materials (gauze and filter paper) which were stored for up to 24 weeks in different temperatures and environmental conditions.

Methods: One ml of 10 different concentrations of positive methamphetamine urine samples were prepared for study by staining each samples on gauze sponge and filter paper. Each set of urine stains were stored at 0 °C, 4 °C, room temperature and outdoor (avoiding water and rain exposure). Urine stains were eluted subsequently at different times as follows: immediately, 3 days, 1 week, 2 weeks, 4 weeks, 12 weeks and 24 weeks, respectively. Then, elution solvent was analyzed for methamphetamine concentration by TDx analyzer.

Results: Methamphetamine concentrations of immediate urine stains on gauze were lower than that of urine in all concentrations. The urine stains on filter paper contained methamphetamine less than urine at a concentration below 5,000 ng/ml. Methamphetamine on gauze and filter paper stored at 0 °C and 4 °C did not change for 24 weeks. Being stored at room temperature and outdoor, methamphetamines on gauze and filter paper significantly decreased during 24 weeks. The amount of methamphetamines on gauze and filter paper at outdoor declined faster than at room temperature within the same time frame.

Conclusions: Methamphetamine recovered from urine stains on filter paper was higher than from gauze sponge. The amount of methamphetamine of urine stain on gauze and filter paper were stable when stored at 0 °C and 4 °C but at room temperature and outdoor they were continuously declined during 24 weeks.

Keywords: Detection; Methamphetamine; Urine Stains

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Nowadays, methamphetamine (MAM) is one of the most common addictive drugs. It has a special tendency to spread among the juvenile. Detection of MAM in urine sample is often a necessary step to verify drug addiction.

Evidences including stains have been investigated extensively in forensic fields and stains may serve as reliable alternative specimens for toxicological analyses in the absence of urine normally taken for such purposes. Examination of clothes, fibers, or stains represents an important step of the forensic investigation done on cadavers and may become important evidence that involves personal contact.¹ As a matter of routine, evidence such as victim's clothing or in case of urine stains, one has the option of either scraping the stain of a surface, cutting out the area of the object bearing. If needed, most evidence can be usually submitted to the laboratory to detect possible existence of drug such as opiate,² cocaine metabolite³ and phenobarbital⁴ either by personal delivery or conveniently through the mail. However, detection of MAM in urine stains from drug abuses has never been reported. Therefore, toxicological analysis of urine stains

on gauze, which is similar to cloth or garment, and filter paper, was investigated. Furthermore, detecting positive urine specimen in the dry state as stains, stability of MAM in urine stains on two materials (gauze and filter paper) stored over time for up to 24 weeks will be determined in different temperatures and environmental conditions.

MATERIALS AND METHODS

Materials

Nonsterile gauze sponge, 2x2 inches (Thai Gauze Co., LTD, Thailand), Whatman No.41 filter paper Ø11cm (Whatman International LTD., Maidstone, England), U-100 insulin syringe (Terumo Corporation Tokyo, Japan), Universal-Indicator paper (Art. 9526, Merck, Germany), reagent grade, sterile water (Thai OTSUKA pharmaceutical Co., LTD, Thailand), TDx[®] automated fluorescence polarization analyzer (Abbott Laboratories, USA) were used in the trial.

Methods

Urine sample collection

Positive urine samples were obtained from MAM users whose urine had been detected positive at the Department

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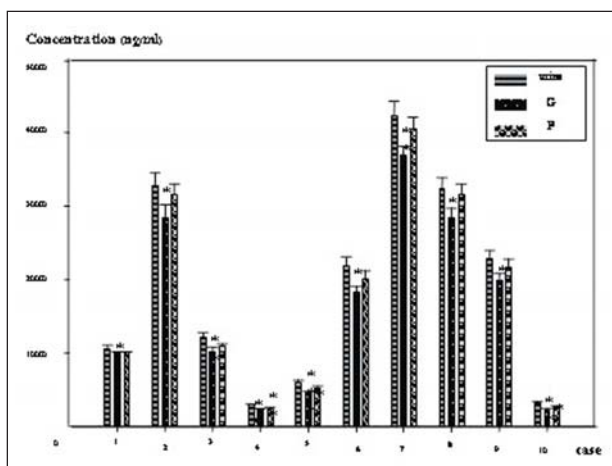


Fig 1. MAM concentration of urine and urine stains on gauze (G) and filter paper (P) at T_0 ; Data are mean \pm SD. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. urine group

of Forensic Medicine, Faculty of Medicine Siriraj Hospital. The ten urine samples were collected in plastic bottle, tightly capped, and kept cool until analyzed.

Staining procedure

The 1/2 piece of Whatman No 41 filter paper and gauze sponge, 2x2 were hanged by a grip. One ml of each positive urine was dropped on filter paper and gauze by U-100 insulin syringe. Then they were left to dry and each set was stored at 0 °C, 4 °C, room temperature (RT) and outdoor temperature (OT). As for the outdoor environment, water and rain exposure were avoided. The stains were eluted at various setting period: immediately (T_0), 3 days, 1 week, 2 weeks, 4 weeks, 12 weeks, and 24 weeks, respectively.

Stain elution procedure

The procedure was modified from the method of DuBey and colleague.⁵ The dried filter paper or gauze was cut into small pieces, approximately 2x2 mm per piece. The small pieces were then placed in a 15 ml test tube. Then sterile water of 8 ml was added to each test tube by 10 ml

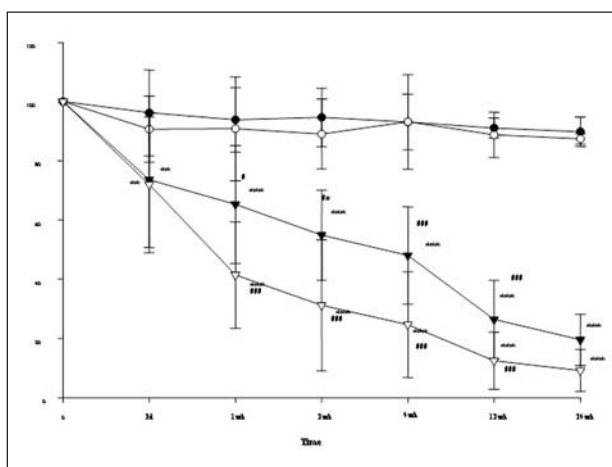


Fig 2. Stability of MAM in gauze stains stored at 0 °C, 4 °C, room temperature (RT) and outdoor (OT) for different time. Data are mean \pm SD of ten samples in each group. ** $p < 0.01$, *** $p < 0.001$ vs. T_0 ; # $p < 0.05$, ## $p < 0.01$, ### $p < 0.001$ vs. 0 °C

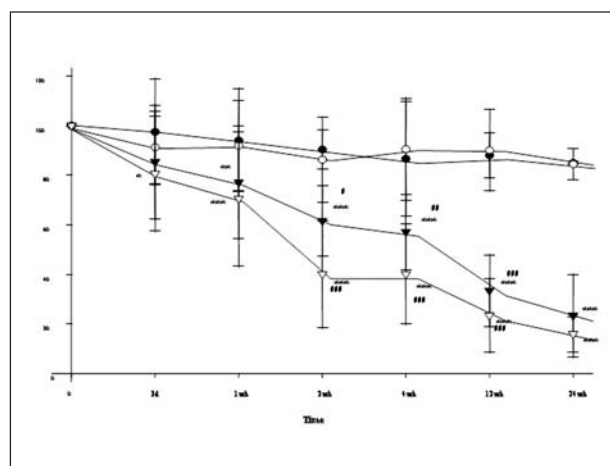


Fig 3. Stability of MAM on filter paper stains stored at 0 °C, 4 °C, room temperature (RT) and outdoor (OT) for different time. Data are mean \pm SD of ten samples in each group. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. T_0 ; # $p < 0.05$, ## $p < 0.01$, ### $p < 0.001$ vs. 0 °C

measuring pipette, vortex at 50 HZ for 3 minutes; the slurry was further macerated for hour, centrifuged at 3000 rpm for 10 minutes and pressed down for minute. Then all solvent was transferred from the filter paper or gauze slurry from each tube with Pasteur pipette into blank 15 ml test tubes, identified by code numbers. This recovered solvent solution of approximately 8 ml containing positive urine was then analyzed by TDx[®] analyzer.

Statistic analysis

For detection of MAM in urine stains on different materials, all data were presented as means and standard deviation (mean \pm SD). One way analysis of variance (one-way ANOVA) was used for comparison among the treatment groups and the significant difference between the two mean values was evaluated by LSD test.

For detection of MAM in urine stains at different durations and temperatures, all data were compared to the MAM concentration at T_0 (100%) as percentage and were presented as means and standard deviation (mean \pm SD). General linear model with repeated measures was used to determine the difference among the timings. Post hoc comparisons were made using LSD test. One way analysis of variance (one-way ANOVA) was used for comparison among the temperature groups and the significant difference between the two mean values was evaluated by LSD test. A difference was considered significant at $p < 0.05$.

RESULTS

Part I. Detection of MAM in Urine Stains on Different Material

All ten cases of urine stains in gauze and filter paper were detected at once when dried. The result is shown in Fig 1. The MAM concentration in all cases can be divided into three groups, i.e., high concentration (28,303.35 to 42,210.80 ng/ml), medium concentration (9,915.20 to 22,933.75 ng/ml), and low concentration (2,247.20 to 6,020.05 ng/ml).

From the graph in Fig 1, for high concentration group (case 2, 7, 8) and medium concentration group (case 1, 3, 6, 9), the MAM concentration in gauze stains demon-

strated significant decrease ($p < 0.05$ for case 1; $p < 0.05$ for case 2; $p < 0.01$ for case 3; $p < 0.05$ for case 6; $p < 0.01$ for case 7; $p < 0.05$ for case 8; $p < 0.05$ for case 9) when compared to the MAM concentration in urine. Interestingly, the MAM concentration on filter paper stains was not significantly different from the concentration in urine.

As for the low concentration group (case 4, 5, 10), the MAM concentration in both gauze and filter paper stains demonstrated a significant difference from that in urine ($p < 0.01$ in gauze and filter paper for case 4; $p < 0.001$ in gauze and $p < 0.05$ in filter paper for case 5; $p < 0.01$ in gauze and $p < 0.05$ in filter paper for case 10). Although the MAM concentration in gauze and filter paper stains showed significant difference from that in urine, it showed that the MAM concentration in filter paper stains revealed higher values than in the gauze stains. Generally, MAM in urine stains from filter paper was recovered at a higher value than that from gauze stains.

Part II. Detection of MAM in Urine Stains at Different Duration and Temperature

2.1 Detection of MAM in urine stains on gauze at different duration and temperature

The result of the stability of MAM concentration in urine stains on gauze at different duration and temperature is shown in Fig 2. As for urine stains on gauze stored at 0 °C and 4 °C, the percentage of MAM concentration was found to be stable when compared to T_0 and not significantly different from T_0 in both temperatures at any time during the storage time for up to 24 weeks.

While gauze stains stored at RT, the percentage of MAM concentration obviously dropped at 3 days when compared to T_0 , and demonstrated significantly decreased difference from T_0 ($F_{6,36} = 33.87$, $p < 0.001$). There were slightly decreased in MAM concentrations through 4 weeks. Then obviously dropped again at 4 weeks through 12 weeks. The results gradually decreased until they reached the lowest values at 24 weeks ($19.54 \pm 8.64\%$) and the values were very low as compared to T_0 , $p < 0.001$. Thus, these results indicated that the storage time for up to 24 weeks could affect MAM concentration in urine stains when stored at room temperature.

Similarly, when gauze stains stored at OT, the percentage of MAM concentration obviously dropped at day 3 through 1 week, when compared to T_0 and demonstrated significantly decreased difference from T_0 . After 1 week, the percentage of MAM concentration continuously declined until it reached the lowest values at 24 weeks ($9.14 \pm 7.09\%$). Similar to those of RT, the percentage of MAM concentration was still significantly lower than T_0 in all storage times, $P < 0.001$. Similar to RT, a significant reduction in percentage of MAM concentration in urine stains on gauze was clearly demonstrated in OT, which verified deprivation of MAM concentration in gauze stains. Therefore, storage time affects MAM concentration in gauze stains in both RT and OT.

In each period, MAM concentrations for gauze stains at different temperature were compared. At day 3, the percentage of MAM concentration at RT and OT was lower when compared at 0 °C and 4 °C. However, there were no significant differences in the changes of MAM concentration among temperatures at this time.

At 1 week, the percentage of MAM concentration at RT and OT were clearly demonstrated lower than at 0 °C while those of OT were significantly lower than those of

RT ($p < 0.05$ for RT and $p < 0.001$ for OT). The decreases from 0 °C in MAM concentration at 2, 4, 12 and 24 weeks were extremely significant following the time. Therefore, these results indicate that temperature could affect MAM concentration in urine stains, which verified deprivation of MAM concentration in gauze stains at both RT and OT when stored after 3 days.

2.2 Detection of MAM in urine stains on filter paper at different duration and temperature

The study in this part is to compare the stability of MAM concentration in urine stains on filter paper when stored at 0 °C, 4 °C, RT, and OT at different durations: T_0 , 3 days, 1, 2, 4, 12, and 24 weeks. The result is shown in Fig 3.

As for urine stains on filter paper stored at 0 °C and 4 °C, the percentage of MAM concentration were found to be stable when compared to T_0 . The results were the same for the urine stains on gauze; the percentage of MAM concentration were not significantly different from T_0 in both temperature at any periods when stored over time for up to 24 weeks. These results thus indicate that urine stains on gauze and filter paper at different duration for up to 24 weeks showed no degradation and did not affect MAM concentration when stored at 0 °C and 4 °C.

While paper stains stored at RT and OT, the percentage of MAM concentration continuously decreased in the same manner until reached the lowest values at 24 weeks ($23.23 \pm 16.56\%$ and $15.75 \pm 7.02\%$) and was still significantly lower than T_0 in all storage times after 1 week ($p < 0.001$). However, the deprivation of MAM concentration for filter paper at RT was slower than those at OT in all periods of time. Therefore, storage time affects the MAM concentration in filter paper stains at both RT and OT.

MAM concentrations on filter paper stains at different temperature were compared in each storage time, 3 days and 1 week. Although the decrease of MAM concentration at OT was lower than RT, they were not significantly different from 0 °C at both storage times.

After 1 week through 24 weeks, the percentage of MAM concentration in all periods were still significantly lower than 0 °C ($p < 0.05$ for RT and $p < 0.001$ for OT at 2 weeks; $p < 0.01$ for RT and $p < 0.001$ for OT at 4 weeks; $p < 0.001$ for RT and OT for 12 weeks; $p < 0.001$ for RT and OT at 24 weeks). Hence, it confirmed that temperature could affect the stability of MAM in urine stains on filter papers at both RT and OT when stored after 1 week.

DISCUSSION

Part I. Detection of MAM in Urine Stains on Different Materials

Up to now, there have been few reports on the potential interest of stain samples in the specific field of forensic toxicology. Especially, detection of MAM in urine stains from drug users' urine has never been reported. Previous studies have been reported that drug-spiked urine stains such as amphetamine, benzoylecgonine, 11-nor-delta-9-tetrahydrocannabinol (THC-COOH), morphine, and phenacyclidine (PCP) on filter paper when kept frozen appear to provide a viable means for storing positive urine specimens⁵ and opiate drugs staining on a piece of clothing and underwear taken from the fatalities can be detected.²

This paper emphasizes on the detection of MAM in

urine stains from drug users' urine samples. The study in Part I was aimed to detect and to compare MAM concentration in urine and urine stains on gauze and filter-paper. Gauze was used as representative of cloths or garments which may be collected as forensic evidence. The advantage of both materials were found suitable for support matrix, stains with a maximum of 1 ml of urine, easily to control and convenient for processing sample before detection and for sending through the mail.

In this study, at the beginning the MAM concentration in all cases can be divided into three levels of concentration, i.e., high, medium, and low. As shown in Fig 1, the high and medium concentration groups in gauze stains demonstrated a significantly decrease but no significant difference in filter paper stains as compared to MAM concentration in urine. As for the low concentration group, although the MAM concentration in both gauze and filter paper stains demonstrated significant difference from that in urine, the MAM concentration in filter paper stains showed higher values than in gauze stains. These results thus indicated that type of material affects the detection of MAM concentration.

Noteworthy, MAM in urine stains from filter paper was recovered more than from gauze stains. Little information exists in the literature about the detection of drug in urine stains in different materials. DuBey and Caplan indicated that amphetamine could be detected in urine drug stains on Whatman No.1 filter paper and Whatman No.3 filter paper and found that the ideal matrix was to be Whatman No.3 filter paper with a maximum of 3 ml of urine. Drug recovery was optimum about 94% with the use of carbonate/bicarbonate buffer pH 9.2 elution solvent.⁵ Tracqui A and colleagues reported that the impregnation of underwear by urine provides detectable levels of opiate drugs extraction; unfortunately, they could not showed recovery of the drugs because of delayed autopsy.²

In this part, the detection of MAM in urine stains on filter paper showed the recovery of MAM about 92% this agreed with previous investigation and seemed to be very close when compared to those reported by DuBey and Caplan.⁵ As for the recovery of MAM concentration from gauze stains, the results were lower than from filter paper stains. The reason for the difference was seemingly because of the structure of gauze which is made of durable cellulose material, when extracted by vortex procedure, the vortex spun and rotated the gauze to be lumpy, or tangle mass. The binding capability of gauze was more durable when compared to filter paper. The structure of gauze contains cellulose, the basic ingredient of cotton and starches are both natural polymers built by combination of several thousand-carbohydrate monomers.¹ Hence, the structure is more complicated and held maximum urine than filter paper which is an advantage of gauze and has been successfully utilized to absorb urine. But this often takes time for solvent to penetrate gauze to displace the drug from its position. Therefore, percentage of recovery from gauze may be lower than it should be. As for filter paper, it is lighter than gauze when the vortex spins and rotates. It is also more dispersible than gauze, and solvent can penetrate it more easily; the percentage of recovery is therefore higher than gauze.

This study also suggests a modification of the method for determination of MAM in urine stain by the application of Whatman No.41 filter paper. It may be used as a choice for urine storage.

Part II. To Detect MAM in Urine Stains at Different Duration and Temperature

Storage of urine stains has been used in forensic science. Temperature and time are critical environmental factors for the storage. This part of the study is to compare the stability of MAM concentration in urine stains on gauze and filter paper when stored at 0 °C, 4 °C, room temperature (RT), and outdoor temperature (OT) at different durations: immediately (T_0), 3 days, 1, 2, 4, 12 and 24 weeks.

In Fig 2 and 3, the storage temperatures at 0 °C and 4 °C for up to 24 weeks did not significantly affect MAM concentration in urine stains on both gauze and filter paper. These data indicated that the suitable temperature for storage urine stains were at 0 °C and 4 °C. Long periods of refrigeration and frozen storage of MAM up to 24 weeks had no effect on MAM. This study demonstrates that it is possible to store urine specimens as dry stains and to recover the drug from the stains.

When stored at room temperature and outdoor temperature, there was some degradation of MAM. For both MAM concentration in urine stain on gauze and filter paper at 3 days, although the percentage of MAM were lower when compared at 0 °C and 4 °C (Fig 2 and 3); there were no significant difference in the change of MAM concentration between temperatures at this time. For 1 week, although the decrease of MAM concentration in urine stains on filter paper at RT and OT was lower than at 0 °C and 4 °C (Fig 3); however, they were not significantly different from 0°C. These results indicated that the MAM concentration on filter paper stains was more stable than on gauze stains within first week when stored in all four conditions. Because of the complicated structure of gauze and more absorbable property than filter paper as described in part I, therefore, percentage of recovery from gauze stains may be lower than it should be.

Storage after 1 week through 24 weeks, the percentages of MAM concentration in all periods were still significantly lower than 0 °C (Fig 2 and 3). The increase of storage and temperature indicated that it could affect the stability of MAM in urine stains from both gauze and filter paper at RT and OT when stored after 1 week. Many factors should be considered, as they may influence MAM concentration during storage. The storage at room temperature and outdoor could not protect specimens from contamination by the external environment such as temperature,^{6,7,8} light and UV⁹, biological cleavage, humidity, oxidation or combinations of these factors which were caused by chemical reactions. Certainly, the important factor that influences MAM concentration during storage is time. When storage time increases, it is also able to increase the effect from those factors and also more contamination from the environment. From Fig 2 and 3, the loss increased as storage time increased, when the storage temperature change was about 25-40 °C (RT and OT) the decrease in MAM was greater.

DuBey and Caplan indicated that amphetamine was stable in dry urine stains stored at room temperature for up to 12 weeks.⁵ It shows that the loss in our study was different from previous experiments. The drug may not persist or not be stable for two reasons: the drug may be degraded by higher temperature or humid environment in Thailand or may be due to certain internal factors such as microorganisms within the urine.

Beside temperature, the interactions of multiple environmental factors also determine the rate of biodegra-

dation. Microorganisms, moisture, oxygen interface are particularly significant in controlling biodegradation. Microorganisms have the efficiency in decomposition. The number of contaminated bacteria attached to the urine stains increases with the test periods. Oxygen is also very important in determining the extent and the rate of biodegradation. There is a direct relationship between oxygen consumption and temperature. Temperatures that enhance microbial activity are in the range of 28-55 °C, with the highest consumption rate of oxygen.^{10,11} In general, aerobic hydrocarbon biodegradation is much faster than anaerobic hydrocarbon biodegradation. Certainly, biological processes increase with increased temperature and the instability of drug relates to the number of bacteria. Therefore, by keeping specimens in 0 °C- 4 °C will be helpful in reducing the possibility of bacterial growth and environmental contamination. This can be concluded that the biological processes are generally decreased with decreasing temperatures. Likewise, specimens which are kept at room temperature may absorb water from the air, active bacterial reactions may be increased. Moreover, keeping samples in the refrigerator can protect light and environmental contamination. Some reports concluded that reduction of drug concentration was considered when the stored specimens were exposed to light.^{12,13}

For OT, the results were similar to RT and it gave some preliminary information to predict the degradation rate of MAM under this condition. Certainly, the specimen exposed to higher degree of temperature, light and UV, it could possibly lose more than RT environment. It was concluded that OT might reduce the stability of MAM. Hence, the degradation process in OT should be higher than RT. Nonetheless, these results indicated that the urine stains provide detectable levels of the drugs throughout 24 weeks of storage time.

In this study, the analytical methods were modified for rapid and reliable routine analysis with a potentiality to be used with a wide variety of drugs of abuse. Although these tests were conducted with MAM, the potentiality for the detection of many other drugs exists. Moreover, these general methods can be utilized in urine stain on toilet- paper, underwear, clothing, and padding which have been derived from the victim. It is much more convenient to send dry specimens to toxicological laboratory by mail instead of biological fluid.

CONCLUSION

The levels of MAM in urine stains from filter paper were recovered more than from gauze and they showed no significant difference from pure urine. Therefore,

storage of urine stains on filter paper may be used to replace pure urine storage.

Detection of MAM in urine stains when stored at 0 °C, 4 °C, room temperature, outdoor temperature for up to 24 weeks showed that the suitable temperature for storage urine stains were at 0 °C and 4 °C. The long periods of refrigeration and freezing of MAM up to 24 weeks had no effect on MAM. This study demonstrates that it is possible to store urine specimens dry, and still the drug can be recovered from them.

Although the storage at room temperature and outdoor temperature revealed some degradation of MAM, it shows that we could detect MAM from urine stains even after a long period, i.e., up to 24 weeks. The results of this study show that even at a low concentration, MAM could be recovered from urine stain analysis. This may still be a good supporting evidence of drug abuse of the owner of the urine stains.

ACKNOWLEDGEMENTS

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บทคัดย่อ

การตรวจหาเมทแอมเฟตามีนในคราบปัสสาวะ

วิชัย วงศ์ณะภัย พ.บ., ป.ร.ค., สุภาพร สุรินทร์ราช วท.ม., วรบุษ อุยประเสริฐกุล วท.ม., สมบูรณ์ ธรรมเกตุกิจ พ.บ.

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วัตถุประสงค์: การศึกษาที่มุ่งตรวจหาเมทแอมเฟตามีนในคราบปัสสาวะบนวัตถุ 2 ชนิด ประกอบด้วยผ้าก๊อช และกระดาษกรองที่เก็บไว้ในอุณหภูมิลดลงและสิ่งแวดล้อมที่แตกต่างกันในระยะเวลา 24 สัปดาห์

วิธีการ: นำน้ำปัสสาวะที่มีเมทแอมเฟตามีนในความเข้มข้นต่างๆ 10 ตัวอย่าง มาเตรียมคราบปัสสาวะบนผ้าก๊อช และกระดาษกรองโดยแต่ละชิ้นใช้น้ำปัสสาวะ 1 มิลลิลิตร โดยแต่ละชุดของคราบปัสสาวะถูกเก็บไว้ในที่อุณหภูมิ 0 องศาเซลเซียส, 4 องศาเซลเซียส, ในห้อง และนอกห้อง โดยหลีกเลี่ยงการถูกน้ำฝน คราบปัสสาวะถูกนำมาตรวจวิเคราะห์หาเมทแอมเฟตามีนด้วยเครื่อง TDx ตามลำดับเวลาดังนี้ ทันที, 3 วัน, 1 สัปดาห์, 2 สัปดาห์, 4 สัปดาห์, 12 สัปดาห์ และ 24 สัปดาห์

ผลการศึกษา: ความเข้มข้นของเมทแอมเฟตามีนในคราบปัสสาวะบนผ้าก๊อชมีค่าต่ำกว่าในน้ำปัสสาวะทุกระดับความเข้มข้นแต่คราบปัสสาวะในกระดาษกรองมีค่าต่ำกว่าในน้ำปัสสาวะเฉพาะที่ต่ำกว่า 5,000 นาโนกรัมต่อมิลลิลิตร เมทแอมเฟตามีนบนผ้าก๊อชและกระดาษกรองที่ถูกเก็บไว้ในที่อุณหภูมิ 0 องศาเซลเซียส และ 4 องศาเซลเซียส ไม่พบการเปลี่ยนแปลงของความเข้มข้นนานถึง 24 สัปดาห์ ส่วนที่เก็บในห้องและนอกห้อง ความเข้มข้นของเมทแอมเฟตามีนในผ้าก๊อช และกระดาษกรองลดลงอย่างต่อเนื่องโดยมีนัยสำคัญทางสถิติ ในช่วงระยะเวลา 24 สัปดาห์ ขณะที่ปริมาณเมทแอมเฟตามีนบนผ้าก๊อชและกระดาษกรองที่เก็บไว้ในนอกห้องลดลงมากและเร็วกว่าที่เก็บไว้ในห้องเมื่อเปรียบเทียบในเวลาเดียวกัน

สรุป: การตรวจพบเมทแอมเฟตามีนจากคราบปัสสาวะบนกระดาษกรองมีค่ามากกว่าบนผ้าก๊อช ปริมาณเมทแอมเฟตามีน ในคราบปัสสาวะบนผ้าก๊อช และกระดาษกรองจะคงที่เมื่อเก็บไว้ในที่อุณหภูมิ 0 องศาเซลเซียส และ 4 องศาเซลเซียส แต่ที่เก็บไว้ในห้องและนอกห้อง ปริมาณเมทแอมเฟตามีนจะลดลงอย่างต่อเนื่องในระหว่าง 24 สัปดาห์