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Storage of urine specimens in point of care (POC) urine drug testing cups reduces concentrations of many drugs

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ABSTRACT

Background: Many clinical toxicology laboratories receive urine specimens in urine cups that contain point of care (POC) drug testing strips. We conducted this study to evaluate the effect on the stability of commonly measured drugs in the clinical toxicology laboratory when urine is exposed to POC urine drug testing cups.
Methods: Drug free urine was spiked with 85 drugs that were measured by a validated liquid chromatography mass spectrometry (LCMS) method after exposure to POC urine drug testing cups at ambient and 2–6 °C temperatures. Alterations ≥20% were defined as significant changes in the drugs concentration.
Results: Concentrations of amitriptyline, cyclobenzaprine, fentanyl, fluoxetine, flunitrazepam, nortriptyline, paroxetine, and sertraline were significantly reduced when urine specimens were stored inside POC urine drug testing cups for 24 h at ambient temperature. Storage of urine in urine chemistry dipsticks reduced the concentration of several drugs. When spiked urine was exposed to an increasing number of POC urine drug testing strips, the concentrations of some drugs were reduced in a dose-dependent manner. The drugs that were absorbed by POC urine drug testing strips were partially back extracted from the strips.
Conclusion: Exposure of urine specimens to POC urine drug testing strips reduces the concentration of several drugs measured by LCMS method.

1. Introduction

Urine drug testing is used by clinicians in pain management clinics to monitor patient's compliance with prescribed drugs and consumption of unprescribed or illicit drugs [1–5].

Two main types of analytical methods are used to perform urine drug testing; immunoassay for presumptive or screening and mass spectrometry for confirmatory or definitive urine drug testing [6,7]. Immunoassay-based methods are performed in clinical laboratories by auto analyzers or at the clinicians' office using point of care (POC) urine drug testing strips. Many pain management clinics use urine cups that contain POC urine drug testing strips to assess the presence of drugs in urine specimens. Urine POC strips use the immunochromatography principle to qualitatively assess the presence or absence of around 10–15 commonly used drugs in urine [8]. Use of POC urine drug testing cups in clinicians' offices is rapid, easy-to-use, and cost effective [9]. However, due to low analytical sensitivity and specificity, the likelihood of false negative and false positive results is high. Therefore, positive results from POC urine drug testing cups are confirmed by a confirmatory method such as liquid chromatography mass spectrometry (LCMS) [10–14].

Some of the urine specimens received by clinical toxicology laboratories for confirmatory urine drug testing are in POC urine drug testing cups. These urine specimens may stay in the POC urine drug testing cups during transportation (24 or 48 h) and may be exposed to hot, summer temperatures. After being received by the clinical toxicology laboratories some of these specimens may be kept in the laboratory for a long period of time in order to be batched and submitted to LCMS. The effects on the concentration of drugs found in urine specimens exposed to POC urine drug testing strips has not previously been explored. However, the widespread assumption between clinicians and clinical laboratories is that the POC urine drug testing cups have no effect on the concentration of drugs. Several previous studies demonstrated that the exposure of blood to the gel of serum separator tubes (SST) alters the concentration of many drugs [15–18]. Therefore, the use of SSTs for measurement of drugs is not recommended. We conducted this study to investigate the stability of drugs that are exposed to POC urine drug testing strips before measurement by LCMS. To the best of our knowledge, this is the first study to report reduction in the concentrations of commonly measured drugs in pain management clinics following exposure to POC urine drug testing strips.

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2. Methods

2.1. Reagents and supplies

Three types of POC urine drug testing cups of Discover Plus (American Screening LLC, Shreveport, LA.), U-Screen (U.S. Screening Source, Inc. Pewee Valley, Kentucky) and First Sign (Hem sure, Inc. Irwindale, CA) were purchased from McKesson Corporation (Irving, TX). Urine chemistry strips, VELOCITY, were purchased from Beckman Coulter (Brea, CA). Syva Enzyme multiplied immunoassay (Emit) reagents were purchased from Siemens (Washington DC) for urine drug screening tests (immunoassay). All certified reference standards and isotope-labeled internal standard solutions were purchased from Cerilliant Corporation (Round Rock, TX). HPLC grade methanol and water were purchased from EMD Millipore Corporation (Darmstadt, Germany). HPLC grade isopropanol and LCMS grade formic acid were purchased from Fisher Scientific (Waltham, MA). Urine toxicology negative control (human drug free urine) was purchased from UTAK (Valencia, CA). β-glucuronidase enzyme and buffer for sample preparation were purchased from Integrated Micro-Chromatography Systems, IMCS (Irmo, SC).

2.2. Instrumentation and conditions

A dilute and shoot confirmatory LCMS method measured 85 drugs and metabolites. These included major categories of illicit drugs and drugs commonly prescribed for chronic pain patients. Table 1 shows the list of drugs/metabolites measured and their cutoff concentrations. LC–MS-MS analysis was performed on Shimadzu Nexera XR high-pressure liquid chromatography (HPLC) system (Shimadzu Corporation, Kyoto, Japan) coupled with a Sciex 4500 mass spectrometer (AB Sciex, Framingham, MA). In both methods, the chromatography separation was performed on a Raptor™ Biphenyl column, 2.7 μm, 50 × 3.0 mm (Restek, Bellefonte, PA) using gradient elution comprising of 0.1% formic acid and 0.1% ammonium formate in water (mobile phase A) and 0.1% formic acid in methanol (mobile phase B). A Raptor Biphenyl EXP Guard Column Cartridge (2.7 μm, 5 × 3.0 mm) was installed preceding the bi-phenyl analytical column. Analytes were detected by mass spectrometry using scheduled multiple reaction monitoring (MRM) in either positive or negative electrospray ionization (ESI) modes. Among the measured drugs 83 were detected in a positive ionization method and 2 in a negative ionization method (butalbital and phenobarbital). Two characteristic MRM transitions were monitored for each analyteThe MRM ratios, which are defined as the peak area ratios between primary and secondary ion transitions, were only acceptable if within ≤30% for all analytes. The data was collected using the AB Sciex Analyst, 1.7 software and quantified with the MultiQuant, 2.1 software. Urine drug screening tests (immunoassay) were performed by Beckman AU 680 chemistry autoanalyzer (Beckman Coulter, Brea, CA). Supplementary table 1 indicates cutoff values for the analytes that were measured with the immunoassay method.

2.3. Sample preparation

In a 1.5 mL microcentrifuge tube, 100 μL of each urine specimen, calibrator, or control was added. Then, 40 μL of IMCS rapid hydrolysis buffer, 30 μL of β-glucuronidase enzyme, (activity > 50 KU/mL) and 10 μL of internal standard mix were added to each tube. Specific deuterated internal standards were used for each analyte. The tubes were vortexed for 10 s, incubated at 55 °C for 30 min, and 500 μL of sample diluent was added to all samples (0.1% formic acid in 75:25 water/methanol). The tubes were vortexed for 10 s and were centrifuged at 3700 rpm for 15 min. To inject the samples into LCMS, 100 μL of supernatant was transferred into a vial.

2.4. Assay validation

The method was developed and validated using Food and Drug Administration recommendations for validation of mass spectrometry methods [19]. Precision, accuracy, analytical measurement range,

Table 1
List of drugs and metabolites and their cutoff concentrations that were measured in the study, using liquid chromatography mass spectrometry method.

N	Analyte	Cutoff ng/ml	N	Analyte	Cutoff ng/mL	N	Analyte	Cutoff ng/mL
1	6-MAM	10	30	Alprazolam,	25	59	Gabapentin	1000
2	Codeine	50	31	Flunitrazepam	50	60	Pregabalin	200
3	Tapentadol	50	32	Hydroxytriazolam	25	61	Quetiapine	50
4	Desmethyltapentadol	50	33	Lorazepam,	50	62	Ritalinic Acid	50
5	Methadone	100	34	Nordiazepam	50	63	Phentermine	100
6	EDDP	100	35	Oxazepam	50	64	Zaleplon	10
7	Fentanyl	2.5	36	Temazepam	50	65	Zolpidem	10
8	Norfentanyl	5	37	Amitriptyline	25	66	Butalbital	100
9	Hydrocodone,	50	38	Nortriptyline	25	67	Phenobarbital,	100
10	Hydromorphone	50	39	Doxepin	25	68	Acetaminophen	250
11	Morphine	50	40	Venlafaxine	100	69	Aripiprazole	50
12	Naloxone	10	41	Desmethylvenlafaxine	100	70	Atomoxetine	50
13	Norhydrocodone	50	42	Paroxetine	50	71	Baclofen	50
14	Noroxycodone	50	43	Sertraline	50	72	Buspirone	10
15	Norpropoxyphene	50	44	Bupropion	10	73	Carbamazepine	50
16	Tramadol	100	45	Citalopram	50	74	Clozapine	50
17	Desmethyltramadol	100	46	Duloxetine	25	75	Haloperidol	50
18	Oxycodone	50	47	Protriptyline	50	76	Levetiracetam	50
19	Propoxyphene	50	48	Amphetamine	100	77	Naproxen	100
20	Oxymorphone	50	49	Methamphetamine	100	78	Olanzapine	50
21	Tapentadol	50	50	MDA	100	79	Risperidone	25
22	Buprenorphine	10	51	MDMA	100	80	Ibuprofen	500
23	Norbuprenorphine	25	5	Pseudoephedrine	25	81	Salicylic Acid	500
24	Naltrexone	50	53	Benzoylecgonine	50	82	Topiramate	50
25	Dextromethorphan	100	54	Phencyclidine	25	83	Cotinine	100
26	Dextrorphan	100	55	THCA	15	84	Ketamine	25
27	7-Aminoclonazepan	50	56	Carisoprodol	50	85	Norketamine	25
28	a-Hydroxyalprazolam	25	57	Meprobamate	100			
29	a-Hydroxymidazolam	25	58	Cyclobenzaprine	25			

sensitivity (limit of detection and limit of quantification), specificity, interference, matrix effect, recovery, carry over limit, and stability of specimens during transportation and storage were assessed. All passed the pre-defined acceptance criteria [19]. Limit of quantification for each analyte was at least 50% lower than the cutoff concertation. Limit of detection for each analyte was at least 50% lower than limit of quantification for each analyte. Precision acceptance criteria was a coefficient variation (CV) % < 15%. All measured analytes had a linear calibration curve within the analytical measurement ranges and a concentration-response relationship fitted with a regression model (r > 0.98 for all the assays). The accuracy of each assay was acceptable when the deviation of each calibrator was < ± 15% from the nominal concentration of the calibrators. Using morphine glucuronide as a hydrolysis control, the hydrolysis efficiency was > 85% (data not shown).

2.5. Effect of POC urine drug testing strips on stability of drugs

Drug free urine specimens were spiked with 85 drugs at the levels of drug cutoff (Table 1), and the concentration of all drugs was measured before exposure to Discover Plus POC urine drug testing cups.

Spiked urines (50 mL) were stored in Discover Plus POC cups without drug testing strips under the same conditions and were used as a control for the experiments. During the experiments, the spiked urine specimens were stored at ambient temperature, in a refrigerator, and in an incubator at 35 °C for various time ranges. Three levels of quality controls materials with low, medium, and high concentrations were used concurrently throughout the analysis. POC urine drug testing cups from three manufacturers were investigated to assess their effects on the drug concentrations: Discover Plus, U-Screen and First Sign.

The urine drug testing strips were used to detect either commonly prescribed groups of drugs in pain management clinics such as opiates, buprenorphine, amphetamines, barbiturates, methadone, and benzodiazepines or illicit drugs or metabolites including cocaine, phencyclidine (PCP), and *tetrahydrocannabinol carboxylic acid* (THC-COOH). An alteration ≥20% was defined as significant change in the drug concentrations. This same level of variation is considered acceptable by the majority of toxicology laboratories for evaluation of accuracy during method development and as an acceptable accuracy range for quality control materials. The drug concentrations were selected at cutoff concentrations to reflect the concentrations used by clinicians to differentiate a positive and negative quantitative result of confirmatory urine drug testing.

To evaluate whether or not the effect of POC urine drug testing strips on drug concentrations depends on the number of drug testing strips, the spiked urines (50 mL) were exposed to increasing number of POC urine drug testing strips for 24 h and the drugs levels were measured.

In the chemistry part of urinalysis, urine chemistry dipsticks are used to test for glucose or protein. Spiked urine (50 mL) was exposed to an increasing quantity of urine chemistry dipsticks to assess whether the effect of POC urine strips on the drug concentrations is a specific reaction.

2.6. Effect of POC urine drug testing strips on the stability of drugs in patient's urine specimens

To test whether urine drug testing strips have an effect on the concentration of drugs in the patients` urine, specimens from 25 patients were evaluated. The specimens were selected from patients of pain management clinics in which one or more drugs were detected in their urine specimens by LCMS method. The specimens were received in regular urine cups and were analyzed as other specimens. The urine (50 mL) was then placed in both a Discover Plus cup with POC urine drug testing strips and a Discover Plus cup without urine drug testing strips (control). Both cups were kept at ambient temperature for 24 h and the concentration of drugs was measured by LCMS method. The concentration of drugs in specimens that were kept in cups with POC urine drug strips were compared to the specimens that were kept in urine cups without POC urine drug testing strips. The data from patients that had a drug concentration that exceeded the laboratory upper limit of quantification were not used as the measurement was not quantitatively reliable. Alterations ≥20% were defined as significant change in the drug concentrations.

2.7. Extraction of drugs from POC drug testing strips and urine chemistry dipsticks after exposure to spiked urine

To evaluate whether the reduction of drug concentrations was due to absorption by POC urine drug testing strips or urine chemistry dipsticks, drug free urine was spiked with 85 drugs at 2.5 X cutoff concentrations (Table 1). Spiked urine (50 mL) was placed in discover Plus POC urine drug testing cups without strips, with 3 sets of POC urine drug testing strips or with 5 urine chemistry dipsticks at ambient temperature. After 24 h, the strips were removed from the cups, air dried for 30 min, and were placed in a cup with drug free urine for two hours while shaking at ambient temperature. After two hours the urine inside the cups was collected and used for the drug measurement.

3. Results

3.1. Exposure of urine to POC urine drug testing cups at ambient temperature or refrigerator reduces concentrations of many drugs

Fifty millimeters of spiked urine was poured in Discover Plus POC urine drug testing cups that had urine drug testing strips or did not contain urine drug testing strips (control) and stored at ambient temperature. The drug concentrations were measured after 24 h using the LCMS method. Concentrations of amitriptyline, cyclobenzaprine, fentanyl, fluoxetine, flunitrazepam, nortriptyline, paroxetine, and sertraline were significantly reduced within a range of 21–65% (Fig. 1). The spiked urine was exposed to POC cups that either had urine drug testing strips or did not contain urine drug testing strips (control) for 24 h in refrigerator (2–6 °C). In the urine that contained urine drug testing strips the concentration of amitriptyline, cyclobenzaprine, paroxetine, sertraline, duloxetine and buprenorphine were significantly reduced (Fig. 2). Exposure for 48 h in the refrigerator added fentanyl,

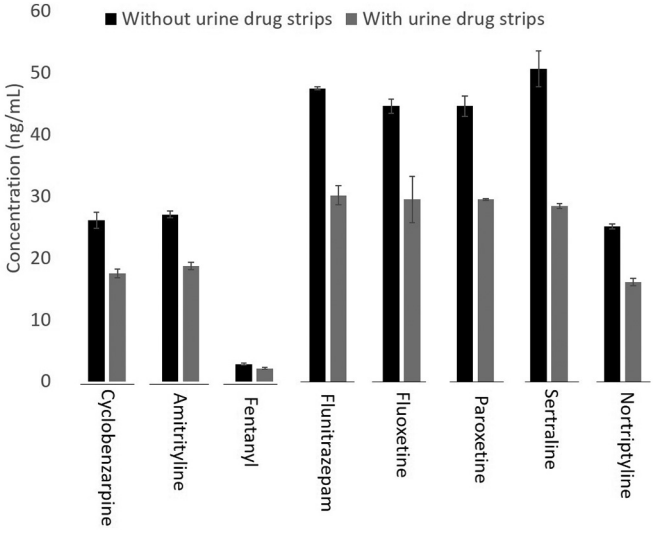

Fig. 1. Drug concentrations measured after exposure of spiked urine to POC urine drug testing cups at ambient temperature for 24 h. Drug free urine (50 mL) was spiked with 85 drugs at their cutoff concentrations and placed in Discover Plus POC urine drug testing cups with and without (control) urine drug testing strips (n = 3).

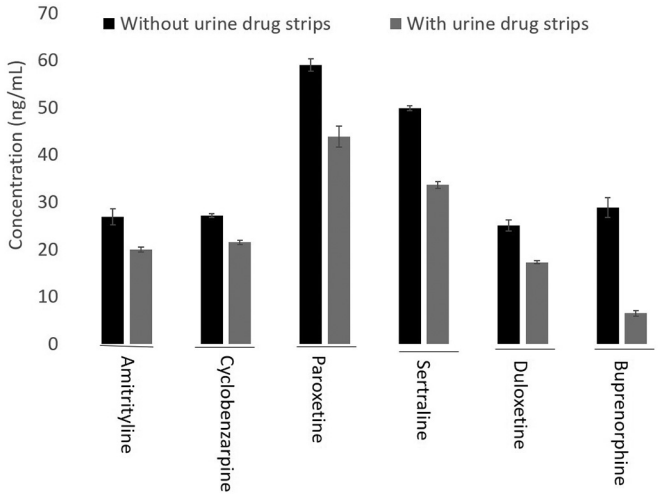

Fig. 2. Drug concentrations measured after exposure of spiked urine to POC urine drug testing cups at refrigerator temperature for 24 h. Drug free urine (50 mL) was spiked with 85 drugs at their cutoff concentrations and placed in Discover Plus POC urine drug testing cups with and without (control) urine drug testing strips (n = 3).

acetaminophen, atomoxetine, bupropion, desipramine, haloperidol, propoxyphene, fluoxetine, nortriptyline, dextromethorphan and doxepin to the list of affected drugs that showed reduction in the analyte concentrations (supplementary Fig. 1). The effects of storage of urine in POC urine drug testing strips on the reduction of drug concentrations was accelerated when spiked urine was exposed to POC urine drug testing strips at 35 °C for 24 h (supplementary table 2).

The effects of urine exposed to POC drug strips on concentration of measured drugs was observed to a similar extent in three commonly used POC urine drug testing cups, Discover Plus, U-Screen and First Sign (supplementary table 3).

3.2. Exposure of patients' urine to urine drug testing strips reduces concentration of some drugs

When urine specimens from 25 patients were exposed to urine drug testing strips for 24 h at ambient temperature, concentrations of nortriptyline, dextromethorphan, bupropion, fluoxetine, cyclobenzaprine, amitriptyline, nordiazepam, oxazepam, paroxetine, and sertraline were significantly reduced. Table 2 indicates the reduction in concentration of the drugs compared to the same urine specimens that were kept at ambient temperature for 24 h in urine cups without urine drug strips.

3.3. The urine drug testing strips not the cup or strip holder are responsible for reduction of drug concentrations after exposure of urine to POC urine drug testing cup

POC urine drug testing cups contain a cup, urine drug testing strips and a plastic frame that holds the strips, plastic strip holder, (supplementary Fig. 2). In each POC urine drug testing cup, cup, plastic strip holder or strips can contribute to the reduction of drug concentrations. Exposure of spiked urine (50 mL) to the either the Discover Plus POC cup without urine drug testing strips or plastic strip holder and to Discover Plus POC cups with the plastic strip holder but no strips did not affect drug concentrations. However, when spiked urine was exposed to POC urine drug testing strips the concentration of drugs was reduced significantly (data not shown). This suggests that the observed reduction of drug concentrations is most likely due to POC urine drug testing strips, not the cup itself or the plastic strip holder.

3.4. POC urine drug testing strips reduce concentration of drugs in urine specimens

When the spiked urines were exposed to an increasing number of POC urine drug testing strips for 24 h, at ambient temperature, the concentrations of several drugs were reduced (Fig. 3). Fig. 3 shows a representative set of drugs in which their concentrations reduced in a linear manner.

3.5. Exposure of urine specimens to urine chemistry dipsticks used in urinalysis reduces the concentration of drugs

To investigate whether or not the effect of POC urine drug testing strips on reduction of drug concentrations is specific, the impact of urine chemistry dipsticks on drug concentrations was examined. Exposure of 50 mL of spiked urine to an increasing number of urine chemistry dipsticks at ambient temperature, for 24 h, showed a reduction in concentrations of several of the measured drugs (Fig. 4).

3.6. The absorbed drugs can be back extracted from POC urine drug testing strips or urine chemistry dipsticks after the exposure

Each POC urine drug testing cup contains a set of strips that has 13 strips. When spiked urine was exposed to either 3 sets of POC urine drug testing strips or 5 urine chemistry dipsticks for 24 h at ambient temperature, the concentrations of many drugs were significantly reduced. A significant portion of the drugs were back extracted from POC urine drug testing strips or urine chemistry dipsticks. Fig. 5 and supplementary Fig. 3 indicate several representative drugs that were back extracted from POC urine drug testing strips or urine chemistry dipsticks, respectively.

4. Discussion

Our studies demonstrated that the exposure of urine to POC urine drug testing strips reduces the concentration of many drugs. The alteration in the concentration of drugs is not specific to POC urine drug testing strips as urine chemistry dipsticks show the same effect.

As we have shown in our study, neither the POC cup nor plastic holder for the strips play a significant role in the reduction of drug concentrations. The effect depends solely upon the presence of urine drug testing strips. We hypothesize that either the materials used in the urine drug testing strips pad or the chemicals embedded in the pad contribute to the effect of POC urine drug testing strips in reducing the concentration of measured drugs. The reduction in the drug concentrations is not specifically related to antibodies embedded in the POC urine drug testing strips pad. This is because most of the affected drugs are not tested by the POC urine drug testing strips and therefore, no specific antibodies against them are present. The POC urine drug testing cups that we evaluated did not measure tricyclic antidepressants and selective serotonin reuptake inhibitors, yet the concentrations of these drugs were reduced after exposure to POC urine drug testing cups. In addition, the effect is not limited to POC urine drug testing strips. Urine chemistry dipsticks also reduced the drug concentrations in a similar manner. It is possible that both POC strips and urine chemistry dipsticks use similar absorbent materials in their pads to absorb the drugs. We were able to partially back extract the absorbed drugs from both POC urine drug testing strips and urine chemistry dipsticks, suggesting that the reduction in the drugs concentration is possibly a physical, not a chemical phenomenon. Further investigation is needed to determine which materials from POC urine drug testing strips are responsible for the effects on the drug concentrations. In most clinical toxicology laboratories urine specimens that are used for confirmatory urine drug testing are considered stable for a week at ambient temperature, two weeks in the refrigerator, and one month or longer in the freezer [19,20]. Our studies indicated that even storage of urine

Table 2
Urine specimens were selected from patients that had a positive result for at least one drug and were exposed to urine cups with or without urine drug testing strips for 24 h at room temperature.

Sample accessioning number	Component name	Concentration, 24 h in regular urine drug testing cups (ng/mL)	Concentration, 24 h in POC urine drug testing cups (ng/mL)	Difference (%)
10,014	Nortriptyline	147	13	−90
10,020	Nortriptyline	118	16	−85
10,008	Nortriptyline	344	72	−79
10,014	Dextromethorphan	477	110	−76
10,007	Bupropion	96	31	−67
10,011	Fluoxetine	300	117	−60
10,016	Cyclobenzaprine	56	25	−54
10,012	Amitriptyline	86	40	−53
10,002	Fluoxetine	99	50	−48
10,010	Fluoxetine	386	206	−46
10,020	Nordiazepam	227	122	−46
10,020	Oxazepam	247	135	−45
10,015	Fluoxetine	468	316	−32
10,013	Paroxetine	78	53	−31
10,017	Sertraline	325	225	−30
10,001	Sertraline	165	114	−30
10,021	Paroxetine	266	189	−28
10,009	Fluoxetine	380	279	−26
10,004	Fluoxetine	218	175	−19
10,008	Amitriptyline	216	179	−17

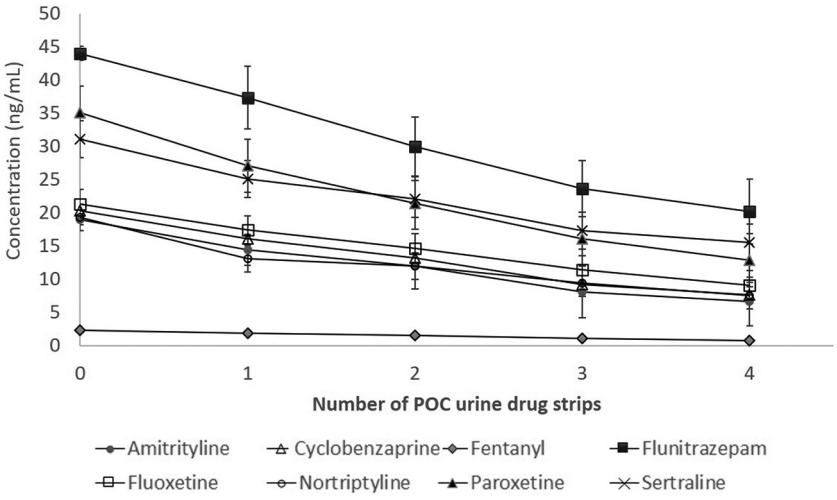

Fig. 3. Drug concentrations measured after exposure of spiked urine to increasing number of POC urine drug testing strips at ambient temperature for 24 h. Drug free urine (50 mL) was spiked with 85 drugs at their cutoff concentrations and placed in Discover Plus POC urine drug testing cups with 0, 1, 2, 3, and 4 sets of urine drug testing strips at ambient temperature (n = 3).

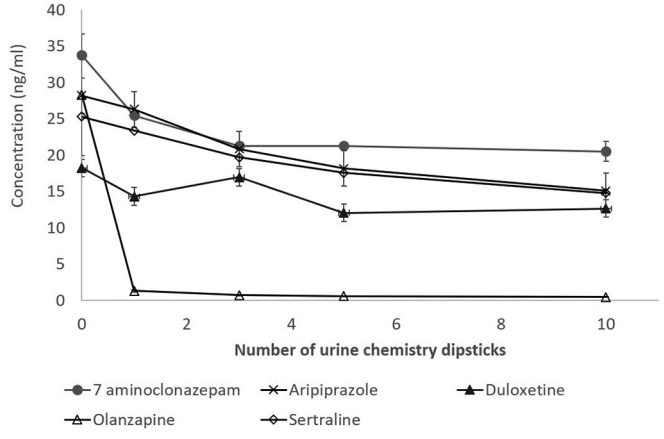

Fig. 4. Drug concentrations measured after exposure of spiked urine to increasing number of urine chemistry dipsticks at ambient temperature for 24 h. Drug free urine (50 mL) was spiked with 85 drugs at their cutoff concentrations and placed in Discover Plus POC urine drug testing cups with 0, 1, 3, 5, and 10 urine chemistry dipsticks at ambient temperature (n = 3).

specimens in the refrigerator cannot stop the effect of POC urine drug testing strips on drug concentrations. The longer the storage time, the more drugs that are affected. Urine specimens are typically transported at ambient temperature, even in the summer. There are times, especially during weekends, that the transportation time is 48 h. In some states of United States of America, the outdoor temperature can exceed 40 °C in the summer months. Our studies indicate that the exposure of urine specimens to POC urine drug testing cups at 35 °C for 24 h can dramatically reduce the concentration of a large list of drugs.

In our studies we found that some drugs, such as tricyclic antidepressants (amitriptyline, nortriptyline, and doxepin) and selective serotonin reuptake inhibitors (fluoxetine, sertraline, and paroxetine) are more susceptible to the effects of POC urine drug testing strips than other classes of drugs. The mechanism behind this susceptibility has not been previously explored and would merit further investigation. However, our personal observation on the stability of these drugs indicates that even when kept in regular urine cups, these drugs are less stable at ambient temperature or in the refrigerator than the other drugs commonly measured at clinical toxicology laboratories (unpublished data). The stability of tricyclic antidepressants and selective serotonin reuptake inhibitors drugs in urine has not been fully investigated. However, some previous studies suggested a shorter

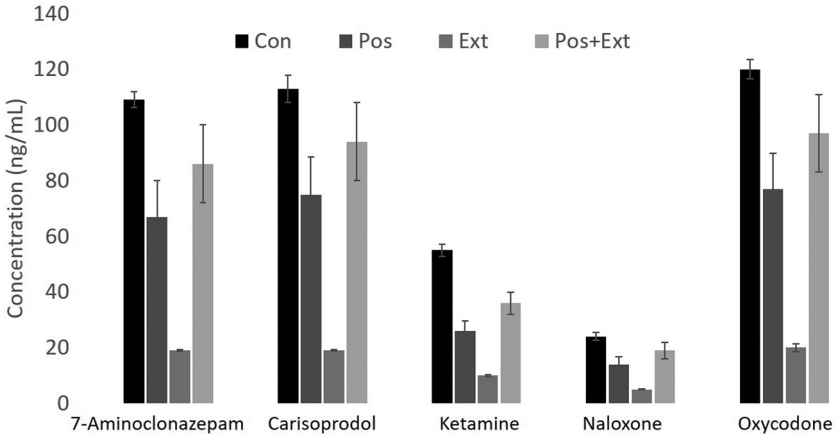

Fig. 5. Several drugs were back extracted from POC urine drug testing strips. Bars show the concentration of drugs when urines were exposed for 24 h to POC cups without urine drug testing strips (Con), POC urine drug testing strips (Pos), first exposed to POC urine drug testing strips then dried and exposed to drug free urine for 2 h (Ext). Pos + Ext, sum of Pos and Ext conditions (n = 3).

stability for urinary levels of these drugs 21,22]. Our studies suggest that the reduction in drug concentrations after exposure to POC urine drug testing cups is not due to conversion of parent drugs to their metabolites. We measured several pairs of parent drugs and their corresponding metabolites such as amitriptyline and nortriptyline, fentanyl and norfentanyl, ketamine and norketamine, and oxycodone and noroxycodone. None of the studied pairs detected a decrease in the parent drug that was associated with an increase in their corresponding metabolite. Van Acker et al. [23] demonstrated that when urine is exposed to urine chemistry strips some agents can be leached out from the strips that can produce many unknown mass spectra in gas chromatography/mass spectrometry (GC/MS). Two of the known chemicals that leached out from the strips were tetramethylbenzidine and caffeine.

4.1. Clinical application

Urine specimens that are exposed to POC urine drug testing strips for longer than 24 h should not be used for measurements of drugs with a confirmatory method (LCMS) of urine drug testing. It is recommended that before the shipment of urine specimen the strips are removed from the POC urine drug testing cups. As an alternative solution, an aliquot of the specimen could be transferred to a regular urine cup to be transported to a clinical toxicology laboratory before exposing it to POC urine drug testing strips.

4.2. Conclusion

Exposure of urine specimens to POC urine drug testing strips at ambient temperature or refrigeration temperature reduces the concentration of several drugs. The reduction in the concentration of drugs is not specific to POC urine drug testing strips as urine chemistry dipsticks show the same effect.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cca.2019.09.001.

References

[1] J.L. Starrels, W.C. Becker, D.P. Alford, A. Kapoor, A.R. Williams, B.J. Turner, Systematic review: treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain, Ann. Intern. Med. 152 (2010) 712–720.
[2] R.A. Deyo, S.K. Mirza, J.A. Turner, B.I. Martin, Overtreating chronic back pain: time to back off? J Am Board Fam Pract. 22 (2009) 62–68.
[3] N. Katz, G.J. Fanciullo, Role of urine toxicology testing in the management of chronic opioid therapy, Clin. J. Pain 18 (2002) S76–S82.
[4] D. Dowell, T.M. Haegerich, R. Chou, CDC guideline for prescribing opioids for chronic pain–United States, JAMA. 315 (2016) 1164–1624.
[5] L. Manchikanti, S. Abdi, S. Atluri, C.C. Balog, et al., American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: part 2–guidance, Pain Physician. 15 (2012) S67–116.
[6] M. Haidari, Essential Knowledge for the Interpretation of Urine Drug Testing Results (a Clinician's Guide), First ed., (2019) Self-published https://www.amazon.com/Essential-Knowledge-Interpretation-Testing-Clinician%60s/dp/0578200112/ref=sr_1_1?keywords=Mehran+Haidari&qid=1562343844&s=gateway&sr=8-1.
[7] P.J. Christo, L. Manchikanti, X. Ruan, M. Bottros, H. Hansen, D.R. Solanki, A.E. Jordan, J. Colson, Urine drug testing in chronic pain, Pain Physician. 14 (2011) 123–143.
[8] Y.Z. Chang, W.F. Yao, K.P. Hsiung, M.S. Chiou, H.Y. Li, Numerical analysis of an immunochromatographic test strip reader in abused drugs screening, J Immunoassay Immunochem. 33 (2012) 180–194.
[9] A. Pesce, M. Rosenthal, R. West, C. West, B. Crews, C. Mikel, P. Almazan, S. Latyshev, An evaluation of the diagnostic accuracy of liquid chromatography-tandem mass spectrometry versus immunoassay drug testing in pain patients, Pain Physician. 13 (2010) 273–281.
[10] R. Gencheva, A. Petrides, M. Kantartjis, M. Tanasijevic, J.L. Dahlin, S. Melanson, Clinical benefits of direct-to-definitive testing for monitoring compliance in pain management, Pain Physician. 21 (2018) E583–E592.
[11] A. Saitman, H.D. Park, R.L. Fitzgerald, False-positive interferences of common urine drug screen immunoassays: a review, J. Anal. Toxicol. 38 (2014) 387–396.
[12] L. Manchikanti, Y. Malla, B.W. Wargo, B. Fellows, Comparative evaluation of the accuracy of immunoassay with liquid chromatography tandem mass spectrometry (LC/MS/MS) of urine drug testing (UDT) opioids and illicit drugs in chronic pain patients, Pain Physician. 14 (2011) 175–187.
[13] K.E. Moeller, J.C. Kissack, R.S. Atayee, K.C. Lee, Clinical interpretation of urine drug tests: what clinicians need to know about urine drug screens, Mayo Clin. Proc. 92 (2017) 774–796.
[14] A. Dasgupta, M.A. Yared, A. Wells, Time-dependent absorption of therapeutic drugs by the gel of the Greiner Vacuette blood collection tube, Ther. Drug Monit. 22 (2000) 427–431.
[15] F. Quattrocchi, H.T. Karnes, J.D. Robinson, L. Hendeles, Effect of serum separator blood collection tubes on drug concentrations, Ther. Drug Monit. 5 (1983) 359–362.
[16] P.J. Orsulak, M. Sink, J. Weed, Blood collection tubes for tricyclic antidepressant drugs: a reevaluation, Ther Drug Moni. 6 (1984) 444–448.
[17] A. Dasgupta, R. Dean, S. Saldana, G. Kinnaman, R.W. McLawhon, Absorption of therapeutic drugs by barrier gels in serum separator blood collection tubes. Volume- and time-dependent reduction in total and free drug concentrations, Am. J. Clin. Pathol. 101 (1994) 456–461.
[18] U.S. Department of Health and Human Services, Food and Drug Administration Bioanalytical Method Validation Guidance for Industry, https://www.fda.gov/downloads/drugs/guidances/ucm070107.pdf, (May 2018).
[19] E. Gonzales, G. Ng, A. Pesce, C. West, R. West, C. Mikel, S. Latyshev, P. Almazan, Stability of pain-related medications, metabolites, and illicit substances in urine, Clin. Chim. Acta 416 (2013) 80–85.
[20] M. Pellegrini, S. Graziano, L. Mastrobattista, A. Minutillo, F.P. Busardo, G. Scarsella, Stability of drugs of abuse in urine samples at ambient temperature by use of a salts mixture, Curr. Pharm. Biotechnol. 18 (2017) 815–820.
[21] R. Das, Y.K. Agrawal, Simultaneous monitoring of selective serotonin reuptake inhibitors in human urine, plasma and oral fluid by reverse-phase high performance liquid chromatography, J. Chromatogr. Sci. 51 (2013) 146–154.
[22] J.L. Poklis, C.E. Wolf, A. Goldstein, M.L. Wolfe, A. Poklis, Detection and quantification of tricyclic antidepressants and other psychoactive drugs in urine by HPLC/MS/MS for pain management compliance testing, J. Clin. Lab. Anal. 26 (2012) 286–294.
[23] J.T. Van Acker, A.G. Verstraete, M.A. Van Hamme, J.R. Delanghe, Falsely increased urinary caffeine attributable to contamination by urine test strips, Clin. Chem. 45 (1999) 1315–1317.