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Rapid Cleanup and Comprehensive Screening of Pain Management Drugs in Urine using Automated Disposable Pipette Extraction and LC-MS/MS

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KEYWORDS

DPX, LC-MS/MS, Sample Preparation, High Throughput Lab Automation

ABSTRACT

This study focuses on the automated extraction of small volumes of urine samples (< 500 μ L) using disposable pipette extraction (DPX) for the comprehensive screening for pain management drugs by LC-MS/MS. Using a GERSTEL MPS autosampler, DPX extractions of hydrolyzed urine were performed, using a reversed phase (DPX-RP-S) sorbent. The resulting eluents from the DPX extractions were automatically diluted and injected into an Agilent® Technologies LC-MS/MS system. Sample preparation was performed just-in-time enabling high throughput screenings, averaging a cycle time of 7 min/sample.

Validation results show that the automated DPX-LC-MS/MS screening method provides adequate sensitivity for over 65 analytes and internal standards. Lower limits of quantitation (LLOQ) ranged between 0.5 - 50 ng/mL and % RSDs were below 10% in most cases.

INTRODUCTION

Toxicology laboratories are trying to find ways to minimize sample preparation and enhance productivity. The adaptation of LC-MS/MS instrumentation is desired due to the high sensitivity, high selectivity, low detection limits (e.g., 1 ng/mL), smaller sample volumes used, and also due to the fact that LC-MS/MS doesn't require chemical derivatization of analytes. Conventional sample preparation methods involve liquid-liquid or solid-phase extraction (SPE). A different approach is to use SPE to extract the sample matrix. In this case, matrix interferences are bound to the sorbent in order to be removed from the analyte solution. The major advantage of this approach is that no separate wash or elution steps are required, enabling rapid sample preparation while still allowing comprehensive screening of the cleaned sample.

Disposable Pipette Extraction (DPX) was developed as an alternative to traditional SPE, combining efficient and rapid extraction with significantly reduced solvent consumption. DPX is a novel dispersive solid-phase extraction technique that uses sorbent loosely contained in a pipette tip enabling highly efficient mixing with the sample solution. The main advantages of DPX technology are: rapid extraction, high recoveries, negligible solvent waste generation, and full automation of the extraction combined with introduction to the chromatographic system.

We have developed a fast automated DPX urine cleanup method using a GERSTEL MultiPurpose Sampler (MPS XL) for comprehensive screening of 49 pain management drugs with LC-MS/MS. The reversed phase sorbent (DPX-RP-S) used in the method allows the removal of salts and proteins present in urine, resulting in reduced matrix effects. The sorbent is chosen to extract the matrix without binding or absorbing the analytes of interest providing high recoveries. The schematic for the DPX "Cleanup" procedure is shown in Figure 2. Since the extraction time (3 min) is less than the analytical LC-MS/MS run time (4 min), the extraction of one sample can be performed during the chromatographic analysis of the previous sample, achieving high throughput while processing each sample "just in time" ensuring that all samples are treated identically.

EXPERIMENTAL

Materials. Stock solutions for the compounds listed in Table 1 were purchased from Cerilliant. An intermediate analyte stock solution was prepared by combining the analyte stock solutions with acetonitrile, at appropriate concentrations, to evaluate the different drug classes.

Deuterated analogues, d_3 -morphine, d_4 buprenorphine, d_3 -norbuprenorphine, d_9 -methadone, d_3 -tramadol, d_5 -fentanyl, d_5 -alpha-hydroxy alprazolam, d_4 -clonazepam, d_5 -oxazepam, d_5 -estazolam, d_3 -cocaine, d_5 -nordiazepam, d_5 -propoxyphene, d_7 -carisoprodol, d_5 amphetamine, d_4 -ketamine, d_4 -7-aminoclonazepam, and d_5 -PCP were purchased from Cerilliant. Table 1 shows which deuterated internal standard was used for each respective analyte during quantitation.

High concentration calibration standard and intermediate QC urine samples were prepared by making appropriate dilutions of the combined intermediate analyte stock solution using analyte free urine to give the concentrations listed in Table 1. Calibration standards were then prepared using a dilution ratio strategy from the high concentration sample of 1:2:2:2.5:2. The high, medium and low QC samples were prepared using a dilution ratio strategy from the high concentration sample of 1:1.33:3.33: 8. ß-Glucuronidase, Type-2, from Helix pomatia, (cat.#G0876-5mL) was purchased from Sigma-Aldrich. Fresh urine was obtained from a male volunteer. All other reagents and solvents used were reagent grade.

Instrumentation. All automated DPX PrepSequences were performed using a MultiPurpose Sampler (MPS XL Dual Tower) with GERSTEL DPX Option as shown in Figure 1. All analyses were performed using an Agilent[®] 1290 Infinity LC with a Zorbax Eclipse Plus C18 column (2.1 x 50 mm, 1.8 μ m, 600 bar), an Agilent 6460 Triple Quadrupole Mass Spectrometer with Jet stream electrospray source and GERSTEL MPS XL autosampler configured with an Active Wash Station (AWS). Sample injections were made using a 6 port (0.25mm) Cheminert C2V injection valve fitted with a 2 μ L stainless steel sample loop.



Figure 1. MPS 2XL multi-purpose sampler with the GERSTEL DPX option for high throughput pain management drug screening.

Sample pretreatment. Hydrolysis of urine was performed by combining 2 mL of urine, 150 μ L of the working internal standard solution, 100 μ L of β-Glucuronidase, and 500 μ L of 0.66M acetate buffer, pH 4, vortex mixing for 30 seconds, and then incubating at 55°C for 2 hours. Aliquots of 260 μ L of hydrolyzed urine samples were added into clean shell vials for automated cleanup and injection.

Figure 2 shows a graphical representation of the general DPX cleanup process. The automated DPX extraction used for this method consisted of the following steps:

Automated DPX Prep Sequence - DPX Cleanup procedure

- 1. Aspirate 750 μL of 100 % acetonitrile from the fast solvent delivery station using the 2.5 mL DPX syringe.
- 2. Pick up a new DPX tip (DPX-RP-S) located within the tray.
- 3. Add 500 μ L of 100 % acetonitrile through the DPX tip, into the urine sample located on the MPS sample tray.
- 4. Wait for 6 seconds to allow the acetonitrile to completely wet the DPX sorbent.
- 5. Aspirate the entire sample followed by 1400 μ L of air into the DPX tip.
- 6. After equilibrating for 5 seconds, dispense the contents of the DPX tip, as well as the remaining acetonitrile found within the DPX syringe, back into the original shell vial in the tray.
- 7. Move the DPX tip to the PipWaste position and dispose of the DPX tip.

- Transfer 100 μL of the upper liquid layer located within the original shell vial, into a clean, empty, capped autosampler vial with magnetic septum cap located on a VT98 tray.
- 9. Dilute the extract by adding 900 μ L of water into the sample vial.
- 10. Inject 50 μL of the sample into the HPLC injection valve.



Figure 2. Graphical representation of the automated DPX urine cleanup process.

Analysis conditions LC.

Pump:	gradient (600 bar),			
	flowrate $= 0.5$ n	nL/min		
Mobile Phase:	A - 5 mM ammonium formate, with			
	0.05 % formic acid			
	B - 0.05 % formic acid in metha			
Gradient:	Initial	5 % B		
	0.5 min	5 % B		
	1.5 min	30 % B		
	3.5 min	70 % B		
	4.5 min	95 % B		
	6.49 min	95 % B		
	6.5 min	5 % B		
Run time:	6.5 minu	ites		
Injection volum	ne: $2 \mu L$ (loo	2 μL (loop over-fill technique)		
Column temper	rature: 55°C			

Analysis condition MS.

Operation:	electrospray positive mode
Gas temperature:	350°C
Gas flow (N_2) :	12 L/min
Nebulizer pressure:	35 psi
Capillary voltage:	4400 V

A total of 124 MRM transitions (98 Analyte qualifier/quantifier and 18 internal standard transitions) were monitored in a 4 minute analytical window followed by a column regeneration time of 2.5 minutes. A retention time window value of 30 seconds was used for each positive ion transition being monitored in the dynamic MRM method. Detailed mass spectrometric acquisition parameters are available upon request.

RESULTS AND DISCUSSION

Figure 3 shows representative dynamic MRM chromatograms for all 49 pain management drugs and internal standards, from a hydrolyzed urine sample spiked sample at the minimum reporting limit (MRL) concentrations after the automated DPX cleanup procedure.



Figure 3. Overlaid chromatograms for all 124 dynamic MRM transitions from an extracted urine sample at the MRL.

Table 1 lists the column retention times, concentrations for the highest calibration standard, MRLs and LLOQs for the 49 analytes in this screening assay. LLOQ concentrations are higher (5 fold factor increase) in comparison to those listed in our previous work performed with an automated concentration step using a solvent evaporation station [1]. However, the LLOQs of this modified cleanup method are still below the original MRLs. Representative calibration curves are shown in Figure 4. Regression analysis for all pain management drugs analyzed within this method resulted in R² values of 0.99 or greater.

Table 1. Retention times, high calibration standard concentrations, MRLs and LOQs for all pain management drugs analyzed.

Compound	Ret. Time [min]	High Cal Std. [ng/mL]	MRL [ng/mL]	LOQ [ng/mL]		
6-MAM ¹	1.60	100	10	5		
Codeine ¹	1.43	500	50	25		
Hydrocodone ¹	1.56	500	50	25		
Hydromorphone ¹	1.01	500	50	25		
Oxycodone ¹	1.51	500	50	25		
Morphine ¹	0.71	500	50	25		
Oxymorphone ¹	0.83	500	50	25		
Meperidine ¹	2.27	500	50	25		
Normeperidine ¹	2.33	500	50	25		
Buprenorphine ²	3.02	100	10	5		
Norbuprenorphine ³	2.60	100	10	5		
EDDP ⁴	2.76	500	50	25		
Methadone ⁴	3.22	500	50	25		
Norpropoxyphene ⁵	2.98	1000	100	50		
Propoxyphene ⁵	3.16	1000	100	50		
o-Desmethyl-cis-Tramadol6	1.71	250	25	12.5		
cis-Tramadol ⁶	2.13	250	25	12.5		
Fentanyl ⁷	2.64	10	1	0.5		
Norfentanyl ⁷	2.04	10	1	0.5		
Meprobamate ⁸	2.58	500	50	25		
Carisoprodol ⁸	3.38	500	50	25		
7-Aminoclonazepam9	2.12	400	40	20		
Clonazepam ¹⁰	3.17	400	40	20		
Oxazepam ¹¹	3.38	400	40	20		
Estazolam ¹²	3.30	400	40	20		
Alprazolam ¹³	3.42	400	40	20		
Diazepam ¹³	3.75	400	40	20		
Flunitrazepam ¹³	3.23	400	40	20		
Lorazepam ¹²	3.39	400	40	20		
Nitrazepam ¹³	3.15	400	40	20		
Temazepam ¹³	3.50	400	40	20		
α-OH-Alprazolam ¹⁴	3.29	400	40	20		
Nordiazepam ¹³	3.63	400	40	20		
Bromazepam ¹²	3.05	400	40	20		
Clobazam ¹³	3.34	400	40	20		
Midazolam ¹³	3.08	400	40	20		
Triazolam ¹³	3.41	400	40	20		
Flurazepam ¹³	2.79	400	40	20		
Ketamine ¹⁵	2.01	1000	100	50		
Norketamine ¹⁵	2.01	1000	100	50		
Amphetamine ¹⁶	1.60	1000	100	50		
MDA16	1.64	1000	100	50		
MDEA ¹⁶	1.82	1000	100	50		
MDMA ¹⁶	1.69	1000	100	50		
Methamphetamine ¹⁶	1.66	1000	100	50		
Methylphenidate ¹⁶	2.16	1000	100	50		
	2.54	50	5	2.5		
Benzoylecgonine ¹⁸	1.99	250	25	12.5		
	2.13	250	25	12.5		
Internal Standards						
1) d3-morphine	6) d3-cistramadol	11) d5-oxaz	epam 16) c	15-amphetamine		
2) d4-buprenorphine	7) d5-Fentanyl	d5-Fentanyl 12) d5-estazolam 17) d5-PCP				
3) d3-norbuprenorphine	8) d7-Carisoprodol 13) d5-nordiazepam 18) d3-cocaine					
4) d9-methadone	9) d4-7aminoclonazepam 14) d5OH-alprazolam					

10) d4-Clonazepam 15) d4-ketamine

5) d5-propoxyphene



Figure 4. Representative calibration curves: morphine, flurazepam, cocaine and ketamine.

The DPX automated sample cleanup time was reduced from 7 to 3 min/sample; the total cycle time per sample for the extraction process and injection was reduced from 13 to 7 min/sample, fitting with the "just in time" sample preparation strategy available using the Maestro software and increasing throughput. Using this automated procedure for extraction and analysis over 200 samples can be processed per day.

The accuracy and precision of the method was measured for all pain management drugs analyzed extracting replicate (n=4) QC samples at high and low concentrations. Table 2 shows the resulting accuracy and precision data for all pain management drugs. Accuracy data averaged 98.0 % (range: 77 % - 108 %) and precision data (% RSD) averaged 4.2 % (range: 1.0 % -12.8 %) for all pain management drugs analyzed.

Table 2. Extracted QC sample % accuracies and % RSDs.

B-MAM 12.5 100.96 12.69 75.0 107.09 4.42 Coderia 62.5 96.24 3.01 375.0 103.52 2.21 Hydronorphone 62.5 96.57 2.28 375.0 101.83 1.82 Ovycocone 62.5 96.87 2.29 375.0 102.07 1.49 Owynophone 62.5 96.84 6.46 375.0 104.10 4.44 Morphe 62.5 100.46 2.67 375.0 104.10 4.44 Normsphore 62.5 100.48 10.78 75.0 102.64 3.85 Bupmonphine 12.5 100.42 1.47 375.0 108.05 4.17 Nortgreeryphine 12.5 100.42 1.47 375.0 108.11 2.21 Norpcopacyphene 12.5 100.42 1.47 375.0 109.11 2.21 Norpcopacyphene 12.5 96.53 1.185 750.0 96.16 151 <td< th=""><th>Compound</th><th>QCL [ng/mL]</th><th>Avg. Accuracy [%] [n = 4]</th><th>% RSD</th><th>QCH [ng/mL]</th><th>Avg. Accuracy [%] [n = 4]</th><th>% RSD</th></td<>	Compound	QCL [ng/mL]	Avg. Accuracy [%] [n = 4]	% RSD	QCH [ng/mL]	Avg. Accuracy [%] [n = 4]	% RSD
Codeins 62.5 98.24 3.01 375.0 105.02 2.31 Hydroxodore 62.6 98.57 2.20 378.0 108.85 1.27 Oxycedore 62.6 98.57 2.20 378.0 100.77 2.44 Morphine 62.6 100.45 2.67 375.0 100.52 3.04 Morphanine 62.6 100.45 2.67 375.0 100.42 3.04 Morphanine 62.6 100.45 2.67 375.0 100.62 3.04 Namsgenine 62.6 100.45 10.79 75.0 100.67 1.72 Morbadrome 62.6 106.72 2.09 375.0 108.17 1.72 Methadore 62.6 106.72 2.99 375.0 108.17 1.72 Methadore 62.6 106.72 2.99 375.0 108.17 1.72 Morphacysphere 12.6 0.05.8 1.85 75.0 10.67 1.52 Pacana	6-MAM	12.5	100.95	12.69	75.0	107.08	4.92
Hydrocodene 62.5 96.07 3.76 375.0 103.65 2.74 Hydrocorphone 62.5 98.67 2.20 375.0 101.83 1.62 Oxycodore 62.5 98.84 6.46 375.0 102.07 1.49 Oxymophone 62.5 97.92 3.15 375.0 100.52 3.64 Morphine 62.5 97.92 3.15 375.0 102.07 1.49 Normsportine 62.5 97.92 3.15 375.0 102.04 3.85 Buprenorphine 12.5 103.48 10.78 75.0 108.05 4.17 Norbupcoxyphene 12.5 106.42 1.47 375.0 108.11 2.21 Norpopoxyphene 12.50 95.59 1.85 75.00 96.67 0.51 p-Desmothydicie-Tarmatol 31.3 94.28 2.06 187.5 93.31 1.26 Tarmatod 31.3 94.28 2.26 187.5 94.07 0.89	Codeine	62.5	98.24	3.01	375.0	105.02	2.31
Hydromerphone 62.5 98.57 2.26 375.0 101.83 1.62 Oxycocone 62.5 98.67 2.90 375.0 103.07 2.84 Morphine 62.5 95.04 6.45 375.0 102.07 1.49 Oxymorphone 62.5 97.32 3.15 375.0 100.52 3.04 Namegoritine 62.5 97.32 3.15 375.0 100.52 4.4 Namegoritine 62.5 103.48 10.78 75.0 106.77 1.72 Northperioritine 12.5 106.76 2.99 375.0 106.71 1.72 Methadone 62.5 106.76 2.99 375.0 108.11 2.21 Nortporyphene 12.50 98.98 1.85 75.0 98.91 1.81 Propoxyphene 12.50 98.93 2.15 175.7 0.91 1.25 Conspropoyphene 12.50 98.93 2.15 175.7 0.92 2.84	Hydrocodone	62.5	96.07	3.78	375.0	103.65	2.74
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Morphine 62.5 96.84 6.46 375.0 102.07 1.49 Oxymorphone 62.5 100.46 2.57 375.0 100.52 3.04 Megeridine 62.5 97.32 3.15 375.0 102.64 3.95 Bagronryphine 12.5 103.48 10.78 75.0 106.05 4.17 Northogenophine 12.5 103.49 10.78 75.0 106.05 4.17 Northogenophine 12.5 106.77 1.72 Methadone 62.5 106.76 2.99 375.0 108.11 2.21 Nortrogenophine 12.50 96.36 1.85 750.0 96.65 1.51 Propaxyphene 12.50 96.30 2.18 750.0 96.57 0.95 o-Desmethyl-di-Tranadol 31.3 94.13 2.253 117.5 94.07 0.89 Pertanyl 1.3 106.86 6.97 7.5 101.72 3.97 Ovarespam 50.0 88.73	Oxvcodone	62.5	98.37	2.90	375.0	103.07	2.84
Oxymorphone 62.5 100.46 2.57 375.0 100.52 3.04 Megendine 62.5 97.32 3.15 375.0 104.16 4.48 Normseynine 12.5 103.48 10.78 75.0 106.05 4.17 Nortugenorphine 12.5 00.69 9.28 75.0 97.44 7.72 EDDP 62.5 106.73 2.99 375.0 108.11 2.21 Nortugenorphine 125.0 96.88 1.86 79.0.0 98.86 1.51 Procoxphine 125.0 96.83 2.18 75.0 97.74 7.22 Softward 31.3 94.28 2.06 187.5 93.31 1.26 Tramadol 31.3 94.28 2.06 187.5 94.07 0.89 Potomyl 1.3 108.86 6.97 7.5 101.72 3.97 Nortestanyl 1.3 98.83 12.11 7.5 98.20 2.24 Megrobantale <td>Morphine</td> <td>62.5</td> <td>96.84</td> <td>6.46</td> <td>375.0</td> <td>102.07</td> <td>1.49</td>	Morphine	62.5	96.84	6.46	375.0	102.07	1.49
Megandine 62.5 97.32 3.15 375.0 104.16 4.48 Nomegendine 62.5 98.07 2.59 375.0 102.64 3.95 Bugenorphine 12.5 100.48 10.78 75.0 97.44 7.72 EDOP 62.5 106.42 1.47 375.0 106.77 1.72 Methadone 62.5 106.76 2.99 375.0 106.77 1.72 Methadone 62.5 106.76 2.99 375.0 106.77 1.72 Norpropoxphene 125.0 96.58 1.85 760.0 96.86 1.51 Propoxphene 125.0 96.30 2.18 750.0 96.57 0.95 o-Desmethyl-cis-Tranadol 31.3 94.13 2.55 187.5 94.07 0.89 Fortanyl 1.3 108.88 12.11 7.5 101.72 3.97 Nortentanyl 1.3 98.89 12.84 375.0 84.49 1.08 <	Oxymorphone	62.5	100.46	2.57	375.0	100.52	3.04
Normeprefine 62.5 98.07 2.59 975.0 102.84 3.85 Bupencophine 12.5 103.48 10.78 75.0 100.05 4.17 Norbupercophine 12.5 100.42 1.47 275.0 106.77 1.72 Methadoce 62.5 106.72 2.99 375.0 108.11 2.21 Norpogosyphen 125.0 96.58 1.85 750.0 96.57 0.95 o-DesmthyLois-Tranadol 31.3 94.28 2.06 187.5 93.31 1.28 Tamadol 31.3 94.82 2.06 187.5 94.07 0.89 Fartanyl 1.3 108.88 6.97 7.5 101.72 3.97 Norfentanyl 1.3 98.89 12.11 7.5 98.20 2.84 Megrobanatle 62.5 89.53 2.84 375.0 84.49 1.08 Z-anisprodol 62.5 89.53 10.12 300.0 91.96 6.18	Meperidine	62.5	97.32	3.15	375.0	104.16	4.48
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Methadone 62.5 108.75 2.99 375.0 108.11 2.21 Norropoxyphene 125.0 96.58 1.85 750.0 96.86 1.51 Propoxyphene 125.0 96.58 1.85 750.0 96.57 0.95 o-Desmethy-instrandol 31.3 94.13 2.55 187.5 94.07 0.89 Fartanyl 1.3 108.08 6.97 7.5 101.72 3.97 Norfentanyl 1.3 108.08 6.97 7.5 94.07 0.89 Carisoprodol 62.5 87.40 3.29 375.0 87.73 1.12 Carisoprodol 62.5 89.53 2.84 375.0 84.49 1.08 7-Aminoclonazepam 50.0 89.73 10.12 300.0 101.38 2.64 Qxazepam 50.0 89.73 10.12 300.0 103.39 2.8 300.0 103.97 5.54 Burtazepam 50.0 97.87 3.81 300.0	FDDP	62.5	106.42	1 47	375.0	106.77	1 72
Norgrossyphene 125.0 96.56 1.85 750.0 96.86 1.51 Proposyphene 125.0 96.30 2.18 750.0 96.57 0.95 o-Dsemtly-cis-Tranadol 31.3 94.28 2.06 187.5 94.07 0.89 Fentanyl 1.3 108.08 6.97 7.5 101.72 3.97 Norfentanyl 1.3 108.08 6.97 7.5 101.72 3.97 Norfentanyl 1.3 98.98 12.11 7.5 98.20 2.84 Meprobamate 62.5 87.40 3.29 375.0 87.49 1.08 7-Aminodonazepam 50.0 89.73 10.12 300.0 91.96 6.18 Chazzopam 50.0 89.93 12.85 300.0 97.32 5.89 Estazolam 50.0 83.90 12.85 300.0 94.41 4.31 Lorazepam 50.0 97.87 3.81 300.0 94.41 4.31 <t< td=""><td>Methadone</td><td>62.5</td><td>106.76</td><td>2.99</td><td>375.0</td><td>108 11</td><td>2.21</td></t<>	Methadone	62.5	106.76	2.99	375.0	108 11	2.21
Non-system Non-	Norpropoxyphene	125.0	96.58	1.85	750.0	96.86	1.51
o-Desmethy/cis-Tamadol 31.3 94.28 2.06 187.5 93.31 1.26 Tamadol 31.3 94.13 2.55 187.5 94.07 0.89 Fentanyl 1.3 108.68 6.97 7.5 101.72 3.97 Nordentanyl 1.3 108.68 6.97 7.5 98.20 2.84 Meprobarate 62.5 87.40 3.29 375.0 87.78 1.12 Carisoprotol 62.5 89.53 2.84 375.0 84.49 1.08 7.Aminodonzepam 50.0 88.94 9.13 300.0 101.33 2.64 Oxazepam 50.0 88.94 9.13 300.0 97.32 5.89 Estazolam 50.0 88.68 3.65 300.0 89.56 3.18 Alprazolam 50.0 97.87 3.81 300.0 96.87 4.44 Flunitrazepam 50.0 97.22 12.63 300.0 96.87 4.97 Nordaz	Propoxyphene	125.0	96.30	2 18	750.0	96.57	0.95
Operation of the second seco	o-Desmethyl-cis-Tramadol	31.3	94.28	2.06	187.5	93 31	1.26
Tombol 01.0 01.0 01.0 0.00 Fentanyl 1.3 108.68 6.97 7.5 101.72 3.97 Nortentanyl 1.3 98.98 12.11 7.5 98.20 2.84 Meprobamate 62.5 87.40 3.29 375.0 87.78 1.12 Carisoprotol 62.25 89.53 2.84 375.0 84.49 1.08 7-Aminockonazepam 50.0 89.73 10.12 300.0 19.96 6.18 Ckonazepam 50.0 88.94 9.13 300.0 101.38 2.64 Oxazepam 50.0 86.68 3.65 300.0 97.32 5.89 Estazolam 50.0 96.68 3.65 300.0 99.22 4.48 Flunitrazepam 50.0 97.87 3.81 300.0 94.21 4.43 Lorazepam 50.0 97.82 12.63 300.0 96.97 4.97 Transzepam 50.0 97.67	Tramadol	31.3	94.13	2.55	187.5	94.07	0.89
Nortentanyl 1.3 96.38 1.11 7.5 98.20 2.24 Maprobamata 62.5 87.40 3.29 375.0 87.78 1.12 Carisoprotol 62.5 89.53 2.84 375.0 84.49 1.08 7.Aminodonazepam 50.0 89.73 10.12 300.0 91.96 6.18 Clonazepam 50.0 83.94 9.13 300.0 101.38 2.64 Oxazepam 50.0 83.90 12.85 300.0 97.32 5.89 Estazolam 50.0 97.87 3.81 300.0 99.22 4.48 Aprazolam 50.0 97.87 3.81 300.0 99.22 4.48 Fluintrazepam 50.0 97.87 3.81 300.0 99.41 4.31 Lorazepam 50.0 97.87 4.81 300.0 98.97 4.97 Temazepam 50.0 97.22 12.63 300.0 98.97 4.97 Temazepam <td>Fentanyl</td> <td>13</td> <td>108.68</td> <td>6.97</td> <td>7.5</td> <td>101.72</td> <td>3.97</td>	Fentanyl	13	108.68	6.97	7.5	101.72	3.97
Note Note 1.2 30.30 1.2.1 1.2.3 30.30 2.2.4 Megrobanate 62.5 87.40 3.29 375.0 87.78 1.12 Carisoprodol 62.5 89.53 2.84 375.0 84.49 1.08 7-Aminoclonazepam 50.0 88.94 9.13 300.0 91.96 6.18 Clonazepam 50.0 88.94 9.13 300.0 97.32 5.89 Estazolar 50.0 86.68 3.65 300.0 89.56 3.18 Alprazolam 50.0 100.33 3.28 300.0 103.97 5.54 Diazepam 50.0 97.87 3.81 300.0 94.41 4.31 Lorazepam 50.0 97.87 3.81 300.0 96.97 4.97 Temazepam 50.0 97.22 12.63 300.0 96.30 2.22 ox-OH-Alprazolam 50.0 97.65 4.13 300.0 97.33 4.35	Norfentanyl	13	08.08	12 11	7.5	08.20	2.84
Mphobanase 02.0 07.40 32.5 07.00 07.10 11.12 Carissoprodol 62.5 89.53 2.84 375.0 84.49 1.08 7-Aminoclonazepam 50.0 89.73 10.12 300.0 91.96 6.18 Okazepam 50.0 83.80 12.85 300.0 97.32 5.89 Estazolam 50.0 86.68 3.65 300.0 89.56 3.18 Alprazolam 50.0 100.33 3.28 300.0 103.97 5.54 Diazepam 50.0 97.87 3.81 300.0 98.22 4.48 Flunitrazepam 50.0 91.83 6.68 300.0 96.97 4.97 Temazepam 50.0 97.22 12.63 300.0 96.97 4.97 Torazepam 50.0 97.22 12.63 300.0 96.97 4.97 Torazepam 50.0 97.55 4.13 300.0 96.97 2.22 CxOH-Alpr	Menrohamate	62.5	87.40	3 20	375.0	87.78	1 12
Calisburg Color Color <thcolor< th=""> Color Color</thcolor<>	Carisoprodal	62.5	80.53	2.84	375.0	84.49	1.12
Arkindodiazepani 3.00 38.73 10.12 300.00 91.33 3.16 Ckonazepani 50.0 88.94 9.13 300.0 101.38 2.64 Oxazepani 50.0 86.84 3.65 300.0 97.32 5.89 Estazolami 50.0 100.33 3.28 300.0 103.97 5.54 Diazepani 50.0 97.87 3.81 300.0 98.22 4.48 Flunitrazepani 50.0 97.87 3.81 300.0 94.41 4.31 Lorazepani 50.0 91.83 6.68 300.0 97.05 8.71 Nitrazepani 50.0 91.83 6.68 300.0 97.05 8.71 Nitrazepani 50.0 91.83 6.68 300.0 96.97 4.97 Temazepani 50.0 91.72 12.63 300.0 96.80 222 COH-Alprazolami 50.0 103.72 11.95 300.0 95.81 5.82 Bromazepani 50.0 101.55 5.26 300.0 97.33 4.35		50.0	80.73	10.12	300.0	01.06	6.19
Okrazepam 50.0 60.54 9.13 30.00 10.135 2.04 Oxazepam 50.0 83.90 12.85 300.0 97.32 5.89 Estazolam 50.0 86.68 3.65 300.0 89.56 3.18 Alprazolam 50.0 100.33 3.28 300.0 103.97 5.54 Diazepam 50.0 97.87 3.81 300.0 98.22 4.48 Flunitrazepam 50.0 91.83 6.68 300.0 94.41 4.31 Lorazepam 50.0 91.83 6.68 300.0 97.05 8.71 Nitrazepam 50.0 94.79 7.76 300.0 98.30 2.22 or-OH-Alprazolam 50.0 76.57 4.13 300.0 79.37 6.21 Nordiazepam 50.0 109.88 10.59 300.0 95.81 5.82 Bromazepam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam </td <td>Clanazanam</td> <td>50.0</td> <td>89.04</td> <td>0.12</td> <td>300.0</td> <td>101.39</td> <td>0.10</td>	Clanazanam	50.0	89.04	0.12	300.0	101.39	0.10
DKazepani 30.0 33.90 12.93 30.00 31.32 33.83 Estazolam 50.0 66.68 3.65 300.0 89.56 3.18 Alprazolam 50.0 100.33 3.28 300.0 103.97 5.54 Diazepam 50.0 108.99 6.88 300.0 98.22 4.48 Flunitrazepam 50.0 198.3 6.68 300.0 94.41 4.31 Lorazepam 50.0 97.22 12.63 300.0 96.97 4.97 Temazepam 50.0 76.57 4.13 300.0 98.30 2.22 C+Alprazolam 50.0 76.57 4.13 300.0 98.30 2.22 C+OH-Alprazolam 50.0 103.72 11.95 300.0 89.70 2.32 Clobazam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 100.56 3.17 300.0 97.94 4.20 Ketamine </td <td>Overanem</td> <td>50.0</td> <td>82.00</td> <td>9.13</td> <td>300.0</td> <td>07.32</td> <td>5.80</td>	Overanem	50.0	82.00	9.13	300.0	07.32	5.80
Estadualit 50.0 80.00 30.00 80.00	Estazolam	50.0	86.69	12.05	300.0	97.52	2.19
Aphzzdam 30.0 100.37 3.00 100.37 0.34 Diazepam 50.0 97.87 3.81 300.0 98.22 4.48 Flunitrazepam 50.0 108.99 6.68 300.0 94.41 4.31 Lorazepam 50.0 97.22 12.63 300.0 96.97 4.97 Temazepam 50.0 97.22 12.63 300.0 98.30 2.22 α-OH-Alprazolam 50.0 97.72 4.13 300.0 98.30 2.22 α-OH-Alprazolam 50.0 76.57 4.13 300.0 98.30 2.22 α-OH-Alprazolam 50.0 109.88 10.59 300.0 95.81 5.82 Bromazepam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine	Alprazolam	50.0	100.33	3.05	300.0	103.97	5.54
Diazgiani 30.0 37.01 30.01 30.02 30.12 4.40 Flunitrazepam 50.0 108.99 6.88 300.0 94.41 4.31 Lorazepam 50.0 91.83 6.66 300.0 97.05 8.71 Nitrazepam 50.0 97.22 12.63 300.0 96.97 4.97 Temazepam 50.0 94.79 7.76 300.0 98.30 2.22 α-OH-Alprazolam 50.0 109.88 10.59 300.0 95.81 5.82 Bromazepam 50.0 103.72 11.95 300.0 89.70 2.32 Clobazam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Flurazepam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.94 4.20 Ketamine	Diazenam	50.0	07.87	3.81	300.0	08.22	1.48
Intrinstactpum 30.0 10.00 30.00 30.00 34.41 4.31 Lorazepam 50.0 91.83 6.68 300.0 97.05 8.71 Nitrazepam 50.0 97.22 12.63 300.0 96.97 4.97 Temazepam 50.0 94.79 7.76 300.0 98.30 2.22 ac-OH-Alprazolam 50.0 76.57 4.13 300.0 79.37 6.21 Nordiazepam 50.0 109.88 10.59 300.0 95.81 5.82 Bromazepam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Triazolam 50.0 101.55 5.26 300.0 97.33 4.35 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 87.67 1.43 Ampheta	Flunitrazenam	50.0	108.99	6.88	300.0	94.41	4 31
Lotacpam 50.0 97.22 12.63 300.0 96.97 4.97 Temazepam 50.0 94.79 7.76 300.0 96.97 4.97 Qc-OH-Alprazolam 50.0 76.57 4.13 300.0 98.30 2.22 Qc-OH-Alprazolam 50.0 109.88 10.59 300.0 98.81 5.82 Bromazepam 50.0 103.72 11.95 300.0 98.81 5.82 Bromazepam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Triazolam 50.0 101.55 5.26 300.0 97.33 4.35 Triazolam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 Amph	Lorazenam	50.0	91.83	6.68	300.0	97.05	8 71
Intracepant 50.0 94.79 7.76 300.0 98.30 2.22 α-OH-Alprazolam 50.0 76.57 4.13 300.0 79.37 6.21 Nordiazepam 50.0 109.88 10.59 300.0 95.81 5.82 Bromazepam 50.0 103.72 11.95 300.0 89.70 2.32 Clobazam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Triazolam 50.0 101.55 5.26 300.0 97.33 4.35 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 87.67 1.43 Ampletamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA <td>Nitrazenam</td> <td>50.0</td> <td>97.22</td> <td>12.63</td> <td>300.0</td> <td>96.97</td> <td>4 97</td>	Nitrazenam	50.0	97.22	12.63	300.0	96.97	4 97
Initiatepant 30.0 34.10 1.10 300.0 79.37 6.21 α-OH-Alprazolam 50.0 109.88 10.59 300.0 95.81 5.82 Bromazepam 50.0 103.72 11.95 300.0 89.70 2.32 Clobazam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Flurazepam 50.0 101.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 Amphetamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA<	Temazenam	50.0	94 79	7 76	300.0	98.30	2.22
Octorn production 50.0 10.01 1.10 50.00 10.01 10.01 Nordiazepam 50.0 109.88 10.59 300.0 95.81 5.82 Bromazepam 50.0 103.72 11.95 300.0 89.70 2.32 Clobazam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Triazolam 50.0 101.55 5.26 300.0 97.33 4.35 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 Amphetamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA <td>α-OH-Alprazolam</td> <td>50.0</td> <td>76 57</td> <td>4 13</td> <td>300.0</td> <td>79 37</td> <td>6.21</td>	α-OH-Alprazolam	50.0	76 57	4 13	300.0	79 37	6.21
Noticized 103.00 103.00 103.00 103.00 300.01 303.01 303.01 303.01 Bromazepam 50.0 103.72 11.95 300.0 89.70 2.32 Clobazam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Triazolam 50.0 99.65 4.17 300.0 104.24 6.29 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 Amphetamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 102.65 1.43 </td <td>Nordiazenam</td> <td>50.0</td> <td>109.88</td> <td>10 59</td> <td>300.0</td> <td>95.81</td> <td>5.82</td>	Nordiazenam	50.0	109.88	10 59	300.0	95.81	5.82
Dromazgam 30.0 100.72 11.33 300.0 00.70 2.32 Clobazam 50.0 101.55 5.26 300.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Triazolam 50.0 99.65 4.17 300.0 104.24 6.29 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 MDA 125.0 90.34 2.48 750.0 102.14 1.47 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDA 125.0 100.78 2.39 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 102.65 1.43 Methamphetamine 12	Bromazenam	50.0	103.72	11.95	300.0	89.70	2 32
Otobazam 30.0 101.33 3.20 30.0 97.33 4.35 Midazolam 50.0 101.55 5.26 300.0 97.33 4.35 Triazolam 50.0 99.65 4.17 300.0 104.24 6.29 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 MDA 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 100.11 2.37 750.0 103.44 1.37 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 101.49 1.39 Methamphetamine 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate	Clobazam	50.0	101.55	5.26	300.0	07.33	4.35
Initiazolarin 30.0 101.33 3.20 300.0 91.33 4.33 Triazolam 50.0 99.65 4.17 300.0 104.24 6.29 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 Amphetamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 99.34 2.48 750.0 102.14 1.47 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDA 125.0 100.78 2.39 750.0 102.65 1.43 Methamphetamine 125.0 100.78 2.39 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 102.65 1.43 PCP	Midazolam	50.0	101.55	5.26	300.0	97.33	4.35
Hiazolam 53.03 44.17 500.0 104.24 0.29 Flurazepam 50.0 100.66 3.15 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 Amphetamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 99.34 2.48 750.0 103.44 1.37 MDA 125.0 101.75 2.49 750.0 102.14 1.47 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 102.65 1.43 Methamphetamine 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 103.49 1.95 PCP 6.3	Triazolam	50.0	00.65	4 17	300.0	104.24	6.29
Hurazepani 30.0 100.00 3.13 300.0 97.94 4.20 Ketamine 125.0 88.19 1.43 750.0 88.72 1.04 Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 Amphetamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 99.34 2.48 750.0 103.44 1.37 MDEA 125.0 101.75 2.49 750.0 102.19 1.67 MDMA 125.0 100.78 2.39 750.0 101.49 1.39 MEthamphetamine 125.0 100.78 2.39 750.0 101.49 1.39 Methamphetamine 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 103.49 1.95 PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecg	Elurazonam	50.0	100.66	2.15	300.0	07.04	4.20
Norketamine 125.0 90.52 2.05 750.0 87.67 1.43 Amphetamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 99.34 2.48 750.0 103.44 1.37 MDA 125.0 101.75 2.49 750.0 102.14 1.47 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 102.65 1.43 Methamphetamine 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 101.49 1.39 Methamphetamine 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 103.49 1.95 PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecgonine <td>Kotamino</td> <td>125.0</td> <td>88.10</td> <td>1 /3</td> <td>750.0</td> <td>88.72</td> <td>1.04</td>	Kotamino	125.0	88.10	1 /3	750.0	88.72	1.04
Nonketanine 125.0 90.32 2.03 750.0 67.87 1.43 Amphetamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 99.34 2.48 750.0 103.44 1.37 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 101.49 1.39 Methamphetamine 125.0 100.78 2.39 750.0 102.65 1.43 Methylphenidate 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 102.65 1.43 PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecgonine 31.3 96.94 3.38 187.5 97.79 2.51	Nerketemine	125.0	00.52	1.43	750.0	87.67	1.04
Antipletamine 125.0 100.11 2.37 750.0 102.14 1.47 MDA 125.0 99.34 2.48 750.0 103.44 1.37 MDA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 101.49 1.39 Methamphetamine 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 103.49 1.95 PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecgonine 31.3 96.94 3.38 187.5 97.79 2.51		125.0	90.52	2.05	750.0	102.14	1.43
MDA 125.0 99.34 2.46 750.0 103.44 1.37 MDEA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 101.49 1.39 Methamphetamine 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 103.49 1.95 PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecgonine 31.3 96.94 3.38 187.5 97.79 2.51	Amphetamine	125.0	00.24	2.37	750.0	102.14	1.47
MDEA 125.0 101.75 2.49 750.0 102.59 1.67 MDMA 125.0 100.78 2.39 750.0 101.49 1.39 Methamphetamine 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 103.49 1.95 PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecgonine 31.3 96.94 3.38 187.5 97.79 2.51		125.0	99.04 404.7F	2.40	750.0	103.44	1.37
Methamphetamine 125.0 100.78 2.39 750.0 101.49 1.39 Methamphetamine 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 103.49 1.95 PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecgonine 31.3 96.94 3.38 187.5 97.79 2.51		125.0	101.73	2.43	750.0	102.09	1.07
Methalphenidate 125.0 101.31 2.59 750.0 102.65 1.43 Methylphenidate 125.0 99.32 2.33 750.0 103.49 1.95 PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecgonine 31.3 96.94 3.38 187.5 97.79 2.51	Mothemphotemine	125.0	101.78	2.39	750.0	101.49	1.39
PCP 6.3 106.94 7.32 37.5 105.36 2.99 Benzoylecgonine 31.3 96.94 3.38 187.5 97.79 2.51	Mothulphanidate	125.0	00.22	2.59	750.0	102.05	1.43
Benzoylecgonine 31.3 96.94 3.38 187.5 97.79 2.51		125.0	39.32	2.33	750.0	103.49	1.95
Defizuyieugunine 31.3 90.94 3.36 187.3 97.79 2.51	Por	24.2	06.04	1.32	37.5	07.70	2.33
	Cassing	21.05	90.94	3.30	107.3	91.19	2.31

CONCLUSIONS

As a result of this study, we were able to show:

- The automated DPX cleanup method using the GERSTEL MPS XL Dual Tower robotic sampler for pain management drug screenings in urine was modified to provide cycle times of approximately 7 min/sample allowing throughput of over 200 samples per day
- 49 pain management drugs can be rapidly and reproducibly isolated from hydrolyzed urine samples using an automated DPX cleanup procedure coupled to LC/MS/MS analysis using the Agilent 6460 Triple Quadrapole Mass Spectrometer.
- Linear calibration curves resulting in R² values 0.99 or greater were achieved with LOQs lower than the minimum reportable limits for the majority of pain management drugs analyzed.
- The DPX-LC/MS/MS method provided good accuracy and precision averaging 98.0 % (range: 77 % 110 %) accuracy with 4.2 % RSD (range: 0.89 % -12.8 %) for all pain management drugs analyzed.

References

[1] Determination of Pain Management Drugs using Automated Disposable Pipette Extraction and LC-MS/MS, Gerstel AppNote AN-2011-06

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