TECHNICAL NOTE

imcs integrated micro-chromatography systems

MicroSep Biological Science

A summary of "Meconium Targeted Drug Screening in 9 seconds per Sample Using Laser Diode Thermal Desorption Mass Spectrometry (LDTD-MS/MS)"

Overview:

Meconiuom from newborns is typically used to screen for drug use by the mother during pregnancy. Drugs accumulate in meconium by fetal excretion into bile and amniotic fluid. Meconium is typically screened for various drug categories via immunoassay. To increase sample throughput while reducing the amount of meconium necessary for testing, a Laser Diode Thermal Desorption Mass Spectrometry (LDTD®-MS/MS) method was developed for analyzing 26 drugs of abuse in meconium. The LDTD ion source uses a laser diode to vaporize dry samples from a 96-well plate, after which the sample is carried by a gas into a corona discharge region, resulting in high efficiency protonation and strong resistance to ionic suppression. The use of the LDTD ion source enables samples to be processed at a run time of only 9 seconds.

Material and Methods:

Meconium samples were prepared by weighing out 0.1 g and adding 1 mL of 0.1 M phosphate buffer, pH 7. After vortexing and centrifugation, the solution was filtered using a 0.45 µm Nylon filter. In preparation for enzyme hydrolysis, 110 µL of meconium solution was combined with 5 µL internal standard solution, 20 µL of IMCSzyme®, and 25 µL of rapid hydrolysis buffer. The samples were then vortexed and incubated at 55°C for 15 minutes. A liquid-liquid extraction was performed which varied depending on the acidity or basicity of the drugs being tested, and 4 µL of the organic upper layer was transferred to a 96-well LazWell™ plate and then dried prior to analysis on the LDTD-MS/MS system.

Results:

For quantitation, drug peak areas were normalized against internal standard areas. All drug curves passed with each concentration point within ± 2 standard deviations of the mean. Thirty meconium patient samples previously tested by ARUP Laboratories via LC-MS/MS or GC-MS were tested with the LDTD-MS/MS method. The results were comparable and the LDTD-MS/MS was successful in obtaining no false negative results for any of the drugs, as seen in **Table 1**.

To measure the hydrolysis efficiency of IMCSzyme, meconium matrices were spiked with an equal concentration of oxazepam and oxazepam-glucuronide. After hydrolysis, the results were compared and revealed a complete hydrolysis of the oxazepam-glucuronide, seen in **Table 2**.

Table 2. Hydrolysis efficiency of IMCSzyme

Sample ID	Mean Ratio Area
Oxazepam-glucuronide (87.2 nM)	3.61
Oxazepam (87.2 nM)	3.35
Enzymatic hydrolysis efficiency	107.5%

Table 1. 30 Patient Samples Comparison

Drug	LC-MS/MS		LDTD-MS/MS		False positive/ negative	
	POS.	NEG.	POS.	NEG.	FALSE POS.	FALSE NEG.
Amphetamine	4	26	4	26	0	0
Methamphetamine	5	25	5	25	0	0
MDA	0	30	0	30	0	0
MDEA	0	30	0	30	0	0
MDMA	0	30	0	30	0	0
Butalbital	1	29	1	29	0	0
Pentobarbital/ Amobarbital	0	30	0	30	0	0
Phenobarbital	0	30	0	30	0	0
Secobarbital	0	30	0	30	0	0
Butabarbital	0	30	2	28	2	0
Oxazepam	4	26	6	24	2	0
Tempazepam	1	29	2	28	1	0
Alprazolam	0	30	0	30	0	0
Diazepam	0	30	0	30	0	0
-OH-Alprazolam	0	30	0	30	0	0
BZE	1	29	1	29	0	0
Methadone	4	26	4	26	0	0
EDDP	4	26	4	26	0	0
PCP	0	30	9	21	9	0
Morphine/ Hydromorphone	14	16	16	14	2	0
Codeine/ Hydrocodone	7	23	9	21	2	0
Oxymorphone	4	26	5	25	1	0
Oxycodone	4	26	5	25	1	0

Conclusions:

The goal of obtaining no false negative results was achieved with this new LDTD-MS/MS method. By combining the efficient and complete hydrolysis capability of IMCSzyme with the ultrafast quantification ability of the LDTD-MS/MS system, meconium patient samples were able to be prepared and screened for 26 different drug analytes in a matter of minutes.

A summary by IMCS from the technical poster "Meconium Targeted Drug Screening in 9 seconds per Sample Using Laser Diode Thermal Desorption Mass Spectrometry (LDTD-MS/MS)" presented by Serge Auger - Phytronix at ASMS 2016

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