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Determination of 17 illicit drugs in oral fluid using isotope dilution ultra-high performance liquid chromatography/tandem mass spectrometry with three atmospheric pressure ionizations

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ABSTRACT

The collection of oral fluid for drug testing is easy and non-invasive. This study developed a drug testing method using ultra-high performance liquid chromatography/tandem mass spectrometry (UHPLC–MS/MS) in selected-reaction monitoring (SRM) mode. We tested the method on the analysis of four opiates and their metabolites, five amphetamines, flunitrazepam and its two metabolites, and cocaine and its four metabolites in oral fluid. 100-μL samples of oral fluid were diluted with twice the amount of water then spiked with isotope-labeled internal standards. After the samples had undergone high-speed centrifugation for 20 min, we analyzed the supernatant. The recovery of the sample preparation ranged from 81 to 108%. We compared the performance of electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI) and atmospheric pressure photoionization (APPI). The ion suppression of most analytes on ESI (28–78%) was lower than that of APCI and APPI. A post-column flow split (5:1) did not reduce the matrix effect on ESI. Direct APPI performed better than dopant-assisted APPI using toluene. ESI, APCI and APPI limits of quantitation mostly ranged from 0.11 to 1.9 ng/mL, 0.02 to 2.2 ng/mL and 0.02 to 2.1 ng/mL, respectively, but were much higher on amphetamine and ecgonine methyl ester (about 2.7–4.7 ng/mL, 8.7–14 ng/mL, and 10–19 ng/mL, respectively). Most of the bias percentages (accuracy) and relative standard deviations (precision) on spiked samples were below 15%. This method greatly simplifies the process of sample preparation and shortens the chromatographic time to only 7.5 min per run and is able to detect analytes at sub-ppb levels.

1. Introduction

Drug abuse comes with serious health problems, increased criminal activity, and the spread of some diseases. According to the 2008 World Drug Report, almost 5% of the world's populations have abused at least one drug in the past twelve months and 0.6% of the world's adults are severely drug addicted [1].

Morphine, heroin (diacetyl morphine) and codeine are narcotics. Amphetamine and its derivatives, including methamphetamine, 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylenedioxyethamphetamine (MDEA), and 3,4-methylenedioxyamphetamine (MDA), act to stimulate the central nervous system (CNS), increasing alertness and decreasing fatigue and appetite. Flunitrazepam, a hypnotic for short-term treatment of chronic insomnia, can debilitate persons and is often used as a date rape drug or for robbery. Cocaine is a CNS stimulant and topical anaesthetic able to produce a euphoric state similar to that induced by amphetamines.

Oral fluid has emerged for drug testing for the last twenty years [2,3]. It is a much simpler matrix than traditional specimens like urine and plasma because it is composed of 99% water, 0.3% proteins, and 0.3% mucin [4]. Its collection is non-invasive, easily performed, and can be done under surveillance or in clinics and workplaces [4], minimizing the chances of sample substitution or adulteration. Parent drugs in oral fluid are usually found in concentrations highly correlated with those in plasma [5–7] and they are much less susceptible to dilution by fluid intake [8–13].

Certain chemicals are better detected than others in suited in the oral fluid from users of illicit drugs. Because heroin has a short half-life in the blood (2–7 min), a better biomarker of heroin use might be 6-acetylmorphine in the oral fluid [14,15]. Codeine is the primary chemical found in plasma and oral fluids of codeine users [16,17]. Amphetamine and methamphetamine are found at higher concentrations in the oral fluid than in the plasma if they are taken orally [18,19]. MDMA and its metabolite MDA are the major chemicals found in the oral fluid from MDMA users [20,21].

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