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Detection and Quantification of Ketamine HCl in Alcohol/Water Matrices using ESI-MSⁿ and LC-ESI-MS

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Abstract. Drug facilitated date rape continues to be a problem around the world. Ketamine HCl (KT) has gained popularity since it is nearly odorless, tasteless, and colorless when dissolved in water/alcohol and a typical street dose (300-400mg) only costs \$20-\$25. A street dose of KT will send the victim into a dissociative state within 10-15 minutes and can cause temporary amnesia. Drug detection is paramount in the prosecution of drug facilitated date rape cases. Currently, detection of KT relies on urine or blood analysis. In this study we have developed a method for detecting and quantifying KT in a variety of different alcohols and mixed drinks.

Mass spectrometry (MS) was used to identify the presence of KT in the alcohol matrices. Liquid chromatography (LC) was used to separate the KT from the rest of the alcohol matrix. Quantification of KT was carried out both by MS and LC/UV absorbance using a series of external standards and plotting the concentration versus the signal intensity. Interestingly, it is possible to distinguish not only between different types of alcohol but also different brands of similar alcohol. KT was clearly visible in the spectrum of KT spiked drinks and did not show any interference from the alcohol matrix. Detection limits were found to be in the 100 pM range and samples were stable for up to 7 days. This method has proven to be robust and a viable way to quantify KT in alcoholic beverages for up to 1 week with very low limits of detection.

Introduction

The department of justice reports that between 2001 and 2005 the annual rate of sexual assault on women was about 1 out of 2000^[1]. Included in this category is drug-facilitated sexual assault. KT is a drug that is highly incapacitating, and has been implicated as a date rape drug^[2,4]. The primary method of delivery for KT, when consumed involuntarily, is the consumption of alcoholic beverages spiked with the drug. KT symptoms are described as a dissociation of perception from sensation, which results in insensitivity to pain, feelings of alternate consciousness, well being, amnesia, out body experiences, etc^[2-3,5]. These symptoms are particularly detrimental to the victims of sexual assault as they may not recall or realize the extent of the crime committed. Detection of the drug is paramount for the prosecution of drug-facilitated date rape cases, but KT is metabolized rapidly by the body into norketamine and dehydronorketamine. Methods have been developed for detection limits as low as 5ng/ml of these metabolites in urine^[6-7]. However, because urine analysis needs to be completed within two days of use, there is a significant need for alternative methods to detect KT that have a higher tolerance for delayed testing^[8-9]. In this study, we have developed analytical methods using LC-MSⁿ for identification and quantification of KT when found in a variety of different alcohols and have shown a minimum stability of KT analysis of 1 week.

Experiment, Results, Discussion, and Significance

Initially, KT was studied in water by collecting ESI-MSⁿ spectra of the stock standard solution. The dominant peak in the spectrum is at 238.1m/z which corresponds to the KT [M+H]⁺ ion. Upon CID of KT, the dominant ion is a loss of 18 mass units. There is also a second ion with a loss of 31 mass units. This CID profile of KT was used to positively identify KT in the alcohol samples. The matrices of distilled alcohols, mixers used in mixed drinks, and mixed drinks were then determined by collecting positive and negative mode ESI-MS spectra.

The spectra were collected with no sample work up. The alcohols used were whiskey, gin, rum, vermouth, tequila, and vodka. Other beverages tested were cola, tonic water, and lemon juice. The mixed drinks used were whiskey and cola, gin and tonic water, vodka and lemon juice, and vermouth and gin. The spectra show a distinct matrix for each alcohol and mixed drink making it possible to distinguish not only between different types of alcoholic drinks but also distinguish different brands from one another.

Once the matrices of the alcohol were collected, the alcohol samples were then spiked with KT. The spectra show the presence of the 238m/z ketamine ion in the matrix of the alcoholic beverages. ESI-MS/MS spectra were collected on the KT peak and the CID spectra confirmed the presence of ketamine. ESI-MS results show a direct correlation between signal intensity and the concentration of the KT added to the solution making it possible to construct a calibration curve by plotting signal intensity versus concentration. The concentration of the samples calculated from the calibration curve had less than a 2% error. As well, 10mL of the stock standard solution was

mixed 1:1 with the different alcohols and mixed drinks and was allowed to stand in a glass cup. After 20 minutes, the alcohol/KT solution was discarded and the residue was allowed to air dry overnight. A cotton swab was used to swab the inside of the cup and was placed in 1mL of 1:1 ethanol:water solution and shaken for 15 minutes. KT was present in the extract, allowing the analysis of residue on a bottle or glass.

Detection limits were determined by running a series of dilute spiked alcohol samples as well as a series of dilute standards. Detection of ketamine was shown down to 100 picomolar concentrations in all of the alcoholic beverages studied as well as for the standard solutions. Stability studies were also conducted under ambient benchtop conditions. Typically samples obtained and sent to a forensics lab will be analyzed in 48 hours or less. Standards and samples were stable for 7 days with less than a 1% decrease in molarity under bench top conditions.

Using an isocratic LC system, KT was successfully separated from the alcohol matrices. KT eluted at roughly 3.8 minutes and showed no interference from the alcohols and mixed drinks used. A calibration curve was constructed by plotting absorbance at 268nm versus concentration of known standards and was used to quantify samples of known concentration. The concentration of the samples calculated from the calibration curve had less than a 2% error.

Conclusions

ESI mass spectra were collected directly from samples of distilled liquor as well as from samples of mixers used to make up mixed drinks. The ESI mass spectra derived from the range of samples are distinct, thus demonstrating the ability to use ESI-MS to distinguish between different types of alcoholic beverages and even different brands of the same type of liquor. KT spiked alcohol samples show that KT is distinguishable from the alcohol matrix in all of the alcohols, mixers, and mixed drinks used. Quantification is possible using ESI-MS. KT can also be detected in the 100 picomolar range for all samples and is stable for at least 7 days under benchtop conditions. Using an isocratic LC system, KT was successfully separated from the alcohol matrices and quantified using absorbance at 268nm. In general, our study shows that ESI-MS and LC can be used to separate, detect and quantify KT at levels much lower than a normal dose given by a spiked drink, and do so with minimal sample preparation.

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