K22 Methcathinone Formation During Analysis of Ephedrine or Pseudoephedrine

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After attending this presentation, attendees will gain awareness of how analytical artifacts can lead to false positive results, as illustrated by the formation of a schedule I substance from over-the-counter cold medicines present in blood and urine specimens. Suggested methods for detecting and avoiding this artifact will also be provided.

This presentation will impact the forensic science community by raising awareness of the potential for controlled substances to form as artifacts in specimens containing high concentrations of ephedrine or pseudoephedrine. The *in vitro* formation of methamphetamine has previously resulted in false positive reports on proficiency tests. Now it appears that methcathinone may also be formed *in vitro* with similar specimens and analytical techniques. Determining the source of the methcathinone in biological samples is essential for correct interpretation in postmortem and DWI investigations.

Methcathinone is a schedule I controlled substance easily synthesized by oxidation of ephedrine or pseudoephedrine. Use of methcathinone peaked briefly in the 1990s, but has since declined; in large part due to stricter control of pseudoephedrine. Methcathinone produces euphoric and stimulant effects similar to, but less intense than, methamphetamine. Methcathinone is not nearly as popular as methamphetamine, but is easier to synthesize, and may serve as a starting point for clandestine chemists. A recent raid in Valdez, AK uncovered a methcathinone lab in the home of an 18-year-old and a 16-year-old was arrested in Irvine, CA for experimenting with a methcathinone recipe she found online. Due to its rarity, methcathinone findings in biological specimens usually arouse suspicions.

Low levels have occasionally been found of methcathinone in blood or urine during forensic drug screening by gas chromatography mass spectrometry (GCMS). There is usually an overload of ephedrine or pseudoephedrine present in these cases, and many do not confirm when methcathinone is tested directly. These observations suggest that methcathinone can form as an artifact during GCMS analysis if high concentrations of ephedrine or pseudoephedrine are present.

The Navy Drug Screening Laboratory reported a similar issue in 1993. Proficiency urines spiked with pseudoephedrine were reported as positive for methamphetamine. Further investigation revealed that GCMS injection above 220°C promoted the loss of a hydroxyl from derivatized pseudoephedrine to form methamphetamine. The addition of a preparatory acetylation or oxidation step was suggested to remove ephedrine and pseudoephedrine in order to avoid false positive results for methamphetamine. While the oxidation of pseudoephedrine does eliminate the possibility of methamphetamine formation, it can also create methcathinone by converting the hydroxyl to a carbonyl group.

Pharmacokinetic studies of methcathinone have established that it is primarily reduced to form ephedrine. This is one explanation for why ephedrine (or its stereoisomer pseudoephedrine) is almost always detected when methcathinone is present in biological specimens. Unfortunately, this creates a chicken-and-egg situation, making it difficult to determine if methcathinone was intentionally ingested or if it might have formed in vitro due to oxidation of ingested ephedrine/pseudoephedrine. A previous report established that ingestion of 60 mg pseudoephedrine did not produce detectable levels of methcathinone in urine. Higher concentrations were not tested.

A series of experiments were conducted to determine the role of analytical conditions in methcathinone formation. Spiked blood samples were analyzed by GCMS and liquid chromatography tandem mass spectrometry (LCMSMS). Neat standards of pseudoephedrine and ephedrine were also tested to exclude the possibility that methcathinone was present as a contaminant in the ephedrine and pseudoephedrine standard materials.

Methcathinone was detected by GCMS from 20 mcg/mL ephedrine and 40 mcg/mL pseudoephedrine in spiked blood samples. Trace amounts were present at ten-fold lower concentrations. Surprisingly, methcathinone was also detected by LCMSMS in blood samples spiked with 40 mcg/mL pseudoephedrine. The methcathinone did not come from the standard material because neat injections of 50 and 100 mcg/mL ephedrine and pseudoephedrine were negative for methcathinone (LOD 1 ng/mL). Instead, methcathinone appears to form as an artifact due to interactions with the biological matrix.

It is important to consider the possibility of in vitro oxidation when methcathinone is detected in the presence of pseudoephedrine/ephedrine. This combination looks very similar to actual methcathinone ingestion since ephedrine is the major metabolite of methcathinone. However, it is possible for methcathinone to form during analysis of specimens that contain high concentrations of pseudoephedrine/ephedrine. Methcathinone formation can be minimized by using analytical procedures that avoid excessive heat (LCMSMS).

Methcathinone, Artifact, Stability

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