



### K4 Prevalence of Norhydrocodone in Authentic Hydrocodone Urine Specimens

Seongshin Gwak, BS\*, 1319 Smither Drive, #7306D, Huntsville, TX 77340; Ayodele A. Collins, MSc, 516 North Loop 250 West, Apartment 1724, Midland, TX 79703; and Cade Park, BS, Scot Chester, BS, and James A. Bourland, PhD, Ameritox Ltd., 9930 West Highway 80, Midland, TX 79706

The goal of this presentation is to evaluate the incidence and disposition of norhydrocodone in authentic urine specimens of pain patients prescribed hydrocodone.

This presentation will impact the forensic science community by demonstrating applicability of norhydrocodone for the reliable confirmation of hydrocodone positive urine samples.

Hydrocodone is a common semi-synthetic opiate used as an antitussive and an analgesic.<sup>1</sup> Hydrocodone is excreted in urine as unchanged drug (49.8%) and metabolites: norhydrocodone (20.7%), conjugated hydromorphone (16.6%), 6-hydrocodol (12.4%), and conjugated 6-hydromorphol (0.4%).<sup>1</sup> The high potential for hydrocodone abuse may be due to the relative ease of purchase and the prevalence of use among chronic pain patients. Urine drug testing of pain patients for such drugs plays a pivotal role in the management of their prescribed medication. Monitoring of drug adherence, possible drug abuse, and diversion of prescribed drugs should be considered. Opiate urinalysis has been challenged by complex biotransformation of parent drugs and the commercial availability of the metabolites, such as hydromorphone.<sup>2</sup> Therefore, it is necessary to detect distinctive biomarkers for more accurate interpretation in the absence of parent drug. Normetabolites are considered unique metabolites indicating the ingestion of parent drugs. This study aims to detect norhydrocodone in urine specimens of pain management patients prescribed hydrocodone.

Authentic urine specimens (n=101) from pain management patients prescribed hydrocodone were obtained. Norhydrocodone was incorporated into the current opiate assay, which includes codeine, hydrocodone, hydromorphone, morphine, noroxycodone, oxycodone, and oxymorphone. The absence of co-elution effects between norhydrocodone and the other opiates was confirmed. The new method was validated to verify the reliability of norhydrocodone detection and quantification. The concentrations of norhydrocodone, hydrocodone, and hydromorphone in urine samples were measured. Urine specimens were treated with acid for the hydrolysis of conjugated glucuronide moiety and then injected into a liquid chromatograph tandem mass spectrometer (LC/MS/MS) equipped with columns utilizing turbulent flow technology.

The limits of detection and quantification (LOD and LOQ) and the upper limit of linearity (ULOL) for norhydrocodone were 100ng/mL, 250ng/mL and 100,000ng/mL, respectively. Intraday and interday precision and accuracy were conducted at 300, 3000, 30000ng/mL and showed <14.4% coefficient of variation and <±14.7% deviation from the target concentrations. Of the total urine specimens, 90.1% were positive for norhydrocodone, demonstrating that it is a common metabolite in hydrocodone urine specimens. Urine specimens containing norhydrocodone alone totaled 3%. The mean relative abundances of hydrocodone, norhydrocodone, and hydromorphone in the urine samples were 31.1%, 62.4% and 11.8%, respectively. This is inconsistent with previous reports showing unchanged parent drug as the major analyte present in urine after metabolism of hydrocodone. The results imply that the chronic use of hydrocodone increases the abundance of norhydrocodone metabolite in urine compared to single-dose usage.

Norhydrocodone is a prevalent and dominant metabolite in urine following the consumption of hydrocodone by chronic pain patients. It is a unique biomarker that can provide more conclusive confirmation and to a lesser extent reduce false negatives in urine drug testing for hydrocodone.

#### References:

- R. Baselt. Disposition of Toxic Drugs and Chemicals in Man. 7<sup>th</sup> ed. 2004. Biomedical Publications.
- E. Cone, et al. Urine testing for norcodeine, norhydrocodone, and noroxycodone facilitates interpretation and reduces false negatives. Forensic Science International 2010; 198:58-61.

#### Norhydrocodone, LC/MS/MS, Prevalence