K8 Determination and Quantitation of Noroxycodone in Human Urine Samples Using High Performance Liquid Chromatography - Electrospray Ionization-Tandem Mass Spectrometry

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After attending this presentation, attendees will have a greater understanding of opiate chemistry, metabolism, kinetics, and pharmacology, as well as be familiar with and implement current LC/MS/MS technology. Attendees will also gain information about an analytical method for determination of noroxycodone, a metabolite of oxycodone, and will understand the metabolic pattern for oxycodone.

This presentation will impact the forensic community by giving greater insight into human metabolism of oxycodone. This information can be utilized to perfect or improve current methods for detecting and quantifying oxycodone and its metabolites in clinical and forensic toxicological settings.

Oxycodone (4,5-epoxy-14-hydroxy-3-methoxy-17-methylmorphi- nan-6-one), is an analgesic, semi synthetic opioid derived from thebaine. Also known by its manufactured names OxyContinä, OxyNormä, Roxicodone™, and others, it comes in a variety of shapes and dosages. Oxycodone is commonly prescribed for significant pain management typically associated with cancer, and has been used clinically for this purpose in the United States for the past eighty years. It has been a “drug of abuse” for nearly 50 years.

Oxycodone is metabolized in the body by two isoenzymes Cytochrome P450 (CYP) 3A4 and CYP2D6. CYP3A4-mediated metabolism of the compound yields N-demethylated metabolites noroxycodone, noroxymorphone, and a and b noroxycodol. CYP2D6- mediated metabolism produces O-demethylation of oxycodone to oxymorphone and a and b noroxymorphol, and 6-keto-reduction to a and b oxycodol.

Human urine samples, collected as part of another study to determine the elimination rate of oxycodone, were used as test samples for the detection and quantitation of noroxycodone. A method developed for the simultaneous quantitation of several opiates, including codeine, hydrocodone, hydromorphone, oxycodone, oxymorphone, and morphine, was modified to also incorporate noroxycodone as one of the compounds using selected ion monitoring (SIM). This method was utilized on a 4-channel multiplexing HPLC system interfaced with triple quadrupole mass spectrometer. Limit of quantitation, as well as between day accuracy and precision (%deviation and %CV) of noroxycodone was established at 100 ng/mL (3.9% and 24.9%).

Urine samples were collected over a period of a week from seven individuals given one of three different concentrations of oxycodone, along with a naltrexone blockade (50 mg per day). Concentrations of noroxycodone, oxycodone, and oxymorphone resulting from the analysis of an individual dosed with 80 mg tablets of oxycodone have shown noroxycodone to be the primary metabolite (70.8%±4.7) followed by oxycodone (18.5%±5.2) and oxymorphone (10.8%±2.1). Results for samples from other individuals will be tabulated and presented. These concentration results indicate that CYP3A4 mediation is the predominant metabolic pathway of oxycodone in humans.

Noroxycodone, High Performance Liquid Chromatography, Tandem Mass Spectrometry

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