Extraction and Quantitation of Carfentanil and Naltrexone in Mammalian Plasma with LC/MS Detection

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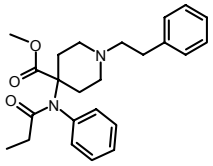
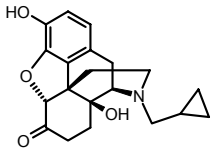
The quantitation of carfentanil and naltrexone at pharmacologically relevant plasma concentrations has not been previously described. This application note reports the sensitive and accurate detection and quantitation of these basic drugs by LC/MS using a ZirChrom®-PBD column. The ability to detect and quantitate carfentanil and naltrexone with a single extraction dramatically decreases the time and money needed to perform sample analysis, especially since both drugs are used concurrently in zoological medicine.



Carfentanil



Naltrexone

Figure 1. Structures of Carfentanil and Naltrexone

Introduction

Carfentanil (CARF) is the most potent opioid agonist currently in use. It is 20× more potent than fentanyl [1], and is approved by the United States Food and Drug Administration for immobilization of free-ranging or confined members of the family Cervidae (i.e. white-tailed deer, elk, & moose). Since its development in 1975, CARF has become the drug of choice for immobilization of a wide variety of non-domestic mammals [1,2], because it allows for rapid and reliable induction of anesthesia with small volumes of CARF in a diverse range of species [3]. Carfentanil is a synthetic derivative of fentanyl (refer to Technical Bulletin # 300). In most situations, CARF anesthesia is reversed using the antagonist naltrexone (NLT) [1].

This analytical method was developed by the Zoological Pharmacology Laboratory, College of Veterinary Medicine, Kansas State University (Manhattan, Kansas, USA) to quantitate the plasma concentrations of carfentanil and naltrexone using a single toluene-based extraction method [4]. The sensitivity of this method is two orders of magnitude lower than previously reported methods [5]. It will assist with providing information on the pharmacokinetics of these compounds.

Experimental

A mixture of carfentanil and naltrexone was separated at room temperature using a ZirChrom®-PBD column and an LCQ_{DUO} LC/MS system manufactured by ThermoFinnigan (San Jose, CA) using an ESI source with positive ionization. The separation conditions were as follows:

Column:	ZirChrom®-PBD, 50 mm x 2.1 mm i.d., 3 micron (Part Number: ZR03-0521)
Mobile Phase:	30/70 (v/v) acetonitrile/10 mM ammonium acetate, 0.1 mM citrate (pH 4.4)
Temperature:	Uncontrolled
Flow Rate:	0.3 ml/min.
Injection:	50 µl
Detection:	LC/MS/MS

The use of LC/MS allows for the determination of plasma levels of carfentanil prior to and following reversal of anesthesia with greater sensitivity and confidence. The limit of quantitation was 8.5 pg/mL for carfentanil and 0.21 ng/mL for naltrexone [4].

Table 1: Chromatographic Results for Carfentanil and Naltrexone

Compound	Retention Time	k'
Naltrexone	~ 1.7	~ 1.5
Carfentanil	~ 2.7	~ 3.0

This method can be tailored to your specific application needs. ZirChrom method developers can help to optimize and transfer this method to your site. Please contact ZirChrom technical support at 1-866-STABLE-1 or support@zirchrom.com for details.

Acknowledgements

R.P. Hunter, D.E. Koch, A. Mutlow, and R. Isaza, Zoological Pharmacology Laboratory, College of Veterinary Medicine, Kansas State University (Manhattan, Kansas, USA)

References

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