Technical Note

Etodolac: An Analytical Profile

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ABSTRACT: Etodolac (Lodine) has been identified in various submissions of illicit heroin seizures in the northeast region of the United States. Etodolac is a nonsteroidal anti-inflammatory drug used in the treatment of mild to moderate pain, and helps relieve symptoms of arthritis, such as inflammation, swelling, stiffness, and joint pain. Analytical data, including gas chromatography, infrared spectroscopy, Raman spectroscopy, mass spectroscopy and proton nuclear magnetic resonance spectroscopy are presented.

KEYWORDS: Etodolac, Heroin, Adulteration, NSAID, Analysis, Forensic Chemistry

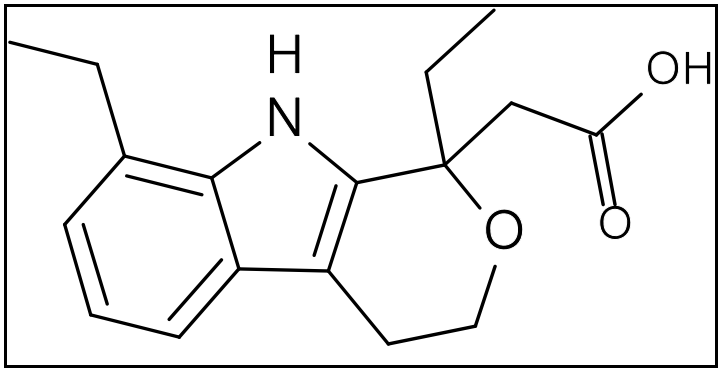

Figure 1. Structure of Etodolac ($C_{17}H_{21}NO_3$; mw = 287.4).

Introduction

The presence of pharmacologically active adulterants and inactive diluents as cutting agents in illicit heroin exhibits is common, and dynamic. Over the past 9 years, this laboratory has received increasing numbers of heroin submissions containing varying amounts of etodolac (trade name Lodine, Figure 1), 1,8-diethyl-1,3,4,9-tetrahydropyranol[3,4-b]indol-1-acetic acid, a prescription nonsteroidal anti-inflammatory drug (NSAID) [1,2] (see Figure 1). Approved by the U.S. Food and Drug Administration in 1997 for acute and long term use in the management of osteoarthritis and rheumatoid arthritis, etodolac is produced by multiple pharmaceutical companies in both capsule and tablet forms [3]. Herein, standard analytical data (GC/FID, FTIR/ATR, Raman, GC/MS, and ^{1}H-NMR) is presented for etodolac.

Experimental

Etodolac Standard: Sigma-Aldrich, Inc. (St. Louis, MO); Lot #121K4049. Because etodolac is *de facto* an indole propionic acid (see Figure 1), it is presumed to be a zwitterionic compound.

Gas Chromatography / Flame Ionization Detector (GC/FID):

Instrument	Agilent 6890N with a flame ionization detector
Column	HP-5, 30 m x 0.25 mm x 0.25 μm film thickness
Injector Temperature	270^{O}C
Oven Temperature	175^{O}C for 1.0 min, ramped 15^{O}C/min to 280^{O}C for 3.0 min
Carrier Gas	Hydrogen ramped flow 2.5 mL/min for 5 min to 3.5 mL/min; split ratio 50 : 1

Utilizing the above experimental parameters, etodolac breaks down into four peaks, three minor peaks followed by one major peak. The retention time for the three minor peaks are 3.940, 4.974, and 5.068 minutes followed by the major peak at 6.056 minutes. The retention times relative to heroin are 0.525, 0.659, 0.676, and 0.807, respectively.

Fourier Transform Infrared Spectroscopy (FTIR/ATR):

Instrument	Perkin Elmer Spectrum One
Number of Scans	16
Resolution	4.000 cm^{-1}
Wavenumber Range	4000 cm^{-1} to 650 cm^{-1}

Data was obtained by direct analysis using an attenuated total reflectance (ATR) attachment on FTIR. The data was not ATR corrected [Figure 2].

Fourier Transform Raman Spectroscopy (FT Raman):

Instrument	Thermo Nicolet Nexus 670 FTIR
Number of Scans	8
Resolution	8.000 cm^{-1}
Wavenumber Range	3701 cm^{-1} to 100 cm^{-1}

Data was obtained by direct analysis using a Smart Golden Gate ZnSe Accessory on FTIR. The data was corrected with the automatic smooth function [Figure 3].

Gas Chromatography / Mass Spectrometry (GC/MS):

Instrument	Agilent 5973
Column	HP-5 MS, 30 m x 0.25 mm x 0.25 μm film thickness
Injector Temperature	255^{O}C
Oven Temperature	90^{O}C for 1.35 min, 35^{O}C/min to 290^{O}C
Carrier Gas	Helium with split ratio = 35 : 1
MS Quad	150^{O}C
MS Source	230^{O}C
Scan Range	40 - 550 amu

Electron impact mass spectrometry data shows a molecular ion at *m/z* 287 and a base ion at *m/z* 228 [Figure 4].

Proton Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR):

Data was obtained using a Varian Mercury 400 MHz NMR. The sample was prepared at a final concentration of 25.2 mg/mL in deuterated methanol (CD_3OD) containing TMS (tetramethylsilane, $Si(CH_3)_4$) as the 0 ppm reference. The spectrum was obtained with 8 scans using a 1.0 second delay, 45^O pulse, and a 2.99 second acquisition time. The scan width was 6410 Hz [Figure 5]. Note that etodolac cannot be analyzed in D_2O, because it is insoluble in water.

Results and Discussion

Although the levels of adulteration have widely varied, etodolac is typically present in heroin at approximately 1% or below. With the exception of the GC/FID chromatography, the presented data is unremarkable. When etodolac is analyzed by GC/FID, four peaks are present due to the thermal breakdown of the compound (the breakdown products were not identified). The presented data will assist in the identification of etodolac.

References

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2. Merck Index. 13th Ed. Whitehouse Station, NJ: Merck Research Laboratories, 2001; 685.

3. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Overview&DrugName=ETODOLAC (last accessed Dec 6, 2008).

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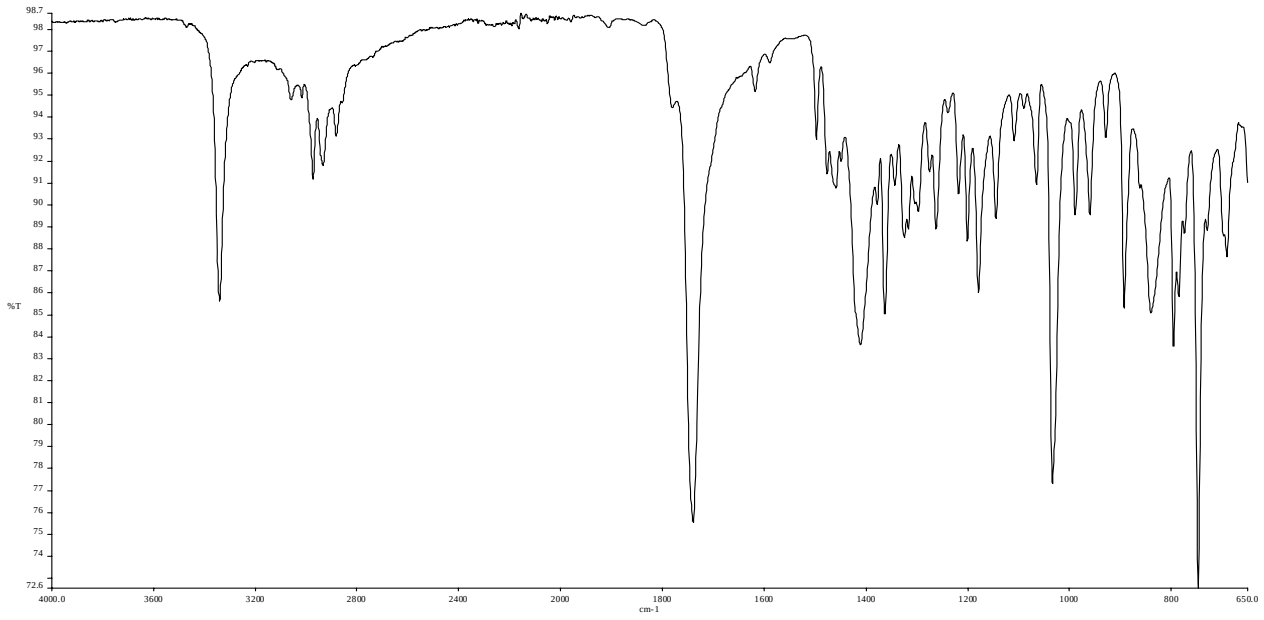

Figure 2. FTIR/ATR Spectrum of Etodolac.

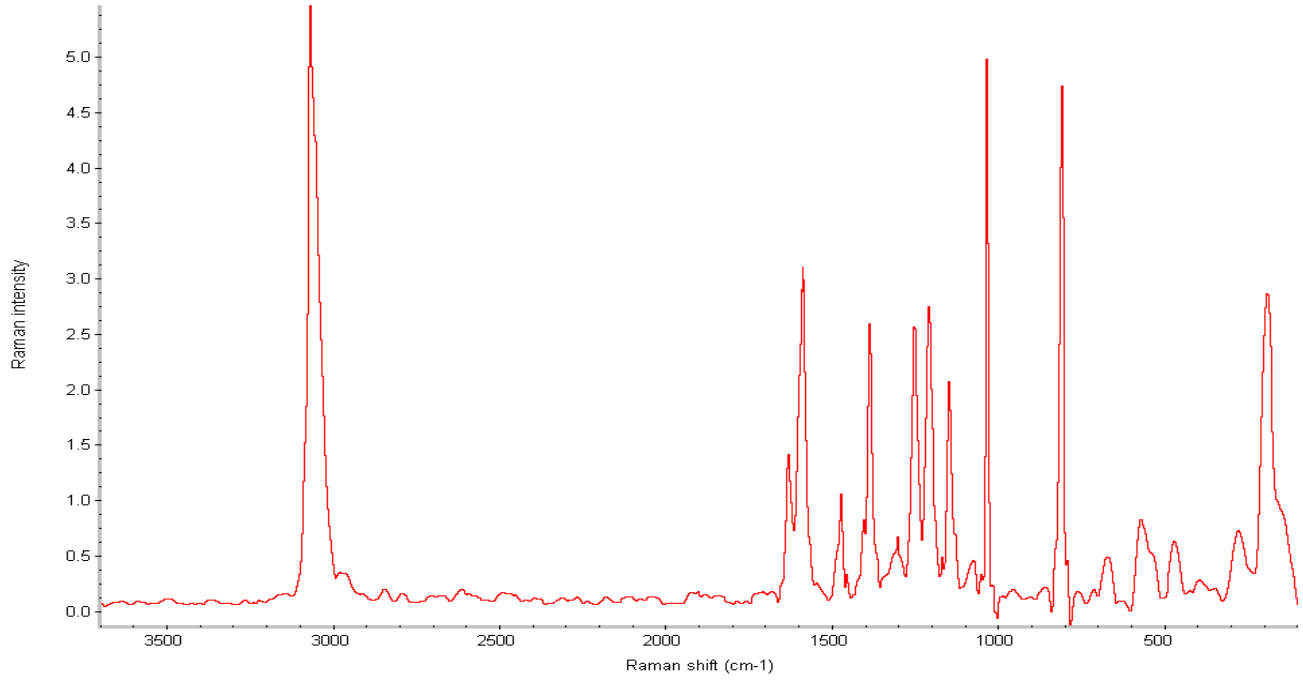

Figure 3. FT Raman Spectrum of Etodolac.

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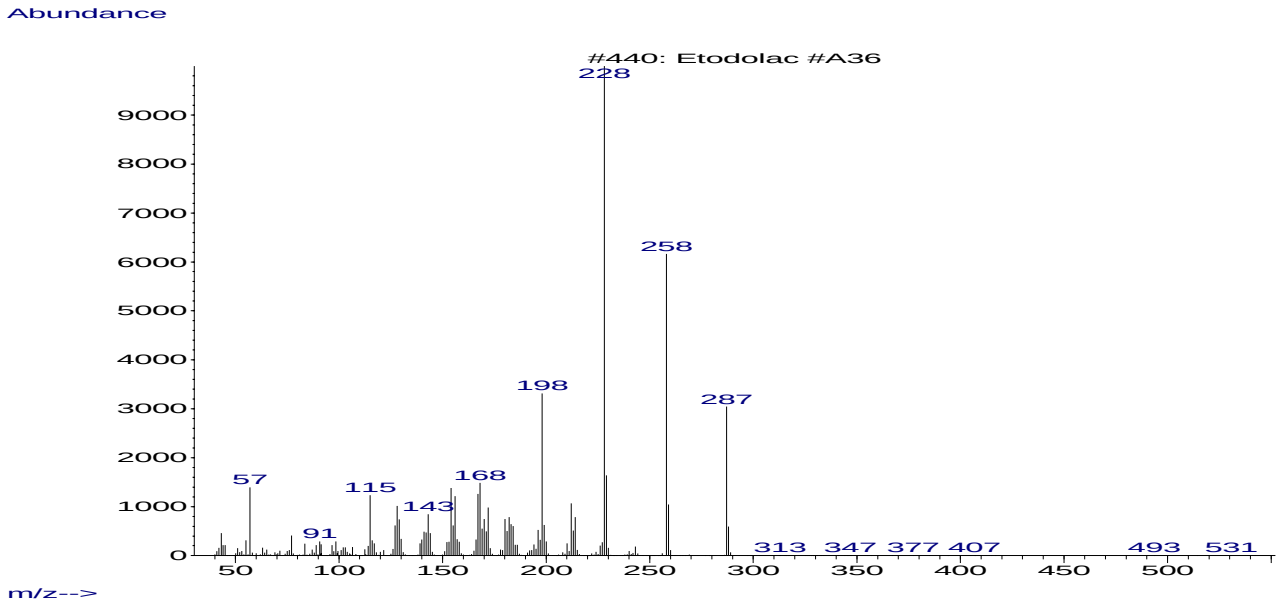

Figure 4. Electron Impact Mass Spectrum of Etodolac.

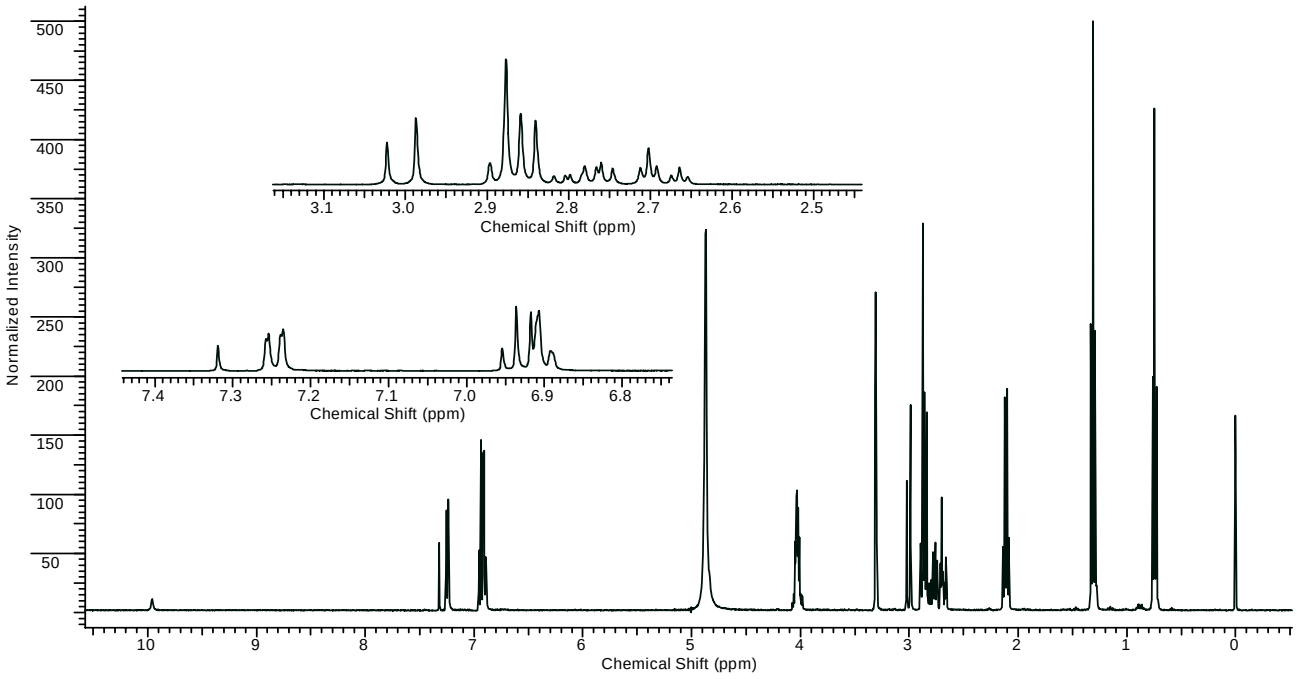

Figure 5. 400 MHz ^{1}H-NMR Spectrum of Etodolac in CD_3OD.

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