

Technical Note

Qualitative and Quantitative Analysis of Ionamin 30 Capsules (Containing a Time-Release Formulation of Phentermine)

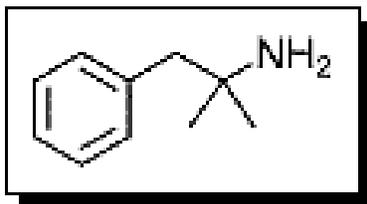
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ABSTRACT: Analysis of a time-release formulation of phentermine required sonication in water for 60 minutes, in order to release the active compound from the matrix.

KEYWORDS: Phentermine, Ionamin 30, Time-Release Formulation, Analysis, HPLC, ¹H-NMR, Sonication, Forensic Chemistry



Phentermine

Introduction

The Mid-Atlantic Laboratory recently received a large submission of multiple exhibits allegedly containing various forms of phentermine. The exhibits were seized in Laurel, Maryland (no further details). One exhibit included 1,494 yellow capsules (14 x 5 millimeters), each labelled as “Ionamin 30” and containing brown resin beads and white powder (see Photos 1 and 2, next page). Ionamin 30 is a time-release formulation of phentermine containing 30 milligrams of phentermine in a cationic exchange resin complex (1). However, preliminary analyses of methanol and chloroform extracts of the capsule contents using GC, GC/MS, and NMR indicated no controlled substances. Further research on drug-resin complexes revealed that the time-release mechanism in these capsules involves a water-permeable/acid insoluble barrier that allows the substance to be slowly released into the body. Herein, a method for the analysis of this type of formulation is presented. The method may be useful for other time-release formulations.

Experimental

Chemicals and Reagents: Phentermine standard was acquired from this laboratory’s reference collection. All other chemicals were of reagent-grade quality or better.



Photo 1



Photo 2

HPLC: Analyses were performed using a Agilent 1100 Series High Performance Liquid Chromatograph. Acquisition Parameters are summarized below:

Column:	RP18 Waters Symmetry Shield; 3.5 μm particle size, 150 mm x 4.6 mm
Detector:	Diode Array (Detection at 210 nm)
Temperature:	30 $^{\circ}\text{C}$
Flow Rate:	1.0 mL/minute
Injection Volume:	3 μL
Buffer:	4000 mL HPLC grade water, 9.6 grams sodium phosphate monobasic, adjusted to pH 2.3 with phosphoric acid, 8.0 mL hexylamine, and 50 milligrams sodium azide
Mobile Phase:	2.3 pH buffer:acetonitrile (85:15)

Standard Solution: A standard solution of phentermine was prepared at approximately 0.5 mg/mL with 0.3 mg/mL resorcinol in 95:5 buffer:acetonitrile.

Sample Solution: A portion of sample was accurately weighed into a volumetric flask, a small amount of room temperature water added, and the mixture was sonicated for at least 60 minutes. The resulting solution was diluted with additional water to give an estimated phentermine concentration of approximately 0.5 mg/mL. The diluted solution was filtered through a 0.2 micron filter before injection onto the HPLC.

Quantitative Procedure: Inject 3 μL of the solution onto the HPLC. The preferred wavelength for phentermine is 210 nm with a bandwidth of 10 nm.

$^1\text{H-NMR}$: Analyses were performed using a Varian Mercury-Plus 400 MHz NMR using a 5 mm Varian Nalorac indirect detection, variable temperature, pulse field gradient probe with PulseTune® (Varian, Palo Alto, CA). The compound was dissolved in deuterated water (D_2O) containing 1 percent (w/w) 3-(trimethylsilyl)-1-propanesulfonic acid, sodium salt as the reference compound. The temperature of the sample was maintained at about 21 $^{\circ}\text{C}$. Standard Varian (vNMR Version 6.1) pulse sequences were used to acquire the proton spectra. Eight scans were acquired for each spectrum. Processing of data was performed using software from Applied Chemistry Development Laboratory, Version 8 (Toronto, Canada).

Results and Discussion

Phentermine is an appetite suppressant (anorectic) used in the management of obesity (1,2). Because it is also a stimulant that is subject to abuse, phentermine is a Schedule IV controlled substance under the U.S. Controlled Substances Act.

Analyses of standard preparations of phentermine is straightforward (3,4). However, time-release formulations of pharmaceuticals require preliminary workup to release the active ingredient from the matrix. In the present study, attempted dissolution of the contents of an Ionamin 30 time-release formulation of phentermine in either methanol or chloroform was ineffective. The resin used in the Ionamin formulation is water-permeable, and it was found that sonication in water was sufficient to release the trapped phentermine. The release was time-dependent; detectable amounts of phentermine (sufficient for a qualitative determination) were released after 10 minutes of sonication, but complete release (required for accurate quantitation) required 60 minutes of sonication (see Figures 1 and 2). The sonicated solution can also be dried down and reconstituted in chloroform/methanol for GC and/or GC/MS analysis, or in deuterated water for NMR analysis (Figures 3a and b).

The white powder in the capsules was not identified, but according to the literature it is a mixture of lactose, magnesium stearate, and titanium dioxide (1).

References

1. Physicians' Desk Reference, 59th ed., Thomson PDR, Montvale, NJ:2005, pp. 1105-1106.
2. The Merck Index, 13th ed., Merck & Co., Inc., Whitehouse Station, NJ:2001, # 7346.
3. Mills III T, Roberson JC. Instrumental Data for Drug Analysis, 2nd ed., Elsevier, New York, NY:1987, pp. 1818-1819.
4. Moffat AC, Osselton MD, Widdop B, Galichet LY, eds. Clarke's Analysis of Drugs and Poisons, 3rd ed., Pharmaceutical Press, London:2004, pp. 1439-1440.

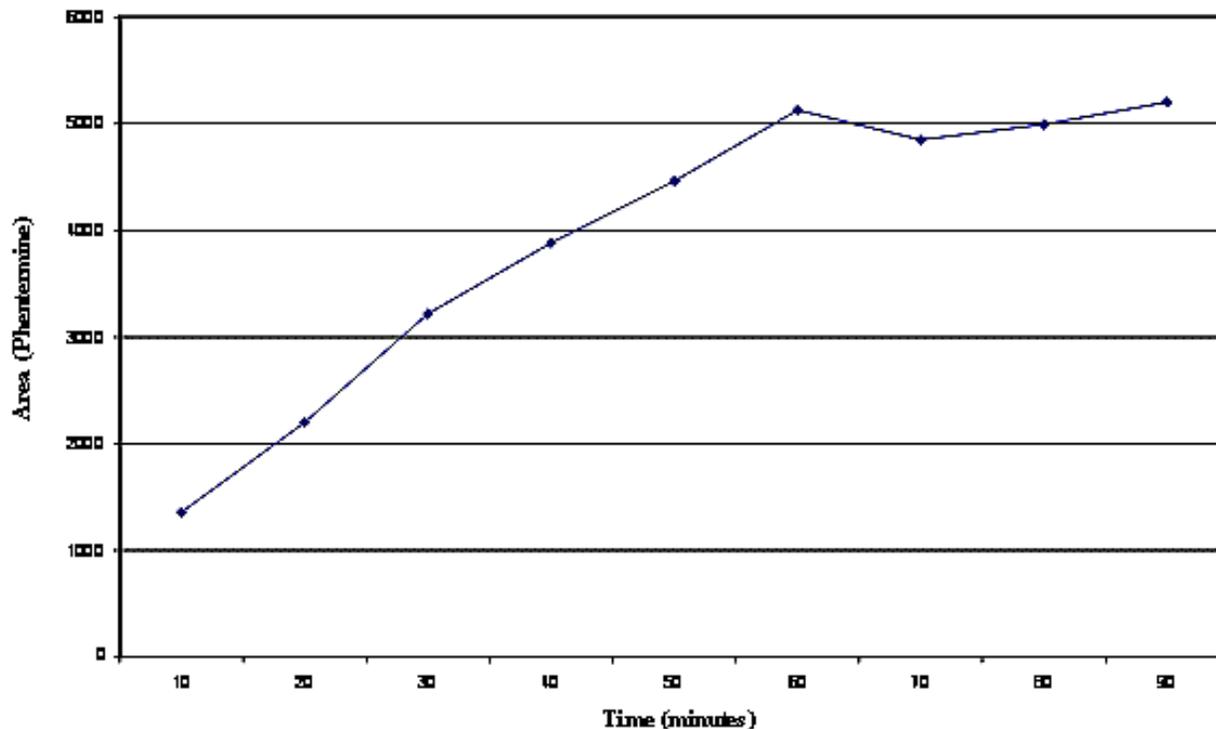


Figure 1. Ten Minute HPLC Qualitative Interval Study of 30 mg Phentermine Capsule.

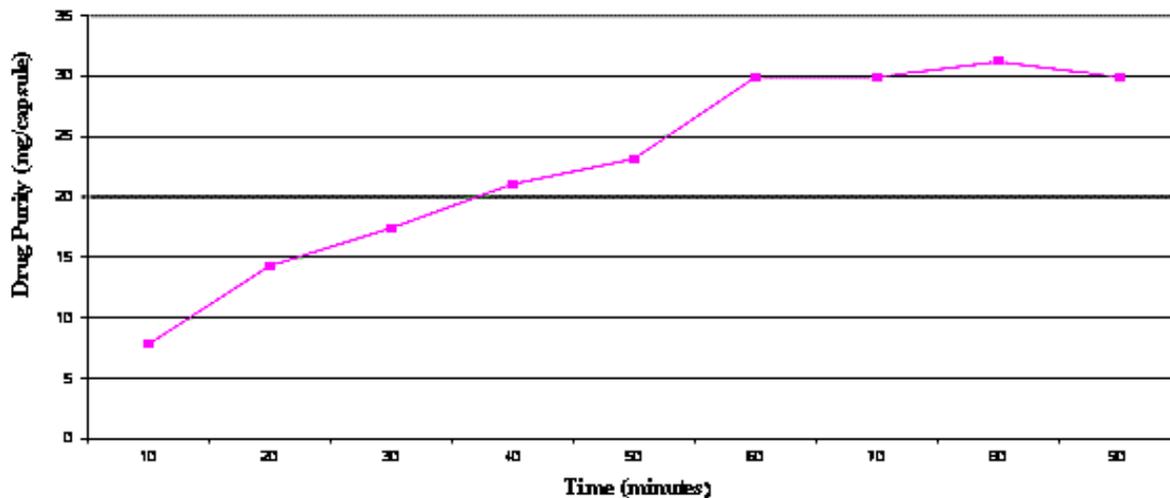


Figure 2. Ten Minute HPLC Quantitation Interval Study of 30 mg Phentermine Capsule.

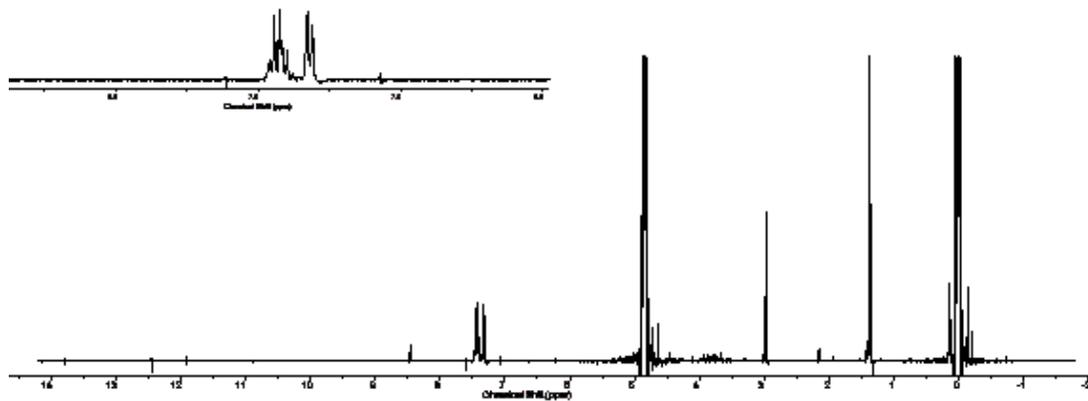


Figure 3a. ¹H-NMR Spectrum of Ionamin 30 Capsule in Deuterated Water.

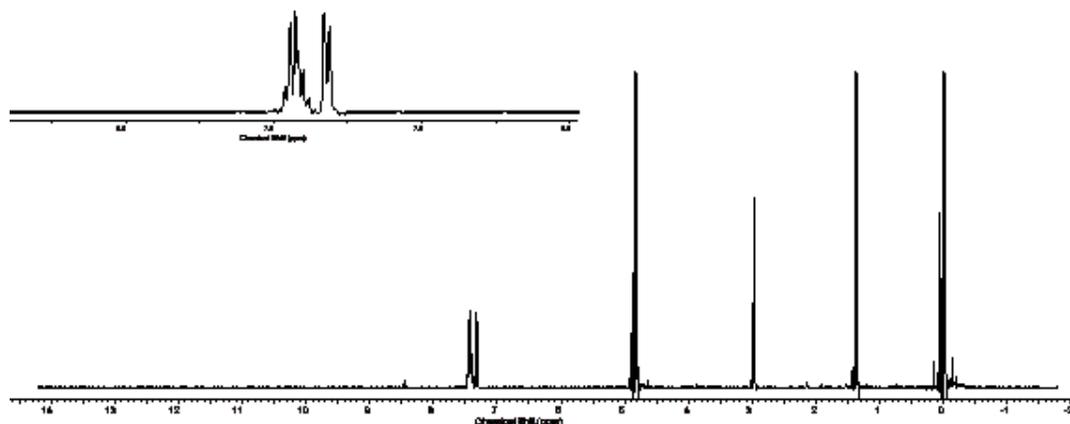


Figure 3b. ¹H-NMR Spectrum of Phentermine Hydrochloride Standard in Deuterated Water.