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The Analytical Investigation of a Designer Drug Proposed to Contain Ethylphenidate

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Abstract

In recent years, designer drugs have flooded the market due to their ability to circumvent current drug laws. Researchers struggle to stay up-to-date due to the constant molecular derivation that occurs among the designer drug market. One such drug is AM-HI-CO Recharge Extra 2B which is advertised to contain (RS)-ethyl 2–phenyl-2-piperidin-2ylacetate better known as ethylphenidate. The website claims this product produces an "*Energizing and Euphoric Collecting Experience*" and is "*Not For Human Consumption*". This compound is structurally similar to methyphenidate which is a Scheduled III drug prescribed to treat narcolepsy and attention deficit hyperactivity disorder. Ethylphenidate is an unscheduled drug and, like other designer drugs sold directly through the internet, very little research has been carried out dealing with the safety effects of the drug. Nonetheless, individuals directly obtain and consume such drugs. We purchased AM-HI-CO Recharge 2B from an online retailer, Bath-Salts-Direct.com and analyzed it using fourier transform infrared spectroscopy (FT-IR), nuclear magnetic resonance spectroscopy (NMR), and gas chromatography-mass spectrometry (GC-MS) in order to obtain an analytical profile. We compared our results to those we obtained for an ethylphenidate standard. Our results showed that the AM-HI-CO Recharge Extra 2B contained approximately 61% pure ethylphenidate with the rest being unknown inorganic filler. These results are relevant since there is no scientific data reported on the contents of AM-HI-CO Recharge Extra 2B. As such, this may serve to aid the forensic and medical communities in the identification and understanding of remnants of such packaging found on an overdose victim.

Keywords: Ethylphenidate; Spectroscopy; Drugs Design

Introduction

Recently law enforcement agencies worldwide have observed an escalation in the use of synthetic designer drugs [1-4]. These products are marketed to children and young adults with attractive labeling and appealing names in order to entice the individual into purchasing them. The products have names such as China White, Ocean Burst Red Extreme, Diablo XXX Extreme, and many others [5]. The compounds within these designer drugs are synthesized to closely mimic the molecular structure of psychoactive drugs that are scheduled control substances. Since the compounds are similar, but not structurally identical, to their controlled counterpart, they are able to slip through the legislative cracks and make their way into head shops, gas stations and online stores around the world [2,3,4]. With modest regulation, little is known pertaining to the contents of these drugs, their effects on the body, and overall toxicity.

Likewise, as a result of the recurring molecular derivatization, new compounds are being synthesized at a rate with which researchers and government officials are struggling to keep up. The synthetic drug market is not unfamiliar to law enforcement agencies. Synthetic drugs have been around for over 45 years and originated in the 1970's with the introduction of a synthetic lysergic acid diethyl amide (LSD) named LSD acet l amide (Orange Sunshine). Shortly thereafter, numerous other compounds were synthesized such as synthetic opioids in the 1980's and the introduction of synthetic cathinones in the 1990's [6]. Many believe the reason for the increased use of these compounds among individuals today is a direct result of technological advancement and aggressive marketing schemes. It is relatively easy for an individual to browse the internet for newly emerging compounds, determine the compound's effects, routes for synthesis and even locations to purchase them without leaving the comfort of their home. Overall, researchers seek to determine the contents of these products, the concentrations at which they are being consumed, and the overall danger these compounds present to the user [7].

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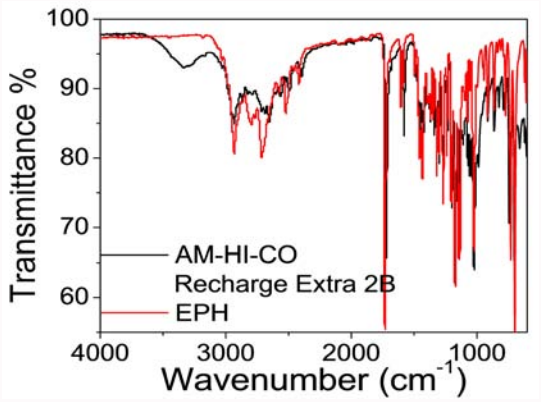

Figure 1: ATR-FTIR spectra for EPH and AM-HI-CO Recharge Extra Formula 2B.

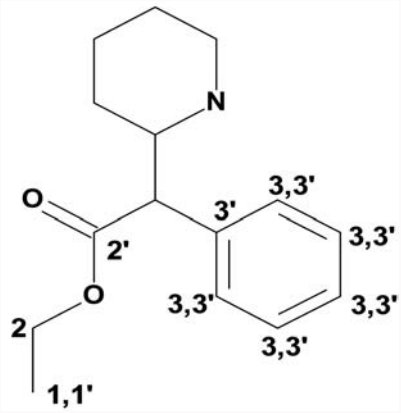

Figure 2: EPH structure ^{13}C abd ^{1}H positions for NMR data.

The designer drug sample under investigation was purchased from *Bath-Salts-Direct.com* and labeled AM-HI-CO Recharge Extra Formula 2B. The website claims this product produces an "*Energizing and Euphoric Collecting Experience*" and is "*Not For Human Consumption*". Moreover, the sample is available to be shipped to all states in the U.S. except for Alabama, Arizona, Florida, Ohio, Oklahoma, Utah, and Vermont. The sample is advertised to contain (RS)-ethyl 2-phenyl-2-piperidin-2-ylacetate or better known by its common name ethylphenidate (EPH) [5]. This compound is structurally similar to methylphenidate (MPH) which is a compound used for the treatment of narcolepsy and attention deficit hyperactivity disorder (ADHD) [7]. Research involving EPH has been extremely limited and predominately involves the *in vivo* transesterification of ritalinic acid when MPH and ethanol are consumed concurrently. However, with an increase in designer drug use, individuals are directly obtaining EPH and consuming it without the knowledge of its effects on the body. The little research that is available on EPH demonstrates similar effects to that of MPH, acting as both a dopamine (DA) and norepinephrine (NE) reuptake inhibitor. In comparison to MPH, EPH has a far greater dopaminergic selectivity which some suggest may lead to an increased dependence versus MPH [8,9]. Blocking the reuptake of DA and NE produces an amphetamine-like stimulating effect which leads to perceived feelings of euphoria, decreased fatigue, increased alertness, and increased libido. However, various negative side effects have been reported on internet drug forums and include chest pains, tachycardia, tremors, diaphoresis, hyperpyrexia, and hyperflexia [8-10].

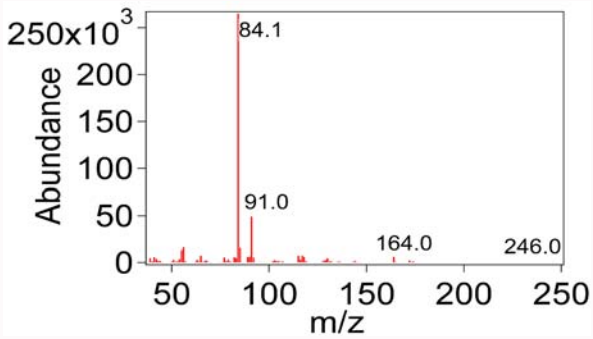

Figure 3: Mass spectrum of AM-HI-CO Recharge Extra Formula 2B.

In this study, we report on the FTIR, NMR, and GC-MS characterization of AM-HI-CO Recharge Extra Formula 2B in comparison to a known ethylphenidate standard.

Experimental

Materials

Chemical materials and reagents: Ethylphenidate (Lot# 0452834) was obtained from Cayman Chemical. The designer drug sample AM-HI-CO Recharge Extra 2B was obtained from *bath-salts-direct.com*. All other chemicals were of reagent-grade quality and obtained from Sigma Aldrich Chemical.

Methods

Fourier-Transform- Infrared Spectroscopy (FTIR): Infrared Spectra were obtained on a Thermo Scientific Nicolet iS10 instrument. The instrument was equipped with a Smart iTR single bounce attenuated total reflectance (ATR) accessory. Instrument parameters were as follows: resolution = 4cm^{-1}, 16 background scans, 16 scans/sample. Data processing was accomplished by means of the provided OMNIC software package.

Nuclear Magnetic Resonance Spectroscopy (NMR): Proton (^{1}H) and Carbon (^{13}C) NMR spectra were obtained utilizing a JEOL 400 MHz NMR.

Samples were dissolved in deuterochloroform ($CDCl_3$). Standard pulse sequences were used to obtain both ^{1}H and ^{13}C spectra. Processing of the data was performed using the provided Delta software.

Gas-Chromatography/Mass-Spectrometry (GC/MS): Mass spectra were obtained on an Agilent 5975C MS detector (MSD) that was interfaced to an Agilent 7890A GC. Samples were dissolved in GC grade methanol. The MSD was operated in the electron ionization mode with an ionization potential of 70eV. The scan range was set for 34-600amu and at a rate of 2.59 scans/second. The GC was equipped with a Restek Rtx-5MS column, 30m X 250µm X 0.25µm, coated with diphenyl dimethyl polysiloxane. The oven temperature program was as follows: Initial temperature = 100°C, 10°C/min ramp rate, final temperature 280°C hold for 6 minutes. The injector was operated in splitless mode with an injection volume of 0.2µL. Data processing was performed using Agilent GC/MSD ChemStation Software.

Results and Discussion

The FTIR spectra collected for the designer drug, Recharge Extra 2B, overlayed with the ethylphenidate standard are shown in Figure 1 and reveal two major functional group peaks present at 1721cm^{-1} and 2929cm^{-1} for the sample. A strong absorbance at 1721cm^{-1} indicating

Table 1: NMR spectra peaks for AM-HI-CO Recharge Extra 2B.

Position	Proton	Carbon
1,1'	1.30 ppm, triplet (R-C**H**$_3$)	13.91 ppm (R**C**H$_3$)
2,2'	4.25 ppm, multiplet (RCOO-C**H**)	172.04 ppm (R**C**OOR')
3,3'	7.30 ppm, multiplet (Ar-**H**)	128.41-134.29 ppm (Ar **C**)
	7.24 ppm, $CDCl_3$ solvent	7.78-77.42 ppm,$CDCl_3$ solvent

the presence of a saturated ketone while the medium absorbance at 2929cm^{-1} corresponds to CH_2 hybridized carbons typically found within a phenyl ring. The two spectra show profound similarities with small differences in absorbance patterns believed to be due to the presence of a filler compound within the designer drug sample. We isolated the filler by means of simple filtration and acquired an FTIR spectrum. The filler's chemical composition could not be determined from this spectrum.

Table 1 shows the ^{1}H and ^{13}C NMR data. The proton NMR spectrum for the designer drug sample shown in Figure 2 displayed an upfield triplet at 1.30ppm, a multiplet at 4.25 from the presence of an ethyl ester proton, and a downfield multiplet at 7.30ppm from the presence of aromatic protons. The carbon NMR spectrum displayed an upfield peak at 13.91ppm from the presence of an R-**C**H$_3$ carbon and a peak at 172.04ppm from the presence of R**C**OOR. The ^{1}H and ^{13}C NMR spectra match the EPH spectra obtained by Casale and Hays. One item worth noting is the lack of filler product present during analysis. The filler component was insoluble in $CDCl_3$ and any other solvent with a greater polarity and therefore was filtered out prior to NMR analysis and all subsequent analyses.

GC/MS analysis of the sample results in one peak with a retention time of 14.6 minutes which also matched the retention time for the EPH standard. The mass spectrum of the designer drug shown in Figure 3 was compared to the mass spectrum of the EPH standard. Both samples displayed the EPH base peak ion at 84 m/z (piperidinium ion) and qualifier ions of 91 m/z (tropylium ion) and 164 m/z (ethyl phenyl acetate moiety). Relative intensities for these ions were similar for both samples with the 91 ion at 18% and 164 ion at 2% relative intensity to the base peak. Both samples also displayed a very weak (>1%) M-1 ion peak at 246m/z which correctly corresponds to the molar mass of ethylphenidate at 247.33g/mol. The sample was shown to contain ~61% ethylphenidate using a one-point calibration. The remainder of the contents could not be identified.

Conclusion

Designer drugs have flooded the market in recent years and with a lack of fundamental research involving these new types of compounds many individuals risk injury or even death when consuming these synthetic compounds. From this investigation, we have confirmed the presence of EPH within AM-HI-CO Recharge Extra 2B and have also determined approximately 61% of the sample is EPH, with the remainder comprised of an unknown filler compound. We believe this is a significant contribution to the forensic science community since it provides the desirable information required for one of these newly emerging designer drugs which (at this current time) is exceedingly limited. This project has laid the groundwork for future work involving EPH and potential analogs to fully comprehend this compound and its potential toxic effects.

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