

Quantitative Determination of Tetrahydrozoline Levels in Eye Drops

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Abstract

Tetrahydrozoline (THZ) is a compound that is commonly found in certain brands of over-the-counter ear drops and eye drops such as Visine, targeting specific symptoms such as redness. This substance is used to give one individual an edge over another: if ingested orally, THZ depresses the central nervous system and leaves victims vulnerable to sexual assault. This compound impairs memory and judgment, and it produces a period of unconsciousness. This drug is not easily identified by typical drug analysis, and it is very easy for an individual to obtain. A recent case study evaluated a woman who had ingested a drink containing unknown amounts of THZ. About 20 hours after the drug had been ingested, both blood and urine samples were taken. No drugs were found in her blood, but 114 ng/mL of THZ was detected in her urine using a method known as gas chromatography (GC).¹ This is the only known value of THZ post-ingestion, and there have been no quantitative studies performed addressing THZ levels via ingestion or deposit in the eyes.

The purpose of this research is to analyze levels of THZ in different brands of eye drops. Protocol for this work includes standard solution preparation and quantitative analysis of these standards by ultraviolet/visible (UV/Vis) spectroscopy. In addition, amounts of THZ are

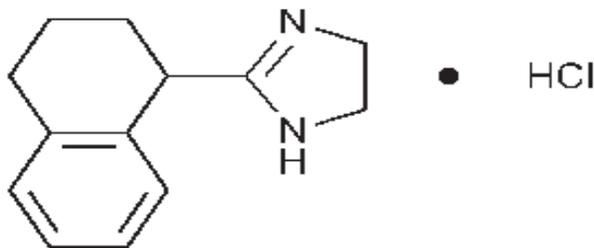


Figure 1: The Structure of Tetrahydrozoline HCl

¹ Spiller, H.A.; Siewert, D.J. "Drug-Facilitated Sexual Assault Using Tetrahydrozoline." *Journal of Forensic Sciences* [Online] 2012 57(3), 835-838.

measured in the different types of eye drops. Ultimately, these results will be beneficial in determining the amount of eye drops that need to be ingested to achieve the desired effects. It will also allow for further investigation of how the THZ interacts with the human body, is metabolized, and produces certain symptoms.

Keywords: Tetrahydrozoline (THZ), UV/Vis spectroscopy, Refractometry, Refractive index

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Very few studies have been conducted on tetrahydrozoline (THZ). Though the topic is on the rise, documentation of research on tetrahydrozoline as a date rape drug is very rare. Due to the nature of this topic, further research and quantification on this issue are pertinent. In order to quantify THZ in eye drops, spectroscopic measurements will be taken as well as the refractive index of the substance.

To investigate the use of THZ as a date rape drug, tetrahydrozoline hydrochloride (THZ) from Sigma-Aldrich, Visine brand eye drops, and Equate brand eye drops were obtained. A stock solution of 0.001M THZ was prepared, and from that, standards of 1.00×10^{-6} , 2.00×10^{-6} , 3.50×10^{-6} , 5.00×10^{-6} , 1.00×10^{-5} , and $2.00 \times 10^{-5} M$ were prepared. Following the solution preparation, 100x dilutions of Visine brand and Equate brand of eye drops were prepared after filtration.

Once standards and dilutions were prepared, spectroscopic measurements were taken. All spectroscopic measurements were obtained using an Ocean Optics Red Tide 650 Ultraviolet/Visual (UV/Vis) Spectrometer and the corresponding SpectraSuite software. A UV/Vis spectrum of THZ was obtained using a midrange standard, and a λ_{\max} was determined at a wavelength of 208nm (Fig. 2). Three absorbance readings were taken at this λ_{\max} for every concentration and then averaged. An average absorbance was determined for a 100x dilution for Visine and Equate brand eye drops.

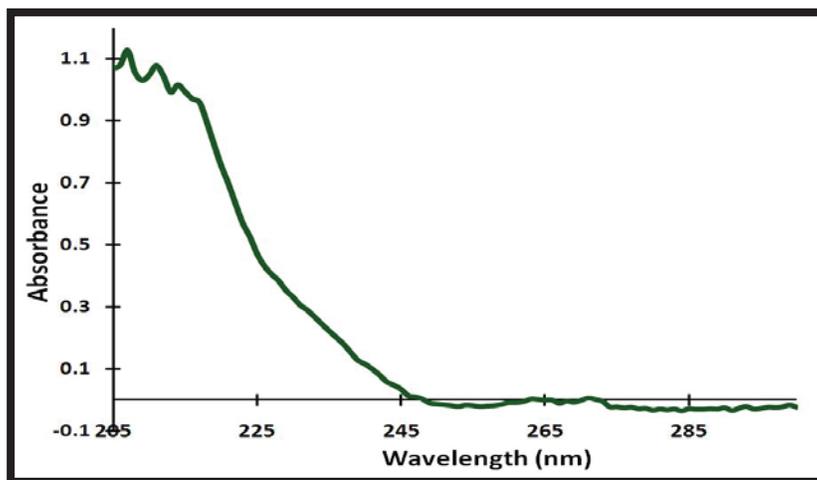


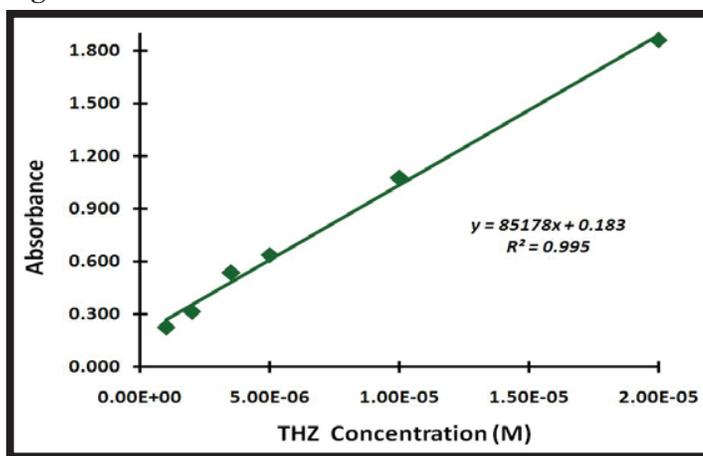
Figure 2: The UV/Vis Spectrum of THZ with a λ_{\max} value at 208 nm

After spectroscopic measurements were analyzed, it was determined that more data was necessary. The refractive index was determined using the ATAGO Pocket Refractometer. This is a qualitative method that identifies the presence of THZ. Measurements were taken for 100X diluted solutions of Visine and Equate brand eye drops, as well as $3.50E \times 10^{-06} M$ THZ.

Results and Discussion

THZ absorbance measurements detected in eye drop samples were consistent with the absorbance measurements of the THZ standards. They were all detected at the 208 nm wavelength. The R^2 value is 0.995, which is an acceptable correlation factor for a calibration curve (Fig. 3). The refractive index was taken, and all of the measurements were relatively close in comparison. This data confirms that there are detectable levels of THZ in certain over-the-counter eye drops.

Figure 3: Calibration curve for THZ Standard Solutions



Eye Drops (Diluted 100 Xs Each)	Diluted Conc. (M)	Actual Conc. (M)	Abs.
Visine	1.90×10^{-6}	1.90×10^{-4}	0.345
Equate	2.05×10^{-6}	2.05×10^{-4}	0.358

Table 1: Calculated Values of THZ in Eye Drops

The quantifiable amount of THZ in Visine and Equate (Table 1) is enough to induce unconsciousness and vomiting when ingested, and is approximately 15% of the LD_{50} concentration in rats. Visine and Equate also produced a refractive index of 1.3345

and 1.3341, reflecting the refractive index of the $3.50 \times 10^{-6} M$ THZ, which was 1.3327 (Table 2). These values represent the potential potency of the misuse of these products,

THZ Concentration	Refractive Index
$3.50 \times 10^{-6} (M)$	1.3327
100x Visine	1.3345
100x Equate	1.3341

Table 2: Refractive Index Measurements

and support the proposition that further analysis of this compound and its metabolites is necessary.

Conclusion

In order to gain complete understanding of the effects of this drug on the human body, further investigation is essential. There is no known dosage of THZ to affect one particular person because there are many factors that interfere; however, it is thought that the addition of THZ to alcohol will elevate the potency of THZ. Because the investigation of this drug is so new, there are many unanswered questions dealing with the mechanism and metabolism of THZ. In the future it will be interesting to determine if the chemical THZ is in fact reacting with the ethanol of certain alcoholic drinks, or if it is interacting with any known chemicals or enzymes in the human body. We know THZ works through the body relatively fast due to the low detection levels. There has been no known human or animal testing done with this chemical, but further investigation will provide the ability to learn the mechanism and by-products of this reaction, greatly benefiting law enforcement and enhancing the scientific understanding of this phenomenon.

References

1. Spiller, H.A.; Siewert, D.J. "Drug-Facilitated Sexual Assault Using Tetrahydrozoline." *Journal of Forensic Sciences* [Online] **2012** 57(3), 835-838.