

SOFT-DFC Snapshot – Tetrahydrozoline

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SOFT-DFC Snapshots are short reports of critical information about the more common drugs associated with drug-facilitated crimes (DFC). They do not have complete literature reviews about the drug or drug class. One key aspect is their focus on the ability to detect a drug after a single-dose administration, as is often the situation in DFC investigations. As such, these summaries also highlight instances in which available data is limited, hoping this will encourage further research studies. Finally, SOFT-DFC Snapshots point to the use of these drugs in actual DFC cases, as cited in the medical and open literature.

Tetrahydrozoline is an imidazole derivative drug that acts as an alpha-adrenergic agonist. It was identified in 1949, went through clinical trials in the 1950's, was patented in 1954, and became available for medical use in 1959 ^(1,2). Tetrahydrozoline is used in many ophthalmic and nasal preparations for its vasoconstrictive and decongestant properties ⁽³⁾. These properties make it ideal to treat congestion, conjunctivitis, dry eye, and eye redness since the drug is rapidly absorbed at the site of application when used topically ^(2,3). Although there is a prescription nasal spray available under the trade name Tyzine®, it is not frequently used anymore ⁽¹⁾. The majority of tetrahydrozoline is found in over-the-counter eye drop preparations.

When used as directed topically in the nasal passages and eyes, tetrahydrozoline interacts with alpha-1 adrenergic receptors ⁽³⁾. Side effects are typically minimal, and central nervous system (CNS) effects may be negligible; however, when ingested orally, tetrahydrozoline can interact with alpha-2 adrenergic receptors, leading to more noticeable and potentially hazardous CNS effects such as miosis, dry mouth, hypotension, bradycardia, drowsiness, hyporeflexia, hypothermia, and respiratory depression ⁽³⁾.

Tetrahydrozoline is widely available as an over-the-counter licit drug, making it easily accessible by people who may want to use it for other illicit or criminal purposes. It is colorless, odorless, tasteless, and often comes in small containers or bottles, making it attractive for criminal perpetrators. These properties have been exploited by criminals in drug-facilitated crimes (DFC) throughout the world ⁽¹⁾. Its' quick onset of action, ease of availability, and ability to cause central nervous system depression when ingested orally make it an enticing drug for use in DFCs.

Drug Class	Alpha-adrenergic agonist
Generic Name	Tetrahydrozoline
Brand Names	Azoline, Murine, Optigene, Visine® ⁽⁴⁾ , Tyzine® ⁽³⁾ Geneye Extra, Geneyes, Opti-Clear, Clarine, Altazine ⁽⁵⁾
Dosage Forms	Ophthalmic Solution: 0.05% ^(3,6) , Nasal Solution: 0.05% & 0.1%, Nasal Spray: 0.1% Ophthalmic 0.05% Solution: 1 to 2 drops up to 4 times per day for people over 6 ⁽⁵⁾ . Nasal Solutions: 0.1%: 2 to 4 drops every 4 to 8 hours for people over

18⁽⁷⁾, 0.05%: 2 to 3 drops every 4 to 6 hours for children between 2 to 6 years old⁽⁷⁾.

Nasal 0.1% Spray: 3 to 4 squirts every 4 to 8 hours for people over 6⁽⁷⁾

FDA Approval

Tetrahydrozoline is approved under Title 21 as an over-the-counter ophthalmic drug in a form suitable for topical administration⁽⁸⁾.

Tetrahydrozoline is one of four approved ophthalmic vasoconstrictors. Its' approved concentrations are 0.01 to 0.05 percent. No warnings regarding oral consumption are required⁽⁸⁾.

Pharmacological Effects:

Tetrahydrozoline exerts its' effects due to its' action on alpha-adrenergic receptors. It can act on both alpha-1 and alpha-2 adrenergic receptors. It has a very quick onset of action ranging from five to ten minutes with a duration of action of four to eight hours⁽¹⁾.

The pharmacological effects and potential toxicity can differ depending on whether it is used topically as directed or ingested⁽³⁾. When used as a topical application, it exerts its effects at the site of administration⁽³⁾. The eyes and nose have alpha-1 adrenergic receptors that allow it to produce vasoconstriction and decongestion with very few other CNS or systemic effects⁽³⁾. It is rapidly absorbed after either topical or oral ingestion⁽²⁾. If it is ingested, tetrahydrozoline is rapidly distributed into the CNS and can interact with alpha-2 adrenergic receptors, potentially causing respiratory depression, hypotension, bradycardia, dry mouth, hyporeflexia, hypotonia, miosis, and hypothermia^(2,3,9). Oral ingestion of the drug can cause profound CNS depression^(3,9). Case reports have suggested that adverse cardiovascular effects after ingestion may last a day or even longer^(9,10).

Metabolism/Elimination

Very limited information is available regarding metabolism and elimination of tetrahydrozoline. Research on half-life is also very limited, with some studies reporting a serum half-life of approximately six hours⁽¹¹⁾.

Single Dose Studies

Limited dosing studies are available for tetrahydrozoline. Dosing studies that have been conducted looked at serum and urine concentrations after receiving ocular doses. One study administered two drops of tetrahydrozoline ocularly to 10 adults at four-hour intervals for twelve hours⁽¹¹⁾. Serum and urine were collected at various intervals for up to 24 hours after the administration⁽¹¹⁾. This study found that tetrahydrozoline was able to be detected in both serum and urine for up to 12 hours after the last dose given when used ocularly as directed by the manufacturer. At 13 hours post-dosing, serum concentrations were detectable in all 10 samples and ranged from 0.068 to 0.360 ng/mL. At

24 hours post-dosing, urine concentrations ranged from 13 to 210 ng/mL while some serum concentrations were below the lower detectable limit. Research suggests that laboratory values above these levels in urine and serum indicate a non-medicinal use such as intentional poisoning, murder, suicide, or drug-facilitated sexual assault.

Non-DFC case studies can provide more information regarding metabolism, blood and/or urine levels, and clinical manifestations. A 17-year-old woman accidentally ingested 10-15 mL. Twenty-five minutes post-ingestion, she exhibited lethargy, slow speech, and ataxia. She continued to exhibit drowsiness 36 hours post-ingestion ⁽⁹⁾. In a second case study, a two-year-old male was brought to the emergency room three hours after ingesting 2-3 mL of Visine®. He was lethargic and unresponsive except to deep pain stimulation. Additionally, he had low oxygen saturation, low blood pressure, low heart rate, and pinpoint pupils ⁽¹²⁾. In another case study, a 76-year-old man was admitted 24 hours after consuming eight bottles (120 mL) of Visine® mixed with wine ⁽¹⁰⁾. He called emergency services after a period of unconsciousness. He presented with irregular heartbeat and low heart rate. An electrocardiogram performed later showed a complete atrioventricular block. The urine drug screen detected tetrahydrozoline ⁽¹⁰⁾. Additionally, a case involving an 18-month-old child who had consumed milk laced with Visine® showed similar manifestations to those previously discussed. He displayed lethargy, pinpoint pupils, and atrioventricular block. His urine concentration was 2430 ng/mL and serum concentration was 21.56 ng/mL. The milk contained a concentration of 2995.4 ng/mL ⁽¹³⁾.

DFC Cases

Tetrahydrozoline has been reported in DFC cases worldwide. When implicated in DFC cases, it is typically ingested orally. One DFC case involved a 16-year-old female ⁽³⁾. She sought medical treatment approximately seven hours post-incident. In this case, there were witnesses that saw a male placing liquid from a Visine® bottle into her drink at a party. She vomited and had periods of intermittent consciousness throughout the evening. Her vital signs were normal at the emergency room with no signs of distress. She was also awake and oriented at that time. Her urine ethanol concentration was 0.15 g/dL and her tetrahydrozoline concentration was 1481 ng/mL ⁽³⁾.

Another reported DFC case involved a 19-year-old female presenting to the emergency room approximately 23 hours post-assault ⁽³⁾. The victim and a male friend were drinking alcohol at a residence. After one drink the victim felt “buzzed”. She had a second drink and began to feel “weird” and “gray out” She also had periods of intermittent

consciousness, vomited, and felt dizzy ⁽³⁾. Her urine was negative for ethanol, and a routine drug screen didn't detect any analytes. Upon further investigation, tetrahydrozoline was reported in her urine at a concentration of 108 ng/mL, using the average of three extractions ⁽³⁾.

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