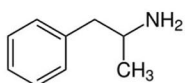


Synonyms: Captagon, fenethylline, amphetaminoethyltheophylline, amfetyline

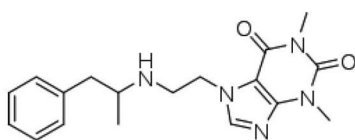


Captagon®, the trade name for fenethylline, an amphetamine prodrug, was originally developed by a German company in 1961 as a psychostimulant and eventually used in the treatment of narcolepsy and attention deficit disorder. Because of its side effects, fenethylline became a Schedule I controlled substance in the United States in 1981, was scheduled internationally in 1986, and its licit manufacture ceased. Most of the remaining stock of Captagon® was destroyed, but some was exported to the Middle East, where it became popular as an illicit stimulant. Once the original supply ran out and fenethylline was no longer available, counterfeit captagon tablets bearing the same monogramming of two offset stylized “C’s” (photo), but containing amphetamine in place of fenethylline began to appear. Today, these tablets also contain a variety of adulterants as discussed below. Counterfeit captagon tablets containing amphetamine are now the major drug used illicitly in the Middle East, where they are predominantly manufactured, although their distribution has now spread to parts of Europe. Although there is illicit demand for amphetamine-type substances (ATS) in the US, as of August 2023, there is no evidence of widespread presence of counterfeit amphetamine-containing captagon tablets in the US. CFSRE and the Colombo Plan encourage vigilance for the emergence of these characteristic counterfeit dosage forms in the US drug supply and would encourage any investigators or laboratories who encounter them to notify us at contact@cfsre.org.

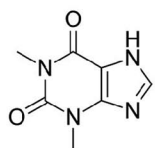
Composition of Counterfeit Captagon Tablets



Amphetamine



Fenethylline



Theophylline

- Fenethylline was a co-drug and pro-drug of both amphetamine and theophylline (see figure) and although the EMCDDA and the UNODC report that amphetamine has replaced fenethylline in all seizures of counterfeit captagon tablets, some of these tablets do contain theophylline as an adulterant. Theophylline, has non-sympathomimetic CNS stimulant properties. Other adulterants identified in captagon tablets by CFSRE and the Forensic and Laboratories Department of the Public Security Directorate in Amman Jordan include caffeine, acetaminophen, diphenhydramine, quinine, methamphetamine, ephedrine, chlorpheniramine and 8-chlorotheophylline. A significant percentage of tablets analyzed contain mostly caffeine and no amphetamine.
- In 2021, EU Member States reported 22,000 seizures of amphetamine, amounting to 7 tonnes.
- Türkiye seized 3.5 tonnes including 13.8 million tablets described as ‘captagon’ (2.9 million in 2020).
- The average purity of amphetamine at the retail level in European markets has increased by 41% over the past decade, while the price has remained relatively stable. Counterfeit captagon tablets seized in Saudi Arabia in 2021 were determined to contain between 16% and 41% amphetamine, along with significant levels of additives such as caffeine. The tablets also contained small amounts (<0.5%) of methamphetamine.
- Based on typical 170mg tablets, this would reflect an average dose of 27 to 71mg of amphetamine per tablet.

Effects of Amphetamine Psychostimulants:

The principal sympathomimetic stimulants in counterfeit captagon tablets are amphetamine, and to a much lesser extent, methamphetamine. These drugs promote the synthesis and release of the neurotransmitters dopamine, serotonin and norepinephrine. Amphetamine is used therapeutically to treat ADHD and narcolepsy. At therapeutic doses (0.25mg/kg), the effects include wakefulness, improved alertness, increased pulse and blood pressure, elevated mood and increased motor activity.

Recreational use of amphetamines typically starts in the 50-100mg single dose range, characterized by marked excitability, euphoria, rapid speech, rapid flight of ideas, marked motor restlessness, tachycardia, and hypertension. Other effects include high blood pressure, rapid heart beat, seizures, and vasoconstriction. With chronic use, there can be paranoia, panic, and delusions. Following repeated high dose use, on cessation, users can experience withdrawal characterized by lethargy, sleepiness, CNS depression, anergia and anhedonia. Effects are more intense with IV or smoked routes of administration.



Adulterants in Counterfeit Captagon Tablets

- Adulterants are added to illicit drugs as cutting agents to add bulk, and sometimes for their additive or synergistic effects. In the case of counterfeit captagon tablets, where only 16 to 41% of the tablet's content may be amphetamine, the remaining constituents will include binders (microcrystalline cellulose, sugars, starch) to help maintain the integrity of the tablet during tableting, but most pills also contain other active pharmaceuticals. In the case of captagon tablets, a number of adulterants have been identified, most commonly caffeine, acetaminophen, diphenhydramine, chlorpheniramine and others. These drugs can contribute to the effect of the amphetamine, or present their own constellation of symptoms. Below, we discuss some of the properties of the major adulterants in counterfeit captagon tablets.

Adulterant	Interactions
Theophylline	Theophylline is similar in chemical structure and effects to caffeine (see below), and is also a bronchodilator used to treat asthma. Side effects include tachycardia and cardiac arrhythmia, nausea/vomiting, stomach/abdominal pain, headache, trouble sleeping, diarrhea, irritability, restlessness, and nervousness. Theophylline can add to the excitatory effects of the amphetamine in counterfeit captagon. Fenethylline itself is broken down in the body to theophylline, so this may be the reason for its selection as an adulterant.
Caffeine	Caffeine is a non-sympathomimetic stimulant that improves wakefulness and alertness, and physical energy. Side effects of caffeine cause insomnia, nervousness, restlessness, nausea, increased heart rate, and other side effects (e.g., abnormal heart rhythm). Larger doses can
Diphenhydramine/ Chlorpheniramine	These drugs are over-the-counter antihistamines with sedative properties and will cause drowsiness. They can also cause dizziness, dry mouth/eyes, blurred vision, and rapid heart rate. Sedatives and stimulants do not cancel out each others cognitive effects, but rather create a more complex impairment with contributions from excitation, euphoria, slowed or fuzzy thinking, impaired decision making, and impulsiveness. During amphetamine withdrawal, antihistamines can add to the depressant rebound effects of the abstinence syndrome.
Ephedrine	Ephedrine is a commonly used over-the-counter stimulant and precursor for amphetamine synthesis that can lead to increased alertness and energy. It can also result in side effects such as restlessness, nervousness, rapid heartbeat, and elevated blood pressure. Combining ephedrine with sedatives or other stimulants can create a more intricate cognitive impact, involving heightened arousal, potential euphoria, as well as challenges with focus, decision-
Allopurinol	Allopurinol is a widely used medication, primarily prescribed for managing conditions like gout and hyperuricemia. By reducing the production of uric acid in the body, allopurinol helps prevent the formation of painful urate crystals. While generally well-tolerated, it's important to be aware of potential side effects such as skin rash, gastrointestinal disturbances, and, rarely, severe hypersensitivity reactions. The drug has also been associated with rare but significant conditions such as leukopenia, thrombocytopenia, agranulocytosis,
Local anesthetics	Local anesthetic agents such as lidocaine, benzocaine, and procaine are frequently used as adulterants in various drugs and have been detected in counterfeit captagon tablets. Large amounts of local anesthetic or rapid absorption into the bloodstream can potentially lead to cardiovascular effects like lowered blood pressure, an irregular heartbeat, or even cardiac arrest. Benzocaine has been associated with methemoglobinemia.
Trimethoprim	Trimethoprim is an antibiotic commonly used to treat bacterial infections. It has also been documented as an adulterant in counterfeit captagon tablets. Serious side effects from excessive exposure to trimethoprim can include lower white blood cell count and liver damage.

Adulterants in Counterfeit Captagon Tablets



Origins of Counterfeit Captagon in the Levant

Recent intelligence has spotlighted major production centers for counterfeit captagon tablets in the Levant, the region of the Middle East encompassing Syria, Jordan, Lebanon, Iraq and parts of Israel and Palestine. The clandestine production of this counterfeit drug has reached significant proportions, fueling a booming black market. The Levant, known for its porous borders and fragmented authorities, has become an ideal location for these illegal activities. Criminal syndicates exploit weak law enforcement, corrupt officials, and political instability, allowing them to establish sophisticated production networks. These networks span across multiple countries, enabling the transit of precursor chemicals and distribution of the final product. Consequently, the Levant is witnessing a surge in drug-related crimes and addiction, posing significant challenges and threats to the region's socio-economic stability. Major seizures of counterfeit captagon have been made in Turkey, Lebanon, Saudi Arabia and major port cities in Southern Europe.

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- [Synthetic stimulants – the current situation in Europe \(European Drug Report 2023\) | www.emcdda.europa.eu](http://www.emcdda.europa.eu)

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