



Study of Adulterants and Diluents in Some Seized Captagon-Type Stimulants

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Introduction

ATS are synthetic compounds belonging to the class of stimulants that excite the Central Nervous System (CNS) to produce adrenaline-like effects such as amphetamine, methamphetamine, fenethylamine, methylphenidate and dextroamphetamine [1,2]. ATS are the second most commonly consumed illicit drugs after cannabis worldwide. According to the UN Office on Drugs and Crime [3,4] the number of ATS users worldwide was estimated at 37 million men, higher than the number of cocaine

and heroin users combined [3,4]. Fenethylamine, 7-(2-amethyl phenyl-amino ethyl)-theophylline, is a theophylline derivative of amphetamine. It is a psychoactive drug which is similar to amphetamine in many ways [5]. Fenethylamine was used for its antinarcotic and antidepressant effects during the 1960s and 1970s. This was also shown to be effective in managing childhood attention deficit disorder. Fenethylamine does not induce a substantial increase in the blood pressure of the treated subjects, as



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compared to amphetamines [6]. Currently, fenethylamine is not included in any FDA-approved medications. Unlike prescription drugs such as heroin and cocaine, it is relatively easy to manufacture ATS with common household chemicals and solvents that are readily available from commercial sources. Additionally, methods of producing such items are readily available on the Internet [7]. It leads to the widespread (illegal) dissemination of these designer drugs among many populations with high adulteration incidences. Unlike many other illegal drugs, ATS is never marketed or used in its purest form. To order to maximize the apparent amount of the drug, they are often heavily combined with a variety of ingredients, adulterants and/or diluents, thus enhancing the dealer's benefit. Identification of potentially harmful substances that contaminate illegal products is very critical as they may be more dangerous than the drug itself [8]. One of the most commonly used methods for fenethylamine manufacturing (Captagon™) relies on using amphetamine and caffeine as starting materials. Therefore, inadequate street manufacture of Captagon™ tablets would undoubtedly lead to the occurrence of these two compounds in a high yield in the final product, and in some cases even the absence of the fenethylamine itself. Analytical separation of psychoactive ATS from adulterating compounds is a major challenge in forensic drug chemistry as some of the adulterants' health hazards may be highly dangerous. Literature review revealed that many methods have been used to screen ATS to detect adulterants using UV, infrared spectroscopy (IR), as well as TLC, [9–10] IR, GC/MS, [11–12] and Capillary electrophoresis.

Captagon: In the whole world

A steady rise in the number of drug consumers and abusers has followed the increasing growth in illegal development of Amphetamine-Type Stimulants (ATS) and psychotropic drugs. It is a global problem that has generated problems in each country of the world not only for those responsible for control and monitoring, but also for technicians working on the research to detect and classify these products. Fenethylamine was first synthesized in 1961 by Chemiewerk Homburg, a subsidiary of German Degussa AG, a specialty chemicals group, as part of a research program on the side effects of theophylline derivatives, particularly on the cardiovascular, pulmonary and central nervous systems [13–16].

For more than two decades, it has been used in Europe as a milder alternative to amphetamine and associated drugs, and as a non-prescription psychostimulant and analeptic agent sold under the brands Captagon, Fitton and Biocapton [13]. The patent for its production dates to 1962, thus, it was used for several years in the treatment of attention-deficit-hyperactivity disorder and to a lesser degree in narcolepsy, epileptic absences and depression [13]. This was also used in the absence of drive, particularly in elderly patients due to organic diseases (e.g., parkinsonism) or other causes, as well as after serious illness or injury (e.g. head injury). Fenethylamine increased resilience in cases of narcolepsy and epileptic absences, and of paroxysms. Nonetheless, the above indications for fenethylamine have never been approved in the United States, as the Food and Drug Administration has not submitted any new investigational drug application [13–16].

Fenethylamine has raised concern in West Asian and Arab countries in recent years, where it is clandestinely synthesized, using simple and inexpensive chemistry techniques and raw

materials, and extensively used. Though illegal, it remains available among militant groups, especially in Syria. Fenethylamine was found to be one of the active ingredients in a large number in tablets trafficked as Captagon [13–15].

Captagon: In the middle east

Information from the International Narcotics Control Board and Interpol disclosed almost a decade ago that the drug was illegally produced in laboratories mainly located in South-East Europe, specifically in Turkey, Bulgaria, Slovenia, Serbia and Montenegro (Drug Enforcement Admin, US Department of Justice, and United States of America [16]. Captagon trade in the Middle East and North Africa is currently a significant, high profit margin of illegal trade [17–19] because it can be clandestinely synthesized using easy and inexpensive chemicals and raw materials [18–20]. Nonetheless, there have been clear signs in recent years based on statistical evidence that Captagon's illicit production has moved to the Middle East region and northern Africa, especially Syria and Iraq (EMCDDA, Portugal, and Europol [21]. More than 1.4 million tablets were confiscated in Syria in 2002, and 107.5 kilograms of the drug were confiscated in Turkey (Drug Enforcement Admin, US Department of Justice [16–19]. Illicit trade is growing exponentially, and 8.8 million pills, mainly containing Captagon, were found in Egypt in 2016 [22], while 11,000 Captagon tablets were seized in Al-Nasiriya City (January 2016), a town southeast of the Iraqi capital Baghdad. Toxicological work has shown the existence of toxins such as amphetamine, cocaine, procaine, caffeine, quinine, metronidazole, theophylline and others, in addition to the absence of fenethylamine [23,24]. While the ongoing civil war persists in Syria, there is a very strong market for illegal drugs like Captagon. The drug also spreads across Iraq, Jordan, Kuwait and Qatar [19]. The quality of items that are illegally sold as Captagon however still needs to be determined. Alabdalla (2005 who performed chemical analysis of falsified Captagon tablets from 124 batches confiscated across Jordan, confirmed the absence of fenethylamine. The analysis was performed via Gas Chromatography–Mass Spectrometry (GC–MS). The fraudulent nature of the Captagon tablets confiscated in Europe was also demonstrated by the review of confiscated Captagon tablets between 2008 and 2011, which revealed that they no longer contained fenethylamine but amphetamine in combination with caffeine and other substances (European Monitoring Centre for Drugs and Drug Addiction, EMCDDA, Portugal, and Europol [19].

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