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Designer Drugs in Egypt: Toxicological and Medicolegal View

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Abstract: Designer drugs are a subcategory of synthetic drugs. They are created by chemically altering the structure of a controlled substance to produce similar effects. The widespread emergence of designer drugs in Egypt poses a challenge alongside classic substances, as they are not listed as illegal and are difficult to detect via standard screening tests. Common Egyptian designer drugs include shabu, strox, and voodoo. These new psychoactive substances simulate the pharmacological effects of classical or original illicit drugs such as cannabis, amphetamine, and cocaine. However, it is difficult to identify their harmful effects at any dose. Shabu is considered one of the synthetic cathinones that produces symptoms like amphetamine, while strox is a synthetic cannabinoid, and voodoo is like strox because it contains different psychoactive compounds, including synthetic cannabinoids. The clinical presentation of designer drug intoxication can vary because of essential variation in concentrations and types of chemical components and other adulterants.

Keywords: Designer Drugs, Egypt, Intoxication, shabu, strox, voodoo

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INTRODUCTION

Drug abuse has become a critical problem in Egypt in recent years because it has significant social and economic impacts. The reports of the National Research on Addiction that were released by the General Secretariat of Mental Health and Addiction Treatment, Ministry of Health, Egypt, indicated that the rate of substance use is increasing over time, and the young adult group was the most represented age group among substance users. A study conducted by the United Nations Office on Drugs and Crime in cooperation with the Ministry of Health in August 2004 found that 15- to 25-year-olds are more prone to drug abuse in Egypt [1].

However, many efforts are underway to combat drug abuse and reduce its spread among this age group, which is considered a cornerstone of development in society. Still, these efforts face many challenges, including the growing number of illicit drug laboratories in the Middle East, particularly in Egypt [2].

Abused drugs are either natural or synthetic. Natural substances are plant-derived, extracted from the leaves, flowers, or fruits of plants. The active ingredient is concentrated in the unripe fruits of the poppy plant, while it is concentrated in the leaves and flowering tops of cannabis. However, the active ingredients of coca and khat are usually concentrated only in the leaves [3].

Synthetic drugs may be totally synthetic or semi-synthetic. Semi-synthetic drugs are usually narcotic substances extracted from narcotic plants and then reacted with other substances to form more potent compounds than the original substances, such as heroin. On the other hand, synthetic drugs are produced through complex chemical reactions between various compounds [4].

Drugs can be classified according to their effect on mental activity and psychological state into depressants (natural, semi-synthetic, synthetic), stimulants (natural, synthetic), and hallucinogens (natural, semi-synthetic, synthetic). However, it is noted that cannabis is considered a depressant in small doses and a hallucinogen in large doses [5].

Therefore, the plants of cannabis (hashish), poppy (opium), coca (cocaine), and khat are classified as natural drugs. In contrast, morphine, heroin (acetylmorphine), and codeine are classified as semi-synthetic drugs, while sedatives and hypnotics, hallucinogens, and volatile solvents are synthetic drugs [6].

Thus, the term synthetic drug refers to any drug made in a professional or illicit laboratory using a chemical process. It includes both legal drugs for medical use, such as fentanyl, and illegal drugs that are detected by standard drug tests. In contrast, designer drugs are a

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subcategory of synthetic drugs that are created by chemically altering the structure of a controlled substance in a clandestine laboratory to produce similar effects. However, they have different molecular structures, are not listed as illegal, and are difficult to detect via standard screening tests [7].

Recently, the drug market in Egypt has been rapidly shifting with the growing drug abuse phenomenon. There is a widespread emergence of designer drugs, which represent a challenge alongside classic substances such as cannabis (hashish) that are becoming more prevalent. This challenge is legal, as the national legal list of drug abuse should be updated, and scientific, for urine screening tests [8].

Designer drugs are synthetic alternatives associated with chemical structural modifications of a controlled substance to maximize psychoactive potency. They are called new psychoactive substances, such as shabu, strox, and voodoo. Major concerns about these compounds have emerged because their quality control has not been met. Designer drugs simulate the pharmacological effects of classical or original illicit drugs such as cannabis and cocaine, but it is difficult to identify their harmful effects at any dose [9].

Furthermore, the rapid evolution of these compounds is considered a challenge because their effects can be dangerous and unpredictable. Moreover, these compounds are not detectable by conventional drug screening tests, and studies on their short- and long-term effects are limited; their classification as illegal substances is considered another challenge. Notably, the terms synthetic drugs and designer drugs are often used interchangeably; designer drugs are synthetic, but not all synthetic drugs are designer drugs [10].

Designer drugs may be different from their parent drug in terms of their effects, whether an increase in potency or a reduction in side effects. However, designer drugs may have similar effects to known drugs, but they have completely different chemical structures. Moreover, designer drugs are considered a broad term that may also be used to indicate synthetic recreational drugs [11].

In Egypt, some designer drugs may be a mix of herbs, tobacco, crude botanical mixtures, and dried plants such as Datura. Moreover, clandestine laboratories can improve the quality of these drugs to increase the efficacy of their psychoactive effects by adding adulterants such as benzodiazepines, tramadol, and ketamine. Thus, the clinical picture of Egyptian designer drug intoxication is usually unpredictable. They have a wide spectrum of dangerous clinical presentations that range from acute toxic psychosis to major cardiovascular morbidity, coma, and death [12]. Therefore, this article focuses on the most common designer drugs in the Egyptian market and their clinically different presentations.

Shabu (Crystal Methamphetamine)

Shabu is considered one of the synthetic cathinones that contain a ketone group at the β-position of amphetamine. Cathinones can be classified into two types based on pharmacological profile and clinical toxicity. The first type is serotonergic cathinone that acts on the serotonin system, like methylenedioxymethamphetamine (MDMA), while the second type is the cocaine-MDMA-mixed cathinone group that is like cocaine and releases serotonin like MDMA [13].

All cathinones induce higher dopaminergic activity when compared with non-keto amphetamine analogs, leading to higher stimulant effects and a greater risk for dependence. Cathinones release dopamine and noradrenaline like methamphetamine. In other words, cathinones inhibit neurotransmitter reuptake by blocking dopamine, serotonin, and norepinephrine transport channels, leading to unnatural monoamine accumulation in the brain's synaptic spaces, inducing intense stimulant or hallucinogenic effects. Therefore, cathinone toxicity produces symptoms like amphetamine, such as euphoria, hallucinations, hyperthermia, hypertension, and locomotor activation, after high or repeated doses [14].

Worthwhile, synthetic cathinones such as shabu and bath salts are derivatives of cathinone, which is a natural stimulant found in the Khat plant. Synthetic cathinones are human-made substances and classified as new psychoactive substances that are potent central nervous system stimulants mimicking the effects of traditional drugs like cocaine, MDMA, and methamphetamine [15].

Shabu is the name of a recreational drug, which is crystal methamphetamine (a synthetic central nervous system stimulant). It is also called ice or bath salts. Methamphetamine is considered the second most prevalent abused drug in the world [16]. It passes the blood-brain barrier rapidly because it is highly lipid-soluble, inducing neurological and psychiatric effects [17]. Recently, crystal methamphetamine (Shabu) has seen a rapid increase in abuse, associated with violent crimes and high addiction rates in Egypt [18].

Clinical manifestations of acute shabu intoxication are sympathomimetic, such as severe tachycardia, palpitations, arrhythmia, hypertension, hyperthermia, and mydriasis, while chronic use leads to cardiovascular failure and seizures. Long-term abuse of shabu may cause irreversible damage to dopaminergic and serotonergic neurons of the brain, leading to memory impairment and cognitive deficits. Furthermore, hyperthermia may induce muscle tissue breakdown (rhabdomyolysis) and renal failure [19].

In addition, psychiatric manifestations of shabu intoxication may include severe persecutory delusions, auditory and visual hallucinations, severe agitation, aggression, impulsivity, behavioral dysregulation, and unprovoked physical violence. Moreover, some studies

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reported that 26% of shabu users have depression, while 23% of them have suicidal attempts during the crash or withdrawal phase [20]. Notably, Egyptian toxicological studies reported that shabu is used with polysubstance abuse, so its intoxication manifestations are severe, and the risk of overdose is high [21].

Strox (Egyptian Spice)

It is a synthetic cannabinoid that clandestine laboratories manufacture. Still, it is not a standard synthetic cannabinoid because it consists of mixtures of herbs or plants (datura), chemicals, and synthetic cannabinoids. It is considered one of the most serious novel psychoactive substances in Egypt. It is widespread because of its low cost and ease of availability. It is classified into two types: green marjoram and tobacco [22].

Strox is the Egyptian version of spice or K2. Strox includes five synthetic cannabinoids, which have high potency exceeding 85 to 100 times the potency of delta-9-THC of natural cannabis. Furthermore, other adulterants may be added to strox, such as amphetamines, tramadol, ketamine, and benzodiazepines [23].

Worthwhile, the components of strox can be changed by adding or removing one, as they are the result of ongoing efforts by underground chemical manufacturers creating non-prohibited analogues by altering cannabinoid molecules to bypass current legal schedules. Toxicological analysis of Strox (tobacco and marjoram packages) that was performed by gas chromatography indicated the presence of methylene dioxy methamphetamine, xylene, and trihexyphenidyl, besides other unidentified substances in some packages [24].

Strox is considered the third most abused substance among addicts in Egypt after natural cannabis and tramadol, according to the Egyptian Addiction Treatment and Abuse Fund, wherein it represents 22% of all cases [25]. There was a spike in strox abuse according to the Fund for Drug Control and Treatment of Addiction (FDCTA), wherein the prevalence rate increased from 2% in 2017 to 20.7% in 2018 [26]. Moreover, a study showed that 14.9% of secondary school students had used strox, while another study conducted among Egyptian university students indicated that 41.3% of them used strox [27].

According to Egyptian poison control centers, the clinical manifestations of acute strox intoxication cases may be neurological, cardiovascular, and gastrointestinal. These manifestations may be nausea, vomiting, tachycardia, palpitations, chest pain, fatal arrhythmias or myocardial infarction in severe cases, blurred vision, conjunctival injection, CNS depression, catatonia, or slow behavior and speech (zombie-like), visual and auditory hallucinations, acute psychosis, irritability, panic attacks, and seizures [28]. In addition, some studies indicated that a high percentage of strox abusers are manifested by severe injuries because strox induces violent agitation, leading to acute psychosis, disorientation, and loss of motor control, and then the user is liable to a high risk of trauma [29].

However, there is a variation in the clinical presentation of strox toxicity based on its different components. An intoxicated patient with strox may have a disturbance in the level of consciousness, but it is transient because of the depressant effect of xylene on the central nervous system, which is added to strox preparations; xylene is considered an aromatic hydrocarbon and has high lipophilic properties, inducing a rapid coma that is transient because of rapid metabolism and elimination of xylene from the body within 24 hours. Furthermore, strox may contain anticholinergic substances such as trihexyphenidyl, hyoscine, and atropine-like substances, which may cause hallucinations, aggression, delirium, coma, and death, as well as ketamine, which induces hallucinations, tachycardia, hypertension, vomiting, and respiratory distress [30].

Voodoo

Voodoo is like strox because it contains different psychoactive compounds, including synthetic cannabinoids. It is the street name for mixing psychoactive compounds, including amphetamine, tramadol, and methadone, MDA, benzodiazepines, morphine derivatives, and synthetic cannabinoids [31].

The synthetic cannabinoid is considered the main compound in voodoo, where it mimics the effects of delta 9 tetrahydrocannabinol (THC), the active principle of cannabis (marijuana). The synthetic cannabinoid binds to CB1 in the central nervous system, regulating coordination, pleasure, memory, and thought. It also binds to CB2 in the immune system and peripheral organs, which is responsible for inflammation and immune response [32].

Therefore, voodoo is also considered a class of designer drugs that are abused to simulate the clinical effects of marijuana; it is similar to herbal incense. Furthermore, voodoo was designed to evade drug regulation laws and standard cannabinoid screening tests in some previous periods. But the Egyptian Ministry of Health listed voodoo in Schedule 1 in 2014 and considered it a highly hazardous addictive substance [33].

The clinical presentation of acute voodoo intoxication can vary because of essential variation in concentrations and types of chemical components and other adulterants. Intoxicated patients with voodoo may present with tachycardia, agitation, hallucinations, respiratory acidosis, and a disturbance of consciousness level [34].

However, the medical records of the Poison Control Center at Ain Shams University Hospitals reported some death cases due to voodoo in 2015 and 2016. Thus, the wide variation in clinical manifestations and outcomes of

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acute voodoo intoxication depends on the quantitative and qualitative composition of the voodoo [35].

Medicolegal view of designer drug screening

Manual multi-drug urine dipstick screening for abused drugs is considered the first diagnostic tool in Egypt. However, its ability to detect designer drug abuse faces many challenges because of several factors [36]. Traditional urine drug screening is designed to detect classical drugs by their specific structures or metabolites, such as delta-9-tetrahydrocannabinol (THC). Still, it fails to detect synthetic cannabinoids because they have distinct molecular structures, unlike those of natural cannabinoids, even though they do well at the CB1 and CB2 receptors [37]. Therefore, synthetic cannabinoids yield false negative results with standard urine screens because they do not cross-react with them due to the lack of structural cross-reactivity [38].

Furthermore, Manual multi-drug urine dipstick screening (immunoassay) cannot detect designer drugs because of the constant and rapid evolution of the structural framework of designer drugs, wherein the development of an antibody assay for a specific designer compound cannot keep pace with the rapid shift in production by clandestine laboratories via modifying side chains or substituting functional groups, producing unlisted, non-prohibited structural variants [39].

In addition, detection of designer drugs via Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) or Gas Chromatography-Mass Spectrometry (GC/MS) represents another challenge because it depends on a specific and up-to-date reference, while the composition of designer drugs may be changed constantly, so toxicological laboratories find unidentified mass spectra that do not correspond to this reference, making the detection of these drugs impossible [40].

In a related context, the results of previous studies indicated that strox may not be detected easily via standard screen drug tests because of its composition and molecular diversity, wherein manufacturers modified the composition of strox after the banning of five specific THC analogs in 2018 [41].

In the same context, another study reported that toxicological analysis of seized strox samples via Gas Chromatography-Mass Spectrometry (GC/MS) in Upper Egypt revealed that it is an evolving and unpredictable mixture, not a single compound, because it contains a cocktail of synthetic indoles, fatty acids, tobacco residues, quinazoline derivatives, and benzodiazepines [42]. Therefore, strox does not yield a positive result on a standard urine drug screen, which challenges physicians when diagnosing emergency cases. Still, medicolegal confirmation of strox use can be achieved via gas chromatography-mass spectrometry (GC-MS) [43].

Furthermore, another study conducted on the prevalence of strox smoking among university students in Egypt confirmed that routine urine dipsticks remain blind to these designer substances. Hence, the true extent of their use is difficult to determine and likely underestimated [44]. In another context, but it is related, a study conducted on the prevalence of substance abuse indicated that standard urine drug screens are strictly for natural herbal cannabis metabolites, so detecting designer drugs such as voodoo is difficult because their analytical profiling contains multiple variant structures, such as the synthetic cannabinoid FUB-AMB and plant-derived alkaloids [45].

CONCLUSION

Designer drugs are synthetic alternatives with chemical structural modifications of a controlled substance made to maximize psychoactive potency, but they may have effects similar to those of known drugs. In Egypt, some designer drugs may be a mix of herbs, tobacco, crude botanical mixtures, and dried plants. The clinical picture of Egyptian designer drug intoxication is usually unpredictable, with a wide spectrum of dangerous clinical presentations that range from acute toxic psychosis to major cardiovascular morbidity, coma, and death. These compounds are not detectable by conventional drug screening tests due to the constant, rapid evolution of their structural frameworks. Recently, shabu, voodoo, and strox have been the most serious novel psychoactive substances in Egypt, with abuse increasing rapidly and associated with violent crimes and high addiction rates.

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