

# The Explosion of a New Designer Drug, Flakka

## Implications for Practice

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### Abstract

There are many challenges facing healthcare professionals. One such challenge is the continuous introduction of new synthetic drugs. Synthetic drugs pose many difficulties to providers, including identification of the drug ingested, management of symptoms, ensuring safety of the patient and his or her environment, and continual monitoring after the initial symptoms, because synthetic cathinones have many long-term effects on an individual. One such synthetic drug, flakka, is a potent second-generation synthetic cathinone. Because flakka inhibits the reuptake of norepinephrine and dopamine, which are involved in one's perception of pleasure, it causes inflated feelings and also causes signs and symptoms of psychosis. Flakka also induces various exaggerated symptoms, such as feelings of incredible strength, disorientation, aggression, and altered thought processes, and also can cause hyperthermia, coma, and death. Healthcare professionals need to understand the nature of flakka ingestion, the various symptoms a user may exhibit, and the long-term symptoms a person may have once the acute recovery phase has ended. Once the initial phase of ingestion is over and the patient is medically stabilized, the patient may experience signs and symptoms of psychosis or other psychiatric disorders. It is paramount that healthcare professionals are able to recognize the signs and symptoms of flakka ingestion, know the steps to take to ensure safety of the patient and those around him or her, and also know how to facilitate the patient's recovery.

**Keywords:** flakka, implications for practice, synthetic cathinones

Healthcare professionals should be aware of a new synthetic designer drug called “flakka.” This drug, a second-generation cathinone, which has alternative names such as x-pyrrolidinopentiophenone, x-PVP, flakka, \$5 insanity, and gravel, is an extremely potent stimulant. Flakka is a variation of the Spanish word “flaca” meaning thin, pretty woman (Miotto, Striebel, Cho, & Wang, 2013). Flakka is a synthetic cathinone similar to another potent drug, bath salts. Flakka inhibits the reuptake of norepinephrine and dopamine and may cause excited delirium, which can mimic extreme psychosis. Users may display a range of different side effects that might include a combination of agitation, anxiety, changes in speech, violent and strange behaviors, high pain threshold, euphoria, increased energy, paranoia, hallucinations, psychosis, and death (Penders, Gestring, & Vilensky, 2012). Flakka has also been known to cause hyperthermia (temperatures up to 41°C [106°F]), which may cause users to remove their clothes and display naked delusional-like behavior (Gregg & Rawls, 2014).

Healthcare professionals must be prepared for varying degrees of symptoms and ensure that safety is paramount. When users are experiencing excited delirium caused by flakka, they show incredible strength because of the adrenaline surge, and they may also become aggressive, making them dangerous to themselves and others. The extreme agitation caused by flakka may lead to excited delirium syndrome in users, which constitutes a medical emergency. One should thus brace for the unexpected with users of synthetic cathinones like flakka. Management must be based on the user's symptoms, which means that, when the user is violent or aggressive, restraints may be necessary. Because flakka and other new designer drugs pose such a serious threat, healthcare professionals must play a key role in the prevention, education, detection, treatment, and removal of these dangerous agents to limit abuse and serious side effects, including death (Califano, 2015).

### PURPOSE

The purpose of this article is to provide a comprehensive overview of a new designer drug called flakka. Information discussed will include physiological and psychological adverse effects and pharmacokinetics. The epidemiology of

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use, health-related complications, treatment strategies, and implications for healthcare providers will also be reviewed. The goal of this article is to inform healthcare providers about the increased use of synthetic cathinones and heighten their awareness about common clinical presentations seen in various clinical settings and management of intoxication.

## BACKGROUND TO THE PROBLEM

In recent years, synthetic cathinone abuse has increased across the United States and around the world, resulting in public health concerns (Maxwell, 2014). The striking increase in usage may be related to media attention as well as accessibility. Synthetic cathinones and amphetamines share a related structure and produce effects similar to those of cocaine and methamphetamine (Khullar, Jain, & Sattari, 2014). There are approximately 30 known synthetic cathinones (Kelly, 2011). It is worth noting that one synthetic cathinone is bupropion, which is widely used to treat depression and in smoking cessation (Stahl, 2014).

Cathinone is a natural stimulant found in the *Catha edulis* (khat) plant. Chewing of khat leaves dates back many centuries and still continues in many parts of Africa, Yemen, and the Jazan region in southwest Saudi Arabia (El-Setouhy, Alsanosy, Alsharqui, & Ismail, 2016). The fresh leaves, twigs, and shoots of the khat shrub are chewed, then retained in the cheek, and chewed intermittently to release the active drug. Only fresh leaves may be used for chewing because the cathinones break down after the leaves are harvested. This decomposition may be the reason chewing of the leaves is limited to specific geographic areas (Capriola, 2013). The amphetamine-like effect of cathinones is said to cause excitement, loss of appetite, euphoria, and increased alertness. Therefore, individuals often chew khat to assist in improving their performance and reduce physical fatigue and hunger. In different parts of the world, chewing khat is socially acceptable and may be used at parties and various celebrations (Kalix & Braenden, 1985).

In the United States, synthetic cathinones are among the new popular designer drugs causing great morbidity and mortality among drug users. Despite the government's efforts to regulate the distribution and sales, synthetic cathinones may be purchased in appealing packages at convenience stores, tobacco outlets, gas stations, tattoo parlors, and truck stops as well as on the Internet (Johnson, Johnson, & Portier, 2013). Synthetic cathinones have subsequently become popular because of the ease of purchase and because they are advertised as safe to use despite being labeled "not for human consumption." These agents may be ingested, snorted, smoked, vaped, or injected, with rectal application as another method used for consumption (Forrester, 2012). Smoking/vaporizing of synthetic cathinones may be a preferred route of administration as it is associated with a rapid onset of effects of less than 10 seconds (Prosser & Nelson, 2012). Users report that the drug is attractive because it increases libido, empathy, openness, and energy (Baumann et al., 2014). Common street names for flakka include Bloom, Cloud Nine, Vanilla Sky, and Scarface (Baumann et al., 2014).

## LITERATURE REVIEW

A literature search was conducted using multiple databases, including Cumulative Index to Nursing and Allied Literature, MEDLINE, and PubMed, limited to the years of 2011–2016 and using the key words "synthetic cathinones," "bath salts," "synthetic designer drugs," "flakka," "legal status," "mental illness," and "patterns of abuse." The search was limited to full-text articles published in English. This produced only over 100 hits in the search on all databases accessed. Relevant citations on the pharmacology, pharmacokinetics, extent of use, effects, and adverse effects were reviewed, and pertinent data were incorporated into the review. The National Institute on Drug Abuse and the Substance Abuse and Mental Health Services Administration sites were also searched to review new emerging trends and alerts.

### Pharmacology of Flakka

Flakka is the common name for the synthetic cathinone  $\alpha$ -pyrrolidinopentiophenone. First developed in the 1960s as a central nervous system (CNS) stimulant and pressor agent,  $\alpha$ -pyrrolidinopentiophenone has structural similarities to ephedrine and other phenylethylamines and therefore exhibits significant amphetamine-like effects. Synthetic cathinones such as flakka are lipophilic and readily cross the blood–brain barrier to interact with monoamine transporter and synapses in the CNS. Flakka is chemically related to 3,4-methylenedioxypropylamphetamine, an earlier synthetic cathinone that acts in a manner similar to cocaine but is 10 times more potent (Kaizaki, Tanaka, & Numazawa, 2014). With regard to its mechanism of action, flakka appears to inhibit the reuptake monoamines such as norepinephrine, serotonin, and dopamine at synapses in the CNS (Ross, Watson, & Goldberg, 2011). Flakka may also stimulate the release of dopamine from CNS neurons, which in turn leads to the activation of both Dopamine 1 and 2 receptors. Activation of central dopamine pathways may be related to the psychotic, psychomotor, and rewarding effects of flakka (Ross et al., 2011).

### Physiological and Psychological Adverse Effects of Flakka

Flakka use has been associated with a condition called "agitated delirium." The condition likely occurs as a result of elevated levels of CNS neurotransmitters such as norepinephrine, serotonin, and dopamine. CNS symptoms are those associated with acute psychosis and may include anxiety, aggression, bizarre behaviors, and disorientation (Crespi, 2016). Paranoid hallucinations may occur, which may be associated with violent or aggressive actions. A case report by Crespi describes a 17-year-old female adolescent who inadvertently ingested flakka that was placed in her school lunch by classmates (Crespi, 2016). The patient was involuntarily admitted to the hospital after experiencing severe episodes of acute psychoses. Psychological and physiological symptoms persisted for nearly a week, despite supportive treatment and administration of olanzapine and lorazepam. It was not until the sixth day of hospitalization

and treatment that the patient became coherent and oriented (Cherry & Rodriguez, 2017).

Physiologic symptoms of flakka use are those associated with sympathetic overactivation, including hypertension, tachycardia, and hyperthermia. These manifestations may be life-threatening. Myoclonus and repetitive motor behaviors have also been observed. Cherry and Rodriguez reported on the case of “an otherwise healthy 41-year-old female” who presented to the emergency department with an anterior myocardial infarction and intracardiac thrombus that occurred after flakka use (Frankel, 2016). The authors reported several other cases of sudden cardiac death cited in the literature that were attributed to flakka use in otherwise healthy young individuals. Autopsy results found that these individuals died from acute heart failure and pulmonary edema (Frankel, 2016).

A number of bizarre episodes have been documented recently in South Florida regarding flakka users. In two instances, flakka users ran naked down the middle of a busy street as they experienced a paranoid delusion. In another incident, a flakka user was impaled on a metal fence he tried to scale near a police station while fleeing imaginary attackers. In one particularly horrific incident, flakka use was associated with an episode of cannibalism (Altrubin, Bowden, & Hamilton, 2015).

### Epidemiology of Flakka Use

The recent wave of several synthetic cathinones emerged in 2010 on the streets of the United States, and use rose rapidly in 2011 (Forrester, 2012). Forrester (2012) described the pattern of over 360 synthetic cathinone exposures reported to Texas poison centers. Texas was one of two states with the highest number of synthetic cathinone reports in 2010. Designer drugs, like flakka, have become attractive because they produce psychoactive effects similar to methamphetamine, yet they are difficult to detect in standard urine toxicology tests (Abbott & Smith, 2015).

Individuals can purchase online a kilogram of flakka for \$1,500, which has a street value of \$50,000, and have it delivered to their door. China has been the primary source of flakka on the streets in the United States. However, in 2015, Chinese officials agreed to ban flakka production, which has resulted in a recent reduction in flakka availability. Essentially, the U.S. government, in coordination with China, halted the production of flakka in late 2015 and early 2016, causing an unprecedented decrease in production and distribution. However, Weaver and Ovalle believe that this decrease in production and distribution may only be temporary (Weaver & Ovalle, 2015). Although media reports of flakka use have declined, there has been a recent increase in report of use. Flakka users continue to appear to EDs frequently (Scaccia, 2016).

### Health-Related Complications

Individuals who ingest flakka are at risk for various health-related complications and other complications including hospital admissions, lifelong effects of the drug, and death. Some of the most disturbing findings include hyperthermia that one can experience, which can reach 41°C (106°F),

and excited delirium, which can lead to seizures. Another challenge healthcare providers encounter with cathinone intoxication is managing an individual’s agitation. Often, the individual experiences extreme agitation and paranoia, along with superhuman strength, which may be caused by the brain being flooded with dopamine (Crespi, 2016). When combined, these symptoms can lead to self-destructive behaviors. Examples of such behaviors include a flakka user who sustained injuries when attacking a fence and another who attempted to copulate with a tree. All of these examples ended with the individual sustaining injuries (Califano, 2015).

Because of the risk of health-related consequences, these individuals often seek medical treatment or may require treatment in hospital emergency departments. They are often known to exhibit violent behaviors because of hallucinations and extreme paranoia. This places the flakka users at risk for multiple health-related complications, with some appearing right away, such as hyperthermia, and others appearing later, for example, excited delirium. Moreover, flakka use is associated with high morbidity and mortality risks for users (Katselou, Papoutsis, Nikolaou, Spiliopoulou, & Athanasis, 2016).

### Treatment Strategies

Treatment of flakka users is aimed at suppressing and managing symptoms. For users experiencing hyperthermia, treatment aims to aggressively lower the temperature while also preventing complications of the body compensating for the extremely high heat. Hyperthermia also places the patient at risk for dehydration, making rehydration integral. Moreover, safety of the patient and those around him or her is paramount, playing a large role in treatment. Some users must be subdued pharmacologically if aggressive behavior is present, and mechanical restraints are often necessary. Medications to treat violent or aggressive behaviors may include intravenous (IV) benzodiazepines such as midazolam (2 mg) or diazepam (5 mg). Alternative medications may include ketamine (250 mg intramuscular) or haloperidol (5 mg intramuscular or IV; Greater Broward EMS Medical Directors Association, n.d.).

Using antipsychotics to treat flakka symptoms is controversial because of efficacy concerns, but they can be used to manage symptoms of paranoia. There are no known antidotes for flakka, and nothing is available to counter its effects. During treatment, all body systems affected by the drug must be supported, and the patient is at a high risk of complications until the acute phase is completed. Once the patient is more stable, paranoia can persist and medication management with antipsychotics is often needed (Abbott & Smith, 2015).

### Legal and Regulatory Status of Synthetic Cathinones

The legal and regulatory status of these drugs varies among countries and is changing continuously. Hence, in an effort to circumvent drug laws, manufacturers of synthetic cathinones often market their products as “not for human consumption.” The U.S. federal government designated synthetic

cathinones, which include bath salts and flakka, as Schedule I drugs under the Synthetic Drug Abuse Prevention Act, a part of the Food and Drug Administration Safety and Innovation Act of 2012<sup>1</sup> (U.S. Food and Drug Administration, 2012). Schedule I drugs have a high potential for abuse and dependency, and they have no acceptable medical use (Abbott & Smith, 2015). As mentioned previously, one of the largest producers of flakka is China, which is followed by Pakistan and India. Clandestine chemists in these countries often illegally produce a type of synthetic cathinones (bath salts). However, the producers of these agents change the chemical structure slightly, so a new drug is made that technically is not illegal in the United States. In early 2015, the U.S. Department of Treasury imposed Kingpin Act sanctions on one of the largest alleged synthetic drug producers in China. The Kingpin Act was designed to deny foreign narcotics traffickers and their related business entities access to the U.S. financial system (U.S. Department of State, 2014). In a nationwide sweep of the United States, the U.S. Drug Enforcement Administration subsequently arrested 151 people in connection with synthetic drugs imported from China (Drug Enforcement Agency, 2016). Reacting to pressure from incidents such as these, the Chinese government imposed new controls over the production and distribution of 116 synthetic drugs, including flakka, in late 2015. On the basis of early data from flakka-related arrests and hospitalizations in Broward County Florida, an area hit the hardest by the flakka epidemic, these efforts appear to be having a positive impact (Frank, 2016).

## IMPLICATIONS FOR HEALTHCARE PROVIDERS

It is important that healthcare providers are knowledgeable about the newest designer drugs and clinically aware of the unique presentation of these agents. Patients under the influence of synthetic cathinones often present with physiological and psychological effects. Healthcare providers must ensure the patient is safe and provide supportive care, which often includes IV fluids, benzodiazepines, and aggressive cooling (McClellan, Anspikian, & Tsuang, 2012). According to Abbott and Smith, haloperidol must be used cautiously and not in isolation because this drug may enhance a catecholamine surge (Abbott & Smith, 2015). Safety is vital; hospital staff members must always be prepared for unexpected behaviors with flakka users. If the user is violent or aggressive, restraints and involvement of law enforcement may be necessary (Maxwell, 2014). In addition, because users often have superhuman strength, additional assistance is required. Healthcare providers should avoid physically struggling with the patient, if possible, because this may exacerbate or cause dehydration in the patient.

Ultimately, management of flakka must be based on the individual patient's symptoms. After the acute phase of treatment is completed, psychiatric treatment may be warranted (Abbott & Smith, 2015). Given that one side effect of flakka is suicidal ideations, all patients who ingest the drug should be placed on suicide precautions (McClellan et al., 2012). For

effective management and care to occur, it is paramount that all healthcare providers are knowledgeable about the effects of synthetic cathinones and to identify patients who present with the clinical manifestations presented previously (Califano, 2015).

## CONCLUSION

In the United States, there has been an explosion of synthetic cathinones' usage, flakka in particular. The reasons for the increase in usage may be attributed to ease of obtainability and media attention. These designer drugs are a serious public health concern. Healthcare providers must therefore be knowledgeable about these agents, including clinical presentation, management, and treatment to deliver optimal care.

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