Designer Drugs: Spice, Bath Salts

Designer drugs (often referred to as novel psychoactive substances or NPS) are created when chemists modify the chemical structure of an existing drug, often to skirt controlled substance regulations. The result is the creation of an analog drug with similar properties that are usually not subject to regulation. Two of the better-understood NPS are synthetic cathinones ("bath salts") and synthetic cannabinoids (commonly marketed as Spice and K-2). These NPS are promoted as "legal highs" and can be easily obtained at gas stations, convenience stores, and online.

Bath Salts (Synthetic Cathinones)

Pharmacology

Synthetic cathinones are synthetic analogues of the Catha edulis plant, commonly known as khat. The exact effects of synthetic cathinones vary based on their pharmacological properties but generally are similar to those of methamphetamine. Cathinones increase levels of brain monoamines, including norepinephrine, serotonin, and dopamine. Examples of synthetic cathinones include methcathinone, mephedrone, bupropion, and methylone.

Signs of Synthetic Cathinone Intoxication and Withdrawal

Sympathomimetic toxidrome (i.e., mimicking the effects of the sympathetic nervous system); similar to amphetamine and cocaine-like psychostimulant effects.

	Stimulant Intoxication	Stimulant Withdrawal
Physical Effects	Restlessness, sinus tachycardia, hyperventilation, mydriasis, bruxism (teeth grinding), headache, diaphoresis, tremor **At higher doses or repeated use** – more serious medical events may include ischemic colitis, acute coronary syndrome – unstable angina, myocardial infarction, tachyarrhythmia; hypertension, seizures, stroke, hyperthermia, rhabdomyolysis	Headache, nonspecific musculoskeletal pain, dental pain, tremor, and chills (usually self-limiting and do not require medical treatment).
Psychological and Behavioral Effects	Increased energy and alertness, increased sociability, elation, euphoria, decreased fatigue, decreased appetite, panic reactions, decreased need for sleep; **At high or repeated stimulant dosing** – anxiety, irritability, interpersonal sensitivity, hypervigilance, suspiciousness, grandiosity, impaired judgment, stereotyped behaviors*, psychosis (hallucinations, paranoia)*, very severe stimulant intoxication may present with symptoms of delirium.	Withdrawal syndrome consisting of depression, irritability, fatigue, difficulty concentrating, anhedonia*, increased drug cravings, increased appetite, hypersomnolence; withdrawal symptoms typically peak in 2-3 days and resolve within 1-2 weeks without treatment; some patients experience a protracted withdrawal ≥ 1 month that includes mild depression and cognitive impairment
Footnotes	*1. Patients intoxicated on stimulants may have symptoms which closely resemble acute schizophrenia and be misdiagnosed. Stimulant-induced hallucinations may be auditory, visual, or somatosensory. Tactile hallucinations are typical of stimulant-induced psychosis (e.g., sensation of something crawling on skin). *2. Stereotyped behaviors - repetitive behaviors (e.g., repeated dismantling of objects, cleaning, doodling, looking for imaginary objects)	*1. Anhedonia is the inability to feel pleasure

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Management of the Behavioral and Psychiatric Symptoms of Cathinone Intoxication

Immediate Safety and Triage:

- Conduct a medical evaluation focused on identifying life-threatening medical conditions that require referral for emergent hospital workup and management
- Evaluate patient for causal factors for agitation and psychosis (besides stimulant intoxication)
- Conduct a mental status examination focused on evaluating whether a patient is a danger to self and others and requires involuntary commitment

Behavioral Interventions:

Utilize verbal and nonverbal de-escalation strategies

Pharmacotherapy Interventions:

- Consider managing stimulant-induced agitation with a medication; benzodiazepines can be considered 1st-line for managing stimulant-induced agitation and/or confusion
- Treat stimulant-induced psychosis with antipsychotic medication.
    - Acuity and symptom severity should determine agent and route. For example, more acute patients may require intramuscular (IM) or intravenous (IV) treatment and should receive an antipsychotic available in those forms.

Clinical Monitoring:

- Monitor patient closely for breakthrough psychosis, suicidality, and trauma symptoms; suicidality may increase during waning intoxication and acute withdrawal
- If agitation and/or psychosis do not respond to your setting's available de-escalation and/or medication management interventions, coordinate transferring the patient to a higher level of care.

Synthetic Cannabinoids

Pharmacology

Synthetic cannabinoids show increased affinity and activity at the cannabinoid receptor 1 (CB-1) compared to naturally occurring cannabis; synthetic cannabinoids do not have the balancing active cannabinoids (i.e., cannabidiol) found in cannabis; this poses greater potential for adverse effects, including psychosis.

Signs of Synthetic Cannabinoid Intoxication and Withdrawal

The effects are largely similar to cannabis but often with higher symptom severity.

	Cannabis Intoxication*	Cannabis Withdrawal	Synthetic Cannabinoid Intoxication Features
Physical Effects	Conjunctival injection (red eyes), tachycardia, palpitations, orthostatic hypotension, dry mouth, poor motor coordination, head jerks	Gastrointestinal distress, diaphoresis, chills, nausea, shakiness, muscle twitches, hypertension. (less common compared to psychological and behavioral effects)	Tachycardia, agitation, and vomiting (common) Increased potential of life-threatening toxic effects - seizures, rhabdomyolysis, myocardial infarction, and severe agitation.

	Cannabis Intoxication*	Cannabis Withdrawal	Synthetic Cannabinoid Intoxication Features
Psychological and Behavioral Effects	Relaxation, euphoria, slowed time perception, altered/intensified sensory perception, increased awareness of environment, impaired concentration, anterograde amnesia, and increased appetite; **At high or repeated dosing use/use in stressful settings** are associated with hypervigilance, anxiety, paranoia, derealization, depersonalization, altered time sense, panic, hallucinations, psychosis, and delirium.	Irritability, anxiety, depression, restlessness, anorexia, insomnia/disturbed sleep	Increased potential to cause neuropsychiatric side effects such as delirium, psychosis, hallucinations, dystonia, dysarthria, short-term memory deficits, paranoia

*Cannabis intoxication is mediated by delta-9-tetrahydrocannabinol (THC) interaction at cannabinoid 1 (CB1) receptors on neuronal membranes.

Management of the Behavioral and Psychiatric Symptoms of Synthetic Cannabinoid Intoxication

Management of synthetic cannabinoids is largely supportive treatment with efforts to decrease environmental stimuli. More interventions may be necessary if severe intoxication symptoms are present.

Immediate Safety and Triage:

- Conduct a medical evaluation focused on identifying life-threatening medical conditions that require referral for emergent hospital workup and management
- Conduct a mental status examination focused on evaluating whether a patient is a danger to self and others and requires involuntary commitment

Behavioral Interventions:

- Utilize verbal and nonverbal de-escalation strategies

Pharmacotherapy Interventions:

- Benzodiazepines can be considered for severe agitation, anxiety, and/or hyperthermia.
- Antipsychotic medication can be considered for psychotic symptoms.
- Synthetic cannabinoid induced psychosis may require higher doses of antipsychotic medications and longer hospital stays compared to naturally derived cannabis.

Clinical Monitoring:

- If agitation and/or psychosis do not respond to your setting's available de-escalation and/or medication management interventions, coordinate transferring the patient to a higher level of care.

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