Synthetic Cannabinoids Fact Sheet

What are Synthetic Cannabinoids?

"Synthetic cannabinoids" or "synthetic cannabis" (**SC**) are laboratory-made substances marketed by illicit manufacturers as being like THC (*delta-9-tetrahydrocannabinol*). THC is the main psychoactive chemical in the cannabis plant that can be smoked as cannabis or used in other cannabis products like edibles. Despite the resemblance in name, SC are not the same as plant-based cannabis and its chemical structures bear no resemblance to the chemical structure of plant-based THC from the cannabis plant. Unlike THC, SC are not one substance, but hundreds of different chemical combinations categorized in a new class of substances called **n**ovel **p**sychoactive **s**ubstances (**NPS**).

As early as the year 2000, SC were sold illegally to consumers in Europe and the USA via the internet, in convenience stores and smoke shops. SC are labeled falsely as "potpourri," "herbal incense," or "natural, herbal and legal" cannabis. Often, these products are marked with a disclaimer such as "not for human consumption" or "for aromatherapy use only" to avoid regulatory scrutiny. "K2" and "Spice" are two early SC products from which many new, modified products have been engineered and sold with new names. Typically, SC are marketed in appealing, brightly colored foil packets, with some featuring familiar children's cartoon characters. These packets contain ground up greenish-brown plant material that has been sprayed with SC. From its original powder form, chemicals such as acetone and ethanol are used to dissolve the powdered SC into a liquid that subsequently is sprayed on and absorbed into the plant material.

In addition to the unregulated nature of SC, the plant material found in these products is neither uniform nor regulated for any type of quality control and may contain unidentified herbs with potentially harmful psychoactive properties. Even within individual packets, there may be different concentrations of chemical substances because the sprayed SC are not distributed evenly, leaving clumps or "hot spots" of SC.

If ingested, the effects of SC are more similar to those experienced from stimulants, like amphetamines, and may include many potentially serious adverse effects (see section below on SC general effects), in contrast to the milder effects typically associated with cannabis.

Because of the misleading name, "synthetic cannabinoids," used to market this group of substances, individuals seeking effects comparable to those effects commonly associated with plant-based cannabis may consume SC unknowingly and be harmed because of SC's increased potency and unpredictable effects. In research reports, comparisons of SC potency to the potency of THC from the cannabis plant vary tremendously from 2 – 800 times more potent depending on the type of SC compound.

- **Youth and synthetic cannabinoids:** Marketing for SC has targeted youth through enticing, playful packaging, and messaging SC as a cheaper alternative to cannabis that is not detected as easily in urine toxicology tests as THC. Both mental and physical health effects of SC use in youth may differ from adults with available studies suggesting greater harm.
  What can we learn from research examining youth and SC use?

  - Estimates of 4.5 - 13.5 % of high school students, differing by geography, report lifetime use of SC versus 29% for cannabis alone.
  - High school students who had used SC were more likely to engage in potentially harmful behaviors detrimental to their sexual and physical health compared to students who used cannabis only. [1]
  - Youth 12- 29 years old represent the largest age group of emergency room visits related to SC intoxication.
  - Severe neurological effects like seizures or coma are more commonly seen with youth using SC versus cannabis only and more commonly seen in youth compared to adults. [2]

The United States Drug Enforcement Agency (DEA) classifies SC as a **Schedule I substance** under the Controlled Substances Act, making this group of substances illegal federally as well as locally in New York State.

It is illegal in New York State to possess, sell, offer to sell, or to manufacture SC.
[Public Health Law Section 225, Title 10, Part 9.]

How are synthetic cannabinoids typically used?

Most commonly, the plant material sprayed with SC is ground up and sold in foil packets or baggies and then rolled and smoked like a "joint." Liquid versions of this substance also are sold in cartridges that may be vaped from an e-cigarette or other vaping devices. Additionally, SC may be ingested orally as a tea or swallowed and/or inserted rectally in capsule or tablet form. Like other psychoactive substances, for example LSD (lysergic acid diethylamide), SC may be ingested orally from blotter paper soaked with liquid SC. Overall, smoking or inhalation is the most popular route of use given its rapid onset of effect while oral ingestion causes a slower onset of effect.

Common names for synthetic cannabinoids

K2, Spice, Kush, Scooby Snax, Green Giant, Geeked Up, Caution, Smacked, Wicked X, AK-47, Herbal Incense, Fake Weed, Yucatan Fire, Skunk, Moon Rocks, Fire, Aroma, Earth impact, Mr. Smiley, Mr. Nice Guy, Zohai, Black Mamba, Dream, and other names.

General effects from synthetic cannabinoid use:

- SC target the same areas of the brain as THC, particularly, the cannabinoid receptors named CB_1 and CB_2. However, the way in which SC interact with these brain receptors is very different from plant-based THC. The result is a significantly more intense and longer-lasting effect than THC in addition to other potential unanticipated adverse effects.
- *After inhaling SC* by smoking or vaping, peak levels of SC are reached in 3 to 20 minutes with effects lasting from 3 – 5 hours to up to 24 hours. In some individuals, the duration of effects may be longer but unpredictable due to the continued activity from an array of SC break down products (metabolites).
- General effects range from feelings of sedation, relaxation, and/or pleasant euphoria to anxiety, agitation, fatigue, problems with thinking and perception. Experiences differ depending on the individual using the substance, the type and amount of SC compound used, other psychoactive substances used together with SC, and the way in which it is consumed (for example, smoking vs. oral ingestion).

Mental and physical health effects of synthetic cannabinoids:

The mental and physical effects of SC range from mild to severe.

- **Potential mental health effects**: Manic or psychosis-like conditions may result from SC use. From emergency room reports, mental health effects may present in several ways including severe anxiety, paranoia, auditory or visual hallucinations, agitation, sedation, and catatonia.

- **Potential physical health effects**: **Many systems in the body can be affected.**
  - *Cardiac or circulatory system*: Tachycardia (rapid heart rate) and other arrythmias (abnormal heart rhythms), elevated blood pressure, heart attacks and strokes
  - *Nervous system*: Seizures
  - *Kidney/urinary system*: Severe kidney injury requiring hospitalization and a possible need for dialysis
  - *Gastrointestinal:* Diarrhea, abdominal pain, dry mouth, and cannabis hyperemesis syndrome (persistent vomiting)
  - *Fatal and non-fatal overdoses* involving SC also have been reported with individuals presenting with severe tachycardia, extreme agitation, and confusion.
  - *Increased risk of needing emergency services:* Compared to people who use naturally occurring cannabis alone, people who use SC are up to 30 times more likely to require hospital emergency services because of severe reactions related to using SC.

- **Potential effects from chronic use may include these symptoms:**

- Difficulty with concentration
- Headaches
- Palpitations (feeling or sensation that the heart is pounding or racing)
- Panic attacks
- Cough
- Fatigue

- **Potential long-term physical and mental health effects:** Long-term effects of chronic SC use are not understood completely and the impact of SC on cognitive, emotional, and physical functioning requires more study.

Substances mixed with synthetic cannabinoids that may make them more dangerous:

- **Other substances** mixed into SC may introduce additional harms to the individual who uses SC in addition to the potential harm related to SC alone. Globally, the type of substances detected have included an array of NPS, including synthetic cathinones ("bath salts"), MDMA ("Ecstasy/Molly") novel synthetic stimulants, and designer benzodiazepines.
- **Other than the substances listed above, less notable additives,** such as vitamin E acetate, have been found in SC and are hypothesized to help mask SC detection in urine toxicology tests. The addition of vitamin E acetate is of particular concern given its association with many cases of e-cigarette or vaping product use-associated lung injury (**EVALI**).[3] In 2018, a rat poison called brodifacoum caused life-threatening bleeding in clusters of individuals using SC.[4] Flavorings like menthol or vanillin also may be added to increase appeal much like e-cigarettes' flavors used in the past.
- There is no reliable method to detect other substances that may be mixed in with SC merely by visual inspection, smell or taste. It also is not possible to predict accurately the potency of a purchased packet of SC by its appearance.

    - **Therefore, individuals who choose to use SC should do so with caution given the likelihood that other chemicals may be present with unpredictable, potentially harmful effects.**

Can using synthetic cannabinoids lead to addiction?

Yes, chronic use of SC may lead to physical dependence and addiction, formally known as *Cannabis Use Disorder (CUD)*. Because SC are full agonists at the CB_1 and CB_2 receptors versus the limited partial agonist effects from THC, SC causes intense activation of these CB receptors. Therefore, when SC are used daily or almost daily for long periods of time and then stopped abruptly, an individual may experience

several mild to moderate withdrawal symptoms including headache, stomach upset, sweating, difficulty sleeping, and anxiety. More severe symptoms include seizures, chest pain, palpitations, and shortness of breath. The severity of withdrawal symptoms may be related to the amount of SC used.

The criteria used to diagnosis a substance use disorder because of SC use include:

- Needing to take more and more SC to get the desired effect
- Using larger amounts of SC or over a longer period than you intended
- Persistent desire or unsuccessful efforts to cut down on SC use
- A lot of time spent doing things to get SC, use SC, or recover from its effects
- Craving, or a strong need or desire to use SC
- Failure to fulfill major role obligations at work, school, or home because of SC use
- Continued SC use despite having persistent or recurrent social or interpersonal problems
- Important things in life are given up because of SC use
- Recurrent SC use in situations in which it is physically hazardous, such a driving a car or operating a machine
- Continued SC use despite knowing its negative impacts on your mental or physical health

(Adapted from the DSM-5-TR criteria for CUD)

Which kinds of treatment work to help people who use synthetic cannabinoids?

- Emergency departments are the most appropriate setting to manage individuals with moderate to severe SC intoxication given the risk of severe or potentially life-threatening complications.
- Research studies demonstrating effective treatments (medications or other) for SC or cannabis use disorder are lacking. Two forms of psychological treatment used effectively to treat other SUDs, **cognitive behavior therapy** and **contingency management,** also may be helpful for people using SC.
- Medical and mental health providers may recommend individual or group counseling or behavioral therapy. These therapies exist in both the outpatient and inpatient treatment settings. Different levels of care are available for individuals seeking help, depending on their needs. Sometimes, an inpatient facility (rehabilitation) or residential program may be the best choice for more intensive treatment.
- It is important to discuss treatment options with medical or mental health treatment providers to see what may work best.

- Identifying and treating *other* co-existing substance use disorders *and* mental and physical health conditions related to SC use disorder are essential to maximize treatment options, reduce harms, and improve health outcomes.

What can be done to reduce the potential harms of using synthetic cannabinoids?

Because the composition of SC is changing constantly with unpredictable potency and effects within and among batches of the same product, strategies aimed at reducing the potential harms associated with SC are recommended:

- Use small amounts of SC at a time if the full effect of using a particular SC is unknown.
- Avoid combinations of other substances with SC, including alcohol.
- Avoid operating vehicles or machinery while using SC.
- If using SC and/or other substances, use with a buddy in case of an unexpected physical or mental reaction.
- If using SC or other substances while alone, consider calling the overdose prevention hotline **Neverusealone.org 1-800-484-3731** whose peers remain on the phone while the caller uses their substance, activating emergency services if an overdose or other severe reaction occurs.
- If an unexpected or severe reaction occurs, seek emergency medical services and bring the SC packet to the emergency room to assist with identification of the chemical substances ingested.

How can I get help for myself or my loved one?

- **For help and hope 24/7, call 1-877-8-HOPENY(467369) or text HOPENY(467369). Toll-free and confidential**
  Office of Addiction Services and Supports

- **The National Suicide and Crisis Lifeline:** call or text 988
  https://988lifeline.org/

- **New York State Office of Drug User Health:**
  Drug User Health (ny.gov)

- **Health Resources Services Administration Poison Help Line:**
  1-800-222-2212
  https://poisonhelp.hrsa.gov/about-us

References

1. Pediatrics (2017) 139 (4)
2. Pediatrics (2019) 144 (2)
3. Toxics. 2020 Mar; 8(1)
4. Am J Case Rep. 2020; 21