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## Synthetic Marijuana – What Do We Know about This Recent Hazard on the Streets?

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## Introduction

Several street drugs under the name of "fake marijuana" have been on the news lately, which appears to be more potent than the plant cannabis and cannot be detected by the drug screens, therefore preferred by drug users. While the recent opioid crisis took attention of all public, media and healthcare professionals on drug addiction, many clinicians still are unaware of the prevalence and severity of physical and psychoactive symptoms and the potentially serious consequences related to the use of these marijuana compounds. This short review aims to provide essential information and update about the imposed risk of synthetic marijuana compounds on health and on public safety.

Synthetic cannabinoids (SC) are lab-made chemicals, structurally similar to delta-9-tetrahydrocannabinol (one of the active substances found in cannabis plant, responsible from euphoric effects of cannabis). Their action is mainly on human cannabinoid (CB1) receptor [1]. Therapeutic effects of CB1 agonists have been extensively studied in variety of conditions such as pain, inflammation, obesity, nerve cell diseases substance use disorders and psychiatric disorders [2,3]. In 2015, the National Institute of Health (NIH) supported 281 projects totaling over \$111 million on cannabis research [4]. However, some SCs such as "K2" or "Spice" can produce severe and even deadly reactions [5]. They are more potent, with severe adverse effects which are not seen with natural marijuana. They are used by spreading on dried/shredded plant chippings, which then can be smoked, vaporized or inhaled.

Anecdotal reports have suggested that the use of these chemicals may cause severe tachycardia, hypertension, lethargy, nausea, vomiting, irritability, chest pain, hallucinations, confusion, and vertigo [6]. Users and bystanders often report the effects of SCs as more incapacitating, even rendering people "zombielike." Users may require physical and chemical restraints since they can suddenly become violent. A recent British clinical study reports that even low dose of JWH-018 (a SC compound also known as "Spice") can cause more 'high' after administration, impaired performance on the tracking, divided attention and stop signal task [7]. Severe conditions such as seizures, permanent cardiovascular and renal damage, stroke, psychosis, aggression and death (through suicide, high risk behavior or overdose) were also reported. In a recent study, compared to marijuana, use of synthetic cannabinoids was associated with high health risk behaviors, particularly for substance use behaviors and sexual risk behaviors [8]. A synthetic cannabinoid product named "Smacked!" has been linked to at least 41 overdoses in New Hampshire since 2014 which caused the government to declare a state of emergency.

In July 2017, more than 100 people in the same Pennsylvania town overdosed in a span of just three days (none were fatal).

It has been observed that patients recovered to normal function in 3-4 h, unless there was a major cardiac or other lifethreatening condition. Panic, anxiety and catatonia may require treatment with benzodiazepines, where agitation and psychosis respond to antipsychotics and further observation. Intravenous fluids, oxygen and supportive care would help individuals to recover faster [6]. There is no specific addiction or detoxification treatment available or necessary for the SC compounds.

The use of SCs among younger individuals is particularly high, especially if they have history of using alcohol, cannabis, or cigarettes. Among college students, 8 to 14% of participants reported the use of SCs. In a recent study of 5947 athletes, 4.5% tested positive for SCs by using specialized urine toxicology screening. The strongest correlation was with a history of cannabis use. SC products have become very popular as "poverty drug" due to its low price and easy access. SCs are often available where incense or marijuana paraphernalia is sold. Per a New York Times article [9], a five-gram bag goes for \$10 in the store, but it is often subdivided and resold on the street as \$1 "sticks," or joints, and \$2 "freestyle" portions — spike poured directly from the bag into the hand of the buyer.

Another popularity of SC compounds comes from the fact that SCs do not cause a positive drug test for marijuana or other illegal drugs, since they are not detectable in standard drug tests [10]. Some screening immunoassays and liquid chromatography-tandem mass spectrometric (LC-MS/MS) methods have been developed for simultaneously quantifying 20 synthetic cannabinoids and 21 metabolites in urine [11]. There is also a K2/Spice Single Test Strip available in the market; however, its reliability is unknown.

Further details and discussions regarding synthetic marijuana and its effects on health and society can be found at an earlier article [12]. More than 140 different SC products have been identified to date available on the street however; they are outlawed by the Food and Drug Administration (FDA) immediately after they have shown up, thus making it illegal throughout the United States (US). A recent survey showed that there was a significant decrease in SC use after the federal ban in the US in 2012 [13], which support the importance of legal regulations. While legal regulations should implement strict regulations, a public health message should be delivered to those users that SCs are not safe alternatives to marijuana and they can be lethal [14].

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