



Review

International trends in spice use: Prevalence, motivation for use, relationship to other substances, and perception of use and safety for synthetic cannabinoids



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ABSTRACT

Synthetic cannabinoids (SC), commonly known as Spice, are a class of compounds that share affinity for the cannabinoid receptors. Recreational use of SCs has grown in recent years. A literature search was conducted of national and international organizations as well as peer-reviewed publications describing SC use in non-clinical populations. Our primary goal was summarizing SC use prevalence within the general population from representative surveys. Our secondary goals included describing SC use frequency, motivation for use, the relationship between SC use and use of other substances, and perception of SC use including beliefs about safety and use by peers. Nationally and regionally representative surveys describe lifetime prevalence of SC use in the general population as between 0.2% and 4%. Longitudinal data, though limited, shows decline in SC use with peak use occurring in the late teens and early twenties. Users tend to be males. The majority of SC users report using only a small number of times and use tends to not be sustained. The most common motive for SC use is curiosity. SC users generally report a history of extensive use of other substances. Perception of SC use by others tends to be significantly greater than actual SC use.

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Abbreviations: ADASM, active duty service members; AOR, adjusted odds ratio; CB, cannabinoid receptor; CB1, cannabinoid receptor type 1; CB2, cannabinoid receptor type 2; DoD HRBS, Department of Defense Health Related Behavior Survey; EDADES, Spanish Household Survey on Alcohol and Drugs; EMCDDA, European Monitoring Center for Drugs and Drug Addiction; ESPAD, European School Survey Project on Alcohol and Other Drugs; ESTUDES, National Survey on Drug Use Among Secondary School Students in Spain; GHB/GBL, γ -Hydroxybutyric acid/ γ -Butyrolactone; GDS, Global Drug Survey; LSD, lysergic acid diethylamide; MDMA, 3,4-methylenedioxy-methamphetamine; MTF, monitoring the future; NC, natural cannabis; NPS, new psychoactive substance; PCP, phencyclidine; SC, synthetic cannabinoids; SNIPE, Social Norms Intervention of the prevention of Polydrug use; THC, tetrahydrocannabinol; UNODC, United Nations Office on Drugs and Crime.

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1. Introduction

In less than a decade, international monitoring organizations have documented an alarming and steady rise in the manufacture, distribution, and use of a new generation of synthetic psychoactive substances (Crime, 2013; Law et al., 2015). These new psychoactive substances (NPS) are designed to mimic naturally occurring molecules or more traditional illicit psychoactive substances (Trecki et al., 2015). Synthetic cannabinoids (SC) are a diverse class of NPS's that share structural or functional similarities to tetrahydrocannabinol (THC) found in natural cannabis (NC) (Castaneto et al., 2014). SCs bind to the two subtypes of cannabinoid receptors, CB1 and CB2, with a varying degree of affinity (Debruyne and Le Boisselier, 2015; Seely et al., 2012). Compared to the partial agonism of THC to the CB receptors, SC compounds can act as agonists, neutral antagonists, or inverse agonists at CB1 receptors (Seely et al., 2012; Trecki et al., 2015; Wiley et al., 2011). Further, SCs lack the naturally occurring cannabidiol present in NC which evidence suggests provides antipsychotic properties (Müller et al., 2010; Zullino et al., 2007).

Progenitor SC compounds were originally designed for research purposes in the 1970s with the goal of better understanding the endogenous endocannabinoid pathway in hopes of developing therapeutic agents for conditions like pain associated with cancer (Loeffler et al., 2012). The scientific literature describing this research was appropriated by clandestine laboratories producing SCs for recreational use (Castaneto et al., 2014). Initially, SC containing products were advertised as legal alternatives to NC consisting of natural spices and herbs (Wiley et al., 2011). Analyses revealed they in fact consisted of inert plant material sprayed with SCs (Loeffler et al., 2012; Wiley et al., 2011).

SCs are impacting the public health of countries around the world. The first evidence of SC use as a recreational drug was in 2004 (Crime, 2011; Debruyne and Le Boisselier, 2015). The widespread use of SCs did not begin until 2008, and the first reported case of SC abuse appeared with the discovery of five compounds (JWH-018, CP 47,497 and its C6, C7, C8 analogs) in herbal blends produced by a German company (Debruyne and Le Boisselier, 2015). The United Nations Office on Drugs and Crime World Drug Report 2015 indicated that SCs are the class of novel psychoactive substances with the most new compounds detected globally, representing 39% of all new psychoactive substances (Nations, 2016). From 2014 to 2015, 177 SCs were reported to the UNODC early warning system, with reports coming in from 58 countries and territories (Nations, 2016).

Secondary to the rapid proliferation of SCs internationally, various countries have compiled data on SC use and related morbidity of users, with among the most extensive data available in the United States. The U.S. Substance Abuse and Mental Health Services Administration reported that Emergency Department visits related to SCs nearly tripled in two years, from 11,406 in 2010 to 28,531 in 2011 (Cassels, 2014). Poison Control Center calls related to SCs increased 229% (1085; 3572) from 2014 to 2015 (Law et al., 2015). Law enforcement agencies observed similar exponential growth trends, with the DEA's national forensics database exploding from fifteen SC reports related to two different substances in 2009 to over 41,200 SC reports in 2012 related to 56 different SC compounds. Compared to NC users, SC users had a 30-fold increased relative risk of requiring emergency medical care (95% CI 17.5–51.2) (Winstock et al., 2015). Multiple geographic clusters of increased morbidity and mortality related to SC use have been reported, with at least 12 states reporting an unprecedented number from March 2015 to May 2015 (Trecki et al., 2015).

Much of the peer reviewed literature on SC use is derived from individuals presenting for medical care, typically emergency department presentations, hospital admissions, poison control center contacts, or substance abuse treatment. Description of SC use patterns outside of these clinical contexts is quite limited. A recent systematic review of the SC literature concluded "SC epidemiology data are limited and derived mostly from cross-sectional surveys of small, self-selected convenience samples. Community-based epidemiological surveys with large, nationally representative samples are needed." (Castaneto et al., 2014).

This study describes our efforts to summarize data of SC use patterns in non-clinical populations.

2. Methods

This paper reviews SC use in non-clinical samples. By non-clinical, we refer to individuals not presenting for medical care such as poison control contacts and clinical encounters (e.g., emergency department visits). Our primary goal was to summarize prevalence of SC use in representative, non-clinical populations. Our secondary goals were to report on other aspects of SC use such as frequency, motivation for use, the relationship between SC use and the use of other substances, and perception of SC use including beliefs about safety and perception of use by peers.

We searched Medline literature using multiple key-words (e.g.; "synthetic cannabinoids"; "synthetic cannabis"; "synthetic marijuana"; "spice"; "fake pot"; etc.). The abstracts of all potential

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