



Original communication

Review of detection frequency and type of synthetic cannabinoids in herbal compounds analyzed by Istanbul Narcotic Department of the Council of Forensic Medicine, Turkey[☆]



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ABSTRACT

In recent years, synthetic cannabinoids have been frequently observed in seized materials all over the world. This new generation of designer drugs, mixed with herbal substances, is also known as “Herbal Highs” or “Legal Highs”.

There are many articles about the history, type and pharmaco-chemical properties of synthetic cannabinoids in the literature; however the number of articles about the frequency of their detection is limited. In this study, we evaluated the type and detection frequency of synthetic cannabinoids in Istanbul and its surrounding area. The reports of the Council of Forensic Medicine-Istanbul Narcotic Department were retrospectively reviewed for the presence of synthetic cannabinoids in herbal compounds sent by the judicial authorities between August 01, 2010 and March 31, 2012. Among 1200 herbal compounds, 1179 of them (98.3%) contained synthetic cannabinoids. Twenty-one samples (1.7%) had other psychoactive substances. The analysis of 1179 samples showed that JWH-018 was present in 1172 (99.4%) of the samples. JWH-081 was found in 777 samples (65.9%) together with JWH-018. Samples had different package names. “Bonzai Aromatic Potpourri” ($n = 755$; 64.0%) and “Bonzai Plant Growth Regulator” ($n = 316$; 26.8%) were the most common product names amongst the herbal products in this study. It is clear from the present study and previous studies that brand name of synthetic cannabinoids that dominate the market exhibit regional differences as to the type and detection frequency of synthetic cannabinoids and the content of herbal highs packages.

The number and diversity of synthetic cannabinoid compounds have increased dramatically in the drug market in recent years. New, different, potent derivatives appear on the market almost every day and this presents important problems that need to be solved by scientists and judicial authorities working to prevent their harm. These problems include the limited knowledge about their frequency, the

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lack of analytical data and reference standards for analysis of these new derivatives, the lack of information on their toxic effects, and information about the metabolism and metabolites for toxicological analysis in human subjects.

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1. Introduction

Cannabinoids are a diverse group of substances acting on cannabinoid receptors CB1 and CB2 and produce a wide range of responses throughout the body. They are classified mainly in three groups: natural cannabinoids, endogenous cannabinoids and synthetic cannabinoids. The most well-known example of natural cannabinoids is delta9-tetrahydrocannabinol (THC), the main active ingredient of marijuana.¹ Endogenous cannabinoids include 2-arachidonoylglycerol and anandamide. The third group, synthetic cannabinoids, consists of the molecules created in laboratories (scientific or clandestine) to mimic the effects of THC.^{2,3}

The first record about marijuana (*Cannabis sativa*) which dates back over 10,000 years to the Stone Age was found in Taiwan.⁴ Its medical use dates back over 5000 years, in the ancient inscription and folklore of India and China.^{4–6} It was reported that, in 2737 B.C., the Chinese Emperor Shen Nung (Chen Nung) discovered marijuana's healing properties and he wrote a monograph about the use of cannabis in treating several diseases including migraine, asthma and some gynaecological disorders.^{4,6} Marijuana continued to be used for medical purposes throughout the centuries in near and far eastern countries. In 1842, Dr W.B. O Shaughnessy, an army surgeon in India, introduced an extensive treatise about medical use (as analgesic, antispasmodic and anticonvulsant) of cannabis to the British medical community.^{5,6} In the following years, cannabis became widely used in Britain and the United States as a part of medical treatment until the beginning of the 20th century.^{4–6}

As a result of long researches aiming at more effective therapeutic uses of cannabis, the first analogues of THC were reported in the early 1940s.⁷ After the 1960s, following the isolation of THC as the main active substance in *C. sativa*, new cannabinoid receptor agonists such as HU-210 (100 times more potent than THC), Nabylone, Dronabinol were synthesized and the number of THC analogues increased rapidly.^{8–10} In 1970s, the cyclohexylphenol (CP) series, which included CP-59,540, CP-47,497 and their n-alkyl homologues were created, and in the years following, up to 1994, most of naphthylindoles and their homologues (including JWH-015, JWH-018, JWH-073, JWH-398), naphthylmethylindoles, naphthylpyrroles, naphthylmethylindenes and phenylacetylindoles (include JWH-250) were developed.¹⁰

Synthetic cannabinoids have been classified according to their chemical structures by Howlett et al.¹¹ This classification was referred, as shown below, in the report on synthetic cannabinoids found in herbal products produced by the United Nations Office on Drugs and Crime (UNODC)¹²:

1. Classical cannabinoids (THC, other constituents of cannabis and their structurally related synthetic analogues, e. g. HU-210, AM-906, AM-411, O-1184)
2. Nonclassical cannabinoids (cyclohexylphenols or 3-aryl cyclohexanols such as CP-47,497–C8, CP-55,940, CP-55,244)
3. Hybrid cannabinoids (combinations of structural features of classical and non-classical cannabinoids, e. g. AM-4030)
4. Aminoalkylindoles (AAls), which can be further divided into naphthylindoles (e. g. JWH-018, JWH-073, JWH-398, JWH-015, JWH-122, JWH-210, JWH-081, JWH-200, WIN-55,212); phenylacetylindoles (e. g. JWH-250, JWH-251); naphthylmethylindoles and benzoylindoles (e. g. pravadoline, AM-694, RSC-4).

5. Eicosanoids (endocannabinoids such as anandamide, and their synthetic analogs, e.g. methanandamide)
6. Others, diarylpyrazoles (selective CB1 antagonist Rimonabant[®]), naphthylpyrroles (JWH-307), naphthylmethylindenes or derivatives of naphthalene-1-yl- (4-pentyloxynaphthalen-1-yl) methanone (CRA-13)

In contrast to this, the British Advisory Council on the Misuse of Drugs (ACMD) classified synthetic cannabinoids in seven groups based on their chemical structure and accordingly suggested a "generic definition" in the legal control of these substances.¹³ These included: 1-Naphthylindoles (e.g. JWH-018, JWH-073, JWH-081); 2-Naphthylmethylindoles (e.g. JWH-185, JWH-199); 3-Naphthylpyrroles (e.g. JWH-369, JWH-370); 4-Naphthylmethylindenes (e.g. JWH-176); 5-Phenylacetylindoles (benzoylindoles: e.g. JWH-250); 6-Cyclohexylphenols (e.g. CP-47,497 and its homologues); 7-Classical cannabinoids (dibenzopyrans: e.g. THC, HU-210).

In recent years, synthetic cannabinoids have frequently been observed in seized materials all over the world. This new generation of designer drugs, which are mixed with herbal substances in sold materials, is also known as "Herbal Highs" or "Legal Highs".¹⁴ According to previous reports, these products, which were named as "herbal incense products", can easily be obtained via the internet and from some specialized shops such as gas stations, convenience stores, and head shops without age restrictions,^{9,10,14–16} with different brand names, including: Spice, Spice Silver, Spice Gold, Spice Diamond, Spice Arctic Synergy, Spice Tropical Synergy, Spice Egypt, K2, Mojo, Aroma, Dream, Chill X, Chaos, Sence, Smoke, Skunk, Silent, Black, Genie, Algerian Blend, Yucatan Fire, Tai, Fun, Sensation, SpicyXXX, Spike 99, Bonsai-18, Banana Cream Nuke, Wicked X, Natures, Organic, Zen, Spice Gold, Silver, Scene, Ex-ses, Spark, Blaze, Highdi's Almdröhner, Earth Impact, Gorillaz, Genie, Galaxy Gold, Space Truckin, Solar Flare, Moon Rocks, Blue Lotus, Scope, Dream, etc.^{9,17–19}

Although there are many articles about the history, type and pharmaco-chemical properties of synthetic cannabinoids in the literature, the number of articles about the frequency of their detection is limited.

In this study, we evaluated the type and detection frequency of synthetic cannabinoids in Istanbul and its surrounding area.

2. Material and methods

The reports of herbal compounds that were analyzed between August 01, 2010 and March 31, 2012 in the Istanbul Narcotic Department of the Council of Forensic Medicine at the request of the judicial authorities were retrospectively reviewed for synthetic cannabinoids. The reports about classical marijuana were not included in the study.

The results were statistically evaluated by the Chi-square test. The level of significance was $p \leq 0.05$.

3. Results

A total of 1200 herbal compounds (except classical marijuana) were reported during a 20-month study period and 1179 of them (98.3%) contained synthetic cannabinoids. The total weight of analyzed herbal compounds was 11786.47 g and of these

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