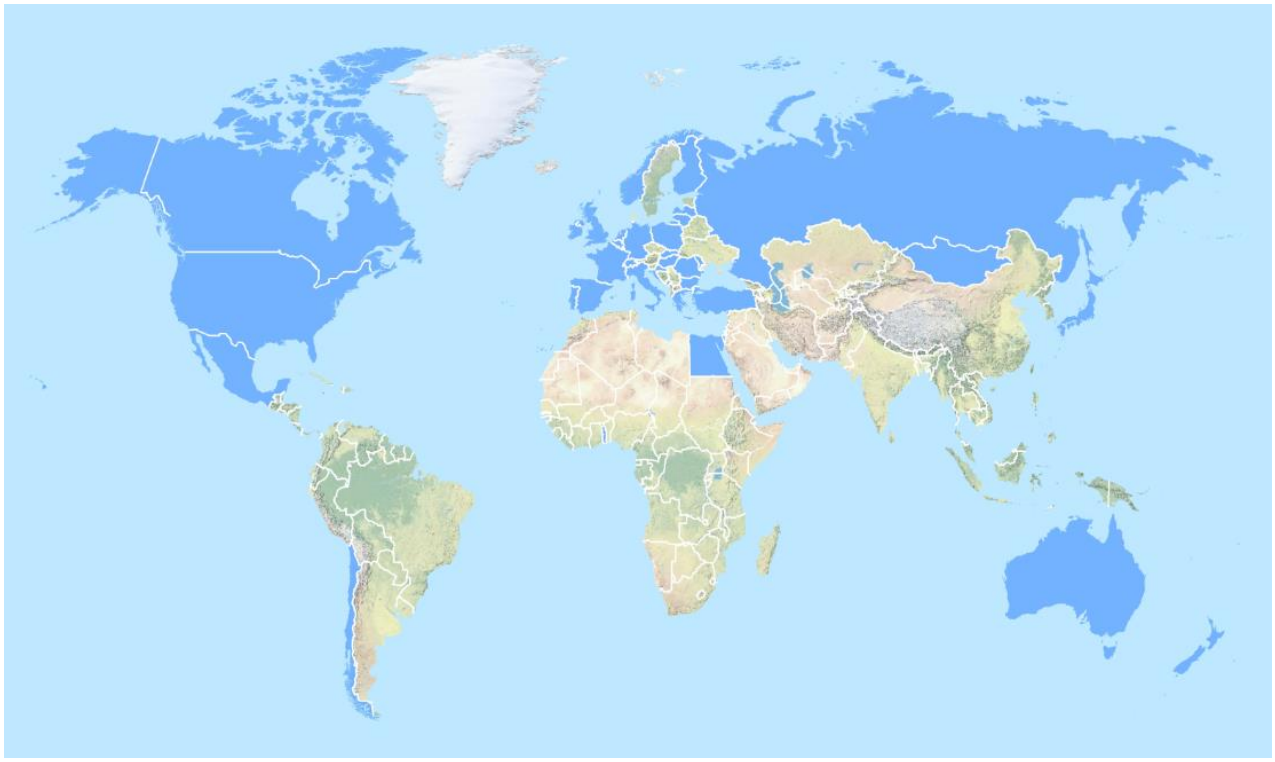
Global emergence of synthetic cannabinoids

Source: https://www.unodc.org/LSS/SubstanceGroup/Details/ae45ce06-6d33-4f5f-916a-e873f07bde02



Source: UNODC questionnaire on NPS, 2012

Background

The appearance of 'herbal highs' in the market is not a new phenomenon. Such products usually consisted of plant mixtures with little psychoactive effects. Since 2004, however, the composition of these herbal products seems to have substantially changed to include potent new psychoactive compounds known as synthetic cannabinoids.

Research on the mechanism of cannabis activity dates back several decades when molecules with similar behaviour to Δ9-tetrahydrocannabinol (THC) were first examined. A synthetic analogue of THC , 'HU-210', was first synthesized in Israel in 1988[1]and is considered to have a potency of at least 100 times more than THC. Due to its similar chemical structure to THC, 'HU-210' is regarded as a 'classical cannabinoid' and has been found in synthetic cannabinoids sold in the United States and other countries.

Non-classical cannabinoids include cyclohexylphenols or 3-arylcyclohexanols ('CP'compounds). 'CP' compounds were developed as potential analgesics by a pharmaceutical company in the 1980s. Respondents to the UNODC questionnaire on NPS have reported the emergence of CP-47,497 and CP-47,497-C8 in numerous countries in all regions except Africa since 2009.

Other structurally dissimilar varieties of synthetic cannabinoids unrelated to THC have also emerged on the market. These include aminoalkylindoles, such as naphthoylindoles (e.g. JWH-018), phenylacetylindoles (e.g. JWH-250), and benzoylindoles (e.g. AM-2233).[2] JWH-018, arguably the most widely known synthetic cannabinoid, belongs to the group of aminoalkylindoles and is considered to be three times as potent as THC. The JWH-compounds had been previously developed as test compounds in the research of receptor-drug interactions by Professor John William Huffman [3]and his team in the United States.

While cannabis and THC are controlled under the international drug control treaties, none of the synthetic cannabinoids are under international control. However, several have been subject to control measures at the national level. In 2012 UN Member States identified JWH-018 as the most widespread synthetic cannabinoid, followed by JWH-073, JWH-250 and JWH-081, all of which are aminoalkylindoles.

Description

Most synthetic cannabinoids are functionally similar to THC. Synthetic cannabinoids are usually available in powder form and are sold as 'Spice Gold', 'Spice Silver', 'Spice Diamond', 'K2', 'Bliss', 'Black Mamba', 'Bombay Blue', 'Blaze', 'Genie', 'Zohai', 'JWH -018, -073, -250', 'Kronic', 'Yucatan Fire', 'Skunk', 'Moon Rocks', 'Mr. Smiley'. They are usually smoked, but oral use has also been

Reported adverse effects

While side effects of cannabis are well documented,[4] data on human toxicity related to the use of synthetic cannabinoids remains limited. As with other NPS, products sold as synthetic cannabinoids often contain several chemicals in different concentrations, making it very difficult to determine substance-specific effects. Available knowledge on the toxicity of these compounds comes from scientific reports and clinical observations.

Health-related problems associated with the use of synthetic cannabinoids include cardiovascular problems and psychological disorders,[5] and it appears that there may be carcinogenic potential with some of the metabolites of the substances contained in these products.[6]

A study published in 2011 on the severe toxicity following synthetic cannabinoid ingestion suggested that JWH-018 could lead to seizures and tachyarrhythmia (irregular heartbeat).[7] In a recent review of clinical reports, addiction and withdrawal symptoms similar to those seen with cannabis abuse were also linked to the use of synthetic cannabinoids.[8] An analysis of synthetic cannabinoids in 'spice-like' herbal blends highlighted the increasing number of reports on suicides associated with preceding use of these products.[9]

Global emergence

Canada, Japan, Liechtenstein, Mexico and Togo reported that synthetic cannabinoids appeared on their markets before 2008, while New Zealand reported their first appearance in 2008. In Europe, synthetic cannabinoids started to emerge on a larger scale in 2008 and 2009, with seven countries eah year reporting their first appearance. In the Americas, synthetic cannabinoids were reported in

2009 from Chile and the United States. In Europe, the appearance of synthetic cannabinoids reached its peak in 2010 when ten countries reported these substances (Belgium, Bulgaria, Croatia, Lithuania, Luxembourg, Malta, Netherlands, Slovakia, Spain and Turkey). Outside Europe, Australia, Egypt, Israel and Hong Kong SAR reported their first emergence in 2010. Greece, Moldova, Mongolia and Singapore reported first appearance of synthetic cannabinoids in 2011.

Seizures

Synthetic cannabinoids are the most frequently seized NPS, with seizures reported from all regions. Over the last four years, seizures of synthetic cannabinoids have spread geographically. Whereas for 2009, only three countries (Finland, France and Germany) reported seizures of more than 1 kg of synthetic cannabinoids, that number had increased to 10 in 2010, 9 from Europe as well as the United States. In 2011, 16 countries reported seizures of synthetic cannabinoids, indicating a further spread to new regions, namely Oceania (New Zealand) and Asia (Saudi Arabia). Some countries reported particularly high increases, in the United States, for example, only 23 seizure cases were reported in 2009, rising to 22,000 cases in 2011.

Several European countries reported significant seizures of synthetic cannabinoids. In Germany, 261 kg of synthetic cannabinoids were seized in 2009. Cyprus, Hungary, Italy and Romania also reported seizures of more than 10 kg. In 2011, the EMCDDA reported that 20,000 packages containing several synthetic cannabinoids were seized at one facility in the Netherlands. [10]

Various countries initiated special operations targeting NPS. The Drug Enforcement Administration of the United States, for example, conducted a nationwide operation in July 2012 which resulted in the seizures of 4.8 million packages of synthetic cannabinoids as well as large quantities of synthetic cathinones.

Substances reported

UN Member States identified 60 different synthetic cannabinoids, the most frequently reported substance being JWH-018. The Republic of Korea reports that 74 per cent of all synthetic cannabinoids analysed by the Customs Laboratory between January 2009 to August 2012 belonged to the JWH class. [11] Similarly, data on synthetic cannabinoids submitted through the National Forensic Laboratory Information System (NFLIS) [12] of the United States, found that most belonged to the JHW class; in 2010, 63 per cent of them were identified as JWH-018, followed by JWH-250 (14%) and JWH-073 (9%).[13]

Top five synthetic cannabinoids reported to UNODC, up to 2012

Source: UNODC questionnaire on NPS, 2012

Please click here for a detailed list of synthetic cannabinoids reported up to 2012

References

[1]Mechoulam, R., Lander, N., Breuer, A., Zahalka, J., 'Synthesis of the individual, pharmacologically distinct, enantiomers of a tetrahydrocannabinol derivative', Tetrahedron: Asymetry, 1990, 1 (5), 315-18

[2]United Nations Office on Drugs and Crime, 'Synthetic cannabinoids in herbal products', Vienna, 2011, 5; see also Hudson, S., Ramsey, J., 'The emergence and analysis of synthetic cannabinoids', Drug Testing and Analysis, 2011, 3, 466–478

[3]John W. Huffman is a US chemist and a retired professor of organic chemistry at Clemson University in the United States, whose research led to the synthesis of non-cannabinoid cannabimimetrics in the 1990s. Dr Huffman's research group focuses on the synthesis of analogues and metabolites of THC with the aim to develop new pharmaceutical products for medical treatment. 'John Huffman', Clemson University (http://www.clemson.edu/chemistry/people/)

[4]For example in Hall, W., Solowij, N., 'Adverse effects of cannabis', to other stimulants (e.g. cocaine, amphetamine and The Lancet, 1998, 352, 1611-6; Ashton, C. H., 'Adverse effects of cannabis and cannabinoids', British Journal of Anaesthesia, 1999, 83 (4), 637-49

[5]Müller, H., Huttner, H.B., Köhrmann, M., Wielopolski, J.E., Kornhuber, J. and Sperling, W., 'Panic attack after spice abusein patient with ADHD', Pharmacopsychiatry, 2010, 43, 4, 152-153; Mir, A., Obafemi, A., Young, A. and Kane, C., 'Myocardial infarction associated with use of the synthetic cannabinoid K2', Jounal of Pediatrics,

2011, 128, 6, 1622-1627; Every-Palmer, S., 'Synthetic cannabinoid JWH-018 and psychosis: an explorative sudy', Drug and Alcohol Dependence, 2011, 117 (2-3), 152-157

[6]Lin, C.Y., Wheelock, A.M., Morin, D., Baldwin, R.M., Lee, M.G., Taff, A., Plopper, C., Buckpitt, A., and Rohde, A, 'Toxicity and metabolism of methylnaphthalenes: comparison with naphthalene and 1- Nitronaphthalene', Toxicology, 2009, 260, 16-27

[7]Lapoint, J., James, L.P., Moran, C.L., Nelson, L.S., Hoffman, R.S., & Moran, J.H., 'Severe toxicity following synthetic cannabinoid ingestion', Clinical Toxicology (Philadelphia), 2011, 49, 760-64

[8]Vardakou, I., Pistos, C., Spiliopoulou, C.H., 'Spice drugs as a new trend: mode of action, identification and legislation', Toxicology Letter, 2010, 197, 157-162

[9]Ludger, E., Krueger, K., Lindigkeit, R., Schiebel, HM., Beuerle, T., 'Synthetic cannabinoids in ''spice-like'' herbal blends: first appearance of JWH-307 and recurrence of JWH-018 on the German market', Forensic Science International, 2012, 222 (1), 216-222

[10]European Monitoring Centre for Drugs and Drug Addiction, '2012 Annual report on the state of the drugs problem in Europe', Lisbon, 2012

[11] Yuk, S., 'Designer drug situation and activities of customs laboratories in Korea', Korea Customs Service, presented at the Group of European Customs Laboratories workshop on designer drugs, Berlin, 27 – 28 September 2012

[12]The National Forensic Laboratory Information System (NFLIS) is a programme of the Office of Diversion Control of the Drug Enforcement Administration that systematically collects drug identification results from drug cases conducted by state and local forensic laboratories across the U.S.

[13]United States, Drug Enforcement Administration, 'Special report: synthetic cannabinoids and synthetic cathinones reported in NFLIS (National Forensic Laboratory Information System), 2009-2010', Department of Justice, Springfield, 2011 (http://www.deadiversion.usdoj.gov/nflis/2010rx_synth.pdf)