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Identification and quantification of synthetic cannabinoids in 'spice-like' herbal mixtures: Update of the German situation in early 2017

Ludger Ernst[a], Kai Brandhorst[b], Uli Papke[c], Anna Altrogge[d], Simone Zodel[d], Nico Langer[d], Till Beuerle[d,*]

[a] Chemistry Department, Central NMR Laboratory, Technische Universität Braunschweig, Hagenring 30, 38106 Braunschweig, Germany
[b] Chemistry Department, Institute of Inorganic and Analytical Chemistry, Hagenring 30, 38106 Braunschweig, Germany
[c] Chemistry Department, Central Mass Spectrometry Laboratory, Technische Universität Braunschweig, Hagenring 30, 38106 Braunschweig, Germany
[d] Institute of Pharmaceutical Biology, Technische Universität Braunschweig, Mendelssohnstr. 1, 38106 Braunschweig, Germany

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A B S T R A C T

In February 2017, eleven "Spice-like" products (14 individual packages including replicates) from German language internet shops were analyzed. In total, three different synthetic cannabinoids (SCs) were identified by gas-chromatography–mass spectrometry (GC–MS), namely MDMB-CHMICA and two, so far only partially described compounds, 5F-Cumyl-P7AICA and Cumyl-PeGACLONE. All analyzed products contained only one synthetic cannabinoid as active ingredient. 5F-Cumyl-P7AICA and Cumyl-PeGACLONE were subject to an in-depth characterization by nuclear magnetic resonance spectroscopy (NMR), electron ionization mass spectrometry (EI-MS), electrospray ionization tandem mass spectrometry (ESI-MS/MS), infrared and ultraviolet-visible spectroscopy (IR and UV/Vis). Cumyl-PeGACLONE shows a rather unexpected structure compared to conventional SCs of the past. Hence a global minima calculation was conducted to demonstrate structural similarity of Cumyl-PeGACLONE to JWH-018, a classical SC.

In addition, all SCs were quantified by a GC–MS method using JWH-018 as internal standard and corresponding response factors. While MDMB-CHMICA was detected in six out of 14 tested products (ranging from 6 to 20 mg/g; average 10 mg/g), 5F-Cumyl-P7AICA and Cumyl-PeGACLONE were detected in three (109–153 mg/g; average 131 mg/g) and five products (15–74 mg/g; average 39 mg/g), respectively.

1. Introduction

In the last ten years, synthetic cannabinoids (SCs) have developed widespread occurrence as designer drugs [1,2]. Since then, these products have been marketed as plant-based incense blends serving allegedly as room fragrances, but the obvious and well known purpose is cigarette-like smoking of the plant material, which is impregnated with SCs, to achieve cannabis like effects.

The first SCs in use, were compounds known from the scientific literature on research chemicals tested in studies as receptor agonists for the human cannabinoid receptors [3,4]. However, the rapid economic success followed by legal prohibition of individual compounds in many countries, resulted in an increasingly faster spinning spiral of regulations and appearance of chemically slightly modified compounds to circumvent these updated regulations. Until recently, the seemingly endless number of possible small chemical modifications allowed the immediate replacement of SCs as soon as new regulations were put into effect. This generated a constant availability of new (unregulated) SCs, until national laws were modified accordingly with the resulting time delay.

As a result, 256 SCs are currently listed by the United Nations Office on Drugs and Crime (UNODC), making SCs the predominant group of new psychoactive substances worldwide [5] (Fig. 1). Similar tendencies were observed on EU (172 compounds) and individually regulated compounds (56) on a national level (Germany) (Fig. 1) [6,7].

The assumed "legal" status as perceived by the consumers, the fact that SCs are not detected by common drug screenings and an easy access via the internet, have contributed to the growing

* Corresponding author at: TU Braunschweig, Inst. f. Pharm. Biol., Mendelssohnstr. 1, 38106 Braunschweig, Germany.
E-mail address: t.beuerle@tu-bs.de (T. Beuerle).

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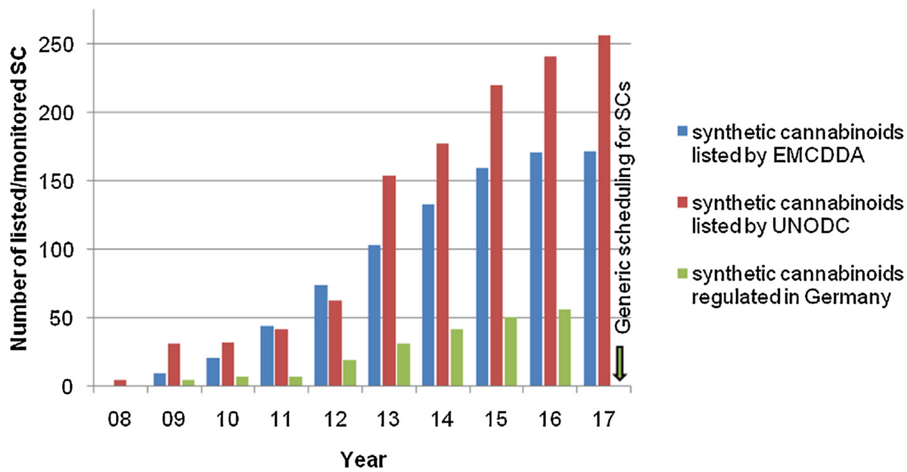

Fig. 1. Summary of the time history and the number of synthetic cannabinoids (SCs) reported by UNODC (United Nations Office on Drugs and Crime) [5], the EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) [6], or regulated by the German BtmG [7].

popularity of the so called "legal highs" to become one of the most widely used designer drugs worldwide. This never-ending flood of new SCs presents a constant challenge for public health, law enforcement agencies and forensic analytics around the world (see Fig. 1).

In order to cope with these developments concerning SCs, but also 2-phenethylamines including cathinones, a new law (NpSG; [8]) became effective in Germany on November 21st, 2016 which constitutes a generic approach to regulate whole classes of compound based on core structural elements and numerous residues/elements (Generic Legislation Model). The aim of this action is to put an end to the minute chemical modifications by the manufacturers in order to synthesize new SCs which are not yet covered by the individual regulation of the BtMG (List Model Approach; [7]). The generic approach of the NpSG is exemplified in Fig. 2.

This approach is rather unique from a legal point of view, since the new law implies a kind of preventive measure, namely predicting/prohibiting crimes of the future, something not commonly seen in the judicial system.

However, many countries, including Japan, the USA and the UK [9], dealing with similar situations, have already installed a generic or analogue control of SCs by their national narcotic laws. In an Analogue System Model, legislation is even much broader than a generic legislation, due to the definition of analogues as substances with substantially similar structure and/or effect to an already controlled substance [9].

The present study deals with the isolation, proof of structure, description of the physio-chemical characteristics and quantification of SCs detected in herbal incenses on the German market in early 2017, in the light of the newly effective legal framework (NpsG, [8]).

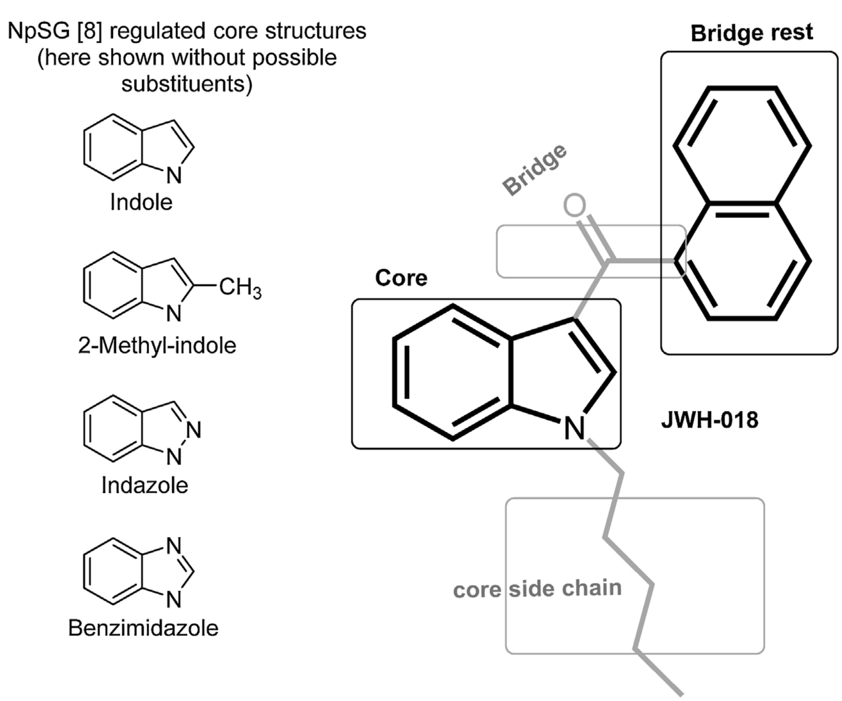

Fig. 2. Summary of the generic regulation of new designer drugs, implemented in Germany in 2016 (NpSG, [8]). The approach is exemplified using JWH-018 as a model compound to demonstrate the different structural elements (core, bridge, bridge rest and core side chain). Each structural element includes a series of variations, here exemplified by the currently regulated variants for the core (indole, 2-methyl-indole, indazole, benzimidazole).