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Short communication

Determination of AB-CHMINACA and its metabolites in human hair and their deposition in hair of abusers

Juhyun Sim, Han Soo Cho, Jaesin Lee, Sangwhan In, Eunmi Kim*

National Forensic Service, 26460, 10 Ipchun-ro, Wonju, Gangwon-do, South Korea

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ABSTRACT

Despite global efforts to control the abuse of synthetic cannabinoids, the high-level of turnover from the market impedes regulation, endangering public health. N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (AB-CHMINACA) is the most popular synthetic cannabinoid in South Korea since its introduction in 2014. Nonetheless, few studies have been carried out on AB-CHMINACA and its metabolites, and its deposition in human hair. The purpose of this study was to develop and validate an analytical method for detection of AB-CHMINACA and its six metabolites in hair using a liquid chromatography tandem mass spectrometry (LC–MS/MS) system, for forensic applications. The methanol extracts of hair samples were evaporated, filtered, and analyzed by LC–MS/MS with electrospray ionization in positive ion mode. The limits of detection and quantification ranged from 0.5 to 10 pg/mg and 2 to 50 pg/mg, respectively. Good linearity was achieved within the range of 5–1000 pg/mg or 10–1000 pg/mg depending on the analyte. Intra- and inter-assay precision and accuracy values were below 15%. No significant variation was observed using different sources of hair matrices. These validation results proved the selectivity, accuracy and reproducibility of the method. The established method was applied to 37 authentic samples from suspected synthetic cannabinoid users. AB-CHMINACA and its two metabolites, AB-CHMINACA M2 and AB-CHMINACA M4, were detected. The concentration of the parent drug was much higher than those of its metabolites, and the amount of AB-CHMINACA M2 was greater than that of AB-CHMINACA M4 in all samples. No other metabolites were detected in the samples.

1. Introduction

Synthetic cannabinoids, originally developed for research of CB_1 and CB_2 cannabinoid receptors [1,2], were first identified in herbal incense in 2008 [3,4]. These herbal incenses, usually called 'spice', have since gained global popularity because they are sold on the Internet and in many head shops under the disguise of normal herbal products [5,6]. In South Korea, synthetic cannabinoids have been widely distributed since 2009 [7–10]. Therefore, a 'temporary drug designation system' was added to the Act on the Control of Narcotics, in order to control rapidly emerging synthetic cannabinoids [8].

N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (AB-CHMINACA), a recently introduced synthetic cannabinoid, was first reported in Japan in 2013 [11] and has spread rapidly worldwide. Due to its prominence, it was placed into Schedule I (i.e., compounds with high abuse potential and no accepted medical use) by the US Drug Enforcement Administration in 2015 [12]. In addition, AB-CHMINACA has been under control by a temporary drug designation system since December 2014 in Korea. Nevertheless, it became widely and rapidly distributed since late 2014.

AB-CHMINACA is one of the AB-INACA family, sharing an indazole-carboxamide (INACA) backbone with an amino-methyl-oxobutanyl (AB) group [13,14]. It is a highly potent agonist of the CB_1 receptor [15] and can cause serious adverse health effects [16]. Its metabolism was investigated *in vitro* and *in vivo* by Erratico et al. [13] (Fig. 1), and the distribution and metabolites of AB-CHMINACA in tissues, urine [17], and plasma [16], have been identified by LC–MS/MS methods. However, AB-CHMINACA and its metabolites in hair have been discussed only in one study by Franz et al. [18] with a single authentic hair sample.

Analysis of drugs in hair has gained attention and been adopted in many forensic and clinical laboratories because of its unique advantages: longer detection window, noninvasiveness, and better sample stability than urine [19]. Recommendations for the anal-

* Corresponding author.
E-mail addresses: jhsim86@korea.kr (J. Sim), chs6938@korea.kr (H.S. Cho), ljstrust@korea.kr (J. Lee), swin@korea.kr (S. In), emkim4725@korea.kr (E. Kim).

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Table 1
MRM transitions, retention times and other conditions for MS analysis of AB-CHMINACA, its metabolites and internal standards.

Compound name	Precursor ion (*m*/*z*)	Product ion (*m*/*z*)	RT (min)	DP	EP	CE	CXP
AB-CHMINACA	357.2	241	6.9	81	10	35	22
	357.2	312	6.9	81	10	21	22
AB-CHMINACA M2	358.2	241	7.6	86	10	27	16
	358.2	145	7.6	86	10	47	14
AB-CHMINACA M3A	374.2	239	4.6	101	10	33	20
	374.2	145	4.6	101	10	45	12
AB-CHMINACA-M4	259.2	241	6	121	10	19	12
	259.2	145	6	121	10	35	10
AB-CHMINACA M5A	275.1	145	3.5	136	10	35	12
	275.1	239	3.5	136	10	21	20
AB-CHMINACA M6	387.1	241	5.4	106	10	33	22
	387.1	145	5.4	106	10	53	10
AB-CHMINACA M7	388.2	241	5.6	81	10	25	14
	388.2	145	5.6	81	10	47	14
JWH-018 N-5-OH M-d_5	363.0	155	5.5	140	10	30	12
	363.0	127	5.5	140	10	65	12
JWH-018-d_9	351.1	155	8.6	75	10	33	14
	351.1	127	8.6	75	10	65	14

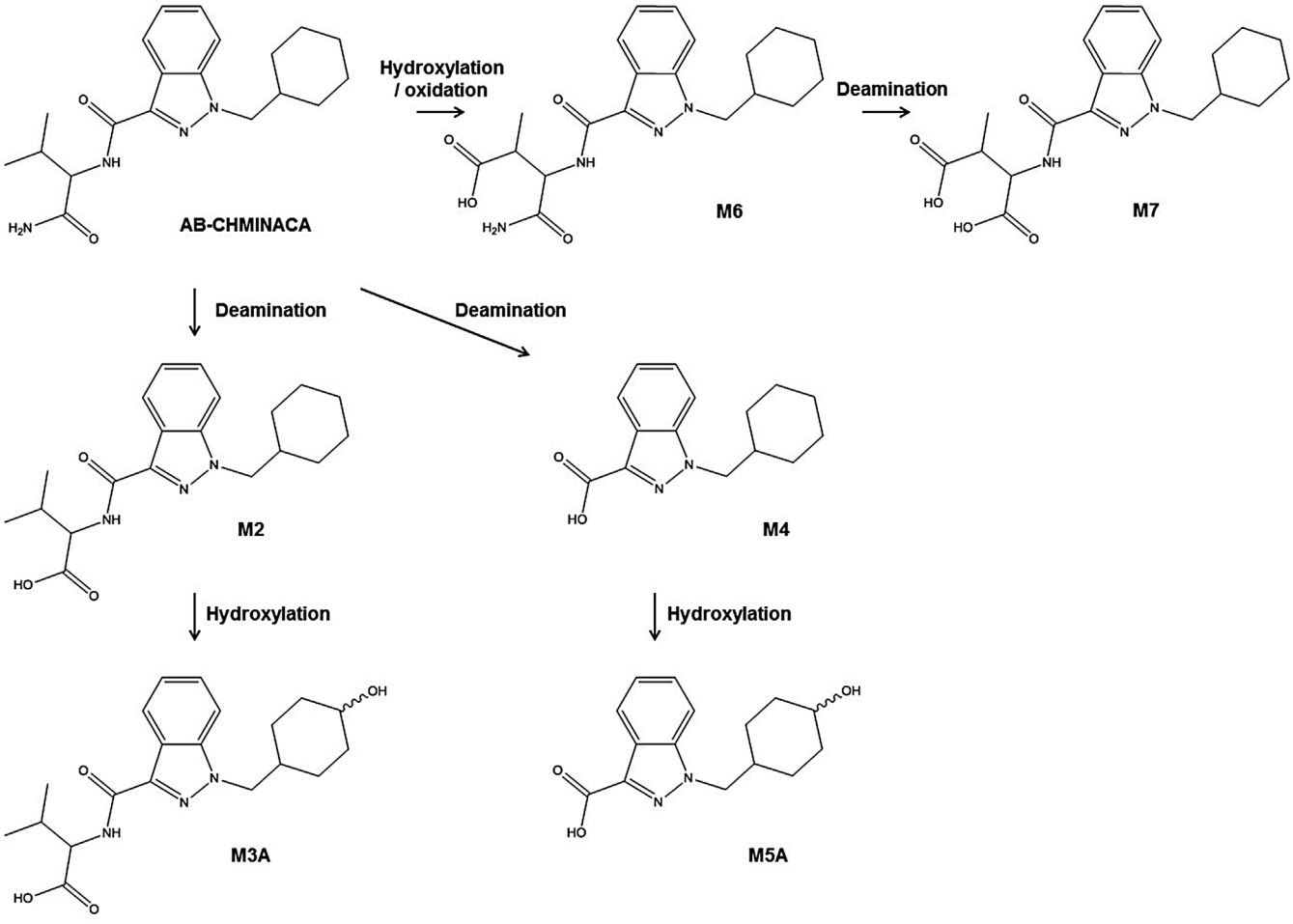

Fig. 1. Chemical structures of AB-CHMINACA and its metabolites.

ysis of hair for drugs of abuse published by the Society of Hair Testing (SoHT) proposed to confirm metabolites of drugs of abuse in hair to rule out passive contamination [20]. For these reasons, we aimed to investigate the distribution of AB-CHMINACA and its metabolites in hair. Herein, we have developed and fully validated a liquid chromatography-tandem mass spectrometry (LC–MS/MS) method for the determination of AB-CHMINACA and its six metabolites in hair. Furthermore, we analyzed 37 authentic hair samples from suspected synthetic cannabinoids users and investigated the incorporated metabolites in hair.