



**World Health
Organization**

**Critical review report:
ADB-BUTINACA**

Expert Committee on Drug Dependence

Forty-fifth Meeting

Geneva, 10–14 October 2022

This report contains the views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization.

© World Health Organization 2022
All rights reserved.

This advance copy will be distributed to the members of the 45th Expert Committee on Drug Dependence before formal publication by the World Health Organization. The document may not be reviewed, abstracted, quoted, reproduced, transmitted, distributed, translated or adapted, in part or in whole, in any form or by any means without the permission of the World Health Organization.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The World Health Organization does not warrant that the information contained in this publication is complete and correct and shall not be liable for any damages incurred as a result of its use.

Contents

Summary	4
1. Substance identification	4
A. International nonproprietary name	4
B. Chemical Abstracts Service registry number	4
C. Other chemical names	5
D. Trade names	5
E. Street names	5
F. Physical appearance	5
G. WHO review history	5
2. Chemistry	5
A. Chemical name	5
B. Chemical structure	6
C. Stereoisomers.....	6
D. Methods and ease of illicit manufacture	7
E. Chemical properties	7
F. Identification and analysis.....	7
3. Ease of conversion into controlled substances.....	8
4. General pharmacology	8
A. Routes of administration and dosage	8
B. Pharmacokinetics	8
C. Pharmacodynamics	8
5. Toxicology.....	9
6. Adverse reactions in humans.....	9
7. Dependence potential.....	10
A. Studies in experimental animals	10
B. Studies in humans	10
8. Abuse potential	10
A. Studies in experimental animals	10
B. Studies in humans	10
9. Therapeutic applications and extent of therapeutic use and epidemiology of medical use.....	10
10. Listing on the WHO Model Lists of Essential Medicines	10
11. Marketing authorizations (as a medicinal product).....	10
12. Industrial use	10
13. Non-medical use, abuse and dependence	11
14. Nature and magnitude of public health problems related to misuse, abuse and dependence...	11
15. Licit production, consumption and international trade.....	11
16. Illicit manufacture and traffic and related information	11
17. Current international controls and their impact.....	11
18. Current and past national controls	12
19. Other medical and scientific matters relevant for a recommendation on scheduling of the substance.....	12
References.....	12

Executive summary

ADB-BUTINACA (Chemical Abstracts Service [CAS] registry number: 2666932-43-8; CAS name: *N*-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-butyl-1*H*-indazole-3-carboxamide) is an indazole-derived synthetic cannabinoid, the *S*-enantiomer being the active compound (CAS No.: 2682867-55-4). It is distinguished from its closely related analogue ADB-BINACA by a butyl tail substituent (rather than the benzyl substituent of ADB-BINACA). The first documented detection of ADB-BUTINACA by government authorities occurred in Sweden in July 2019. Since then, the compound has been detected in seized products or biological samples in 11 countries. ADB-BUTINACA is not under international control, and the specific compound does not appear to be under national control.

Little information on ADB-BUTINACA is available in the scientific literature. Online forum posts by people who self-report use of ADB-BUTINACA suggest that its primary route of administration is inhalation by smoking after the chemical has been sprayed onto herbal material or by vaping of the chemical solubilized in a vehicle. Oral use has also been reported.

Its extensive metabolism is mediated primarily by three isoforms of the CYP450 enzyme system (CYP2C19, CYP3A4 and CYP3A5), and monohydroxylation is a predominant phase I metabolic pathway. The dihydrodiol metabolite has been proposed for use as a primary urinary biomarker. ADB-BUTINACA binds to CB1 and CB2 receptors with high affinity ($K_i = 0.299$ nM and 0.912 nM, respectively) and is a potent full agonist at both receptors, with an efficacy (E_{max}) ranging from 101% to 290% depending on the assay and comparison control compound (e.g., CP55,940 or JWH-018). *In vivo*, ADB-BUTINACA caused a pronounced, dose-dependent drop in core body temperature in mice (maximum, ~ 6.5 °C decrease at 3 mg/kg intraperitoneally) and fully and dose-dependently substituted for Δ^9 -tetrahydrocannabinol (THC) in rats ($ED_{50} = 0.038$ mg/kg).

In the USA, analytically confirmed use of ADB-BUTINACA has been associated with six fatal and eight non-fatal poisonings, the latter requiring emergency room visits. By the time most patients came to the attention of medical personnel, they were minimally responsive or unconscious; however, the cause of these adverse effects could not be definitively assigned to ADB-BUTINACA, as toxicology often showed use of more than one substance. Products containing ADB-BUTINACA have been seized by law enforcement officers in prisons, suggesting that it is smuggled in and used by incarcerated people. Reports on online forums provide evidence that ADB-BUTINACA is used intentionally for its intoxicating effects, and it has also been detected in seized samples as an adulterant of substances marketed as cannabis.

The primary source of information about its psychological effects is online forums. The reported effects in intentional users include feeling “mad stoned”, sedation, euphoria, sleepiness (at higher doses) and “warm, fuzzy” sensations. Unintentional use (e.g., in adulterated cannabis) resulted in different symptoms, which included extreme paranoia, dissociation and unconsciousness. Online posts should be considered anecdotal reports, as there was no analytical confirmation of sole use of ADB-BUTINACA.

1. Substance identification

A. International nonproprietary name

Not available.

B. Chemical Abstracts Service registry number

2666932-43-8 ((*N*-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-butyl-1*H*-indazole-3-carboxamide)

2682867-55-4 ((*S*)-enantiomer) (*N*-[(1*S*)-1-(aminocarbonyl)-2,2-dimethylpropyl]-1-butyl-1*H*-indazole-3-carboxamide)

C. Other chemical names

N-(1-Amino-3,3-dimethyl-1-oxobutan-2-yl)-1-benzyl-1*H*-indazole-3-carboxamide

N-(1-Amino-3,3-dimethyl-1-oxobutan-2-yl)-1-benzylindazole-3-carboxamide

2-[(1-Butyl-1*H*-indazol-3-yl)formamido]-3,3-dimethylbutanamide

N-[1-Amino-3,3-dimethyl-1-oxobutan-2-yl]-1-butyl-1*H*-indazole-3-carboxamide

ADB-BUTINACA

ADB-BINACA

The name ADB-BINACA has been used to refer to ADB-BUTINACA (*N*-[1-amino-3,3-dimethyl-1-oxobutan-2-yl]-1-butyl-1*H*-indazole-3-carboxamide), the analogue with the 1-butyl substituent on the indazole ring instead of the 1-benzyl substituent (ABD-BINACA). ADB-BINACA is the name used for the analogue with the benzyl substituent on the indazole ring as the tail portion (*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-benzyl-1*H*-indazole-3-carboxamide), while ADB-BUTINACA contains a butyl moiety as its tail (1–3).

D. Trade names

The (*S*)-enantiomer (*N*-[(1*S*)-1-(aminocarbonyl)-2,2-dimethylpropyl]-1-butyl-1*H*-indazole-3-carboxamide) is sold by Cayman Chemicals as an analytical standard under the trade name “ADB-BUTINACA” (4).

E. Street names

Although no specific information was available on the street names for ADB-BUTINACA, it is likely that the substance is sold under the name “Spice”, which is typically used for smoking mixtures containing synthetic cannabinoid receptor agonists. Other common names for such mixtures depend on the country, region, product type, brand name and user groups (5).

F. Physical appearance

The (*S*)-enantiomer of ADB-BUTINACA has been described as a crystalline solid (4). Pure ADB-BUTINACA is typically available as a beige or yellowish powder, but it is easily blended into other street drugs. Thus, small amounts of ADB-BUTINACA in a sample may be difficult to identify, as other components can mask its colour, smell and taste. Moreover, solutions of synthetic cannabinoids such as ADB-BUTINACA are usually sprayed onto plant material or into blotting paper and smoked, vaped or consumed orally (6).

G. WHO review history

ADB-BUTINACA has not previously been reviewed by the WHO Expert Committee on Drug Dependence.

2. Chemistry

A. Chemical name

IUPAC name:

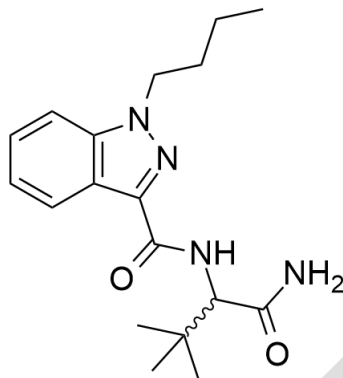
N-[1-(Aminocarbonyl)-2,2-dimethylpropyl]-1-butyl-1*H*-indazole-3-carboxamide

Chemical Abstracts index name:

1*H*-Indazole-3-carboxamide, *N*-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-butyl- (ACI)

B. Chemical structure

Free base:

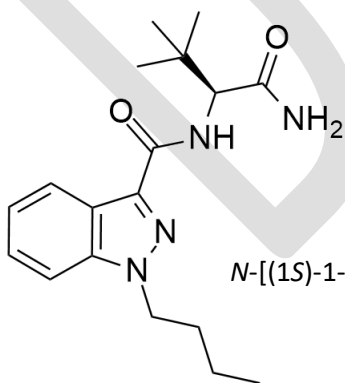


Molecular formula: C₁₈H₂₆N₄O₂

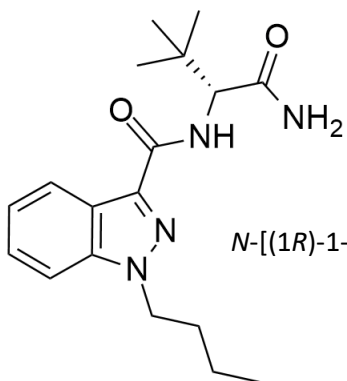
Molecular weight: 330.43 g/mol

C. Stereoisomers

The presence of an asymmetric carbon atom gives rise to the (*R*)- and (*S*)-enantiomers of ADB-BUTINACA. Although structurally related synthetic cannabinoid receptor agonists typically show the (*S*) configuration, the same substance with either (*R*)-configuration or the racemic mixture may be present in seized samples. Although structurally related synthetic cannabinoid receptor agonists typically show the (*S*) configuration, the same substance with either (*R*)-configuration or as the racemic mixture may be present in seized samples.



N-[(1*S*)-1-(Aminocarbonyl)-2,2-dimethylpropyl]-1-butyl-1*H*-indazole-3-carboxamide



N-[(1*R*)-1-(Aminocarbonyl)-2,2-dimethylpropyl]-1-butyl-1*H*-indazole-3-carboxamide

D. Methods and ease of illicit manufacture

No information was available on the manufacture of ADB-BUTINACA seized or collected on the market. Preparation of this substance is, however, straightforward and follows standard procedures with cheap, readily available reagents. Two examples are the synthetic procedures for obtaining (*S*)-ADB-BUTINACA in three steps, starting from methyl indazole-3-carboxylate, described by Cannaert et al. (7) and Sparkes et al. (8). Although the process is simple, it requires the equipment of a chemical synthetic laboratory and qualified personnel.

E. Chemical properties

Melting-point

148.2–148.4 °C (7)

Boiling-point

No information was found.

Solubility

ADB-BUTINACA is soluble in dimethylformamide at 20 mg/mL and in dimethyl sulfoxide at 10 mg/mL. In ethanol, it is soluble at 20 mg/mL (4).

F. Identification and analysis

Synthetic ADB-BUTINACA was characterized by proton and carbon nuclear magnetic resonance (¹H NMR and ¹³C NMR), mass spectrometry (MS), ultraviolet spectrophotometry and infra-red spectroscopy (2, 7). ADB-BUTINACA and two of its metabolites, ADB-BUTINACA *N*-butanoic acid and ADB-BUTINACA *N*-(4-hydroxybutyl), are available as reference materials from commercial suppliers for use in forensic and clinical investigations (4, 9, 10).

Analytical methods for identification of ADB-BUTINACA in seized samples have been published. They include gas chromatography (GC)–MS, GC–infra-red spectroscopy, liquid chromatography (LC)–MS, ionic chromatography, ¹H NMR and ¹³C NMR (11, 12).

ADB-BUTINACA and its major metabolites were identified and quantified in human hepatocytes, liver microsomes, hair, urine, blood and post-mortem kidney and liver samples by LC coupled with high-resolution MS and LC coupled with triple-quadrupole MS (1, 13, 14).

No information was available on the enantiomeric composition of ADB-BUTINACA, but the substance available on the market is most likely to be the (*S*)-enantiomer, like most other closely related synthetic cannabinoids. The (*S*)-enantiomer has not, however, been identified

in analysed samples, and the presence of the (*R*)-enantiomer (including as an impurity) cannot be excluded.

3. Ease of conversion into controlled substances

No information was available in the literature.

4. General pharmacology

A. Routes of administration and dosage

Posts on online forums by people who use drugs indicate that ADB-BUTINACA has been inhaled by vaping after solubilization (15–17). Oral and sublingual use have also been reported (17). ADB-BUTINACA has been found in seizures of various products: adulterated cannabis or hemp plant material prepared for smoking (18–20), paper infused with the chemical (used mainly to smuggle material into controlled environments such as prisons) (2) and powders for making formulations and products (18, 19). In many cases, ADB-BUTINACA was not the sole substance identified in tested samples.

The dosage required for intoxication is unclear. One person reported vaping a 500- μ g/mL solution of ADB-BUTINACA, while others reported smoking 1 mg and taking 75 μ g sublingually (17). The duration of effects ranged from 30 min to 3 h (16). These online forum posts should be considered anecdotal, as there was no analytical confirmation of the purity of ADB-BUTINACA.

B. Pharmacokinetics

Like many synthetic cannabinoids, ADB-BUTINACA undergoes extensive hepatic biotransformation in the body, with an estimated half-life after exposure to human liver microsomes of < 30 min (1). The parent compound is not usually found in urine samples from live humans (1, 13) but may be found in post-mortem samples (13). The parent compound has also been reported in human blood samples and in tissue (kidney and liver) samples (13). The number of identified phase-I and -II metabolites ranged from 21 to 40, depending on the assay (urine samples, human hepatocytes or human liver microsomes), but three published studies concur in specifying mono-hydroxylation as a dominant phase I reaction, resulting in some of the most abundant metabolites (1, 2, 13). While Kavanagh et al. (13) and Kronstrand et al. (2) recommended use of the dihydrodiol metabolite as a primary urinary biomarker, Sia et al. (1) reported that this metabolite is not abundant and recommended one of the hydroxylated metabolites as the most stable urinary biomarker, with half-lives of 48–190 min. Kavanagh et al. (13) suggested that the mono-hydroxylated metabolites (or the parent compound) would be the most reliable biomarker in blood. Three isoforms of CYP450 (CYP2C19, CYP3A4 and CYP3A5) appear to be the predominant enzymes involved in the metabolism of ADB-BUTINACA (1).

C. Pharmacodynamics

ADB-BUTINACA binds to both human type 1 cannabinoid (hCB1) and hCB2 receptors (expressed in HEK-293 cells), with a three times greater affinity (K_i) for hCB1 than for hCB2 receptors: pK_i (CB1) = 9.52 ± 0.05 M (K_i = 0.299 nM) and pK_i (CB2) = 9.04 ± 0.16 M (K_i = 0.912 nM) (8). In an evaluation of functional activation of the CB1 receptor (8), ADB-BUTINACA was found to be a full, potent agonist at both cannabinoid receptors in a fluorescence-based membrane assay in AtT20 cells, with greater potency for activation of CB1 than of CB2

receptors: half maximal effective concentration (EC_{50}) = 0.67 nM, E_{max} = 113% \pm 3 (compared with CP55,940) for the CB1 receptor and EC_{50} = 4.1 nM, E_{max} = 101% \pm 3 (compared with CP55,940) for the CB2 receptor. Using the same assay, Cannaert et al. (7) reported that ADB-BUTINACA was almost 10 times less potent (EC_{50} = 6.36 nM, 95% confidence interval: 2.88 nM; 11.9 nM) at CB1 than CB2 receptors (8) but had greater efficacy (E_{max} = 290%), although efficacy was compared with that of JWH-018 rather than CP55,940. A third study (2) found a potency (EC_{50}) of 11.6 nM (95% CI: 9.8 nM; 13.4 nM) for increasing calcium flux in recombinant Chinese hamster ovary cells expressing hCB1 receptors. ADB-BUTINACA also showed pronounced biased agonism at the CB1 and CB2 receptors through recruitment of β -arrestin 2, with EC_{50} = 19 nM (E_{max} = 728% when compared with CP55,940) and EC_{50} = 1.79 nM (E_{max} = 83% when compared with CP55,940) for the CB1 and CB2 receptors, respectively (8).

ADB-BUTINACA has been evaluated in one in-vivo assay in mice, in which it caused a pronounced, dose-dependent decrease in core body temperature (maximum \sim 6.5 °C decrease at 3 mg/kg intraperitoneally), with maximal effects 45 min after injection and dissipation of the effect by 135 min after injection (8). A decrease in temperature of this magnitude is commonly observed after administration of synthetic cannabinoids to mice (21).

5. Toxicology

No preclinical studies or systematic studies of human toxicology with ADB-BUTINACA were identified.

6. Adverse reactions in humans

Summary information from the US Drug Enforcement Administration provided to the ECDD Secretariat indicates that analytically confirmed use of ADB-BUTINACA has been implicated in at least six fatal poisonings and at least eight non-fatal poisonings that required medical treatment. By the time most patients came to the attention of medical personnel, they were minimally responsive or unconscious. In two of the non-fatal poisonings, patients were reported to be “excitable” before becoming lethargic. Most of the patients were given naloxone, which had no notable effect on their symptoms. Five of the non-fatal and five of the fatal poisonings were in people who were incarcerated at the time of the poisoning. All the deceased were men, as were four of the six people involved in nonfatal poisonings. The age range for all poisoning cases was 27–60 years. The cause of death of one person was listed as cardiac arrest, while the causes of death of the other patients were not available. Several patients had a history of non-cannabinoid substance use, and one had high cholesterol and schizophrenia. While ADB-BUTINACA and/or its metabolites were detected in serum or urine in each case, the effects of ADB-BUTINACA in these poisonings could not be specified because of the presence of other substances in the blood or urine of all but one patient. This non-fatal case had been observed using other substances (alcohol and cocaine contaminated with fentanyl) the night before the poisoning, complicating attribution of his symptoms to ADB-BUTINACA, as the serum or urine concentrations of the other substances might have dissipated overnight.

Phrases used to describe the sensations experienced after intentional use of ADB-BUTINACA at doses that did not result in unresponsiveness include: “it gets me mad stoned, very sedating and warm and pleasant”, “giggle euphoria munchies warmth, and then sleep with higher doses” and “It is quite a nice high, warm, fuzzy, euphoric and a little rushy. It is my favourite noid so far” (17). In cases in which use of ADB-BUTINACA was unintentional (also see section 19), users reported sensations such as “extreme paranoia”, “felt like K2/Spice”, “tripping sensation”, “got an allergy-like reaction at injection site”, “out-of-body experience”, “blacked out for 5 hours, didn’t remember anything” (18). These user posts should be considered anecdotal, as sole use of ADB-BUTINACA was not analytically confirmed.

7. Dependence potential

A. Studies in experimental animals

No studies were available.

B. Studies in humans

No studies were available.

8. Abuse potential

A. Studies in experimental animals

No published studies on the abuse potential of ADB-BUTINACA in experimental animals were available; however, unpublished studies of drug discrimination provided by the US Drug Enforcement Administration (22) showed that intraperitoneal ADB-BUTINACA substituted for THC in six male Sprague-Dawley rats trained to discriminate 3 mg/kg THC (intraperitoneally) from vehicle in a two-lever discrimination test. The substitution was dose-dependent, with maximal substitution (100% THC-lever response) at 0.1 mg/kg but no effect on the response rates. The ED₅₀ for THC-like discriminative stimulus effects for ADB-BUTINACA was 0.038 mg/kg.

B. Studies in humans

No studies were available.

9. Therapeutic applications and extent of therapeutic use and epidemiology of medical use

ADB-BUTINACA has no known therapeutic applications and is not used medically.

10. Listing on the WHO Model Lists of Essential Medicines

ADB-BUTINACA is not listed on the 22nd WHO Model List of Essential Medicines or on the 8th Model List of Essential Medicines for Children.

11. Marketing authorizations (as a medicinal product)

There are no known marketing authorizations for ADB-BUTINACA.

12. Industrial use

ADB-BUTINACA has no known industrial use.

13. Non-medical use, abuse and dependence

ADB-BUTINACA appeared on the European drug market in September 2019 in Sweden (20). Reports on online forums by people who use drugs provide evidence that ADB-BUTINACA has been used intentionally for its intoxicating effects (see section 6), and this substance has been detected in seized and biological samples in 11 countries (see section 16 for listing) and as an adulterant in substances marketed as cannabis (18, 19, 23, 24).

No information was found on the prevalence of chronic use of ADB-BUTINACA and dependence.

14. Nature and magnitude of public health problems related to misuse, abuse and dependence

ADB-BUTINACA has been detected in infused paper in post sent to prison inmates in Scotland. Between January and June 2021, ADB-BUTINACA was one of the most prevalent synthetic cannabinoids seized in Scottish prisons, with a total of 76 (60.3%) samples positive for this substance (2). In 2021, the United Nations Office on Drugs and Crime Tox Portal included 23 cases in Singapore in which ADB-BUTINACA was detected in biological samples (25). No other substances were detected in four post-mortem samples, and ADB-BUTINACA was designated high on the causality scale used in the system. ADB-BUTINACA was also designated as high on the causality scale for 16 of the clinical admissions and as contributory (medium) for the other three cases. No details of the nature of the symptoms or the clinical course were available. The Republic of Korea reported seven additional detections, and France and the United States each reported one case, again with no information on the nature of the symptoms. At least six deaths in which ADB-BUTINACA was found toxicologically post-mortem have occurred in the USA, and at least eight non-fatal poisonings severe enough to require emergency medical attention were reported in a summary document provided by the US Drug Enforcement Administration to the Secretariat of the Expert Committee on Drug Dependence; however, as noted in section 6, ADB-BUTINACA was not the only substance ingested.

15. Licit production, consumption and international trade

ADB-BUTINACA is not legally produced, consumed or in international trade.

16. Illicit manufacture and traffic and related information

The first documented seizure of ADB-BUTINACA in Europe was in Sweden in September 2019 (20). Since that report, ADB-BUTINACA has been detected in seized products or biological samples in 11 countries: Austria (19, 23), China (13, 26), France (25), Republic of Korea (25), Russian Federation (13), Singapore (1, 25), Slovenia (23), Sweden (23), Switzerland (19), the United Kingdom (2, 27) and the USA (19, 25). Most of the reports were made during 2020 and 2021.

17. Current international controls and their impact

Currently, there are no international controls specifically for ADB-BUTINACA.

18. Current and past national controls

ADB-BUTINACA does not appear to be controlled under the national regulations of any country, although it may be covered by generic or analogue legislation or regulations. Although a summary document provided by the US Drug Enforcement Administration to the Secretariat of the Expert Committee on Drug Dependence stated that ADB-BUTINACA has been designated as schedule I in the USA, a search for the compound in the *Federal Register* did not confirm a current status of “schedule I” for ADB-BUTINACA.

19. Other medical and scientific matters relevant for a recommendation on scheduling of the substance

No information was available.

References

1. Sia CH, Wang Z, Goh EML., Tan YL, Fong CY, Moy HY et al. Urinary metabolite biomarkers for the detection of synthetic cannabinoid ADB-BUTINACA abuse. *Clin Chem.* 2021;67:1534-1544.
2. Kronstrand R, Norman C, Vikingsson S, Biemas A, Valencia Crespo B, Edwards D et al. The metabolism of the synthetic cannabinoids ADB-BUTINACA and ADB-4en-PINACA and their detection in forensic toxicology casework and infused papers seized in prisons. *Drug Test Anal.* 2022;14:634–52.
3. Wang Y, Pan Y, Yang H, Liu J, Wurita A, Hasegawa K. Quantification of MDMB-4en-PINACA and ADB-BUTINACA in human hair by gas chromatography–tandem mass spectrometry. *Forensic Toxicol.* 2022;40:340–8.
4. ADB-BUTINACA (Item No. 29350). Ann Arbor (MI): Cayman Chemical Co.; 2022 (<https://www.caymanchem.com/product/29350/adb-butinaca>, accessed 13 June 2022).
5. EMCDDA initial report on the new psychoactive substance 4F-MDMB-BICA. Lisbon: European Monitoring Centre for Drugs and Drug Addiction; 2020.
6. ADB-BUTINACA. Lutherville (MD): National Association of Drug Diversion Investigators; 2021 (<https://www.naddi.org/glossary/adb-butinaca/>, accessed 13 June 2022).
7. Cannaert A, Sparkes E, Pike E, Luo JL, Fang A, Kevin RC et al. Synthesis and in vitro cannabinoid receptor 1 activity of recently detected synthetic cannabinoids 4F-MDMB-BICA, 5F-MPP-PICA, MMB-4en-PICA, CUMYL-CBMICA, ADB-BINACA, APP-BINACA, 4F-MDMB-BINACA, MDMB-4en-PINACA, A-CHMINACA, 5F-AB-P7AICA, 5F-MDMB-P7AICA, and 5F-AP7AICA. *ACS Chem Neurosci.* 2020;11:4434–46.
8. Sparkes E, Cairns EA, Kevin RC, Lai F, Grafinger KE, Chen S et al. Structure–activity relationships of valine, *tert*-leucine, and phenylalanine amino acid-derived synthetic cannabinoid receptor agonists related to ADB-BUTINACA, APP-BUTINACA, and ADB-P7AICA. *RSC Med Chem.* 2022;13:156–74.
9. ADB-BUTINACA N-(4-hydroxybutyl) metabolite (Item No. 30295). Ann Arbor (MI): Cayman Chemical Co.; 2022 ([https://www.caymanchem.com/product/30295/adb-butinaca-n-\(4-hydroxybutyl\)-metabolite](https://www.caymanchem.com/product/30295/adb-butinaca-n-(4-hydroxybutyl)-metabolite), accessed 13 June 2022).
10. ADB-BUTINACA N-(4-hydroxybutyl) metabolite (Item No. 30295). Ann Arbor (MI): Cayman Chemical Co.; 2022 ([https://www.caymanchem.com/product/30295/adb-butinaca-n-\(4-hydroxybutyl\)-metabolite](https://www.caymanchem.com/product/30295/adb-butinaca-n-(4-hydroxybutyl)-metabolite), accessed 13 June 2022).
11. Analytical report ADB-BINACA monograph (1-butyl-N-[1-carbamoyl-2,2-dimethyl-propyl]indazole-3-carboxamide). Vodovodna, Ljubljana: Slovenian National Forensic Laboratory; 2017.
12. Analytical report ADB-BUTINACA (C18H26N4O2) 2-[(1-butyl-1*H*-indazol-3-yl)formamido]-3,3-dimethylbutanamide. Vodovodna, Ljubljana: Slovenian National Forensic Laboratory; 2019.

13. Kavanagh P, Pechnikov A, Nikolaev I, Dowling G, Kolosova M, Gigoryev A. Detection of ADB-BUTINACA metabolites in human urine, blood, kidney and liver. *J Anal Toxicol.* 2021;46:641–50.
14. Liying Z, Min S, Baohua S, Hang C, Xin W, Hongxiao et al. Application of a UPLC-MS/MS method for quantitative analysis of 29 synthetic cannabinoids and their metabolites, such as ADB-BUTINACA and MDMB-4en-PINACA in human hair in real cases. *Forensic Sci Int.* 2022;331:111139.
15. 5cl-adb-a and adb-butinaca vape liquid ratio. San Francisco (CA): Reddit Inc; 2021 (https://www.reddit.com/r/noids/comments/m8itf3/5cladba_and_adbbutinaca_vape_liquid_ratio/, accessed 20 July 2022).
16. Mixing CBD with ADB-BUTINACA. San Francisco (CA): Reddit Inc; 2021 (https://www.reddit.com/r/noids/comments/nm1am7/mixing_cbd_with_adbbutinaca/, accessed 20 July 2022).
17. Everyone with experience with ADB-Butinaca needed! San Francisco (CA): Reddit Inc; 2022 (https://www.reddit.com/r/noids/comments/uqpnu9/everyone_with_experience_with_adbbutinaca_needed/, accessed 20 July 2022).
18. Synthetic cannabinoid “ADB-BUTINACA” aka “ADB-BINACA” detected in dope/heroin/fentanyl. Public health alert on ADB-BUTINACA. Waltham (MA): Opioid Policy Research Collaborative, The Heller School for Social Policy and Management, Brandeis University; 2021 (<https://heller.brandeis.edu/opioid-policy/pdfs/adb-butinaca-community-one-pager-final.pdf>, accessed 20 July 2022).
19. ADB-BUTINACA. Test results positive for ADB-BUTINACA. Grass Valley (CA): Erowid Center, DrugsData.org; 2022 (<https://www.drugsdata.org/search.php?substance1=2546>, accessed 20 July 2022).
20. New psychoactive substances: Global markets, global threats and the COVID-19 pandemic. An update from the EU Early Warning System (December 2020). Lisbon: European Monitoring Centre for Drugs and Drug Addiction; 2020.
21. Wiley JL, Marusich JA, Thomas BF. Combination chemistry: Structure–activity relationships of novel psychoactive cannabinoids. *Curr Top Behav Neurosci.* 2017;32:231–48.
22. Forster MJ, Gatch MB, Hill RD. ADB-BUTINACA: Test of substitution for the discriminative stimulus effects of delta(9)-THC. Contract report. Springfield (VA): US Drug Enforcement Administration; 2021.
23. New psychoactive substances: 25 years of early warning and response in Europe. An update from the EU Early Warning System (June 2022). Lisbon: European Monitoring Centre for Drugs and Drug Addiction; 2022.
24. European Drug Report 2022: Trends and developments. Lisbon: European Monitoring Centre for Drugs and Drug Addiction; 2022.
25. Early Warning Advisory Tox-Portal: ADB-BUTINACA. Vienna: United Nations Office on Drugs and Crime; 2022 (<https://www.unodc.org/tox/#/login>, accessed 25 July 2022).
26. Fan X, Zhang J, Fu X, Zhou B, Xu Z, Huang H et al. Analysis of synthetic cannabinoids in wastewater of major cities in China. *Sci Total Environ.* 2022;827:154267.
27. Synthetic cannabinoid receptor agonists (SCRA): An updated harms assessment and a review of classification and scheduling under the Misuse of Drugs Act 1971 and its Regulations. London: Advisory Council on the Misuse of Drugs; 2020 (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/929909/FOR_PUBLICATION_-_ACMD_SCRA_report_final.pdf, accessed 25 July 2022).