More Than ‘Spice’: Understanding Synthetic Cannabinoid Toxicity in Kentucky

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University of Kentucky

Program Objectives

- Understand the evolving landscape of synthetic cannabinoid use in Kentucky, including variability in product composition
- Recognize the common clinical presentations associated with synthetic cannabinoid exposure, and differentiate these from other toxicities
- Review the limitations of routine hospital toxicology testing in detecting synthetic cannabinoids and discuss the implications for clinical decision-making
- Outline management strategies for synthetic cannabinoid toxicity

Disclosures

- The author of this continuing education activity has made reasonable efforts to ensure that all information is accurate in accordance with the latest available scientific evidence at the time of presentation. However, because information regarding medications, treatment guidelines, laws/regulations, and other healthcare information is subject to constant change, the participant is advised to always confirm practice resources and information before applying any learned information in practice.
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- Generative AI was not used to assist in the development of content. Microsoft Copilot was used for editorial and formatting assistance only. All scientific and clinical content was independently developed by the author.

Understand the evolving landscape of synthetic cannabinoid use in Kentucky, including variability in product composition

Cannabinoids

Endocannabinoids

Synthetic Cannabinoids

Phytocannabinoids

https://pmc.ncbi.nlm.nih.gov/articles/PMC8625816/

Cannabinoids

Endocannabinoids

- Produced naturally in the body
- Plays role in regulation of multiple bodily functions
- Anandamide
- 2-arachidonylglycerol (2-AG)

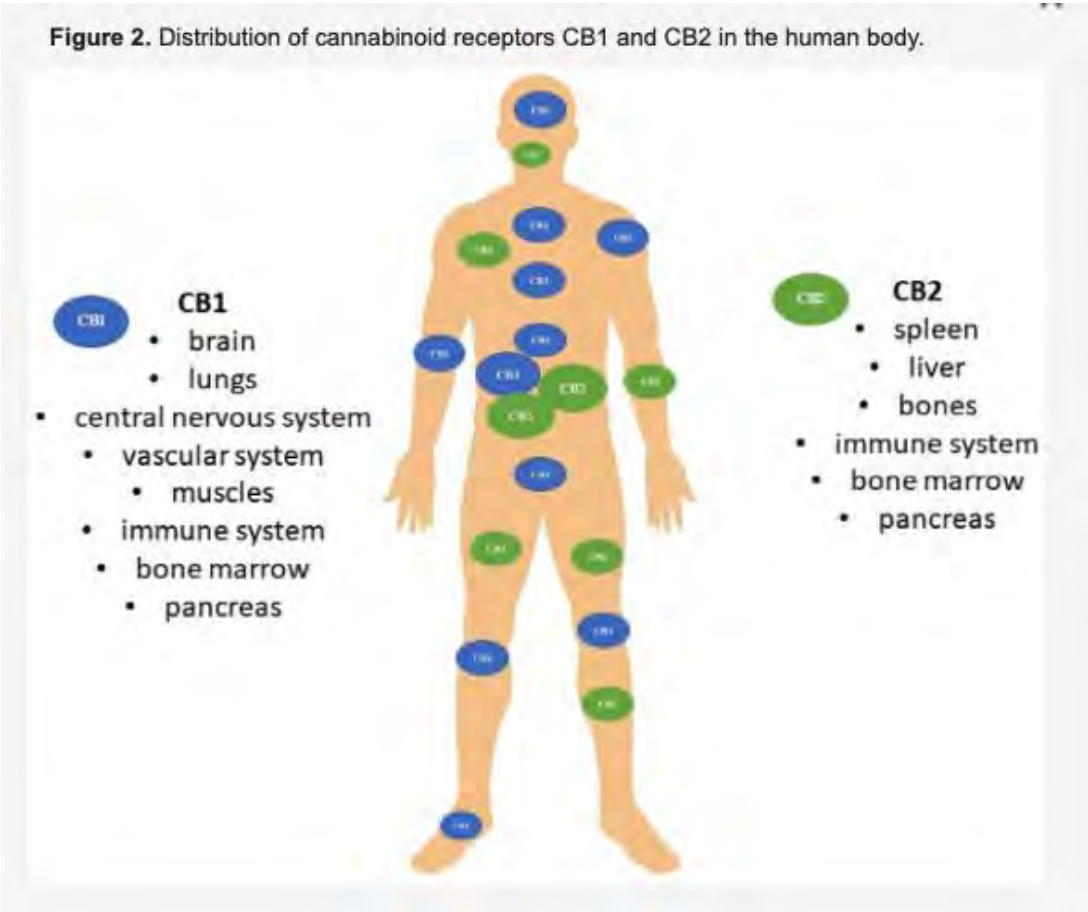
Synthetic Cannabinoids

Phytocannabinoids

https://pmc.ncbi.nlm.nih.gov/articles/PMC8625816/

Endocannabinoid System

- Regulates and controls many body functions
  - Learning and memory
  - Emotional processing
  - Sleep
  - Temperature control
  - Pain control
  - Inflammatory and immune responses
  - Appetite



Duczmal D, Bazan-Wozniak A, Niedzielska K, Pietrzak R. Cannabinoids—Multifunctional Compounds, Applications and Challenges—Mini Review. *Molecules*. 2024; 29(20):4923. https://doi.org/10.3390/molecules29204923

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Synthetic Cannabinoids

Phytocannabinoids

- Plant Derived
- Chemically complex containing more than 500 different components

>100 have been identified

- Tetrahydrocannabinol (THC)
- Cannabidiol (CBD)
- Cannabinol (CBN)

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Cannabinoids

Endocannabinoids

- Produced naturally in the body
- Plays role in regulation of multiple bodily functions
- Anandamide
- 2-arachidonylglycerol (2-AG)

Synthetic Cannabinoids

- Laboratory Derived
- Potent

Novel psychoactive substances (NPS)

- JWH-018
- WIN (WIN-55,212-2)
- CP (CP-55,940)

Phytocannabinoids

- Plant Derived
- Chemically complex containing more than 500 different components

>100 have been identified

- Tetrahydrocannabinol (THC)
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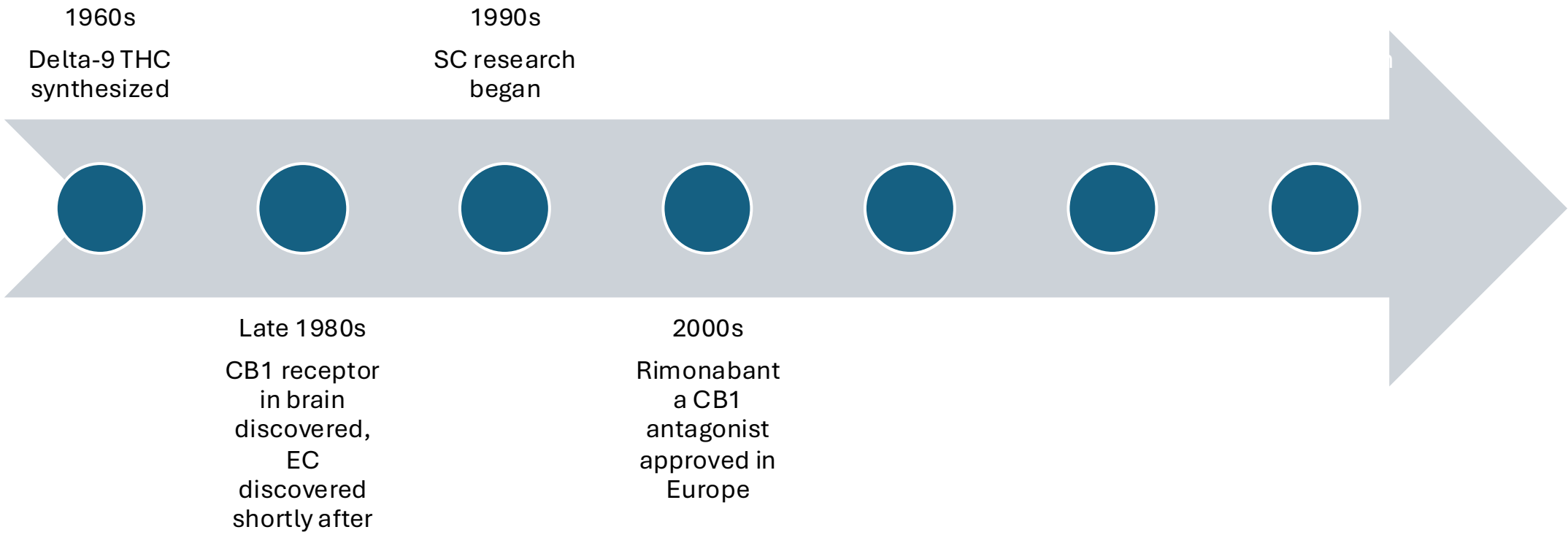
Cannabinoid Discovery Timeline



PC = Phytocannabinoids
EC = Endocannabinoids
SC = Synthetic Cannabinoids

Wiley JL. Hijacking of Basic Research: The Case of Synthetic Cannabinoids. *Methods Rep RTI Press*. 2011;2011:17971. doi:10.3768/rtipress.2011.op.0007.1111
https://pmc.ncbi.nlm.nih.gov/articles/PMC11810933/
https://pmc.ncbi.nlm.nih.gov/articles/PMC3136184/
https://www.smithsonianmag.com/science-nature/the-scientific-history-of-cannabinoids-180981561/
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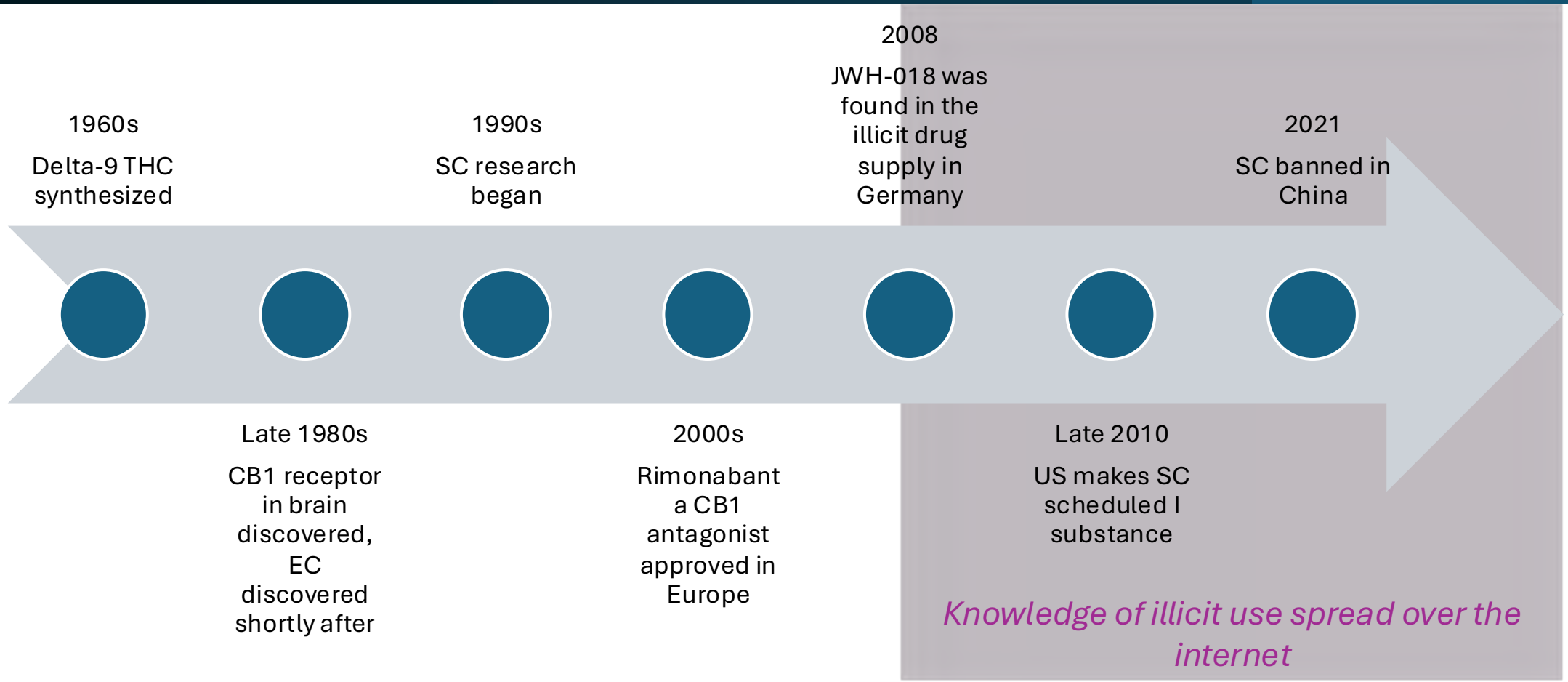
Cannabinoid Discovery Timeline



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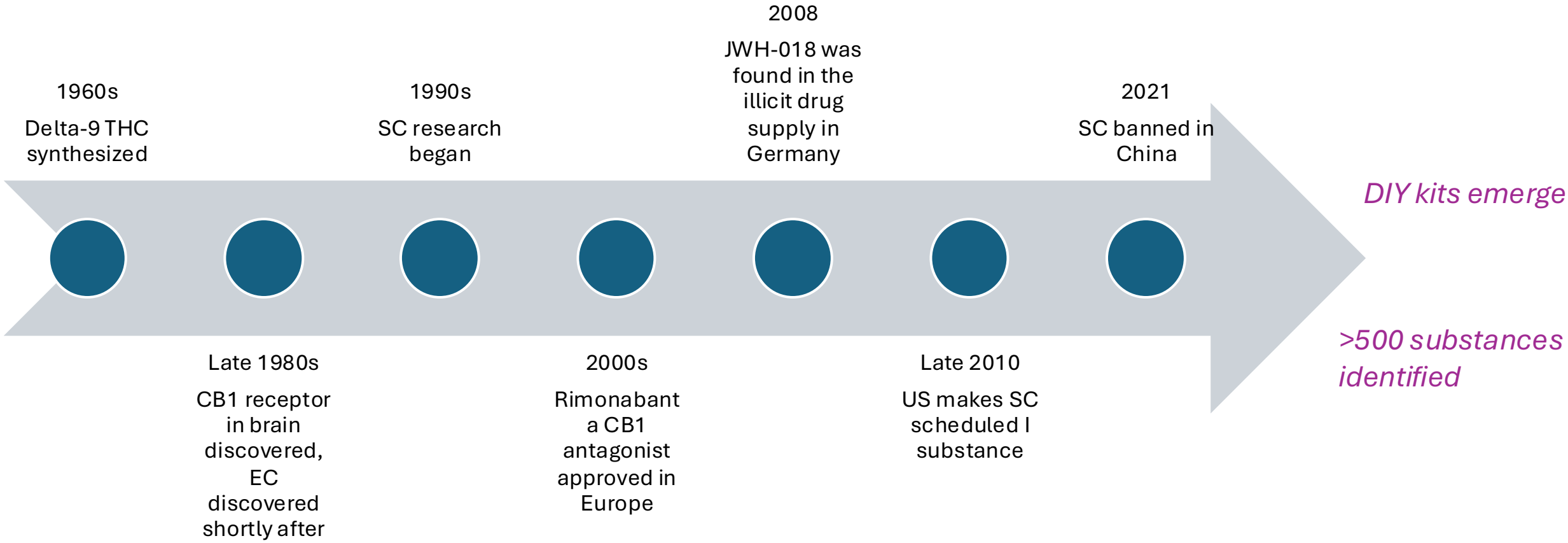

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SEMI-SYSTEMATIC ALPHA-NUMERIC SCHEME

SIMPLE NAMING SCHEME

Head – Tail.Core.Linker

Examples: *ADB-BUTINACA, MDMB-PICA, CH-PIATA*

COMPLEX NAMING SCHEMES

WITH MODIFICATIONS AND/OR SUBSTITUTATIONS

Tail Substitution:

Tail.Sub – Head – Tail.Core.Linker

Examples: *5F-MDMB-PICA, 4CN-CUMYL-BUTINACA*

Tail Modification:

Head – Tail.Mod – Tail.Core.Linker

Examples: *ADB-4en-PINACA, MDMB-3en-BUTICA*

Core Substitution:

Head – Core.Sub' – Tail.Core.Linker

Examples: *ADB-5'Br-PINACA, CHO-4'Me-5'Br-FUBOXPYRA*

Complex Combinations:

Tail.Sub – Head – Core.Sub' – Tail.Core.Linker
Head – Core.Sub' – Tail.Mod – Tail.Core.Linker
Tail.Sub – Head – Core.Sub' – Tail.Mod – Tail.Core.Linker
Head – Core.Sub – Core.Linker

Examples: *ADB-5'Br-4en-PINACA, 5F-MDMB-5'F-PINACA*

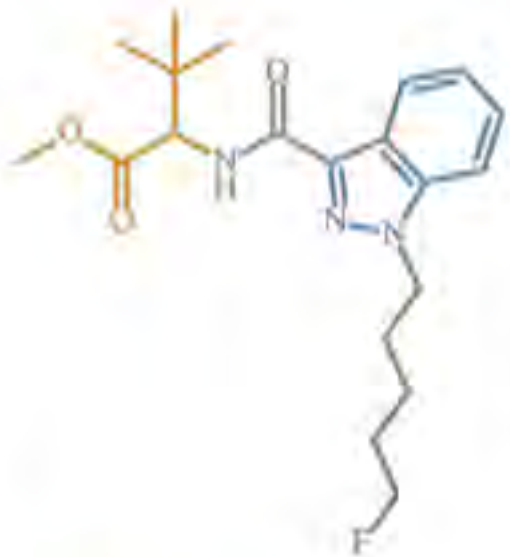


Figure 1: Synthetic cannabinoid *5F-MDMB-PINACA* showing the four structural subcomponents.

Note: *All components of the scheme will not be present within every molecule so the appropriate scheme should be selected for naming.*

Definitions: Substitution = Replacing one atom (e.g., hydrogen) with another atom (e.g., fluorine, chlorine) (pentyl to 5F-pentyl).
Modification = Exchanging one group with another group (e.g., alkane to alkene chain) (pentyl to 4en-pentyl).

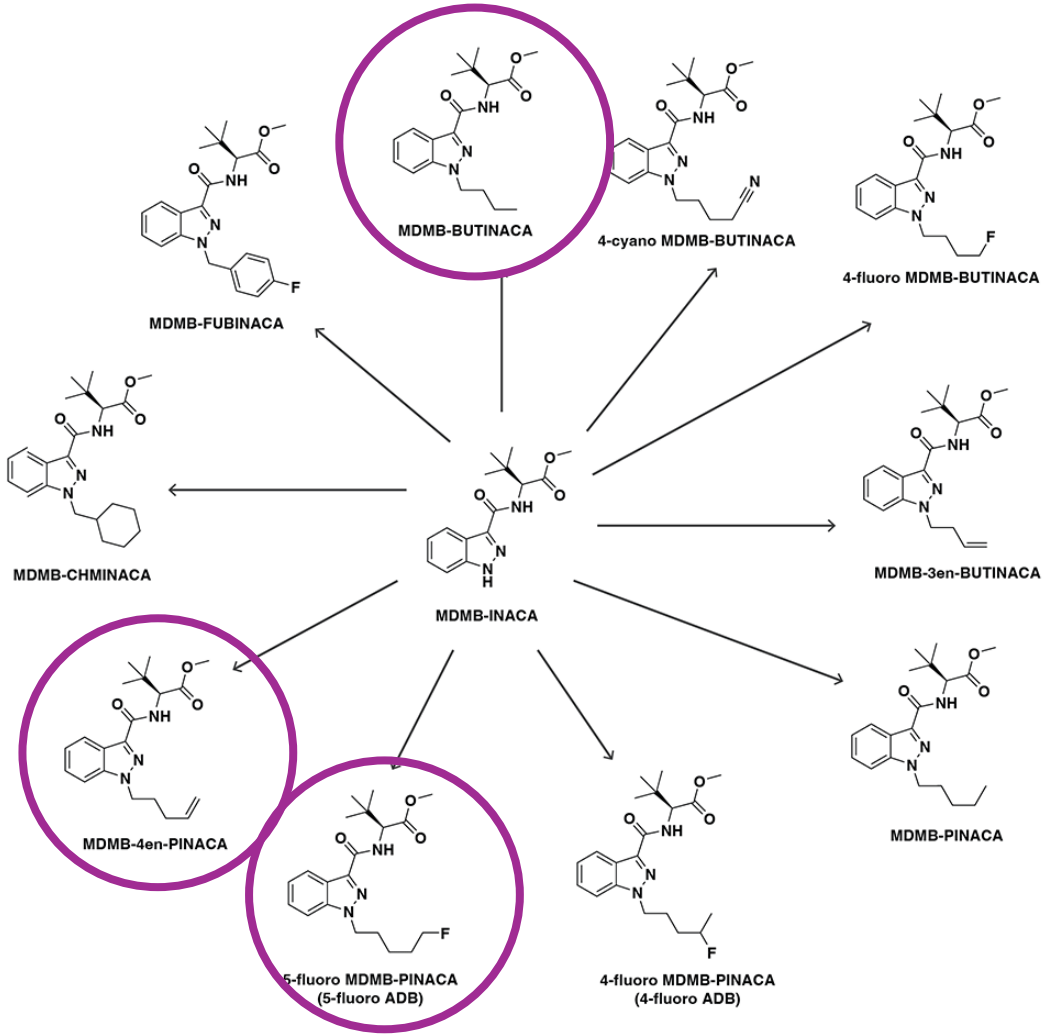
https://www.cfsre.org/images/toolkits/CFSRE_NPSD_Synthetic_Cannabinoid_Naming_Guide_December_2024.pdf

Synthesis of Synthetic Cannabinoids

Proliferation of DIY kits where precursors are provided sold as “Semi-finished”

MDMB-INACA can be used to synthesize many synthetic cannabinoids

If the reaction is incomplete, will show up in samples of the desired finished product



https://www.caymanchem.com/news/emerging-synthetic-cannabinoids-webinar-highlights?srsltid=AfmBOooMxAs1LnNPQF9umPkkB3hK05DFec8Si8dVZTQSwIyXhvUnz6Wr

Synthetic Cannabinoids

- Sprayed or mixed on plant material
- Commonly smoked or inhaled
  - Rapid onset
  - Can be ingested orally from blotter paper
    - Slower onset of effect

https://oasas.ny.gov/system/files/documents/2023/04/synthetics-facts-sheet.pdf

Why are Synthetic Cannabinoids Being Used?

- Described as being “like THC” but more potent
- Drug test evasion
- Low-cost
- Easy access

https://www.health.ny.gov/professionals/narcotic/synthetic_cannabinoids/sample_images.htm
https://oasas.ny.gov/system/files/documents/2023/04/synthetics-facts-sheet.pdf

The New York Times

THE NEW DRUG WAR

No Pills or Needles, Just Paper: How Deadly Drugs Are Changing

Lab-made drugs soaked into the pages of letters, books and even legal documents are being smuggled behind bars, killing inmates and frustrating investigators.

JAMA Network Open

Original Investigation | Substance Use and Addiction

Identification and Health Risks of an Emerging Means of Drug Use in Correctional Facilities

David Kuai, MD; Liz Eneida Rivera Blanco, MD; Alex Krotulski, PhD; Sara Walton, MS; Max Denn, MS; Byron Kelly, MD; Emily Kiernan, DO; Alaina Steck, MD; Joseph Carpenter, MD

Sample and paper No.[a]	Components[b]	
	Major	Minor
Sample 1		
Paper 1	MDMB-4en-PINACA (1p)	ADB-BINACA (minor), ADB-4en-PINACA (minor), MDMB-INACA (precursor), ADB-INACA (precursor)
Paper 2	MDMB-4en-PINACA (1p)	ADB-BINACA (minor), ADB-4en-PINACA (minor), MDMB-INACA (precursor), ADB-INACA (precursor)
Paper 3	MDMB-4en-PINACA (1p)	None
Sample 2		
Paper 1	MDMB-4en-PINACA (1p)	ADB-BINACA (minor), ADB-4en-PINACA (minor), 4F-MDMB-BINACA (minor), MDMB-INACA (precursor), ADB-INACA (precursor)
Paper 2	MDMB-4en-PINACA (1p)	ADB-BINACA (minor), ADB-4en-PINACA (minor), 4F-MDMB-BINACA (minor), MDMB-INACA (precursor), ADB-INACA (precursor)
Paper 3	MDMB-4en-PINACA (1p)	None
Sample 3		
Paper 1	MDMB-4en-PINACA (1p)	ADB-BINACA (minor), ADB-4en-PINACA (minor), MDMB-INACA (precursor), ADB-INACA (precursor)
Paper 2	MDMB-4en-PINACA (1p)	MDMB-INACA (precursor)
Paper 3	MDMB-4en-PINACA (1p)	MDMB-INACA (precursor)
Sample 4		
Paper 1	MDMB-4en-PINACA (1p), AB-CHMINACA (0.8p)	2F-2oxo-PCE (0.2p), ADB-4en-PINACA (0.1p), metonitazene (trace), MDMB-INACA (trace), fentanyl (trace), MDMB-5Me-INACA (trace), UR-144 (trace)
Paper 2	MDMB-4en-PINACA (1p)	ADB-4en-PINACA (0.3p), MDMB-INACA (0.2p), MDMB-5Me-INACA (0.1p), ADB-INACA (trace), 2F-2oxo-PCE (trace), methamphetamine (trace), 2F-deschloronorketamine (trace)
Paper 3	MDMB-4en-PINACA (1p)	AB-CHMINACA (0.3p), 2F-2oxo-PCE (0.1p), ADB-4en-PINACA (0.1p), metonitazene (trace), MDMB-INACA (trace), methamphetamine (trace), fentanyl (trace), 2F-deschloronorketamine (trace), xylazine (trace)
Sample 5	MDMB-4en-PINACA (1p), AB-CHMINACA (0.6p)	ADB-4en-PINACA (0.1p), 2F-2oxo-PCE (0.1p), metonitazene (trace), MDMB-INACA (trace), UR-144 (trace), MDMB-CHMINACA (trace), 5-methyl etodesnitazene (trace)
Sample 6	MDMB-4en-PINACA (1p), AB-CHMINACA (0.6p)	ADB-4en-PINACA (0.1p), 2F-2oxo-PCE (trace), metonitazene (trace), MDMB-INACA (trace), UR-144 (trace), 5-methyl etodesnitazene (trace), caffeine (trace)
Sample 7, paper 1	MDMB-4en-PINACA (1p), AB-CHMINACA (0.5p)	2F-2oxo-PCE (0.1p), ADB-4en-PINACA (trace), metonitazene (trace), MDMB-INACA (trace), UR-144 (trace), caffeine (trace)

Lack of Uniformity or Regulation

- Common with other substances
  - Stimulants
  - Synthetic cathinones (“bath salts”)
  - Novel synthetic stimulants like MDMA (”Ecstasy/Molly”)
  - Designer benzodiazepines
- Vitamin E acetate, hypothesized to help mask SC detection in urine toxicology tests
- Flavorings like menthol or vanillin to increase appeal

Campus Police Drug Paraphernalia Testing

UK PD Drug Seizures → Sampled by research team prior to destruction → Sent for Non-targeted testing with RaDAR

October 2018 to October 2025
233 samples collected
85 cases had multiple samples taken
159 unique cases
6 contain synthetic cannabinoids
Only 24 samples were tested by the state, none of these cases met state testing criteria

https://www.nist.gov/programs-projects/radar

Campus Police Drug Paraphernalia Testing

UK PD Drug Seizures → Sampled by research team prior to destruction → Sent to NIST for Non-targeted Testing

Date Collected by Law Enforcement	Description by Officers	Compound 1	Compound 2	Compound 3	Other relevant information
2023-02	One partially smoked marijuana joint	MDMB-4en-PINACA	MDMB-INACA		
2024-09	Suspected Synthetic Marijuana	MDMB-4en-PINACA	MDMB-BUTINACA	MDMB-INACA	
2025-02	MARIJUANA plant	MDMB-BUTINACA			
2025-07	Baggie of suspected marijuana	5-fluoro ADB	MDMB-INACA		BT: Methamphetamine
2025-07	Brownish marijuana Cigarette/Cigar	5-fluoro ADB	MDMB-INACA	Nicotine	
2025-09	One (1) partially smoked rolled paper containing Serenity [A] One (1) folded dollar bill containing Heroin/\powder [B]	Fentanyl	MDMB-INACA		BT: 4-ANPP

Kentucky Overdose Data to Action (KY OD2A)

Research supported by the Kentucky Injury Prevention and Research Center and funded by the Centers for Disease Control and Prevention (CDC)

Characterize substances involved in nonfatal drug overdoses treated in the emergency department

Identify novel substances of abuse

Kentucky Overdose Data to Action (KY OD2A)

Suspected Overdose

- Identified by emergency department clinical team
- Illicit opioids
- Other synthetics

Remnant Samples

- Blood: serum, plasma, whole blood
- Urine
- Drug paraphernalia

Targeted Analysis

- Local hospital lab
  - GC/MS
  - LC/MS/MS

Nontarget Analysis

1. Synthetic drug, where remainder of drug screen has produced little or no viable options to explain the symptoms
2. Opioid, where remainder of drug screen has produced little or no viable options to explain the symptoms
3. Exposure where story or UDS does not match clinical symptoms

N = ~3,030 patient encounters

~460 nontarget analysis
17 identified with synthetic cannabinoids

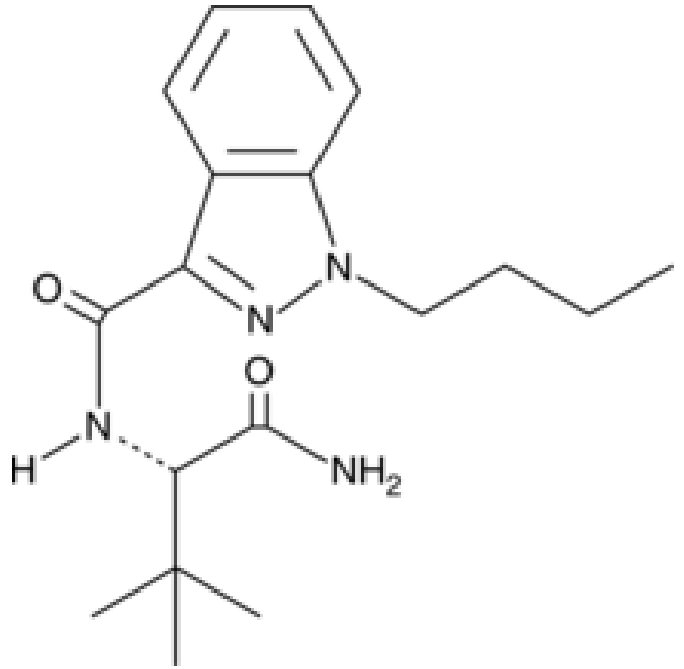
Kentucky Overdose Data to Action (KY OD2A) Synthetic Cannabinoid Cases

	ADB-BUTINACA	ADB-INACA	MDMB-BUTINACA	MDMB-4en-PINACA acid	4-CN-CUMYL-BUTINACA	5F-ADB acid	Fentanyl or Metabolite	Methamphetamine or Amphetamine	Cocaine or Metabolite
September-21	1								
December-22	1							1	1
December-22			1						1
January-23	1						1		
February-23	1								
April-23	1	1							1
May-23	1			1				1	
May-23	1								
June-23		1					1	1	1
October-23				1					
January-24				1					1
March-24			1	1			1		
September-24	1			1					1
October-24	1	1							
November-24					1			1	1
May-25				1				1	
June-25				1		1			

Synthetic Cannabinoids Cases – OD2A

- ADB-BUTINACA
  - N-[(1S)-1-(aminocarbonyl)-2,2-dimethylpropyl]-1-butyl-1H-indazole-3-carboxamide

  - 7 patients identified
  - Decreased responsiveness
  - Hypotension



Common clinical presentations associated with synthetic cannabinoid exposure, and differentiate these from other toxicities

Comparing Clinical Presentations

Synthetic Cathinones | **Synthetic Cannabinoids** | **Phytocannabinoids**

Classified as Novel Psychoactive Substances

- Mimic illicit drugs: Cannabis, Cocaine, MDMA, LSD, PCP
- Constantly changing chemical structures to evade legal action

Synthetic cathinones	**Phenethylamines**	**Synthetic cannabinoids**
Tryptamines	**Piperazines**	**Novel benzodiazepines**

Cannabidiol	Delta-8 THC
Delta-9 THC	Delta-10 THC
Hexahydrocannabinol	Cannabinol

Comparing Clinical Presentations

Synthetic Cathinones

- Common names:
  - Bath Salts, Plant Food, Jewelry Cleaner, Phone Screen Cleaner
- Origin:
  - Laboratory made chemicals
  - Khat shrub in East Africa
- Formulation:
  - White or brown crystal like powder
  - Abused by ingestion, insufflation, inhalation, injection

Synthetic Cannabinoids

- Common names:
  - Spice, Synthetic marijuana, K2, Joker, Black Mamba, Kronic, Herbal or Liquid Incense
- Origin:
  - Laboratory made chemicals
- Formulation:
  - Liquid – sprayed onto plant material or used in e-cigarettes / vape juices

Cannabinoids (Delta-9 THC)

- Common names:
  - Weed, Pot, Chronic, Ganga
- Origin:
  - Plant Derived
- Formulation:
  - Edibles
  - Oils
  - Smoked
  - Tinctures and lotions
  - Vape pens

Pharmacol Toxicol 1992 Feb; 70(2):77-86
Clin Pharmacol. 2013; 5: 109–115
CRITICAL REVIEWS IN TOXICOLOGY 2020, VOL. 50, NO. 5, 359–382

Comparing Clinical Presentations
Mechanism of Action

Synthetic Cathinones	Synthetic Cannabinoids	Cannabinoids (Delta-9 THC)

• Effects on:
  • Dopamine
  • Norepinephrine
  • Serotonin levels
 	
Amphetamine like
	• Effects on:
	  • CB1 and CB2 receptors
	  • With higher potency and efficacy
		• Effects on:
		  • CB1 and CB2 receptors

Comparing Clinical Presentations
Common Symptoms

Synthetic Cathinones

Sympathomimetic

- Tachycardia
- Hypertension

Neurologic Symptoms

- Agitation/irritability (40%)
- Lethargy (7%)
- Altered mental status (13%)
- Hallucinations/Delusions (18%)
- Seizures (3%)

Synthetic Cannabinoids

Mixed toxidromes

- Sympathomimetic
  - Tachycardia
  - Hypertension
- Anticholinergic
  - Dry mouth, dry skin
  - Blurred vision
  - Urinary retention

Neurologic Symptoms

- Agitation/irritability (25%)
- Lethargy (14%)
- Altered mental status (12%)
- Hallucinations/Delusions (11%)
- Seizures (4%)

Cannabinoids (Delta-9 THC)

<u>Naïve</u>

- Central nervous system
  - Lethargy/somnolence
  - Altered mental status
- Musculoskeletal systems
  - Tremors/jitters
  - Hypo or hypertonia

<u>Chronic Use</u>

- Digestive system
  - Nausea/vomiting
  - Abdominal pain
- Cognition, perception, emotional state, and behavior
  - Agitation/psychosis
  - Self-injurious behavior

Heizer J, et al. Pediatr Emerg Care. 2018;34(7):457-462.
Hassamal, etal. Psyc Times. 2021; 38(7)

Synthetic Cannabinoids Case 1 – OD2A

- 29y/o M EMS was called after the patient went to get a vape pen and came back agitated, confused, and combative
- Presented hypertensive and tachycardic

	DRUG ABUSE SCREE...
Presumptiv...	Amphetamine Screen Urine
Negative	Benzodiazepines Screen Urine
Negative	Cannabinoid Screen Urine
Negative	Cocaine Screen Urine
Negative	Barbiturate Screen Urine
Presumptiv...	Opiate Screen Urine
Presumptiv...	Methadone Screen Urine
Negative	Buprenorphine Screen Urine
Presumptiv...	Fentanyl Screen Urine
Negative	Oxycodone Screen Urine

Confirmed Drug (ng/mL)
1. Fentanyl (93.5)
2. Norfentanyl* (38.1)
3. Beta-Hydroxy Fentanyl (10.2)
4. 4-ANPP (7.9)
5. ADB-BUTINACA (4.9)
6. *para*-Fluorofentanyl (1.4)
7. Diphenhydramine
8. Ketamine

Synthetic Cannabinoids Case 2 – OD2A

- Unknown age female, from rehab center, unresponsive with questionable seizure activity
- 12mg of naloxone administered on scene, no response
- GCS 3, hypertensive

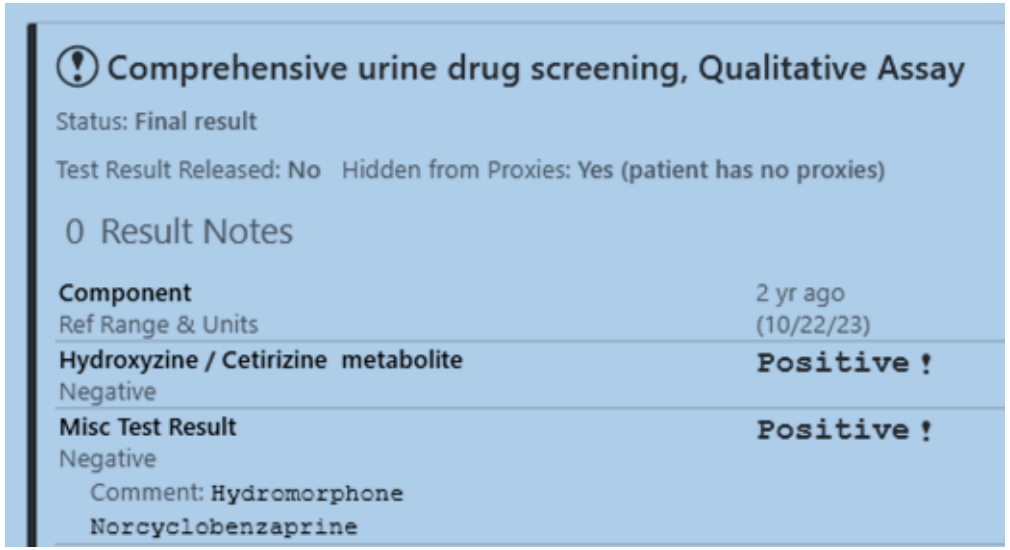
	DRUG ABUSE SCREE...
Negative	Amphetamine Screen Urine
Negative	Benzodiazepines Screen Urine
Negative	Cannabinoid Screen Urine
Presumptiv...	Cocaine Screen Urine
Negative	Barbiturate Screen Urine
Negative	Opiate Screen Urine
Negative	Methadone Screen Urine
Negative	Buprenorphine Screen Urine
Negative	Fentanyl Screen Urine
Negative	Oxycodone Screen Urine

	PAIN MANAGEMENT ...
>1,000	Benzoylecgonine

Confirmed Drug (ng/mL)
1. Benzoylecgonine* (66.8)
2. ADB-BUTINACA (63.3)
3. MDMB-4en-PINACA acid metabolite* (12.0)
4. MDMB-4en-PINACA (0.4**)
5. Cocaine (0.3)
6. Cotinine*
7. Diphenhydramine
8. Duloxetine
9. Ecgonine Methyl Ester*
10. Naloxone
11. Nicotine

Synthetic Cannabinoids Case 3 – OD2A

- 28 y/o M MVC versus tree, seizure activity on scene, combative on scene



Comprehensive urine drug screening, Qualitative Assay

Status: Final result

Test Result Released: No Hidden from Proxies: Yes (patient has no proxies)

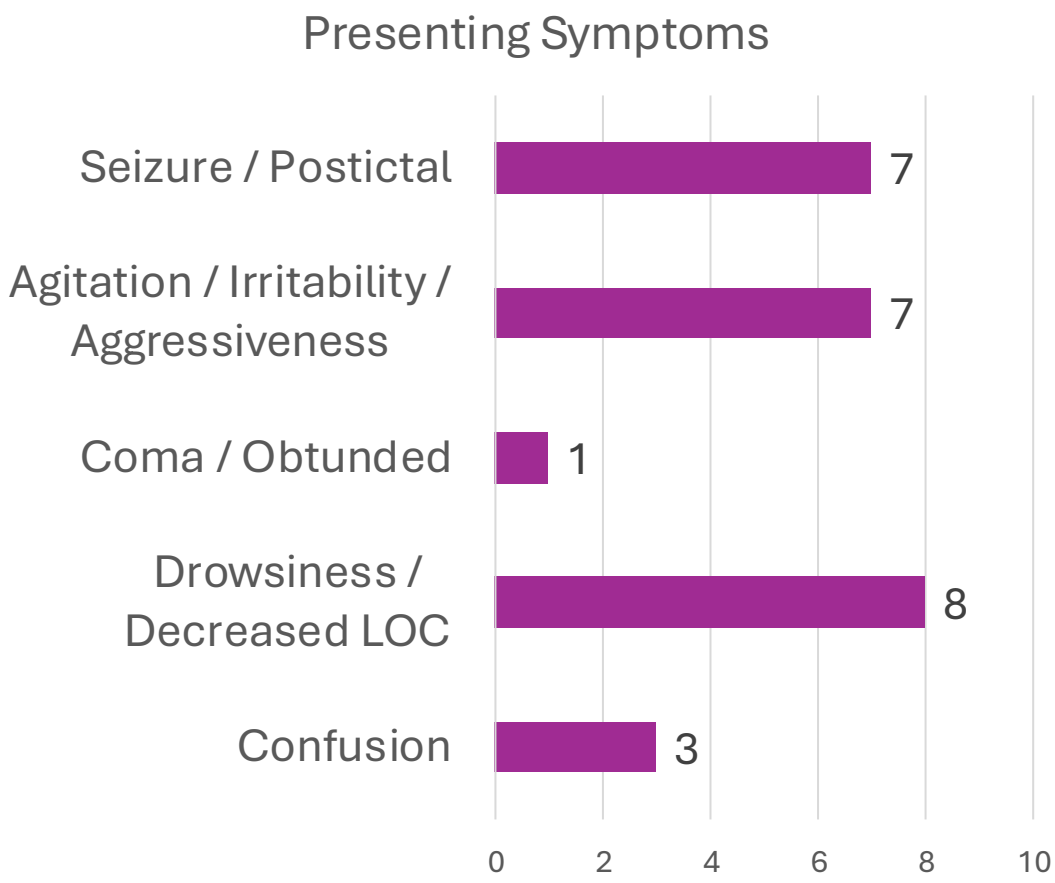
0 Result Notes

Component Ref Range & Units	2 yr ago (10/22/23)
Hydroxyzine / Cetirizine metabolite Negative	Positive !
Misc Test Result Negative Comment: Hydromorphone Norcyclobenzaprine	Positive !

Confirmed Drug (ng/mL)
1. MDMB-4en-PINACA Acid Metabolite* (72.4)
2. MDMB-4en-PINACA (1.1)
3. Lorazepam
4. Midazolam
5. Sertraline

Synthetic Cannabinoids Cases – OD2A

- 17 cases with synthetic cannabinoid
- ~70 % Male
- Average age 48.4 years
- 2 required ICU admission



JAMA Network Open

Original Investigation | Substance Use and Addiction

Identification and Health Risks of an Emerging Means of Drug Use in Correctional Facilities

David Kuai, MD; Liz Eneida Rivera Blanco, MD; Alex Krotulski, PhD; Sara Walton, MS; Max Denn, MS; Byron Kelly, MD; Emily Kiernan, DO; Alaina Steck, MD; Joseph Carpenter, MD

- All patients except 1 experienced central nervous system (CNS) depression (17 patients [94%])
- Most common vital sign derangement was bradycardia, seen in 11 of 18 patients (61%)

Table 1. Characteristics of Patients With Clinical Intoxication From Drug-Soaked Paper Strips.

Characteristic	Patients, No. (%)
Male sex	18 (100)
Age, median (IQR), y	27.5 (18.0-45.0)
Vital signs	
Nadir heart rate, median (IQR), beats/min	57 (50-61)
Hypotension present	7 (39)
Hypoxia present	6 (33)
Hypothermia present	4 (22)
Signs and symptoms	
Central nervous system depression	17 (94)
Agitation and/or combativeness	6 (33)
Seizures	4 (22)
Nausea and/or vomiting	3 (17)
Cardiac arrest	1 (6)
Glasgow Coma Scale score, median (IQR)[a]	
At jail	8 (7-13)
At emergency department presentation	14 (13-15)

https://pmc.ncbi.nlm.nih.gov/articles/PMC11667344/

Review the limitations of routine hospital toxicology testing in detecting synthetic cannabinoids and discuss the implications for clinical decision-making

Types of Toxicology Testing

Presumptive testing by immunoassay (“drug screen”)

- Presence of drug classes and/or their metabolites in a urine sample
  - If the concentration of a drug is high enough
- Typically, the first test used to identify drug classes in the urine
- Available in most hospitals

Confirmatory testing by gas or liquid chromatography

- Used to confirm a positive drug screen result or to definitively identify a detected substance
- Detects the presence of specific drugs and/or metabolites in a urine sample
- Available at larger institutions

https://legislativeanalysis.org/wp-content/uploads/2024/01/Fentanyl-Screening-in-Hospitals.pdf

Common Hospital Testing

Immunoassay	Gas chromatography/mass spectrometry (GC-MS)	Liquid chromatography tandem mass spectrometry (LC-MS/MS)
• Antibodies to detect the presence of selected drugs and/or metabolites	• Chromatography • Confirmatory or definitive testing	• Chromatography • Requires small volumes of substrate
• Fast	• Slower (6-24 hours)	• Slower (12-24 hours)
• Cheap	• Expensive	• Expensive
• Qualitative	• Qualitative	• Quantitative
• Limited library • Known detection thresholds	• Lower detection thresholds	• Lower detection thresholds
• Lacks specificity • Followed by a confirmatory test	• Low likelihood of false results	• Analysis has a second analytical separation step • Lower susceptibility to false results caused by concomitant usage
• NIDA 5: marijuana, cocaine, opiates, amphetamines, and phencyclidine • 10-panel • Drugs of Abuse Screens	• Comprehensive urine drug screen	• Pain management drug screens • Drugs of abuse screen (reflex)

Immunoassay	Gas chromatography/mass spectrometry (GC-MS)	Liquid chromatography tandem mass spectrometry (LC-MS/MS)

• Amphetamines
• Benzodiazepines
• Cannabinoids (Phytocannabinoids)
• Cocaine
• Barbiturate
• Opiate
• Methadone
• Buprenorphine
• Fentanyl
• Oxycodone
	• >450 substances
	• Many prescription and OTC medications
	• Common opioids
	• Common stimulants
	• Common benzodiazepines
	• MDMA
	• Ketamine
	• PCP
	• Xylazine
	• Naloxone
	• Medications for Opioid Use Disorder (MOUD)
		• Detects both prescription and illicit
		  • Opioids
		  • Benzodiazepines
		  • Stimulants
		  • Associated metabolites
		• Barbiturates
		• THC
		• PCP
		• MOUD

Not detected on Immunoassays due to structural differences

Detection is unlikely due to manufacturers frequently changing compounds, making detection difficult

Synthetic Cannabinoids Case 1 – OD2A

- 29y/o M EMS was called after the patient went to get a vape pen and came back agitated, confused, and combative
- Presented hypertensive and tachycardic

	DRUG ABUSE SCREE...
Presumptiv...	Amphetamine Screen Urine
Negative	Benzodiazepines Screen Urine
Negative	Cannabinoid Screen Urine
Negative	Cocaine Screen Urine
Negative	Barbiturate Screen Urine
Presumptiv...	Opiate Screen Urine
Presumptiv...	Methadone Screen Urine
Negative	Buprenorphine Screen Urine
Presumptiv...	Fentanyl Screen Urine
Negative	Oxycodone Screen Urine

	PAIN MANAGEMENT ...
<50	Amphetamine
<50	Codeine
125	Codeine Glucuronide
<50	Desmethyl Tramadol
<50	EDDP - Methadone Metabolite
<50	
>100	Fentanyl
<50	Hydrocodone
<50	Hydromorphone
<50	Hydromorphone Glucuronide
<50	MDA
<50	MDMA
<50	Meperidine
<50	Methadone
<50	
<50	Methamphetamine
<10	Heroin/6-MAM
98	Morphine
>1,...	Morphine Glucuronide
<50	Naloxone

Confirmed Drug (ng/mL)
1. Fentanyl (93.5)
2. Norfentanyl* (38.1)
3. Beta-Hydroxy Fentanyl (10.2)
4. 4-ANPP (7.9)
5. ADB-BUTINACA (4.9)
6. *para*-Fluorofentanyl (1.4)
7. Diphenhydramine
8. Ketamine

Synthetic Cannabinoids Case 2 – OD2A

- Unknown age female, from rehab center, unresponsive with questionable seizure activity
- 12mg of naloxone administered on scene, no response
- GCS 3, hypertensive

	DRUG ABUSE SCREE...
Negative	Amphetamine Screen Urine
Negative	Benzodiazepines Screen Urine
Negative	Cannabinoid Screen Urine
Presumptiv...	Cocaine Screen Urine
Negative	Barbiturate Screen Urine
Negative	Opiate Screen Urine
Negative	Methadone Screen Urine
Negative	Buprenorphine Screen Urine
Negative	Fentanyl Screen Urine
Negative	Oxycodone Screen Urine

	PAIN MANAGEMENT ...
>1,000 ▲	Benzoylecgonine

Confirmed Drug (ng/mL)
1. Benzoylecgonine* (66.8)
2. ADB-BUTINACA (63.3)
3. MDMB-4en-PINACA acid metabolite* (12.0)
4. MDMB-4en-PINACA (0.4**)
5. Cocaine (0.3)
6. Cotinine*
7. Diphenhydramine
8. Duloxetine
9. Ecgonine Methyl Ester*
10. Naloxone
11. Nicotine

Synthetic Testing

Cathinones

- Routine testing limited
- Very minimal cross reactivity with immunoassays for amphetamines

Cannabinoids

- Routine testing limited
- Very minimal cross reactivity with immunoassays for THC

Testing for Natural Cannabis Products at UKHC

★ Tests for THC, CBD, and metabolites → cross-reactive

Urine screen

★

- Drug abuse
  - Qualitative = 4 hours
    - Immunoassay
  - Reflex to quantitative
    - LCMSMS
- Comprehensive
  - 6-24 hours
  - GC-MS

Blood screen

★

- Takes 24-72 hours to get results
- LCMSMS

Meconium

- Tests for 9-carboxy THC
- Takes up to 72 hours to get results

Hair

- Send-out
- Takes up to 7 days to receive the final results

GC-MS: gas chromatography-mass spectrometry
LCMSMS: liquid chromatography with tandem mass spectrometry

Ninnemann A, et al. Addict Behav. 2016;63:72-73.
https://www.usdtl.com/media/mediaarticles/synthetic-cannabinoids-and-drug-testing. Accessed May 3, 2023.
UK Laboratory. Communication May 18, 2023.
Goldfrank's Toxicologic Emergencies, 11e. Chapter 74: Cannabinoids.

Commercially Available Synthetic Cannabinoid Testing

LabCorp
Synthetic Cannabinoids

- AB-CHMINACA
- AB-FUBINACA
- AB-PINACA
- F-AB-PINACA
- ADBICA
- 5F-ADBICA
- ADB-PINACA
- 5F-ADB-PINACA
- AKB-48, 5CI-AKB-48
- 5F-AKB-48
- AM2201
- BB-22, BB-22 hydroxyquinolines
- JWH-018, JWH-073, JWH-122, JWH-250
- MAB-CHMINACA
- MAM-2201
- PB-22, PB-22 hydroxyquinolines
- 5F-PB-22, 5F-PB-22 hydroxyquinolines
- UR-144
- XLR-11

Quest Labs
Novel Psychoactive Substances

- ADB-4en-PINACA
- ADB-5Br-BUTINACA
- ADB-5Br-PINACA
- ADB-FUBIATA
- 5F-ADB
- CH-PIATA
- MDMB-BUTINACA
- 4F-MDMB-BUTINACA
- MDMB-4en-PINACA
- MDMB-INACA
- 5F-MDMB-PICA
- MMB-4en-PINACA

All are utilizing LC-MS/MS

ARUP Laboratories
Synthetic Cannabinoids Metabolites

- 5-fluoro-PIC-ACID
- 5-fluoro-PICA 3,3-dimethylbutanoic acid
- 5-fluoro-PINAC-ACID
- 5-fluoro-PINACA 3,3-dimethylbutanoic acid
- 5-fluoro-PINACA 3-methylbutanoicacid
- CHMIC-ACID
- CHMINACA 3,3-dimethylbutanoic acid
- CHMINACA-3-methylbutanoic acid
- FUBINACA 3-methylbutanoic acid
- K2
- K3
- Spice
- FUBICA 3,3-dimethylbutanoic acid
- FUBINACA 3,3-dimethylbutanoic acid
- 4-carboxy-AMB-PINACA
- 4-carboxy-CUMYL-BINACA
- 4-carboxy-NAPIM and FUBIC-ACID

Limitations of Hospital Drug Testing

- No cross-reactivity exists due to structural differences
- Substance must be known and in the testing library
  - Most synthetic cannabinoids are not part of routine libraries
- Testing varies greatly between facilities and commercial companies
- Takes time
- Testing has minimal impact on initial patient care

Management strategies for synthetic cannabinoid toxicity

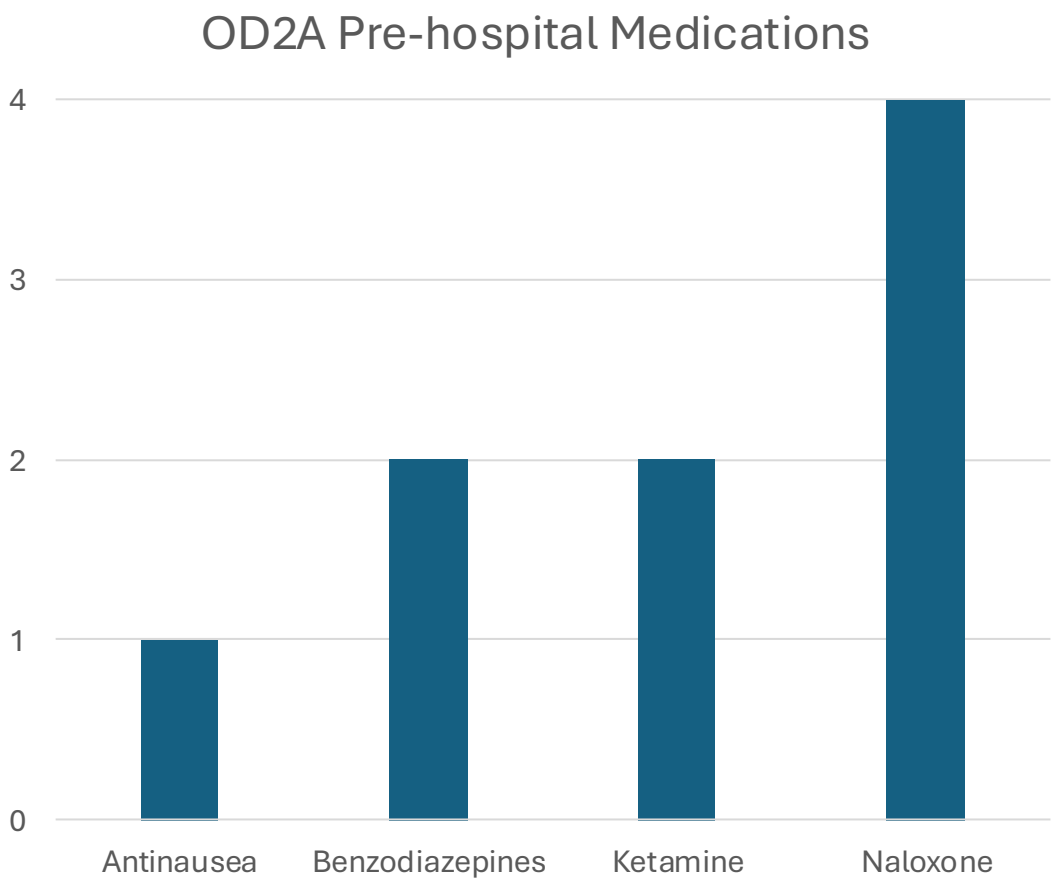
Prehospital Treatment

JAMA Network | Open

Original Investigation | Substance Use and Addiction

Identification and Health Risks of an Emerging Means of Drug Use in Correctional Facilities

Variable	Patients, No. (%)
Prehospital treatment	
Naloxone	14 (78)
Atropine	2 (11)
Intravenous fluids	2 (11)
Sedative medications	2 (11)
Hospital treatment	
Intravenous fluids	16 (89)
Sedative medications	6 (33)



https://pmc.ncbi.nlm.nih.gov/articles/PMC11667344/

Symptomatic and Supportive

- No targeted antidotal therapy
- Focus on respiratory and hemodynamic status
  - Hypotension
    - IV boluses of crystalloid: 20 mL/kg in children and 500-1000 mL in adults
    - Vasopressors if refractory
  - Bradycardia
    - Atropine 0.5 mg every 3-5 minutes (maximum dose 3 mg)
    - Vasopressors if refractory

ABCs

Managing Neurologic Symptoms

- Agitation, anxiety, and convulsions should be treated with benzodiazepines

- CNS depression should be evaluated for other causes

Additional Considerations

- Electrolyte disturbances
- Cardiovascular
- Renal injury
- Musculoskeletal
  - Aggressive crystalloid fluid resuscitation should be given for rhabdomyolysis and acute kidney injury

Conclusions: Synthetic Cannabinoids

- Products are ever-changing making analytic testing difficult
- Mixed clinical pictures
- No direct antidote
- Symptomatic and supportive care

More Than ‘Spice’: Understanding Synthetic Cannabinoid Toxicity in Kentucky

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