Intoxicating Hemp-Derived Cannabinoids:

What Healthcare Professionals Need to Know

Recognizing the differences between regulated medical cannabis and intoxicating hemp-derived cannabinoids (IHDCs) to promote patient safety.

Descheduling Hemp Derivatives Created Perceived Loophole on Legality

The 2018 Agricultural Improvement Act, also known as the Farm Bill, removed hemp (*Cannabis sativa* L.) and derivatives of cannabis with <0.3% THC by dry weight from the definition of marijuana and from Schedule I in the Controlled Substance Act.

Key Differences at a Glance

Medical Cannabis Program Products	Intoxicating Hemp Products
• State-regulated, licensed dispensaries	• Loosely regulated under the Farm Bill . State regulations vary considerably.
• Potency and contaminant testing is required	• Inconsistent or absent testing
• Standard labeling requirements	• Labels often inaccurate or misleading
• Requires certification and patient evaluation	• No clinical oversight
• Based on state-approved conditions	• Marketed broadly without evidence

Did You Know?

Hemp is an inefficient source for extracting some cannabinoids, which is why many IHDCs rely on synthetic cannabinoids instead.

Public Health Concerns and Risks

- Unregulated IHDCs may contain unknown potency and/or contaminants, such as heavy metals, pesticides, bacteria, mold, adulterants, and synthetic cannabinoids.
- No clinical trials or evidence-based medicine to support the medicinal use for IHDCs.
- Patients may experience unexpected psychoactive effects or drug interactions.
- Common adverse effects: anxiety, sedation, impaired coordination, or gastrointestinal distress.
- Populations most at risk: children, elderly, polypharmacy patients, and those with liver or cardiovascular conditions.
- IHDCs are often packaged like popular candies, increasing the risk of accidental pediatric ingestion.

Consumer Alert

Some IHDC products in MS had 5,000 mg of cannabinoids, including synthetic THCP which is 30x more potent than THC.

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The Endocannabinoid System and Cannabinoids:

The endocannabinoid system (ECS) is a diverse cell-signaling system that regulates many physiological processes. Endogenous and exogenous cannabinoids interact with the ECS.

Endogenous Cannabinoids

Anandamide (N-arachidonoylethanolamine)
Partial agonist at CB1 and CB2 receptors

2 AG (2-Arachidonoylglycerol)
Key regulator in CNS neurotransmitter release; full agonist at CB1 and CB2 receptors.

Cannabinoid Receptor Locations

Cannabinoid Receptor 1

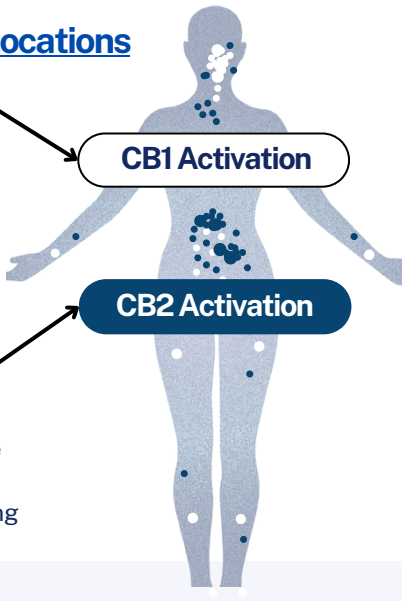
Primarily located at the central and peripheral neurons. CB1:

- control the release of neurotransmitters
- help regulate mood, memory, appetite & pain
- is responsible for psychoactive effects

Cannabinoid Receptor 2

Primarily expressed by immune cells. CB2:

- is responsible for modulating inflammation and pain



Exogenous Cannabinoids

Cannabinoid Name		Cannabinoid Description	Psychoactivity
CBD	Cannabidiol	• Available over the counter, in stores, and via the internet • Mild central nervous system depression may occur at the maximum recommended daily dose	Non-impairing
CBN	Cannabinol	• A product of THC degradation, typically caused by prolonged storage	Mildly psychoactive at higher doses
THCV	Tetrahydro-cannabivarin	• Primarily found in combination with Δ9-THC • Acts as a CB1 antagonist at lower doses and weak agonist at higher doses	Mildly intoxicating when compared to Δ9-THC
Δ^8- THC	Delta-8-Tetrahydro-cannabidiol	• Has less affinity for CB1 receptors when compared to Δ9-THC • Synthesized from CBD	Similar but has milder effects than Δ9-THC
Δ^{10}-THC	Delta-10-Tetrahydro-cannabidiol	• Has less affinity for CB1 receptors compared to Δ9-THC • Synthesized from CBD	Similar but has milder effects than Δ9-THC
HHC	Hexahydro-cannabinol	• Hydrogenated analog of Δ9-THC but slightly lower affinity to CB1 receptors • Can be synthesized from CBD	~20% less potent than Δ9-THC but more potent than Δ8-THC and Δ10-THC
Δ^9-THC	Delta-9-Tetrahydro-cannabidiol	• Major naturally occurring psychoactive component responsible for the "high" associated with cannabis use • Also produced by decarboxylating THCA	THC is impairing
THC-O	Delta-9-Tetrahydro-cannabinol acetate	• Acetylated derivative of Δ9-THC with increased bioavailability • May cause lung damage by releasing toxic ketene gas during thermal decomposition, a suspected contributor to EVALI	Reported to be 2-3 x more potent than Δ9-THC
THCP	Tetrahydro-cannabiphorol	• Structurally similar to Δ^9-THC but with strong affinity for CB1 receptors • Generally synthetic	30 x more potent than Δ9-THC

Increasing Psychoactivity ↓

Intoxicating Cannabinoids: Δ^8-THC, Δ^9-THC, Δ^{10}-THC, HHC, THC-O, THCP

Effects are dose dependent and psychoactivity is also based on relative potency

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Cannabinoid Pharmacology

Absorption

Peak concentrations depend on route of administration.

Distribution

THC is lipid soluble and highly protein bound, rapidly distributing to vascular tissues before accumulating in fat.
THC crosses the placenta and enters breast milk.

Metabolism

THC undergoes hepatic hydroxylation and oxidation.

Excretion

The terminal half-life of THC varies with use patterns, body habitus, and metabolic factors but ranges from 24-36 hours.

Common Formulations and Considerations

Route	Product	Considerations	Onset (Minutes)	Duration (Hours)
Oral Ingestion	Tinctures Edibles Oils	Avoids inhalation First-pass metabolism - Delayed onset Peak is dependent on metabolism/ food intake	30-180+ mins	5-8+ hrs
Inhalation	Smokable Flower or Vapes	Avoids first-pass Vapes are typically high concentrates Can vape flower with specific vaporizers to avoid combustion.	1-15 mins	2-4 hrs
Oromucosal	Dissolvable Tabs or Strips	More likely to be ingested orally if not formulated or used correctly	15-20 mins	4-6 hrs
Transdermal	Patch	Formulation is key to absorption	15-20 mins	6-12 hrs
Topical	Salve Balm Lotion	Formulation is key to absorption	20 mins	2-3 hrs
Rectal	Suppository	Formulation is key to absorption (hemisuccinate) THC will be felt if formulated correctly	Variable 15-20 mins	Variable

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Cannabis Adverse Effects and Potential Risks, Use in Special Populations, and Contraindications

ADVERSE EFFECTS

- **Mild**: somnolence, drowsiness, tachycardia, dry mouth, ataxia, nystagmus, conjunctival injection
- **Moderate**: anxiety, paranoia, hallucinations, lethargy and sedation, inability to concentrate, slowed reaction time, slurred speech
- **Severe**: psychosis, seizures, dysrhythmias, coma

POTENTIAL RISKS

- **Lung disease**: obstructive lung disease, asthma exacerbations, EVALI
- **Cardiovascular risk**: MI, sudden death, arrythmias, stroke. Adverse effects are more likely to occur with inhalation in the first 5-15 minutes.
- **Psychosis:** potential for developing psychosis or schizophrenia-like symptoms.
- **Cannabis Hyperemesis Syndrome:** associated with chronic, heavy cannabis use. Presents as persistent nausea and vomiting with relief from hot showers/baths.

SPECIAL POPULATIONS

- **Pregnancy and Lactation**: Δ^9-THC crosses the placenta and enters breast milk. Use during PG has been associated with low birth weight, preterm delivery, NICU admission.
- **Adolescents**: use during adolescence, especially heavy use, can have permanent effects on behavior, learning, and cognition, and increase risk of developing addiction and dependency.
- **Pets**: cannabis can cause toxicity in cats and dogs.

CONTRAINDICATIONS

Cannabis use has no specific contraindications but caution and consider avoiding use during pregnancy/lactation and in children/teens, in those with history of psychosis, and in those with heart disease or conduction abnormalities. Those with pulmonary disease should avoid smoking.

Call Mississippi Poison Control at 1-800-222-1222 for assistance in the treatment and management of cannabis toxicity

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