Endocannabinoids: Defining the Health in Public Health Impact

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RTI International is an independent, nonprofit research institute. Our mission is to improve the human condition by turning knowledge into practice.

Learning Objectives
- Describe the major components and physiological roles of the endocannabinoid system.
- Compare and contrast the effects of plant-based cannabinoids, endogenous cannabinoids, and synthetic cannabinoids.
- Describe how cannabis acts on the endocannabinoid system to produce its behavioral effects.

What is cannabis?
- Marijuana leaf
- Hashish
- Flowering Marijuana Plant
- Dried Marijuana
- Hashish Oil
- Hemp

Cannabidiol Profiles (THC vs CBD)
- Psychoactive
  - High concentrations in recreational
- Non-psychoactive
  - May have higher concentrations in medicinal

Cannabis sativa
Cannabis indica

Δ⁹-tetrahydrocannabinol (THC)

many other cannabinoids
+ terpenoids and other chemicals

Tetrahydrocannabinol (THC)
Cannabidiol (CBD)
**THC vs THCA**

- Most THC in the plant is in the non-psychoactive acid form (THCA).
- Decarboxylation results in conversion to THC.

![Diagram showing the conversion of THCA to THC](image)

**How is cannabis used?**

- Cannabis infused beverages and edibles
- Smoking / Vaping

**Pharmacological effects of cannabis (THC)**

- Altered state of consciousness (e.g., euphoria, intoxication)
- Altered time perception / slowed reaction time
- Short-term memory deficits
- Tachycardia (fast heart beat)
- Analgesia (pain relief, anti-inflammatory properties?)
- Increased appetite (“munchies”)
- Reddening of eyes / lowered intraocular pressure

**THC and the brain**

*Endorphins are the body’s opioids.*

**“Cannabis” (CB₁) Receptor**

*Δ⁹-THC* = primary cannabinoid receptor in the brain
*CB₂* = cannabinoid receptor primarily in periphery

Endocannabinoids are the body’s cannabinoids.


Anandamide (arachidonoyl ethanolamide)

Where do endocannabinoids come from?

• “On demand” synthesis
• Activity dependent release
• Inactivation mechanisms

Endocannabinoids Formation and Inactivation

Neurotransmission (anterograde)

Neurotransmission (retrograde)
Depolarization-induced suppression of excitation (DSE)

Glutamate: Excitatory
Fatty Acid Amide Hydrolase (FAAH)

Inhibitory effect

Depolarization-induced suppression of inhibition (DSI)

Monoacylglycerol Lipase (MAGL)
GABA = Inhibitory

Regulation of Crucial Physiological Processes

Homeostasis

Distribution of CB1 & CB2 Receptors in the Body

CB1 present:
- Brain
- Lungs
- Vascular system
- Muscles
- GI tract
- Reproductive organs

CB2 present:
- Spleen
- Bones
- Skin

CB1 and CB2 present:
- Immune system
- Liver
- Bone marrow
- Pancreas

Distribution of CB1 Receptors in the Brain

Functions of the Endocannabinoid System

Appetite regulation & energy balance
**Summary: Endocannabinoid System**

- **Endogenous cannabinoids**
  - 

- **Receptors**
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- **Neurotransmitters**
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- **Synthetic Cannabinoids**
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Figure from: Velasco et al. (2012). Nat Rev Cancer, 12: 436-444.
What are synthetic cannabinoids?

- Synthetic cannabinoids are research chemicals that have been diverted and are being used as alternatives to illegal psychoactive drugs.

**Synthetic cannabinoids:** Herbal incense, Spice, K2, fake marijuana

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**WIN 55,212-2**

Δ⁹-Tetrahydrocannabinol


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**Manufacture**

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**Packaging**

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**Purchase & Use**
Symptoms of Synthetic Marijuana Use

Psychological Symptoms
- Increased agitation
- Paranoid delusions
- Depression
- Hallucinations
- Exaggerated thoughts of suicide
- Feelings of impending doom
- Panic attacks
- Exacerbation of previous psychiatric symptoms

“Glazed expression,” Red eyes

Marijuana-like intoxication

Increased BP & heart rate

Body Temperature Fluctuation, Inability to Feel Pain, Seizures

Increased BP & heart rate

Temporary Paralysis, Cramping

Kidney Failure

Nausea, vomiting

Endocannabinoids

Phytocannabinoids

Synthetic Cannabinoids vs THC

- Most synthetic cannabinoids are more potent than THC.
- Synthetic cannabinoids may have toxic properties that are not seen with THC.
- Specific chemicals contained in packets of “product” may differ over time.
- Many synthetic cannabinoids have not ever been tested in a living organism before appearing in “product.”

Synthetic Cannabinoids vs THC

Endocannabinoids

Phytocannabinoids

Cannabinoid Antagonists