Endocannabinoids: Defining the Health in Public Health Impact

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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

Cannabis sativa
Cannabis indica

Δ⁹-tetrahydrocannabinol (THC)

+ many other cannabinoids
+ terpenoids and other chemicals

Cannabinoid Profiles (THC vs CBD)

• Psychoactive
• Non-psychoactive
• High concentrations in recreational
• May have higher concentrations in medicinal
**THC vs THCA**

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

- ![Chemical Diagram](image)

**How is cannabis used?**

- Smoking / Vaping
- Cannabis infused beverages and edibles

**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” (CB<sub>1</sub>) Receptor

CB<sub>1</sub> = primary cannabinoid receptor in the brain

CB<sub>2</sub> = 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)

GABA = Inhibitory

Monoacylglycerol Lipase (MAGL)

Inhibitory effect


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

Areas of the Brain Affected by Cannabinoids

Basal Nuclei: Reward system, motor and emotion control
Cerebral Cortex: Sensory, motor, executive, and emotion control
Hippocampus: Learning, memory, and emotional regulation
Amygdala: Reward system, motor, and emotion control
Medulla: Initiation of movement, tone, and respiration

Functions of the Endocannabinoid System

Appetite regulation & energy balance
Functions of the Endocannabinoid System

- Memory
- Brain reward system (pleasure)
- Functions of the Endocannabinoid System
- Pain and inflammation
- Motor activity & coordination
- Functions of the Endocannabinoid System
- Sleep / Wake Cycles

Summary: Endocannabinoid System

- 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

WIN 55,212-2

Δ⁹-Tetrahydrocannabinol


Manufacture

Packaging

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

**Symptoms of Synthetic Marijuana Use**
- "Glazed expression,"
- Red eyes
- Marijuana-like intoxication
- Inability to speak
- Body temperature fluctuation, inability to feel pain, seizures
- Increased BP & heart rate
- Temporary paralysis, cramping
- Kidney failure
- Nausea, vomiting

**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."

**Endocannabinoids**

**Phytocannabinoids**

**Synthetic Cannabinoids**

**Cannabinoid Antagonists**

**Phytocannabinoids**

**Synthetic Cannabinoids**

**Endocannabinoids**