Cannabis and its Pharmacologic Properties

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Cannabis and its Pharmacologic Properties

1. Describe, generally, the components of the endocannabinoid system and their effect on physiologic function
2. Describe the main components of cannabis and its pharmacologic properties
3. Discuss the uses, advantages and disadvantages of available prescription cannabinoids

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What Is the Endocannabinoid System

- A lipid signaling system
- Components include:
  - Cannabinoid Receptors:
    - CB-1 – Primarily in the central and peripheral nervous systems
    - CB-2 – Primarily in the immune system
  - Endogenous Cannabinoids:
    - Anandamide (AEA)
    - 2-arachidonoyl-glycerol (2-AG)
  - Degrading enzymes:
    - fatty acid amide hydrolase (FAAH)
    - monoacylglycerol lipase (MAGL)

Information for Health Care Professionals; Cannabis (marihuana, marijuana) and the cannabinoids, Health Canada October 2018

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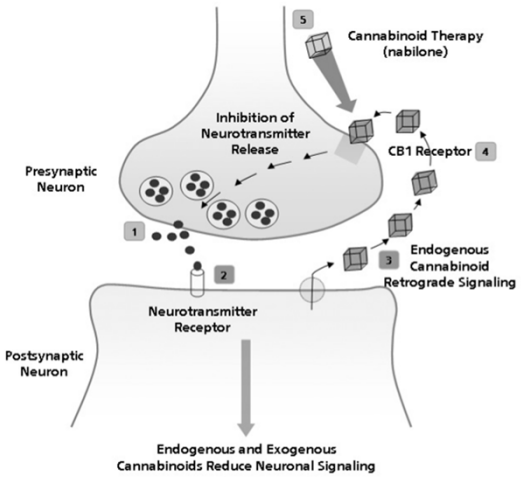
A Retrograde Signaling System

- Endocannabinoids are produced in the post-synaptic terminal in response to cellular demands.
- They bind to the cannabinoid receptors on the cell surface of the pre-synaptic terminal.
- Once stimulated, cannabinoid receptors activate a signaling cascade which suppresses the release of neurotransmitters.
- Neurotransmitter suppression changes the frequency of post-synaptic neuronal firing.



Ware MA et al. Ther Clin Risk Manag. 2008 Feb; 4(1): 99–107.

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Regulating Physiologic Function

Neural Development

Stress Regulation & Emotional State

Memory

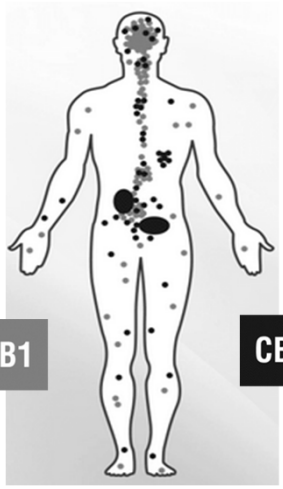
Synaptic Plasticity & Learning

Bone Development & Density

Appetite

Digestion

Metabolism & Energy Homeostasis



Wake/sleep Cycles

Psychiatric Disease

Psychomotor Behaviour

Cardiovascular Function

Pain

Reproduction

Inflammation

Immune Function

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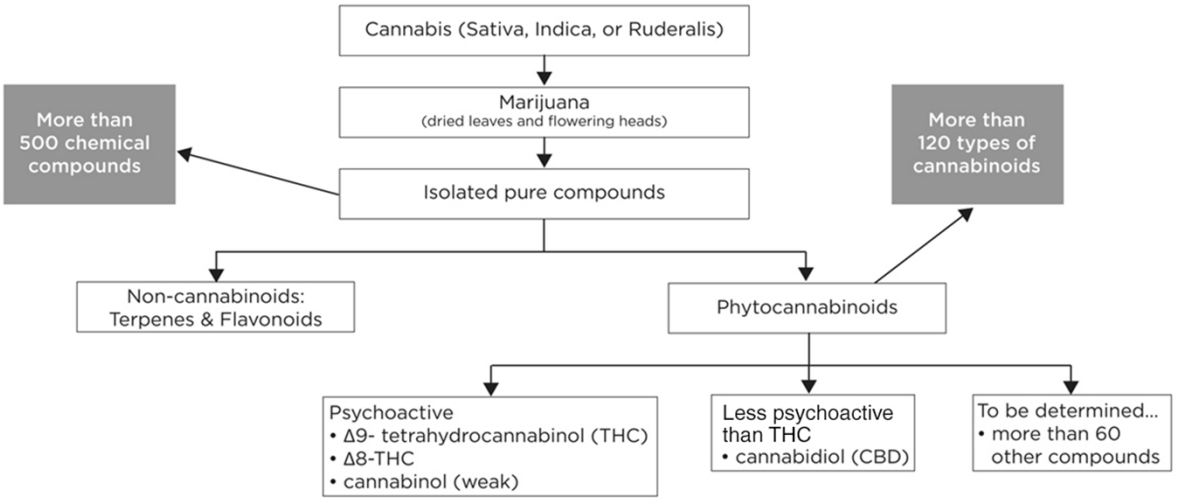
What is in cannabis?



Kalent, H. Pain Res. Manag. 2001 Summer;6(2):80-91

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Comparison of THC & CBD

	THC	CBD
Mechanism of action:	Partial CB1 and CB2 agonist	Not well understood - affects activity of other enzymes, receptors, ion channels
Psychoactive:	Yes, through activity at CB-1	Less - seems to oppose the action of THC on CB-1
May be effective for:	Relief of chronic neuropathic pain and muscle spasms, controlling nausea and stimulating appetite	Anti-inflammatory, analgesia, anti-emetic, antipsychotic, anxiolytic, antiepileptic

The ratio of THC (tetrahydrocannabinol) to CBD (cannabidiol) in the plant influences the therapeutic effects.

THC responsible for feeling "high"; can cause psychoactive adverse events

Information for Health Care Professionals; Cannabis (marihuana, marijuana) and the cannabinoids, Health Canada October 2018
Whiting PF et al. JAMA. 2015;313(24):2456-2473

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What kinds of cannabinoids are available?

Endocannabinoids

Endogenous cannabinoids that are naturally produced in the human body (e.g. AEA, 2-AG)

Phytocannabinoids

Cannabinoids produced naturally by the cannabis plant (THC, CBD, many others). Found in cannabis plant material and extracts
Available via regulated (medical, recreational) channels, and unregulated

Prescription cannabinoids

Pharmaceutical grade cannabinoid-containing prescription medications (nabilone, nabiximols).

Synthetic cannabis

Manufactured illicit products containing highly potent CB1/CB2 receptor agonists (Spice, K2)
Outside regulatory system

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Nabilone

- Synthetic THC analogue (no CBD)
- Indicated for Chemotherapy-Induced Nausea and Vomiting (CINV)
- Off-label use for chronic pain, sleep aid, adjunct to other pain medications
- Designated as a controlled substance
- Available as 0.25 mg, 0.5 mg and 1 mg oral capsule (dose consistency)
- Delayed onset of action, longer duration of action
- May cause drowsiness, vertigo, psychological high, dry mouth
- Relatively inexpensive, often covered under insurance plans

Valeant Canada Limited. Cesamet Product Monograph.

Nabiximols

- Extract of cannabis plant (pharmaceutical product)
- Indicated for spasms associated with MS, adjunctive treatment for neuropathic pain and cancer pain
- Not designated as a controlled substance
- Available as an oromucosal, buccal spray that includes standardized amounts of THC:CBD (2.5:2.7%; approx. 1:1 ratio) plus other components
- Rapid absorption and onset
- May cause dizziness, confusion, tachycardia, blurred vision
- Relatively expensive and not usually covered under insurance plans

GW Pharma. Sativex Product Monograph

Comparison of Prescription Cannabinoids

	Potential Advantages	Potential Disadvantages
Nabilone	• Most clinical evidence – indicated for CINV • Dose consistency • Longer duration of action • Likely insurance coverage, relatively inexpensive	• High incidence of sedation • Slower onset of action • Synthetic THC analogue (no CBD) • Single route of administration (oral)
Nabiximols	• Some clinical evidence • Standardized THC:CBD ratios • Possible entourage effect • Rapid absorption, onset of action • Ease of administration	• Single formulation • May irritate buccal mucosa • Contains ethanol • Costly, unlikely to be covered by insurance
Dronabinol	• Synthetic THC • Used for severe CINV and AIDS related anorexia	• Available in US only (discontinued from Canadian market) • Capsules and solution
Cannabidiol	• Recently FDA approved • CBD only • Similar to high CBD oil extracts • Indicated for Dravet and Lennox-Gastaut seizure syndromes	• Not yet available in Canada

Abbot Laboratories Limited. Marinol Product Monograph
Epidiolex (cannabidiol) monograph (FDA)

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The Legal Landscape: Access, Possession and Use

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