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Cannabis for medical use

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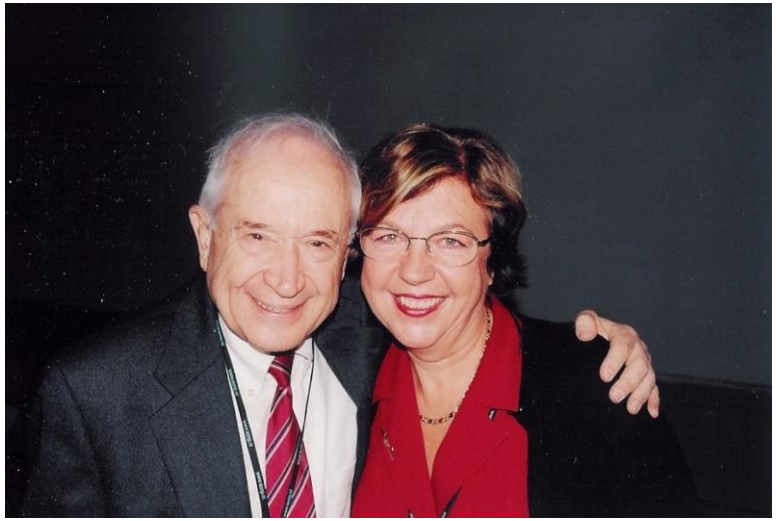
Cannabinoids

Group of 21 carbon terpenophenolic compounds uniquely produced by hemp plants



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NEED FOR A CHANGE OF THE ORIGINAL MEANING

Development of synthetic cannabinoids

Discovery of endogenous cannabinoids
(endocannabinoids)

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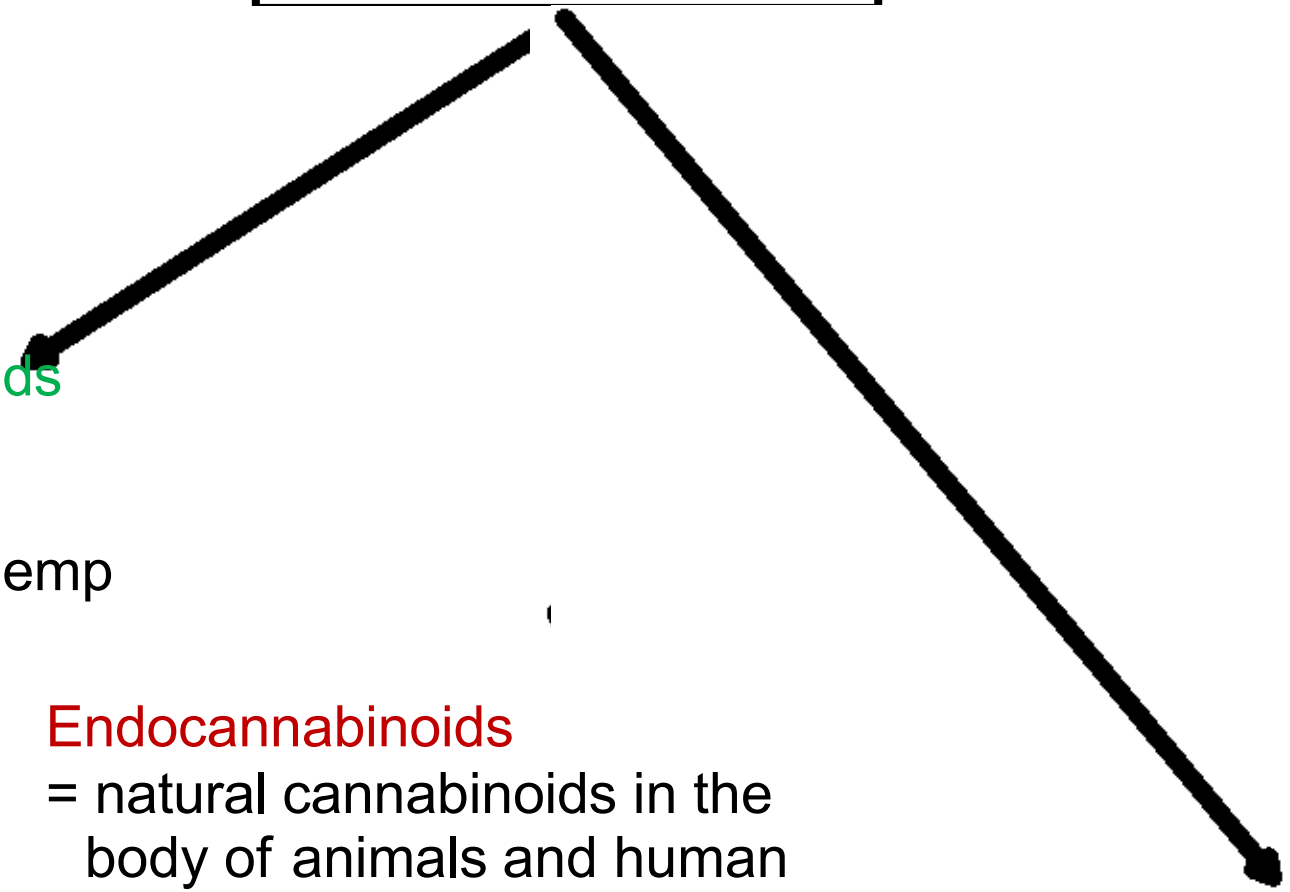
Cannabinoids



Phytocannabinoids
= substances
contained
specifically in hemp

Endocannabinoids
= natural cannabinoids in the
body of animals and human
beings

Synthetic
cannabinoids
= artificially

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Phytocannabinoids

subclasses according to Elsohly et al. (2005):

1) cannabigerol type

2) cannabichromene type

3) cannabidiol type (CBD)

4) Δ9- trans-tetrahydrocannabinol type (THC)

5) Δ8-trans-tetrahydrocannabinol type

6) cannabicyclol type

7) cannabielsoin type

8) cannabinol type

9) cannabinodiol type

10) cannabitriol type

11) miscellaneous types

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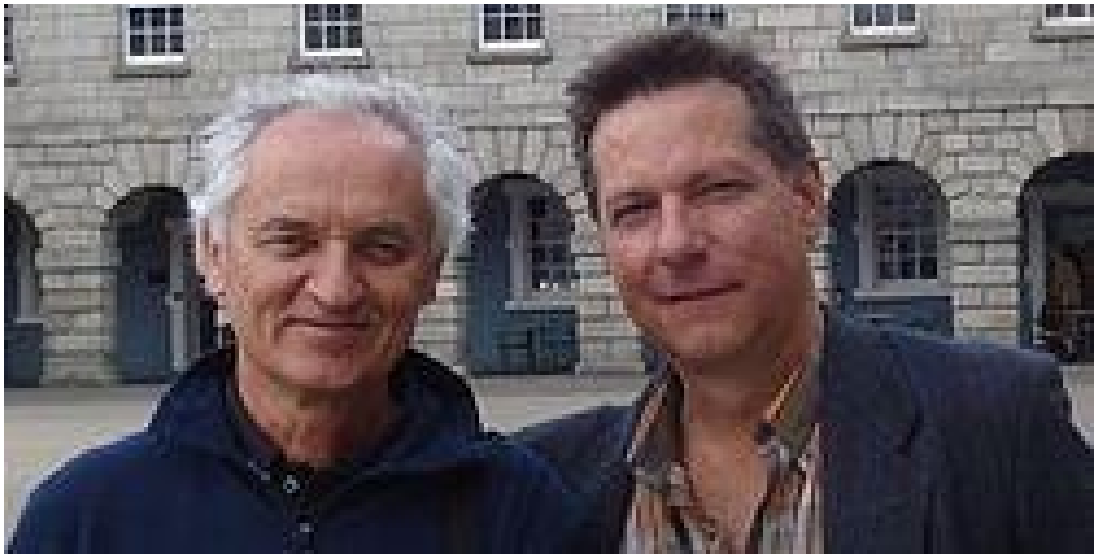
Endocannabinoids



https://cs.wikipedia.org/wiki/Soubor:HanDev.jpg

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Endocannabinoids

anandamide (N-arachidonoyl-ethanolamine, AEA) (Devane et al. 1992)

name based on the Sanskrit word ‘ananda’ (internal bliss)

2-arachidonoyl-glycerol (2-AG) (Mechoulam et al. 1995)

N-arachidonoyl-dopamine (NADA) (Bisogno t al. 2000)

noladin ether (2-arachidonyl-glyceryl ether, 2-AGE) (Hanus et al. 2001)

virhodamine (O-arachidonoyl-ethanolamine) (Porter et al. 2002)

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Synthetic cannabinoids

Main purpose:
study of distribution and pharmacological properties of cannabinoid receptors

HU-210 (CB_1 a CB_2 receptor agonist)

methanandamide (CB_1 receptor agonist)

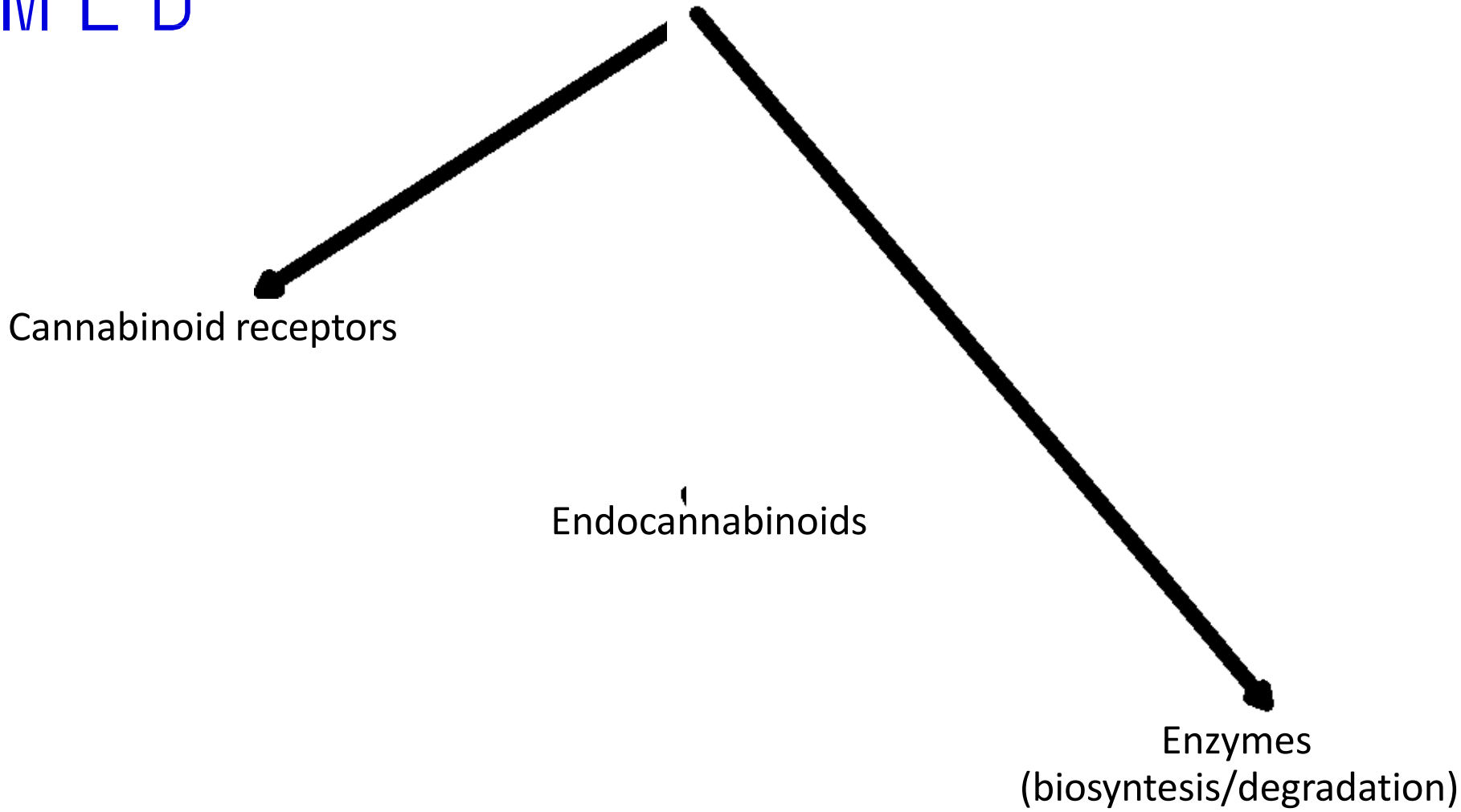
CP 55,940 (CB_1 a CB_2 receptor agonist)

WIN 55,212-2 (CB_1 receptor agonist)

JWH 015 (CB_2 receptor agonist)

AM 251 (CB_1 receptor antagonist)

Cannabinoids - mechanism of action (endocannabinoid system)



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Endocanabinoid system (ECS)

Cannabinoid receptors CB_1 and CB_2

CB_1 receptors - primarily in the CNS

regions of the brain responsible for **pain modulation**: certain parts of the spinal cord, periaqueductal grey (Grotenhermen 2006)

movement: basal ganglia, cerebellum

memory and learning: hippocampus, cerebral cortex

emotions: amygdala

sensory perception: thalamus (Velasco et al. 2012)

RESPONSIBLE FOR PSYCHOACTIVE EFFECTS

CB_2 receptors - particularly in the periphery

on immune cells, especially B-cells and natural killer cells (Pertwee 1997), also expressed in tonsils or spleen (Galiegue et al. 1995)

Endocannabinoid system (ECS)

Other known cannabinoid receptors:

TRPV1 receptors

transient receptor potential cation channels subfamily V member 1

- also known as the “capsaicin receptor” and “vanilloid receptor (Ross 2003)

GPR18, GPR55, GPR119

(also called putative or non-classical cannabinoid receptors)

- structural similarity to CB_1 and CB_2
(Alexander et al. 2013; Zubrzycki et al. 2014)

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Endocannabinoid system (ECS)

Synthesizing enzymes:

phospholipases

Degrading enzymes:

FAAH

(fatty acid amide hydrolase; post-synaptically)

MAGL

(monoacylglycerol lipase; pre-synaptically)

(Pertwee 2005; Muccioli 2010; Battista et al. 2012)

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Endocannabinoids - mechanism of action

NTs bind to their receptors →
activated postsynaptic neurons synthesize endocannabinoid precursors

→ subsequent release of endocannabinoids

(This is generally induced by an increase in the cytosolic concentration of free Ca^{2+})

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Endocannabinoids - mechanism of action (THC)

Endocannabinoids act as retrograde synaptic messengers → bind to presynaptic CB_1 cannabinoid receptors

→ inhibition of NTs release: glutamate and GABA (Guzman, 2003).

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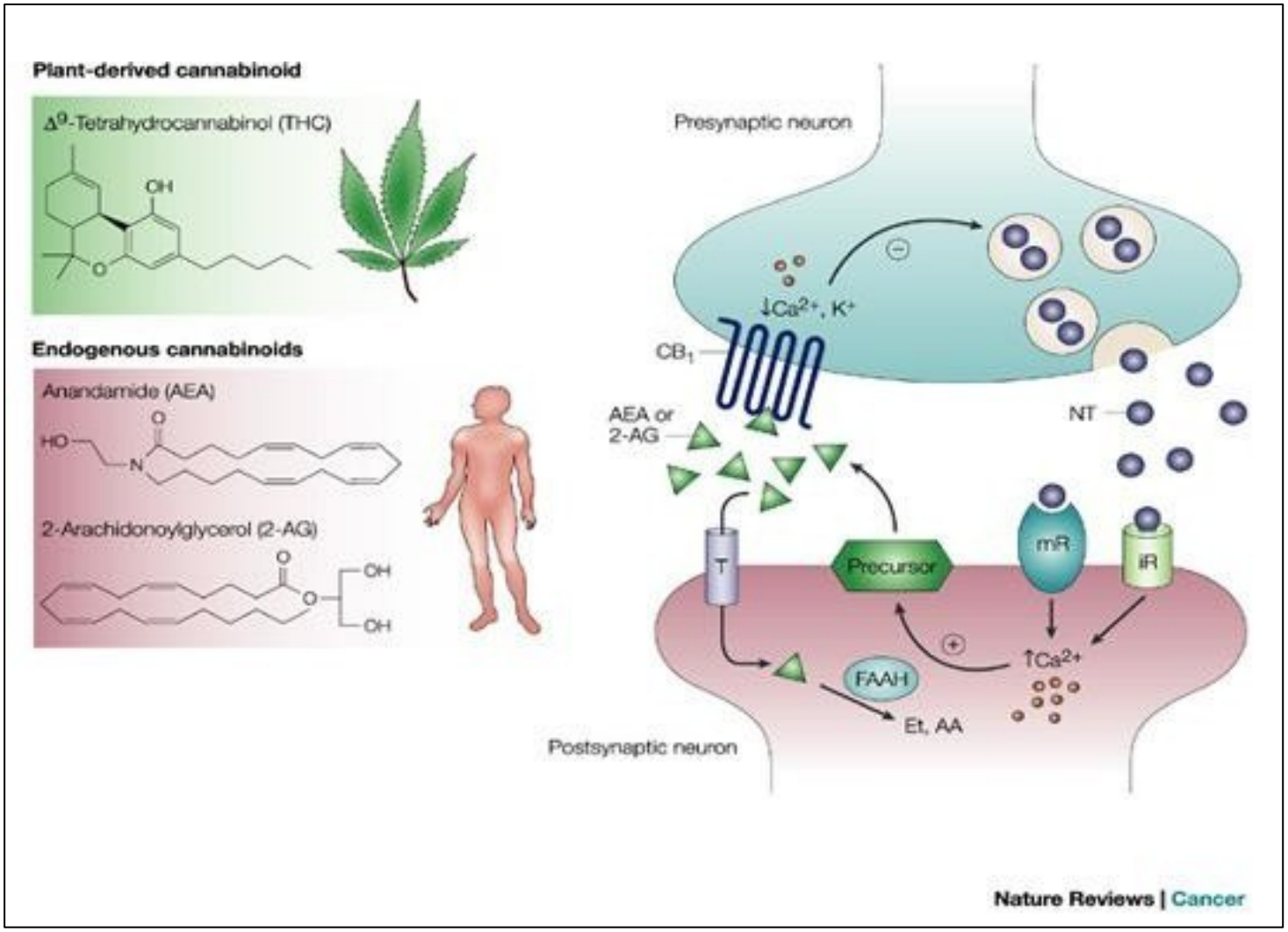

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Endocannabinoid system (ECS)

Physiological functions of ECS are very complex:

motor coordination

memory

appetite

modulation of pain

neuroprotective effects

maintaining of homeostasis, etc. (Pacher et al., 2006).

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Effect of THC on dopamine release → dependence potential

THC stimulates neurons in dopamine reward system to release (indirectly)

GABA normally suppresses amount of dopamine released in nucleus accumbens.

GABA is blocked by THC → increase in dopamine release

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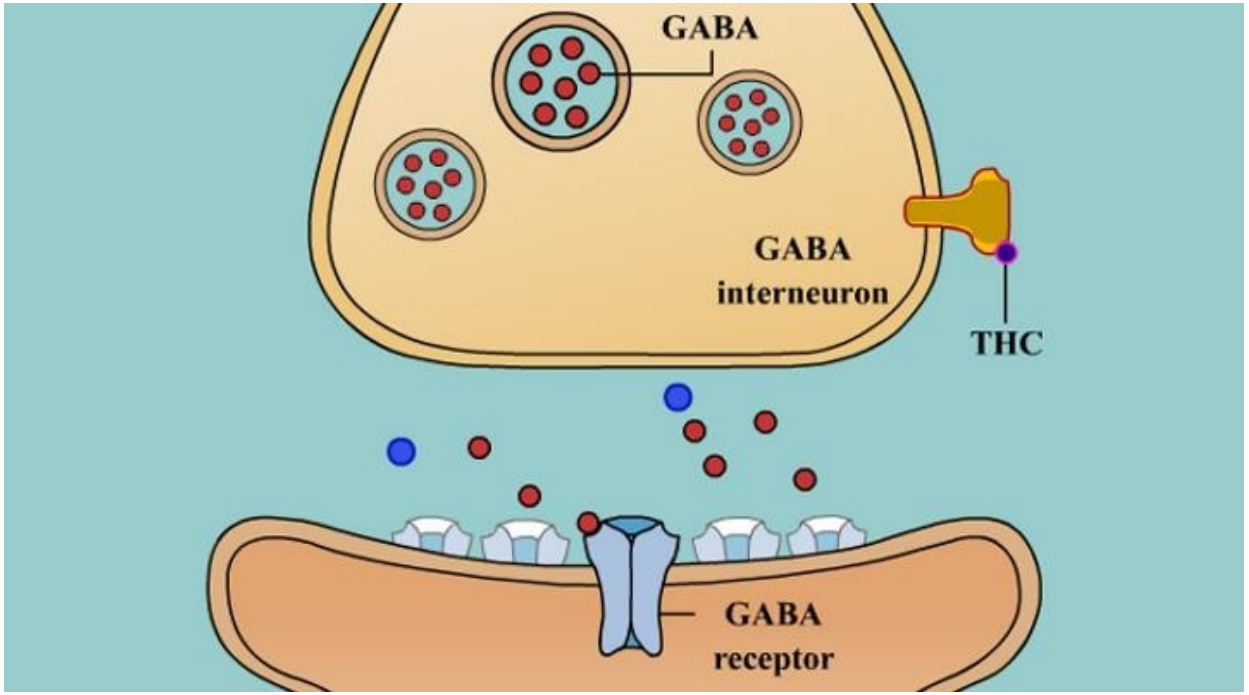
Effect of THC on dopamine release → dependence potential



thebrain.mcgill.ca

Main medical purposes of use

chronic persistent pain – especially in association with cancer,

neuropathic pain, pain associated with glaucoma,

pain associated with degenerative disease of the musculoskeletal system,

spasticity and pain in multiple sclerosis,

tremor caused by Parkinson's disease,

nausea and vomiting particularly following cancer treatment,

stimulation of appetite in cancer and HIV patients,

Tourette syndrome

superficial treatment of dermatosis and mucosal lesions