PainWeek

ADVANCED EDUCATION

CERTIFICATION SERIES

CANNABINOIDS

Cannabis & Cannabinoid Pharmacology

Mark Garofoli, PharmD, MBA, BCGP, CPE

Faculty Disclosure

- **Consulting Fee**: HealthXL, Speranza
- **Other**: Expert Witness—Cardinal Health

This presentation was not a part of the presenter's official duties at the WVU and does not represent the opinion of WVU

Learning Objectives

- Distinguish between cannabis, cannabis sativa, cannabis indica, hemp, marijuana, and cannabinoids with particular attention to cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC).
- Recall the physiological effects of the human endocannabinoid system stemming from CB1 and CB2 receptors, PPARs, TRPVs, GCPRs, fatty acid binding proteins, biosynthesis enzymes, and degradation enzymes, all in relation to the physiological effects.
- Recall the respective pharmacology of cannabinoids including endocannabinoids, phytocannabinoids, and synthetic cannabinoids.

“Multiple Cannabis Personality Disorder”

Cannabis

Weed

CBD

Hemp

THC

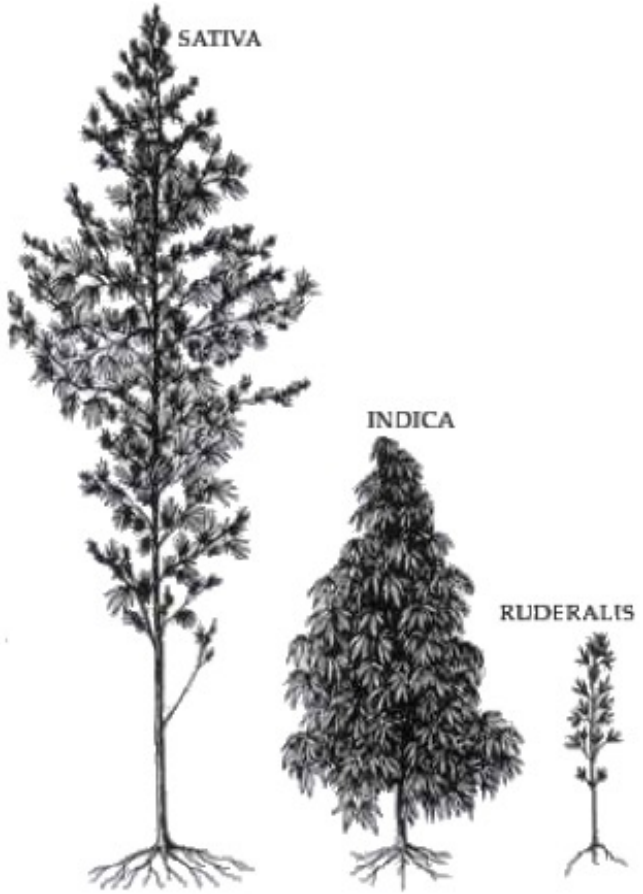
Marijuana

*Not real. Conceptual.

Cannabis Plants

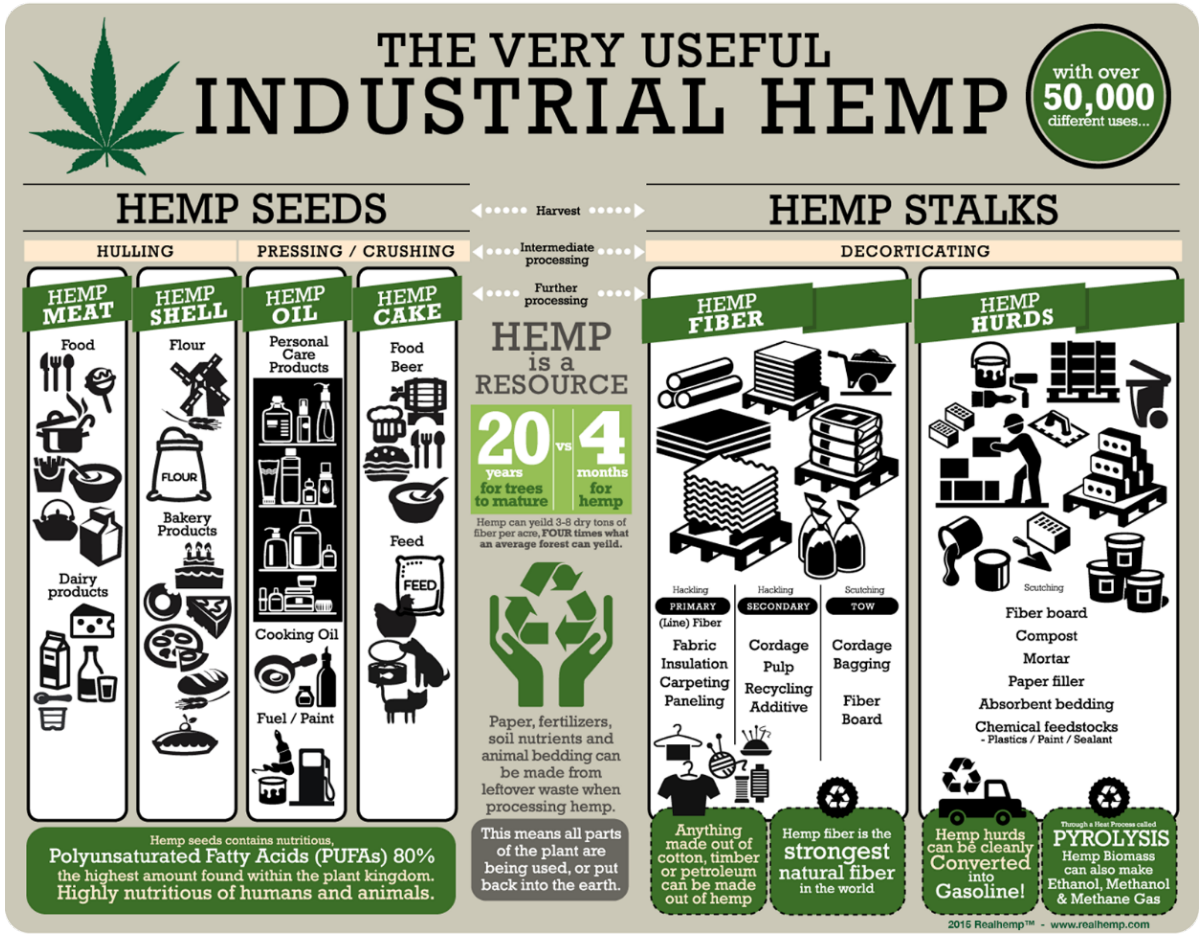
www.amaweed.com/en/blog/what-s-the-real-difference-between-hemp-and-weed/.

Cannabis Plants



www.amaweed.com/en/blog/what-s-the-real-difference-between-hemp-and-weed/.

Industrial Hemp



nationalhempassociation.org/getting-started-in-the-industrial-hemp-industry-one-perspective.

Cotton versus Cannabis

An Alternative American HIGHstory

	Cotton	Cannabis
Land for Growing	2x	1x
Water for Growing 1 kg	10 liters	2 liters
Pesticide Utilization	Pollution due to pesticides/herbicides (25% of all world pesticide use)	N/A
Crop Rotation	N/A	Can grow for 14 years on same land, or be rotated
Environmental Effects	N/A	Returns up to 60% of nutrients to soil when dried in the field

Industrial Hemp

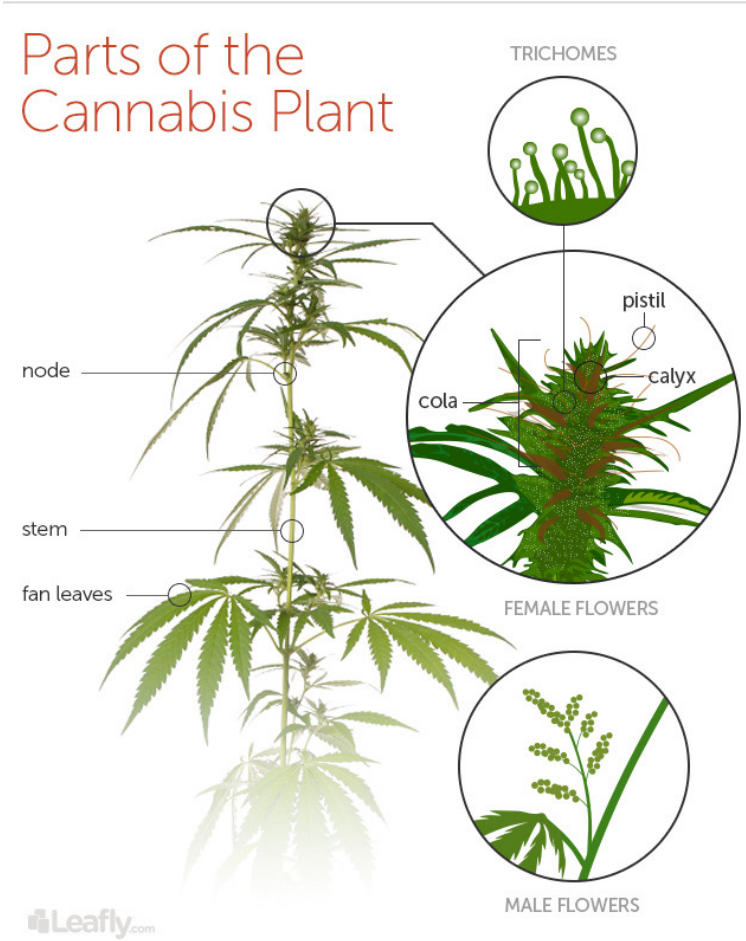
< 0.3% THC

No regulation on CBD %

me.me/i/cotton-vs-hemp-o-cotton-needs-twice-as-much-hemp-7985639.

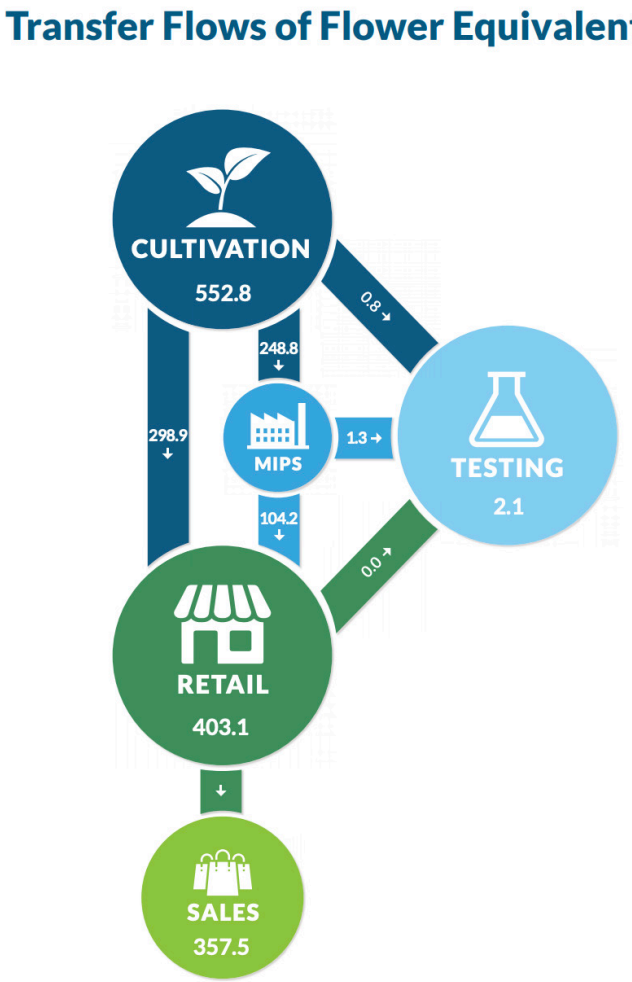
The Cannabis Plant

- *THC cultivation*
  - Low grade: male and female plants
  - Medium grade: fertilized females
  - High grade: isolated females
- Sinsemilla: “without seeds”

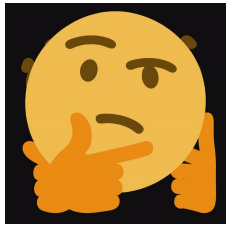


Elsohly. *Life Sci*. 2005;78(5):539-548.
D'Souza. *JAMA.* 2015;313(24):2431-2432. doi:10.1001/jama.2015.6407.

Marijuana Flower Testing and Sales



Then again, are
FDA-approved products
tested at a greater frequency?



www.colorado.gov/pacific/sites/default/files/2019%20Regulated%20Marijuana%20Market%20Update%20Report%20Final.pdf.

Terpenes

Wines

Natural Rubber

www.blockheadbrands.com/articles/2017/10/14/medicinal-properties-of-terpenes-terpenoids.

Terpenes & Terpenoids

- Terpenes are aromatic compounds responsible for the odor of flowers, fruits, seeds, leaves, woods, & roots
  - Particularly Confers
  - Plants develop terpenes to attract pollinators and reject predators
  - 30,000 natural products with the formula $(C_5H_8)_n$

- Terpenoids are terpenes modified with functional groups (typically oxygen-containing)
  - 25,000 exist

www.sciencedirect.com/topics/chemistry/terpene.

Terpenes & Terpenoids

- The terms terpenes and terpenoids are often used interchangeably

- Factors that affect cannabis terpene levels include:
  - Climate, soil type, harvest time, and maturation level

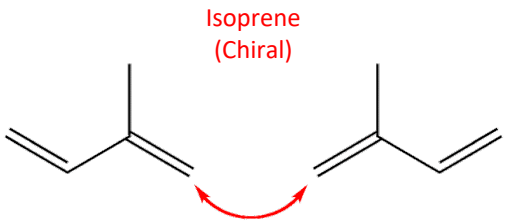
- Research suggests that these compounds can have medicinal properties

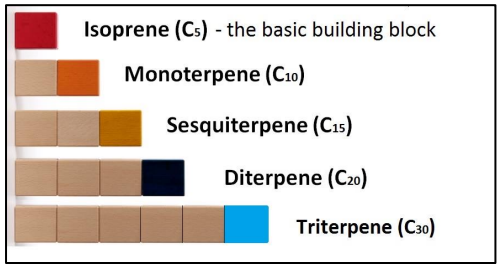
www.sciencedirect.com/topics/chemistry/terpene.

Terpenes

- Terpenes are grouped together because of their distinctive carbon skeleton of isoprene (2-methyl-1,3-butadiene)
- Monoterpene is alpha-pinene, a major component of turpentine
- About 50 monoterpenic compounds have been isolated from wines

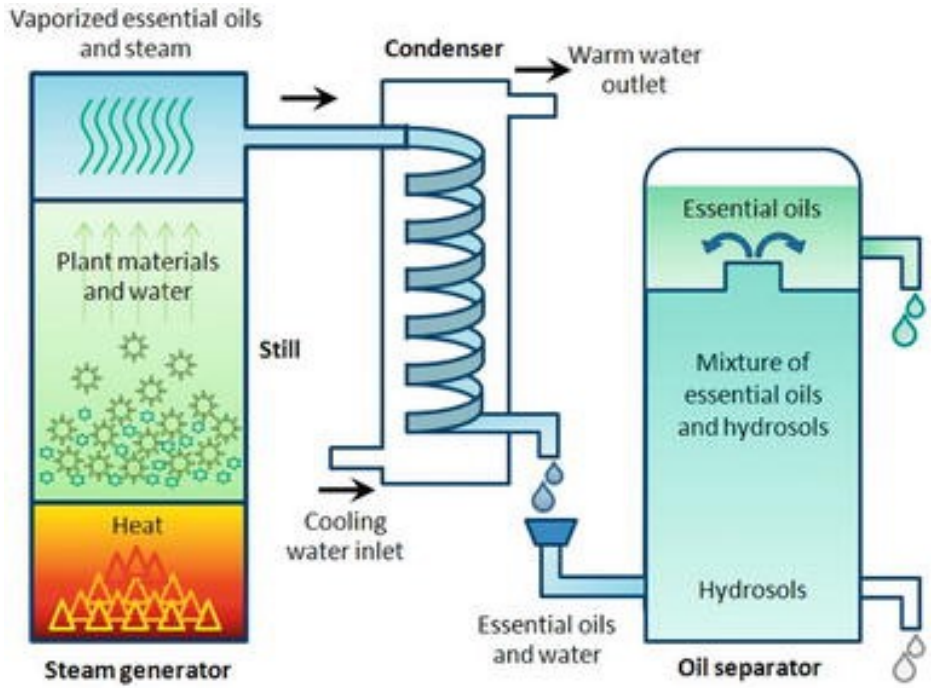
Terpene	Isoprene Units	Formula
Hemiterpene	1	C_5H_8
Monoterpene	2	$C_{10}H_{16}$
Sesquiterpene	3	$C_{15}H_{24}$
Diterpene	4	$C_{20}H_{32}$
Triterpene	6	$C_{30}H_{48}$
Sesquarterpene	7	$C_{35}H_{56}$
Tetraterpene	8	$C_{40}H_{64}$
Polyterpene	Many	N/A





www.sciencedirect.com/topics/chemistry/terpene.

Terpene Extraction

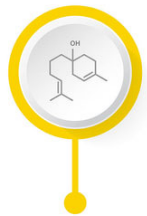


Essential Oils

www.intechopen.com/books/essential-oils-bioactive-compounds-new-perspectives-and-applications/terpenoids-as-important-bioactive-constituents-of-essential-oils.

TERPENES IN CANNABIS

THERE ARE MORE THAN 100 TERPENES IN JUST ONE CANNABIS FLOWER. HERE ARE SOME OF THE MOST WELL KNOWN TERPENES RIGHT NOW, MOST OF WHICH YOU'LL FIND IN LEGAL CANNABIS PRODUCTS IN YOUR AREA.

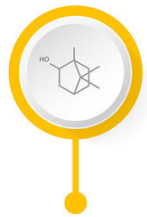


Bisabolol

floral

Properties
anti-inflammatory
anti-irritant
anti-microbial

Common Uses
cancer, skin lesion

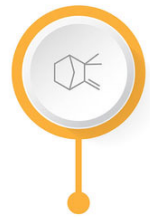


Borneol

mint

Properties
anti-inflammatory
antinociceptive

Common Uses
eyesight, pain relief



Camphene

fir needles, musky earth

Properties
anti-oxidant
skin lesion

Common Uses
cardiovascular diseases

Caryophyllene

spicy

Properties
anti-bacterial
anti-inflammatory
anti-fungal

Common Uses
insomnia, muscle spasms
pain relief

Delta 3 Carene

pine, rosemary

Properties
anti-inflammatory
bone stimulant

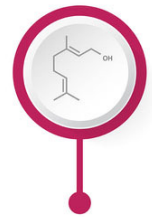
Common Uses
memory

Eucalyptol

mint

Properties
anti-bacterial
anti-fungal

Common Uses
alzheimer's
pain Relief



Geraniol

peach, rose grass

Properties
anti-cancer
anti-oxidant
neuroprotectant

Common Uses
cancer, pain relief

Humulene

earthy

Properties
anti-bacterial
anti-inflammatory
anti-tumor effects

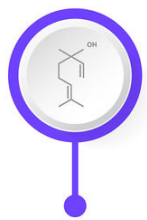
Common Uses
cancer, infections
appetite suppression

Limonene

bitter citrus

Properties
anti-anxiety
anti-cancer
digestion, gallstones

Common Uses
liver detoxification
weight loss, sleep aid

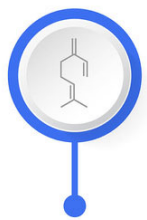


Linalool

floral

Properties
anti-anxiety
anti-epileptic
anti-psychotic
pain killing

Common Uses
depression, convulsions
insomnia, pain relief



Myrcene

citrus, cloves

Properties
relaxing
sedating

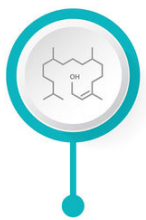
Common Uses
inflammation, insomnia
spasms, pain

Pinene

pine

Properties
anti-depressant
anti-inflammatory
anti-microbial

Common Uses
asthma, bronchitis
cancer, depression
memory, mental alertness



Phytol

balsamic, floral

Properties
anti-insomnia
immunosuppressant

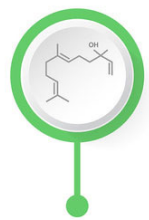
Common Uses
reduce itching
sleep aid
wound healing

Terpinolene

smoky, woody

Properties
anti-bacterial
anti-fungal
anti-insomnia
antiseptic

Common Uses
cancer
heart disease
sleep aid

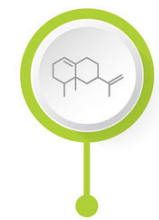


Trans-nerolidol

citrus, rose

Properties
anti-cancer
anti-microbial
anti-oxidant,
anti-parasitic

Common Uses
relaxing
skin lesion



Valencene

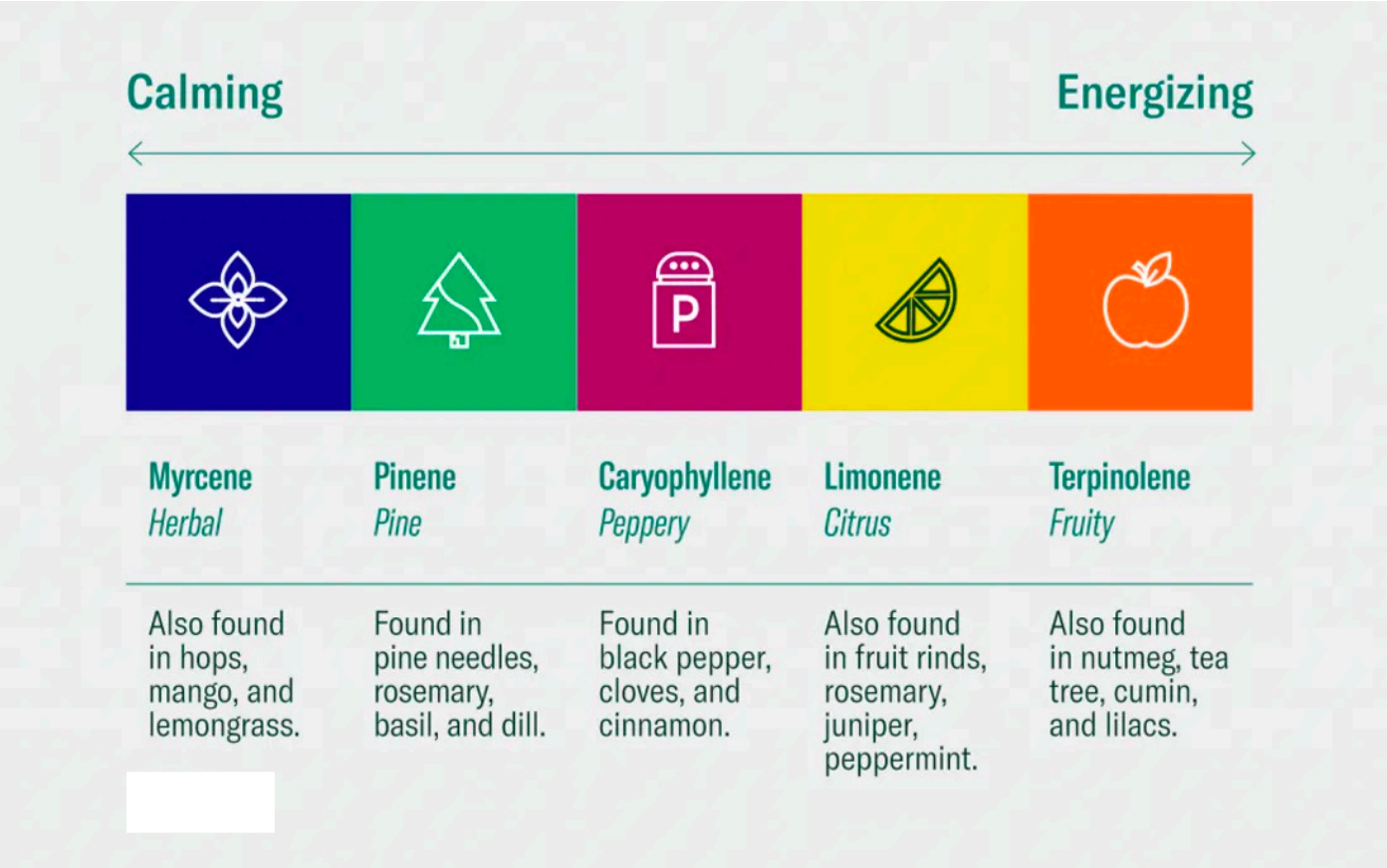
sweet citrus

Properties
anti-inflammatory
anti-melanogenesis
antiallergic

Common Uses
memory
skin lesion

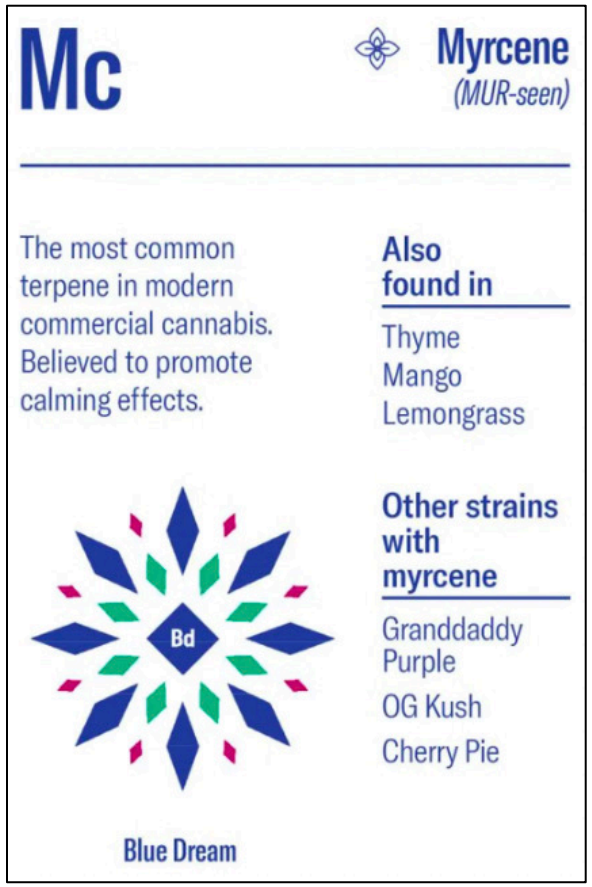
www.mybpg.com/blog/cannabis-terpenes/.

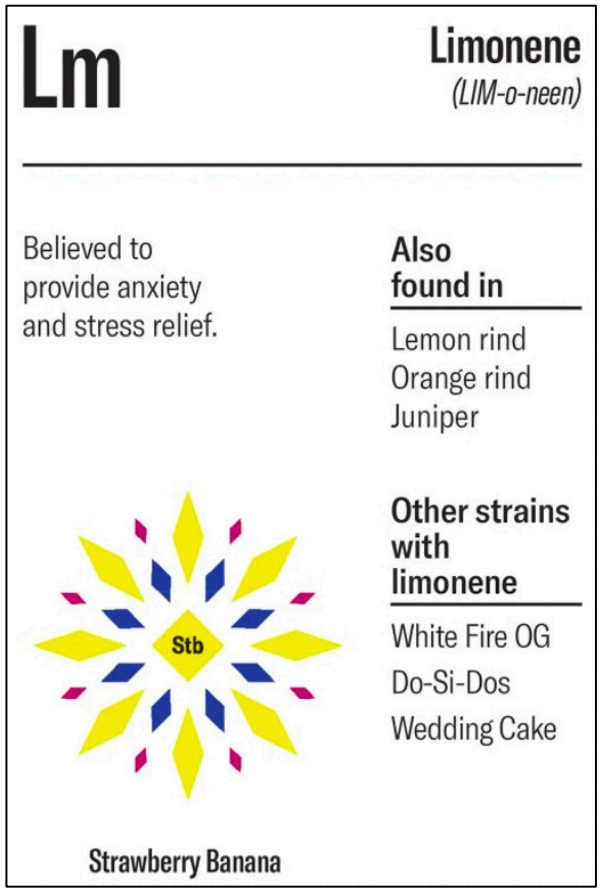
Cannabis Terpenes

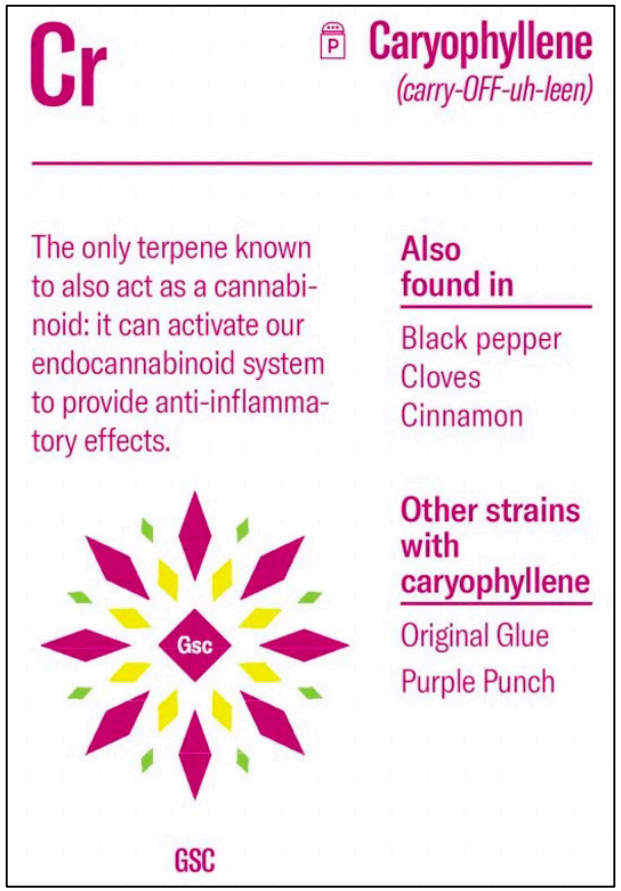


www.leafly.com/news/cannabis-101/terpenes-the-flavors-of-cannabis-aromatherapy.

Cannabis Terpenes

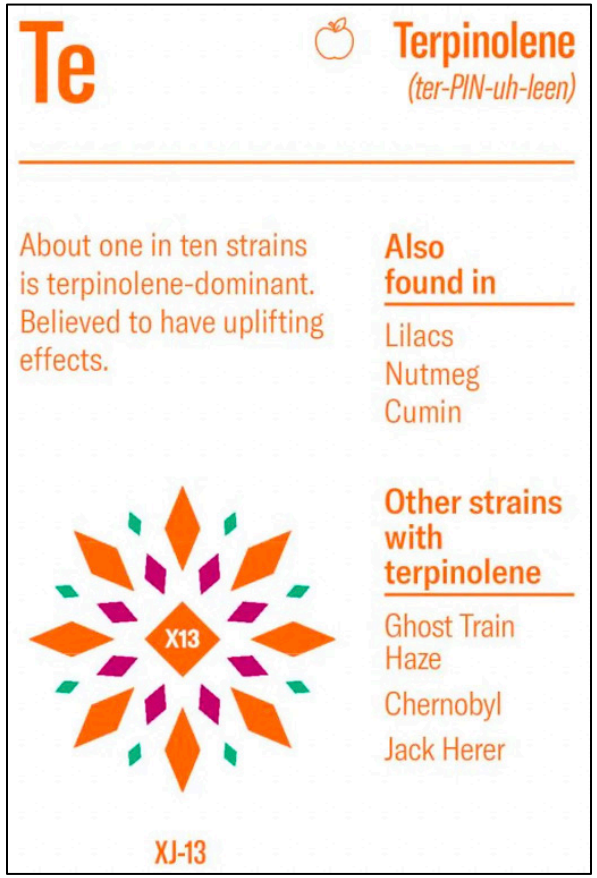


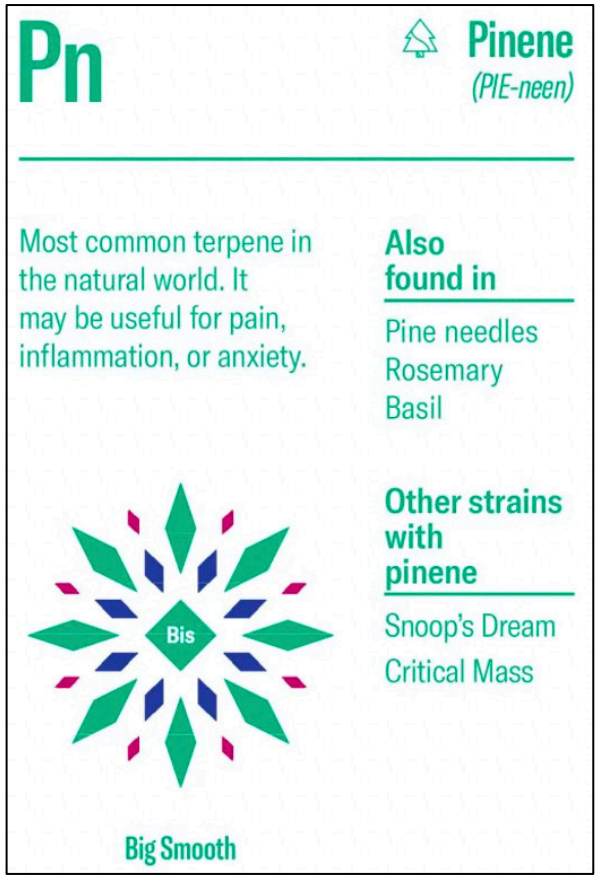


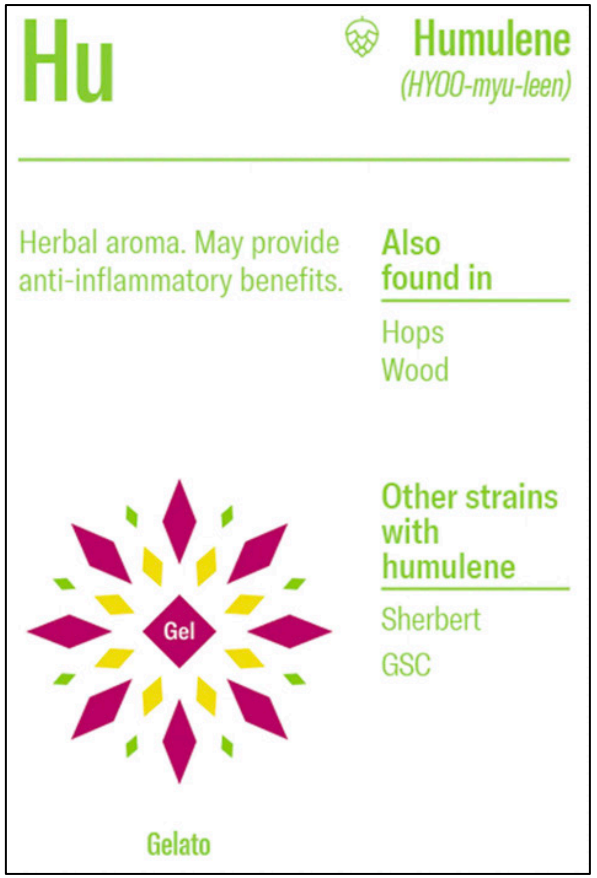


www.mybpg.com/blog/cannabis-terpenes/.

Cannabis Terpenes

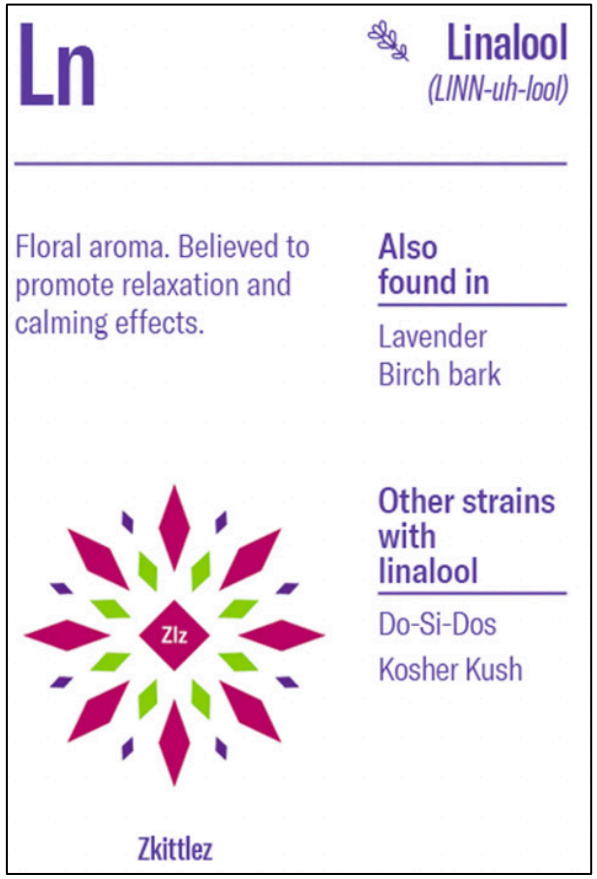






www.mybpg.com/blog/cannabis-terpenes/.

Cannabis Terpenes

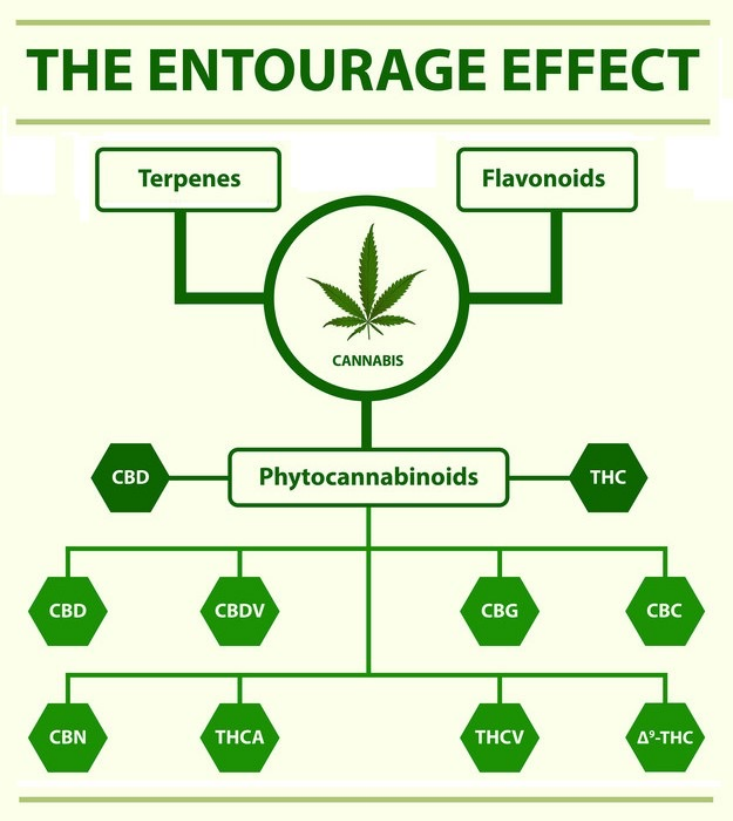


www.mybpg.com/blog/cannabis-terpenes/.

“The Entourage Effect”

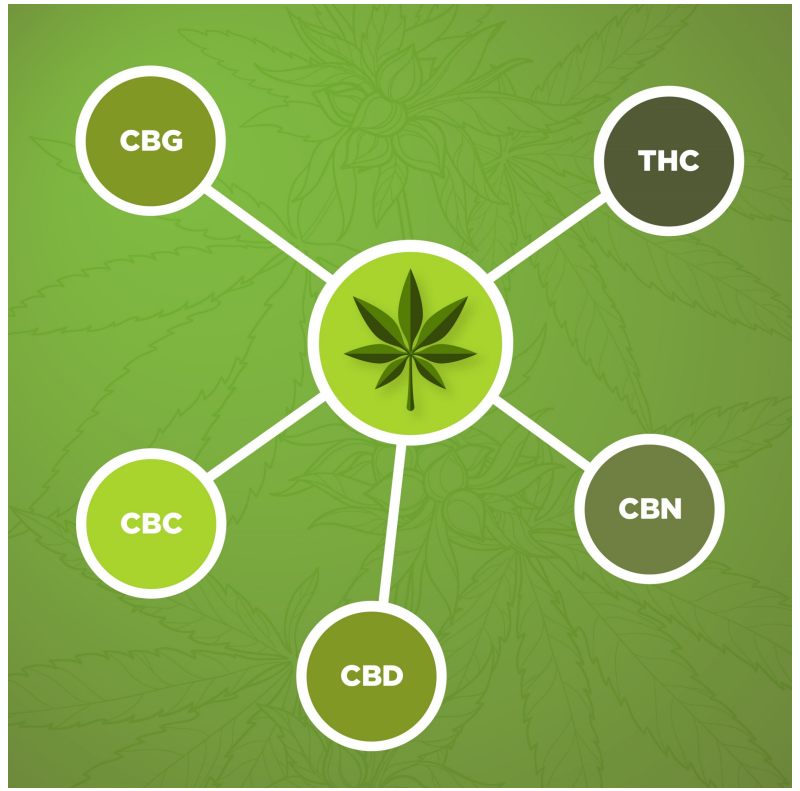
- Cannabis terpenes are said to optimize the effects of cannabis cannabinoids, known as the “Entourage Effect”

- Terpene(s)-to-cannabinoid(s) ratio
  - May affect respective pharmacological outcomes



www.sciencedirect.com/topics/chemistry/terpene.
www.mybpg.com/blog/cannabis-terpenes/.

Cannabinoids



Cannabinoids

Endo-Cannabinoids

Phyto-Cannabinoids

Synthetic Cannabinoids

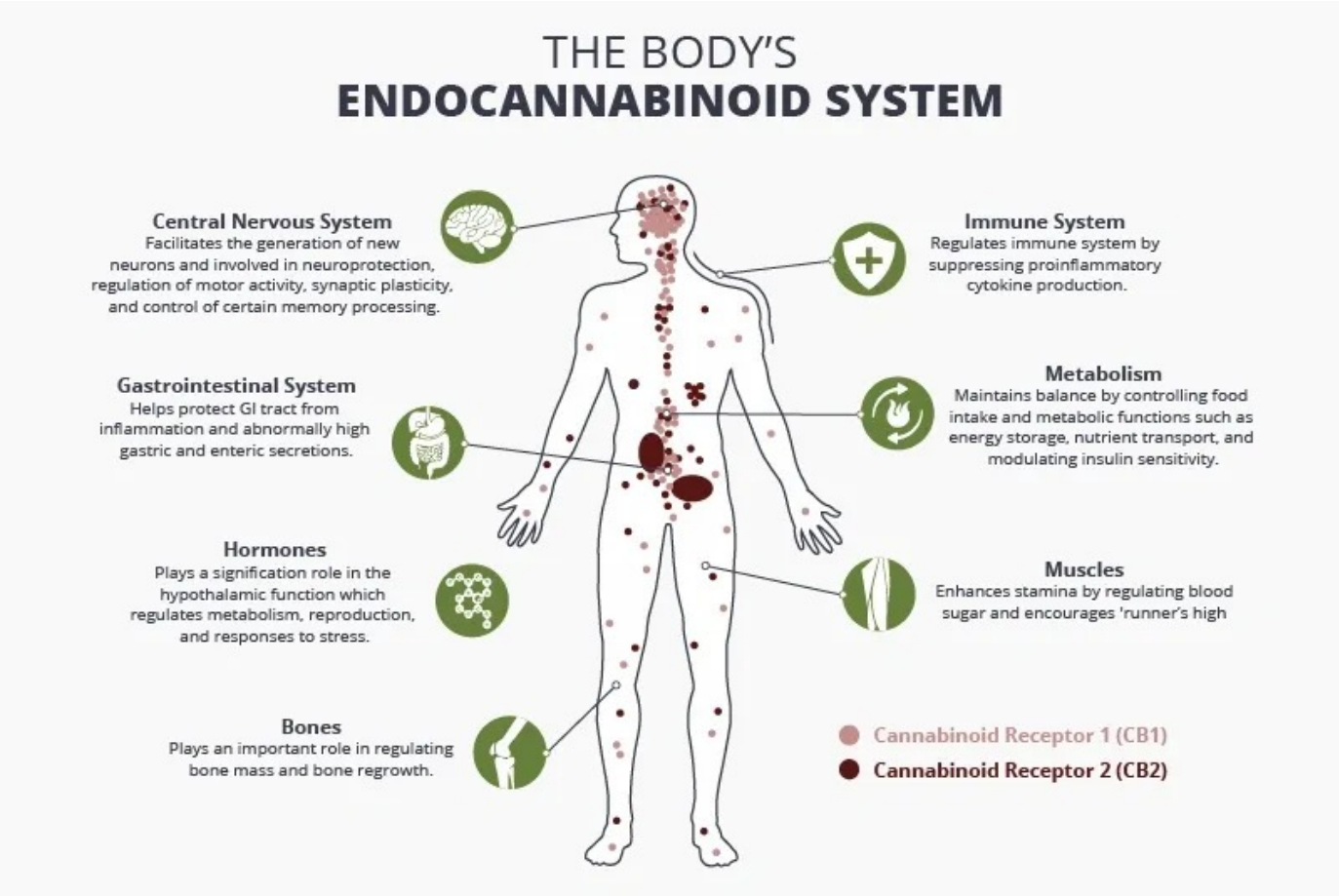
Cannabinoids

Endo-Cannabinoids

Phyto-Cannabinoids

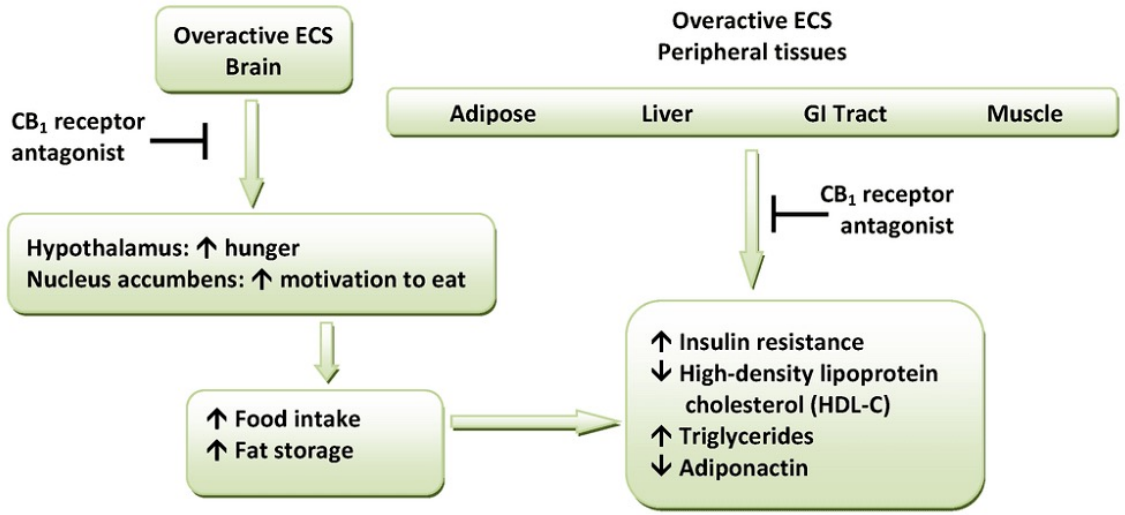
Synthetic Cannabinoids

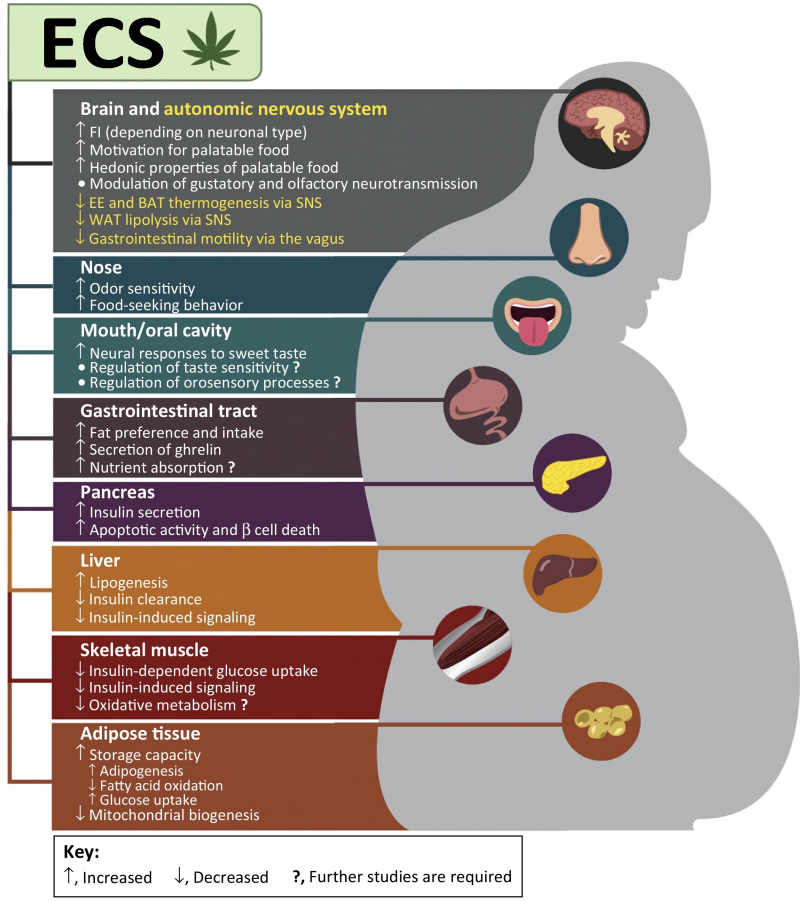
Endocannabinoid System (ECS)



summitreleaf.com/2020/05/04/the-endocannabinoid-system/.

ECS Endocrinology & Metabolism

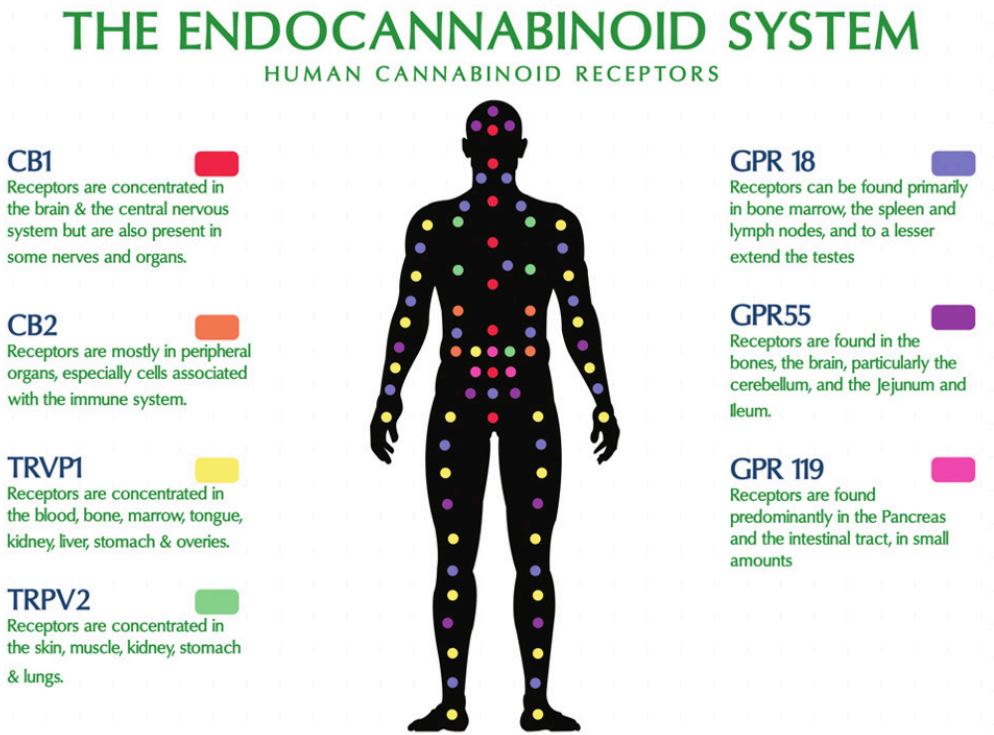


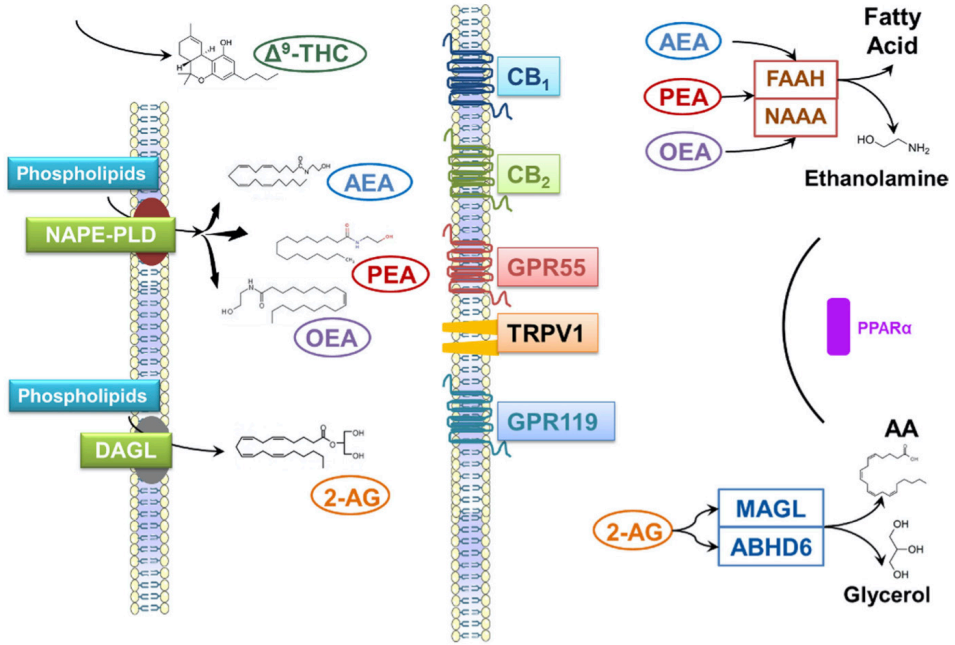


biologydictionary.net/endocannabinoid-system/.

Mazier. *Trends Endocrinol Metab*. 2015;26(10):524-537.

Endocannabinoid Receptors





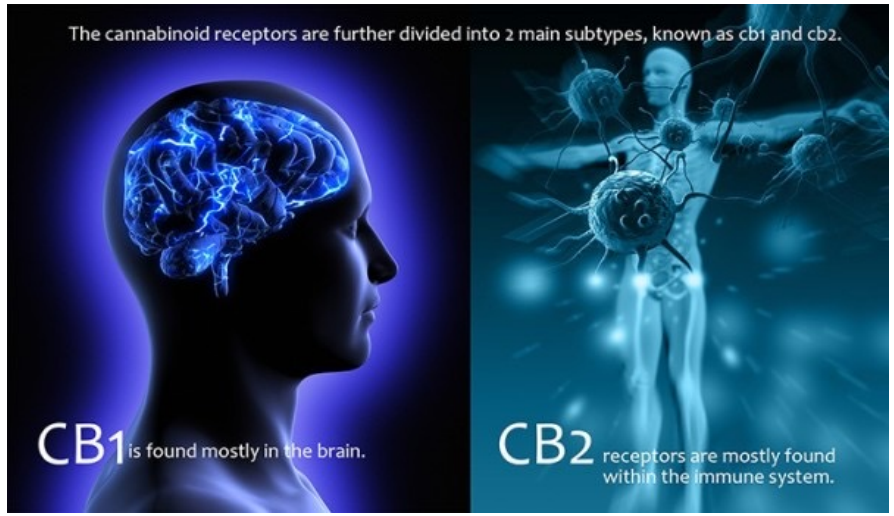
mcanz.org.nz/the-endocannabinoid-system/.

Cani. *Diabetes Metab*. 2014;40:246-257.

Cannabinoid Receptors
CB1/CB2

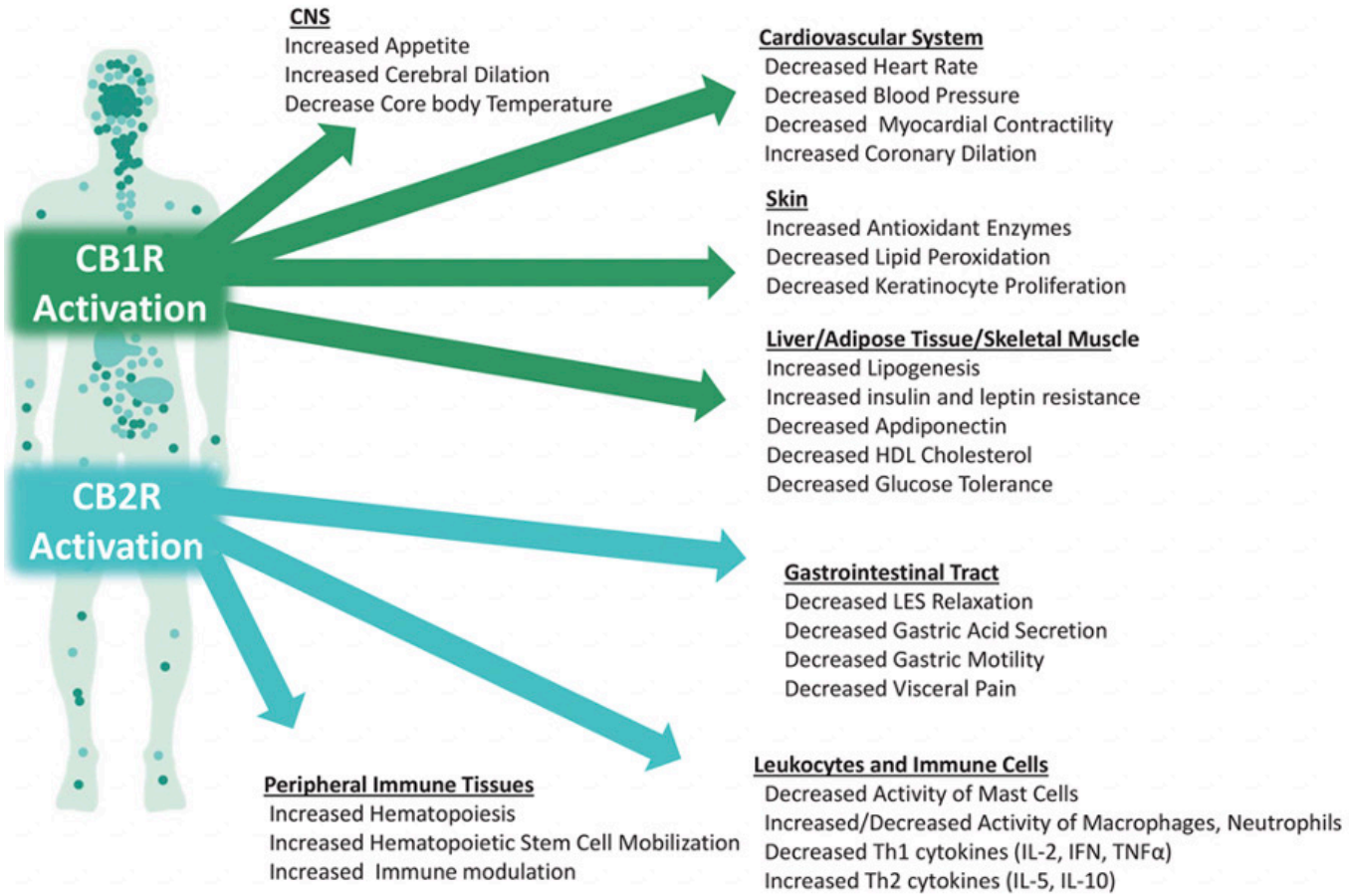
CB1 receptors
- Primarily in CNS
- Also connective tissue, gonads, glands, and organs
- Analgesia, euphoria, and anticonvulsive

CB2 receptors
- Primarily in immune system and GI tract
- Inflammation and digestion



https://cannabisholism.com/endocannabinoid-system-discovery/

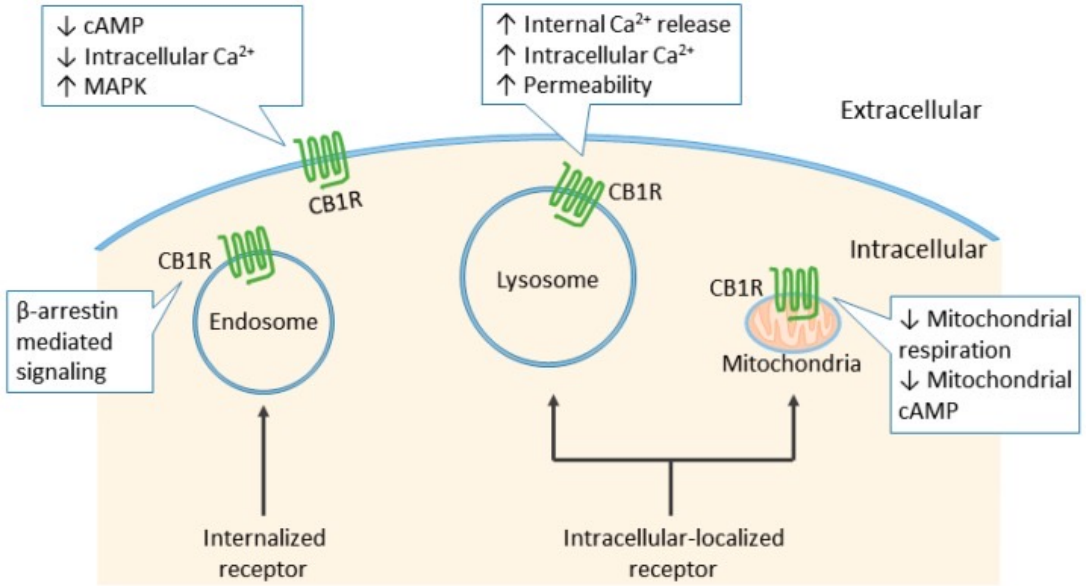
Cannabinoid Receptors
CB1/CB2



Robert. *Circulation*. 2020;142(10):e131-e152.

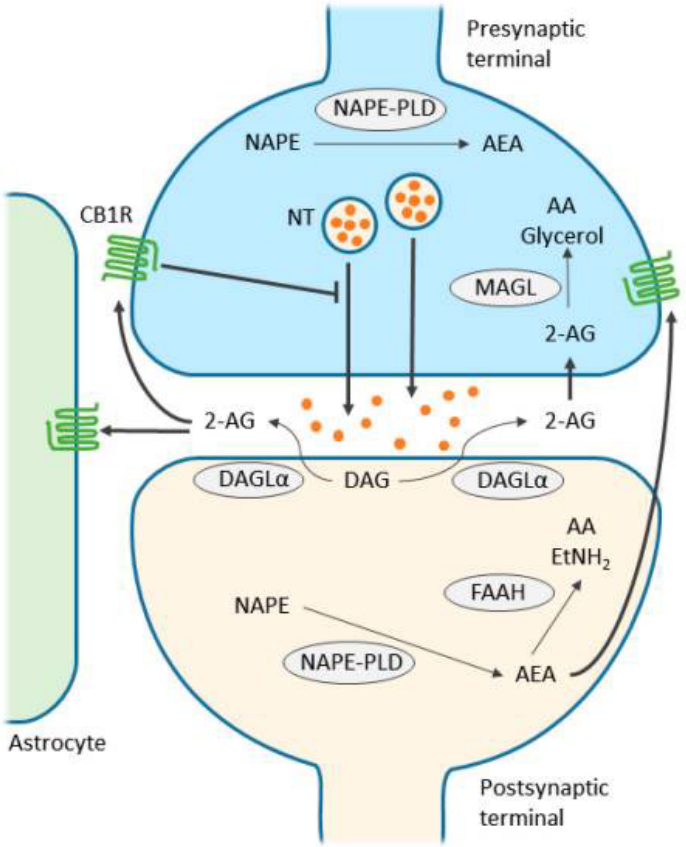
CB1 Receptor Processes

- Surface CB1s inhibit cyclic adenosine monophosphate (cAMP) formation and calcium influx
- Intracellular CB1s mediate signal pathways through β-arrestin
  - Lysosome CB1s: increase intracellular calcium
  - Mitochondrial CB1s: decrease cellular metabolism
    - By inhibiting cellular respiration and cAMP production



Zou. *Int J Mol Sci*. 2018;19(3):833.

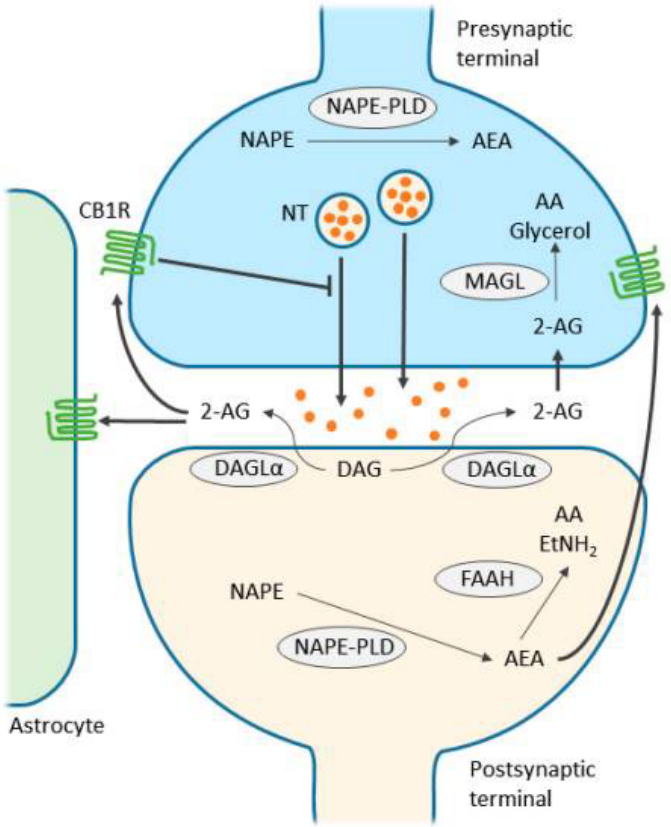
ECS Pre/Post Synaptics & Astrocytes



- 2-AG: 2-Arachidonolglycerol
- DAG: Diacylglycerol
- DAGL: Diacylglycerol Lipase-Alpha
- AEA: Anandamide
- NAPE: N-Acyl-Phosphatidylethanolamine
- NAPE-PLD: NAPE-Specific Phospholipase D
- NAT: N-acyltransferase
- GPCR: G-Protein-Coupled Receptor
- AA: Arachidonic Acid
- NMDA: N-Methyl-D-Aspartate
- VGCC: Voltage-Gated Calcium Channels
- MAGL: Monoacylglycerol Lipase
- TRPV1: Transient Receptor Potential Subfamily V Member 1
- FAAH: Fatty Acid Amide Hydrolase

Zou. *Int J Mol Sci*. 2018;19(3):833.
De Fonseca. *Alcohol Alcohol.* 2005;40(1):2-14.

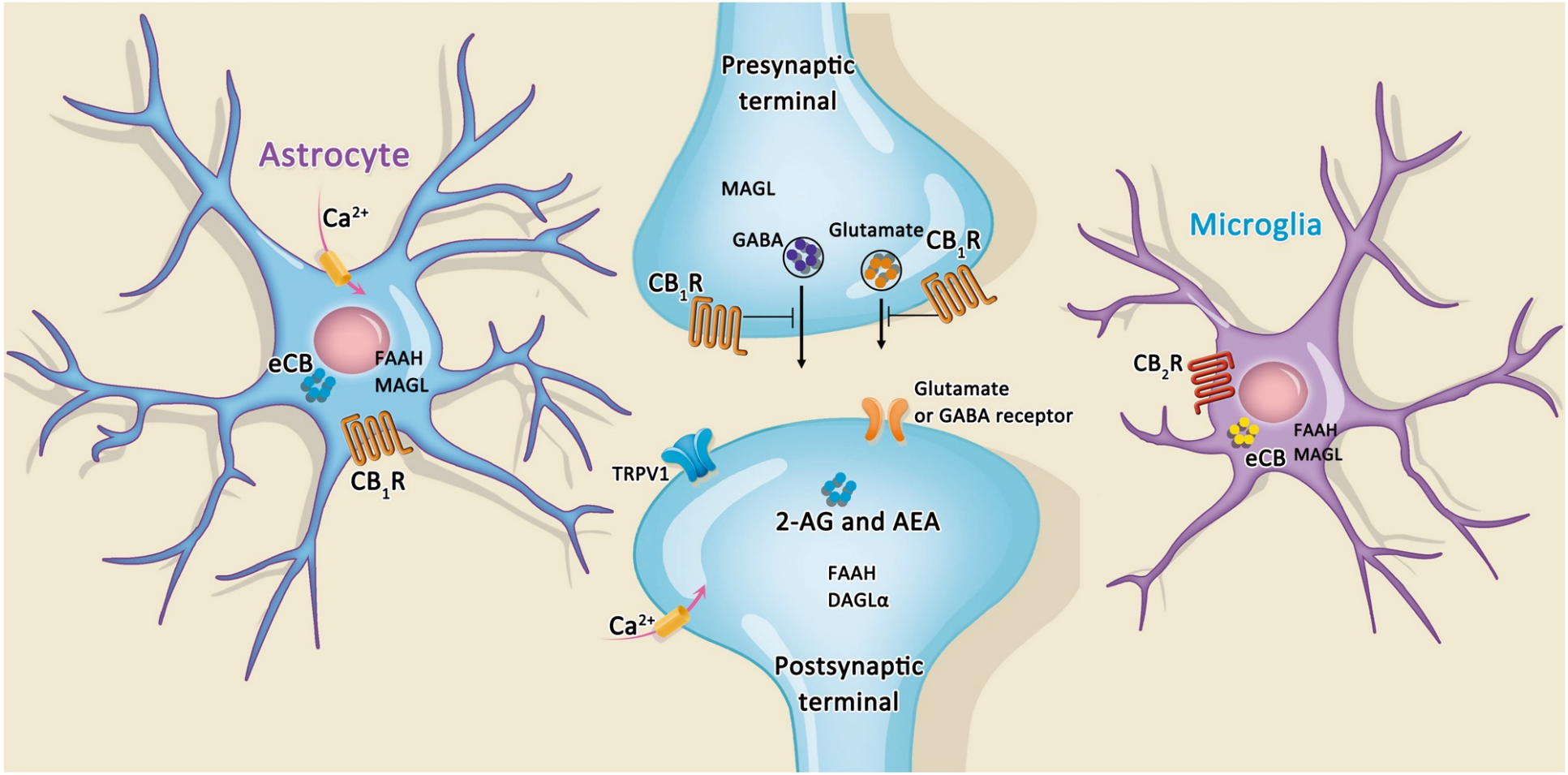
ECS Pre/Post Synaptics & Astrocytes



- Postsynaptic
  - 2-AG is biosynthesized from DAG by DAGL-alpha
  - AEA is synthesized from NAPE by NAPE-PLD activated by GPCR depolarization
    - NAPE biosynthesis catalyzed by NAT, which is activated by Ca and cAMP
  - AEA activates TRPV1
  - AEA regulates dopamine release via K channels and protein kinases
    - Protein kinase A and MAPK
  - AEA is degraded to AA and ethanolamine ($EtNH_2$) by FAAH
- Presynaptic
  - 2-AG and AEA (lipids) cross presynaptic membranes to active CB1, which regulate GABA and glutamate release via VCGG and NMDA receptors
  - 2-AG is degraded to AA and glycerol by MAGL
- Astrocytes
  - 2-AG activates CB1 on astrocytes, which releases glutamate

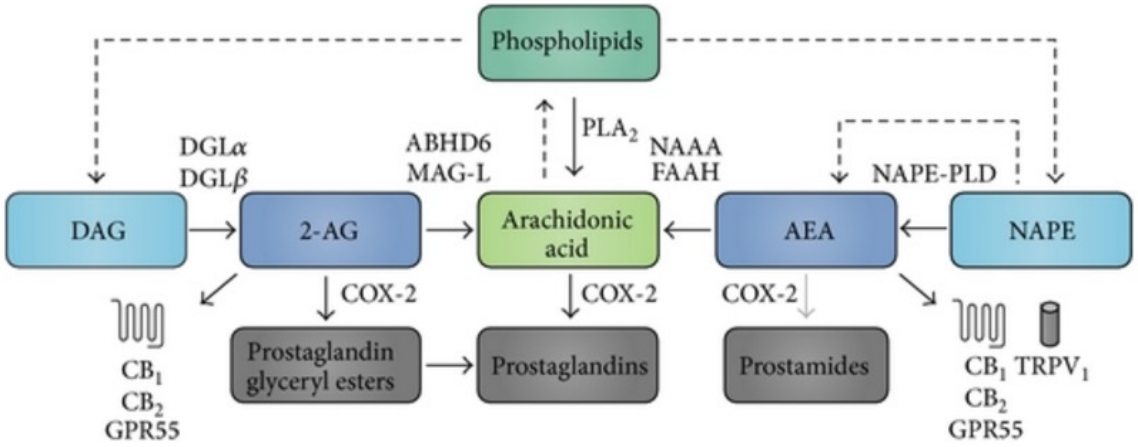
Zou. *Int J Mol Sci*. 2018;19(3):833.
De Fonseca. *Alcohol Alcohol.* 2005;40(1):2-14.

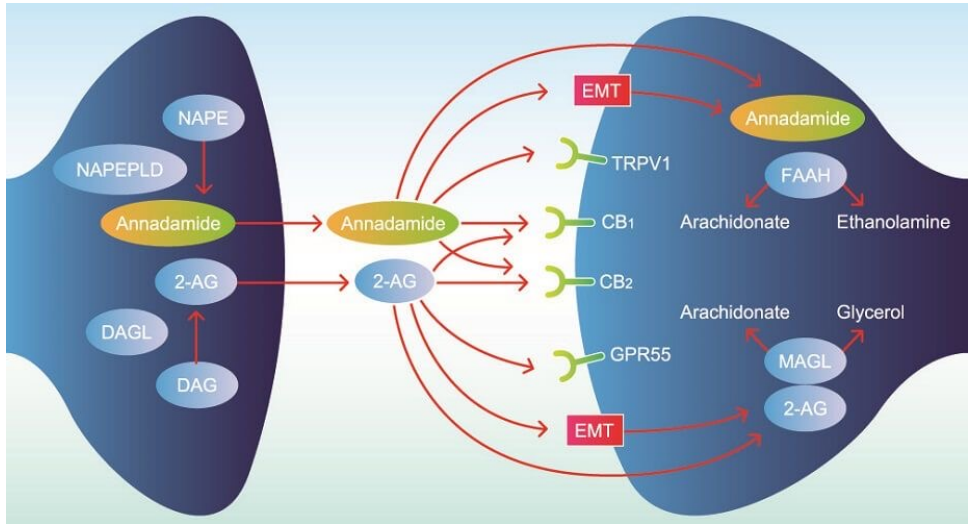
Pre/Post Synaptics, Astrocytes, & Microglia



Yin. *Acta Pharmacol Sin.* 2019;40:336-341.

Biosynthesizing & Degradation Enzymes



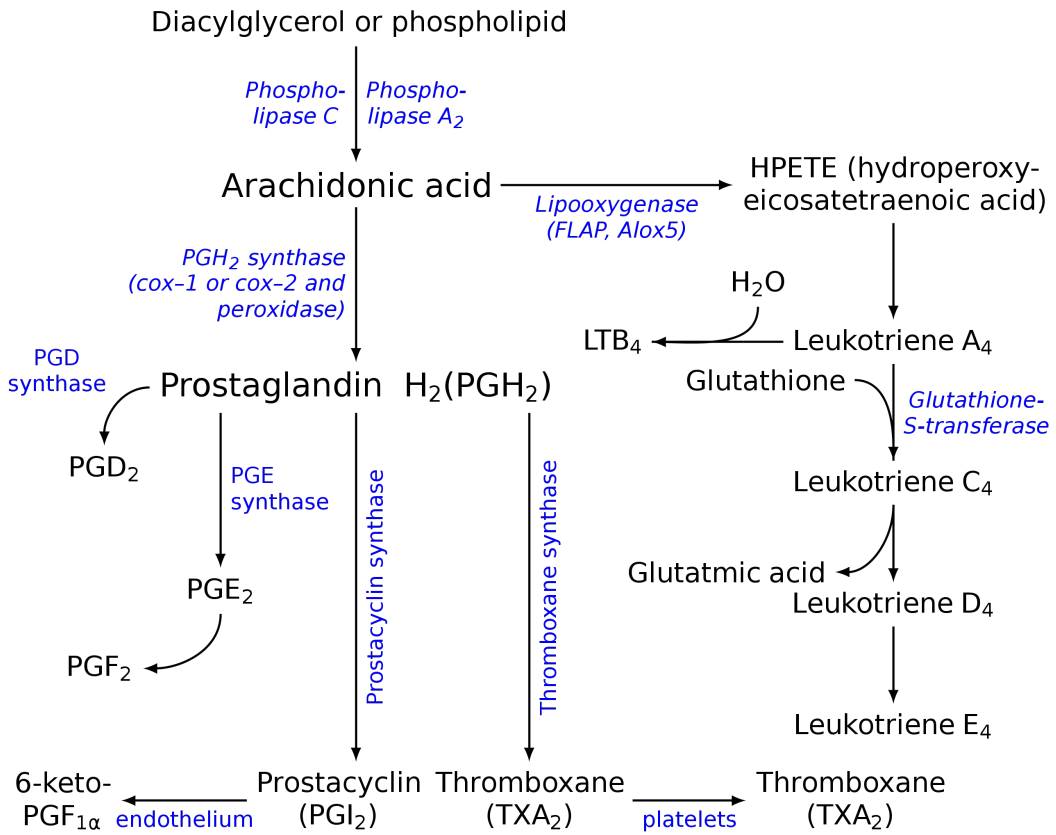


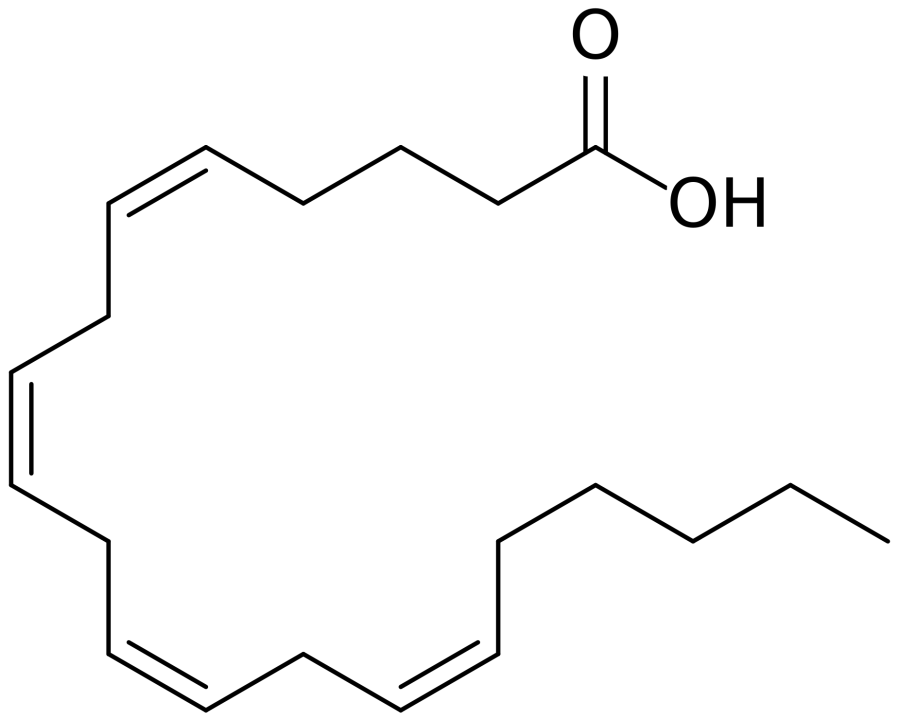
- DAG → 2-AG (via DAGL-alpha)
  - 2-AG is degraded to AA and glycerol by MAGL
- NAPE → AEA (via NAPE-PLD)
  - AEA is degraded to AA and ethanolamine ($EtNH_2$) by FAAH

biologydictionary.net/endocannabinoid-system/. Ramer. *Front Pharmacol*. 09 May 2019.

Arachidonic Acid

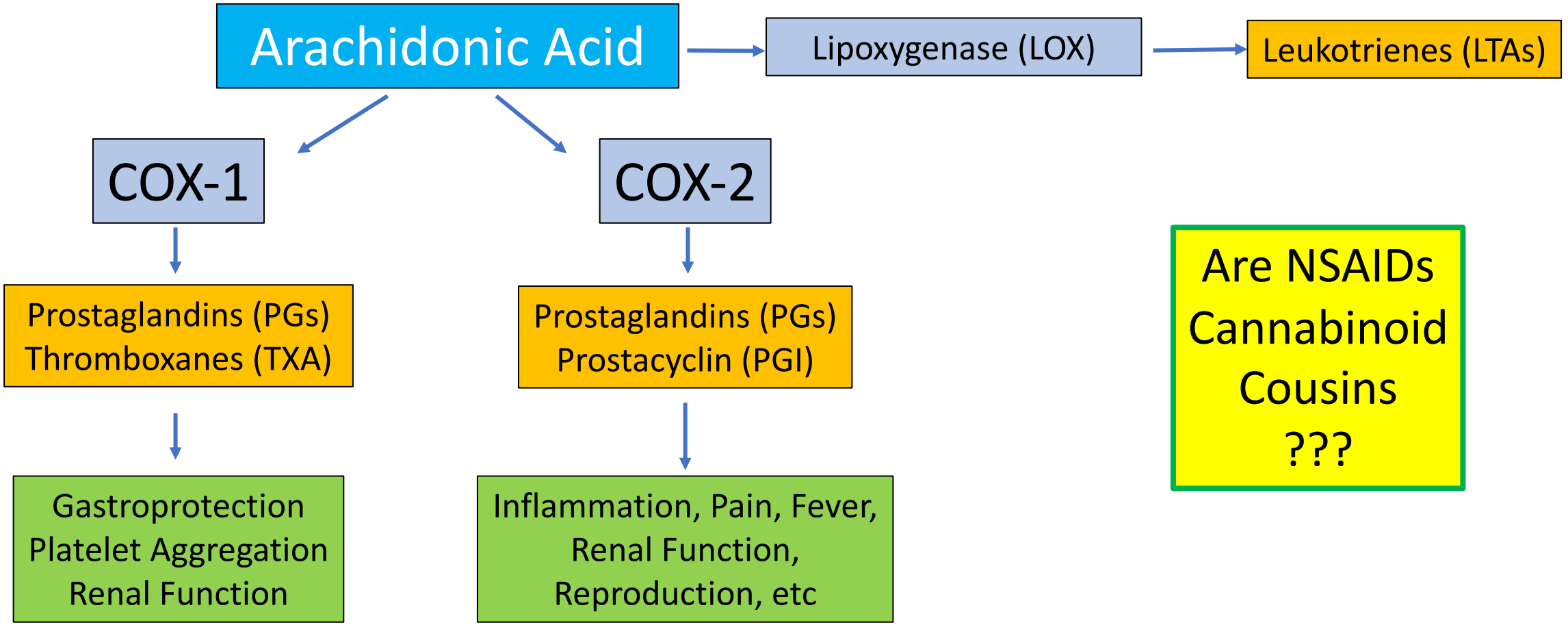
An Omega-3 Fatty Acid





www.painresearchforum.org/news/51110-peripheral-gaba-relieves-trpv1-sensitization-thermal-hypersensitivity. Ramer. *Front Pharmacol*. 09 May 2019.

Arachidonic Acid Cascade



Major Side Effects of NSAIDs & COX-2 Selective Inhibitors. March 2017. tmedweb.tulane.edu/pharmwiki/doku.php/nsaid_side_effects.

PPARs

Peroxisome Proliferator-Activated Receptors

- Alpha
  - PPARα influences fatty acid metabolism and lowers lipid levels (increases HDL)
  - Fibrates are PPARα activators
- Gamma
  - PPARγ is involved in adipogenesis, energy balance, and lipid biosynthesis
    - Increase glucose uptake and glycogen synthesis
  - PPARγ plays a crucial role in the functioning of the nervous system
  - Thiazolidinediones are PPARγ agonists
- Beta and delta
  - Participate in fatty acid oxidation
  - Regulate glucose and cholesterol
  - Studied as prevention of obesity with a high-fat diet

➢PPAR-α/γ dual agonists are being studied

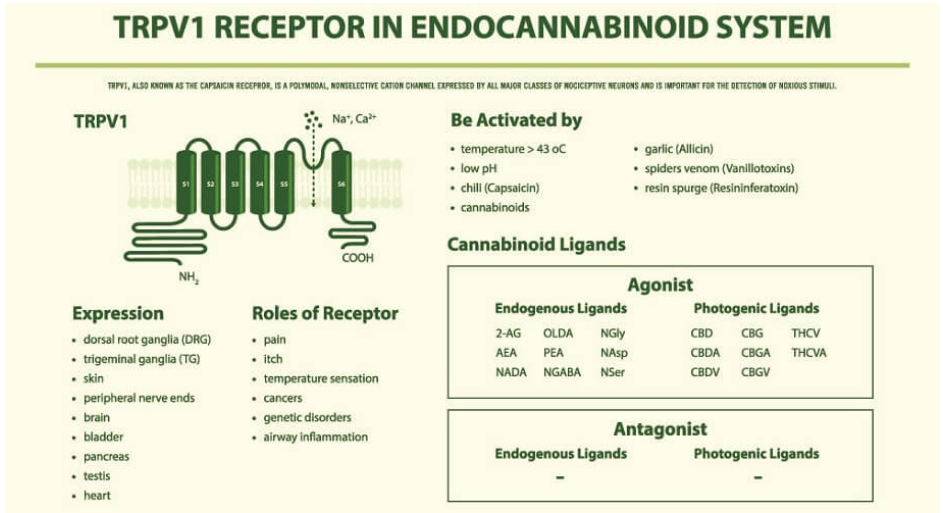
➢Hypolipemic, hypotensive, anti-atherogenic, and anti-inflammatory

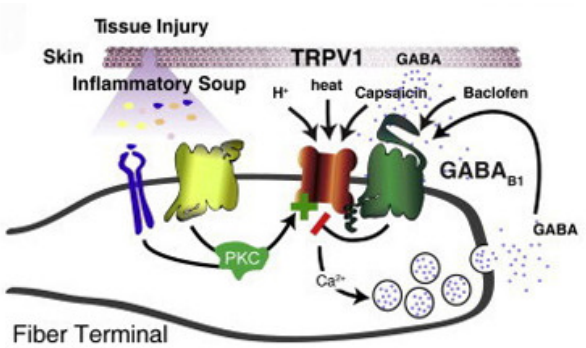
Grygiel-Górniak. *Nutr J*. 2014;13:17.

TRPVs

Transient Receptor Potential Subfamily V Member 1

- Transient receptor potential (TRP) family
- Activated by AEA and CBD
- Main function: detect and regulate heat
- Acts as an integrator of inflammatory signal
- Medication with TRPV MoA: capsaicin

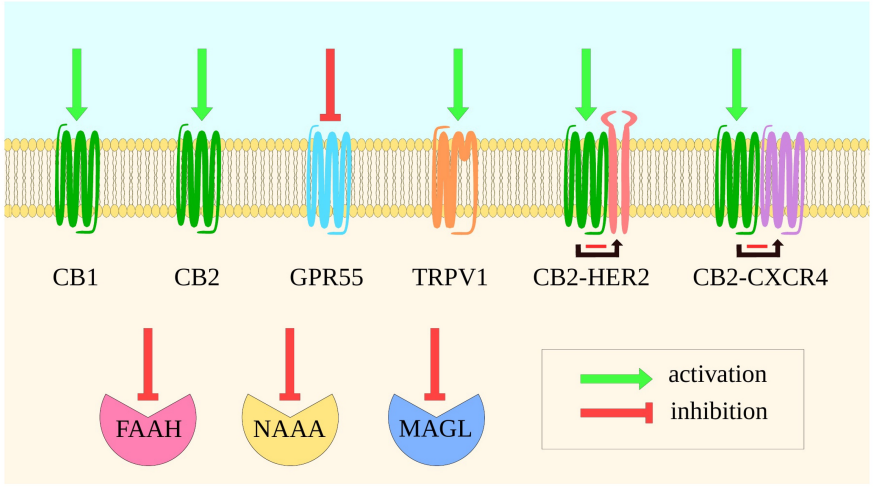


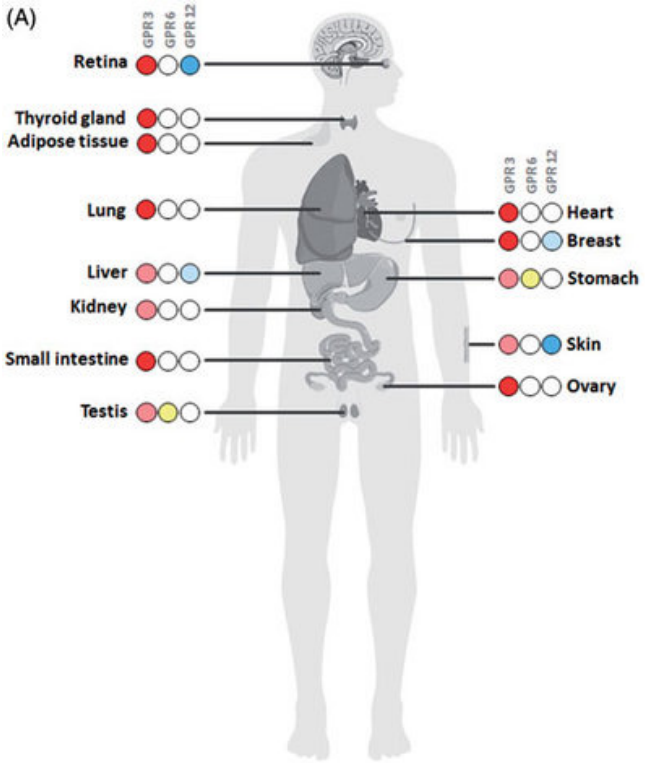


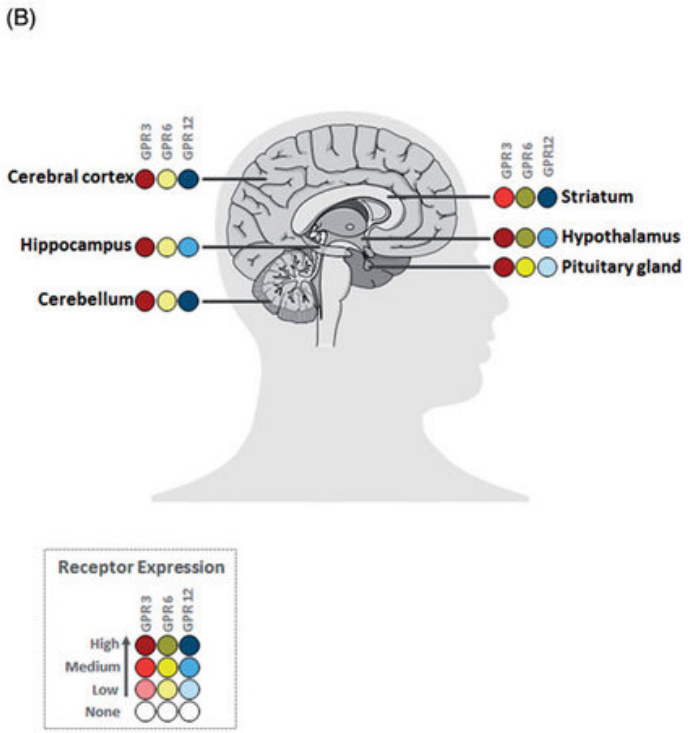
biologydictionary.net/endocannabinoid-system/.
www.painresearchforum.org/news/51110-peripheral-gaba-relieves-trpv1-sensitization-thermal-hypersensitivity.
Ramer. *Front Pharmacol*. 09 May 2019.

GPRs & GCPRs

- G-coupled proteins
- G-coupled protein receptors





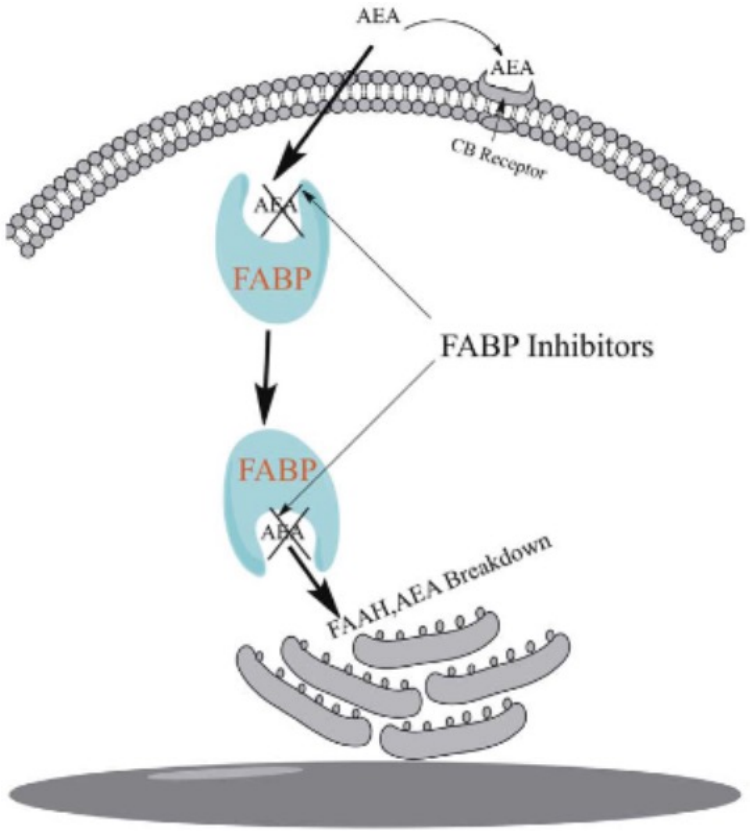


www.painresearchforum.org/news/51110-peripheral-gaba-relieves-trpv1-sensitization-thermal-hypersensitivity.
Ramer. *Front Pharmacol*. 09 May 2019.

FABPs

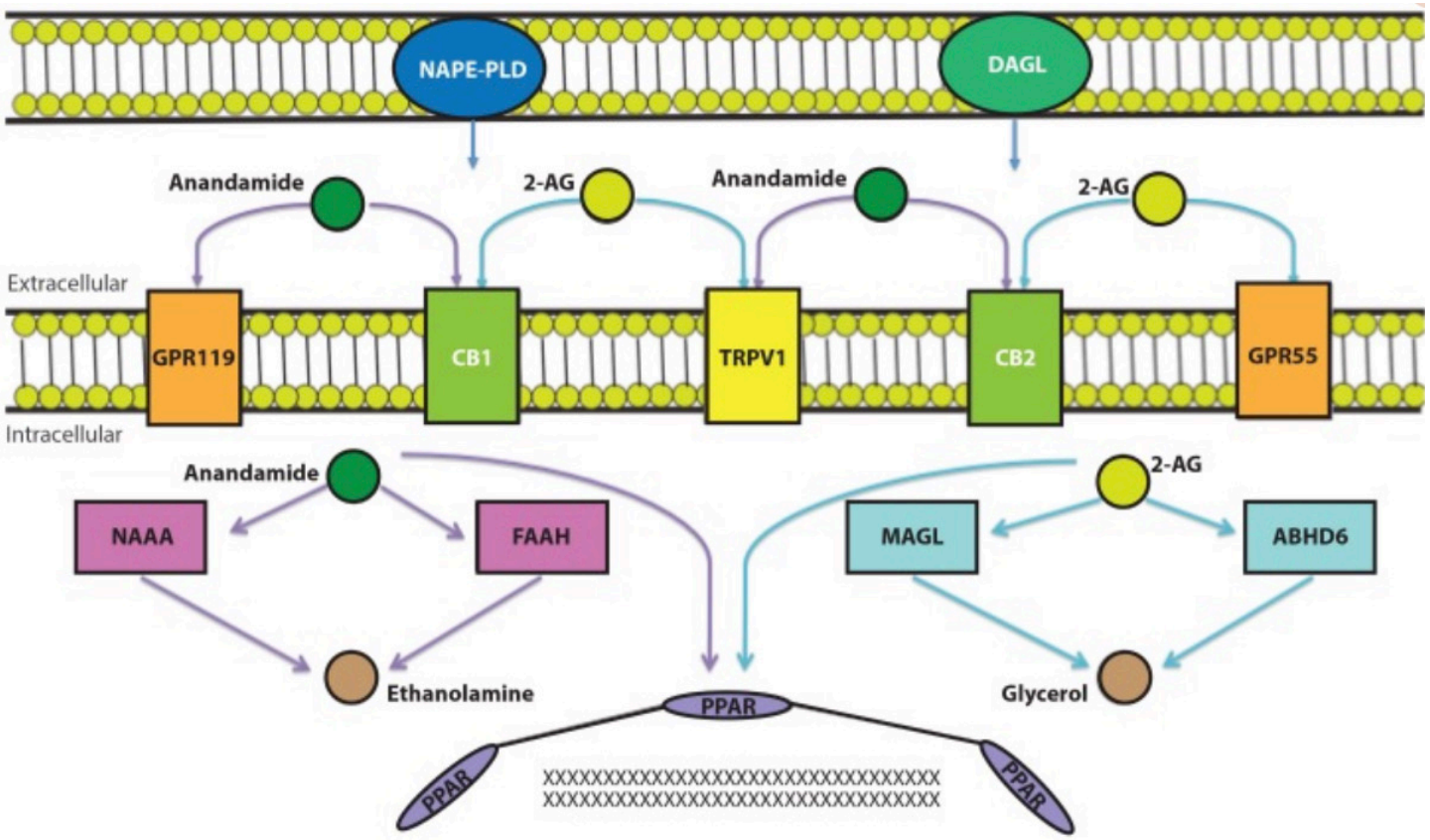
Fatty Acid Binding Proteins

- Transport AEA and 2-AG to PPAR
- Transport 2-AG to MAGL (for breakdown)
- Transport AEA to FAAH (for breakdown)
- FABP inhibitors attenuate AEA degradation by FAAH



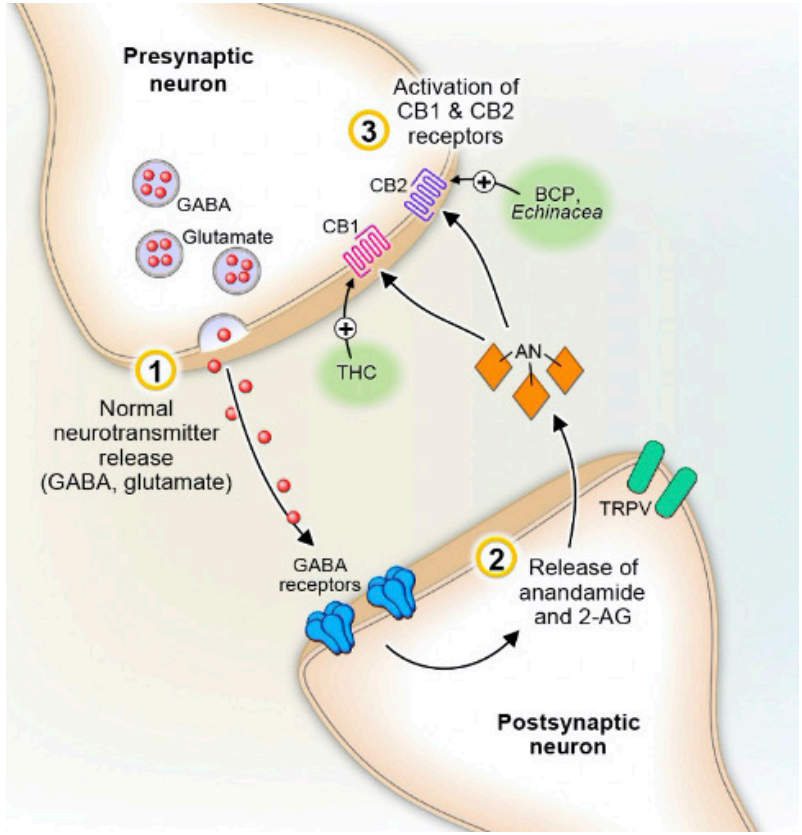
www.painresearchforum.org/news/51110-peripheral-gaba-relieves-trpv1-sensitization-thermal-hypersensitivity.
Ramer. *Front Pharmacol*. 09 May 2019.

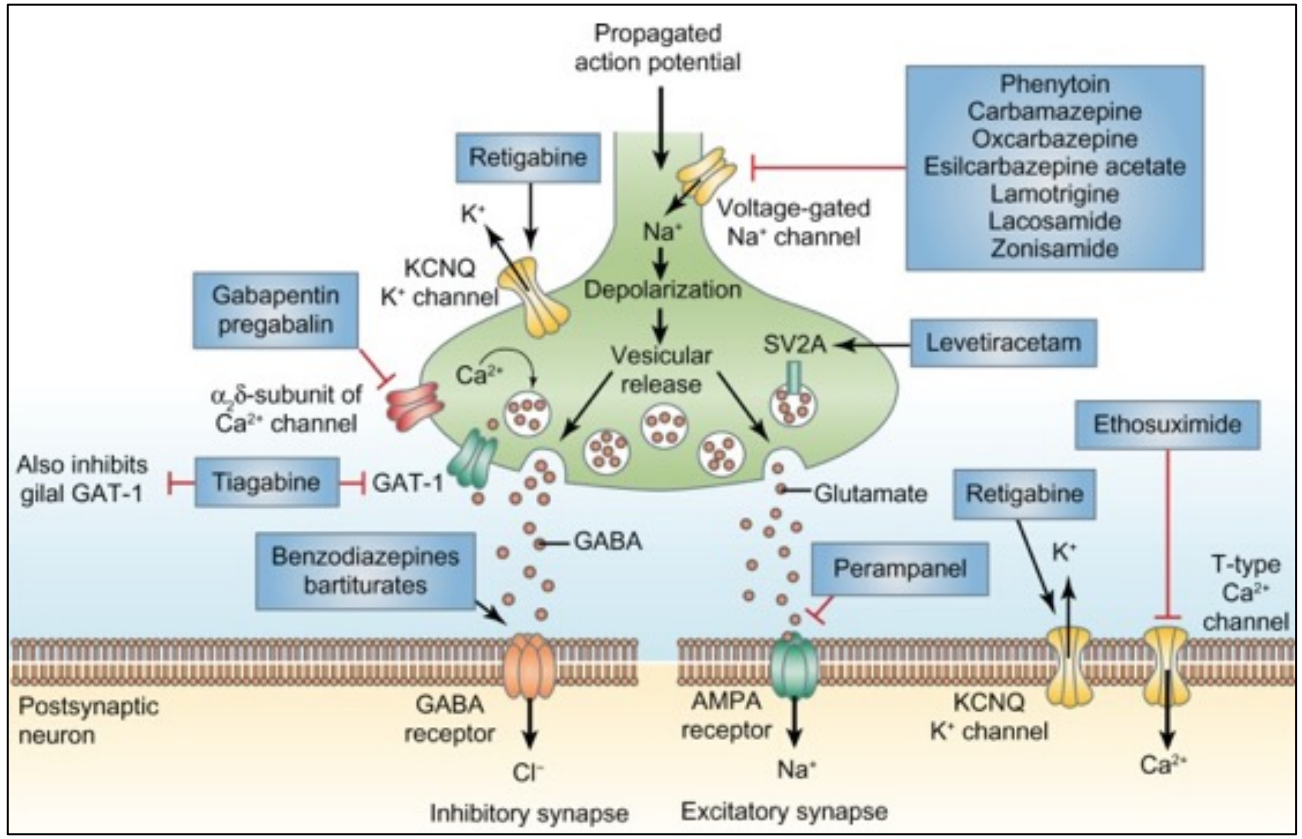
ABCannabinoids



Ahmed. *Gastroenterol Hepatol (N Y)*. 2016;12(11):668-679.

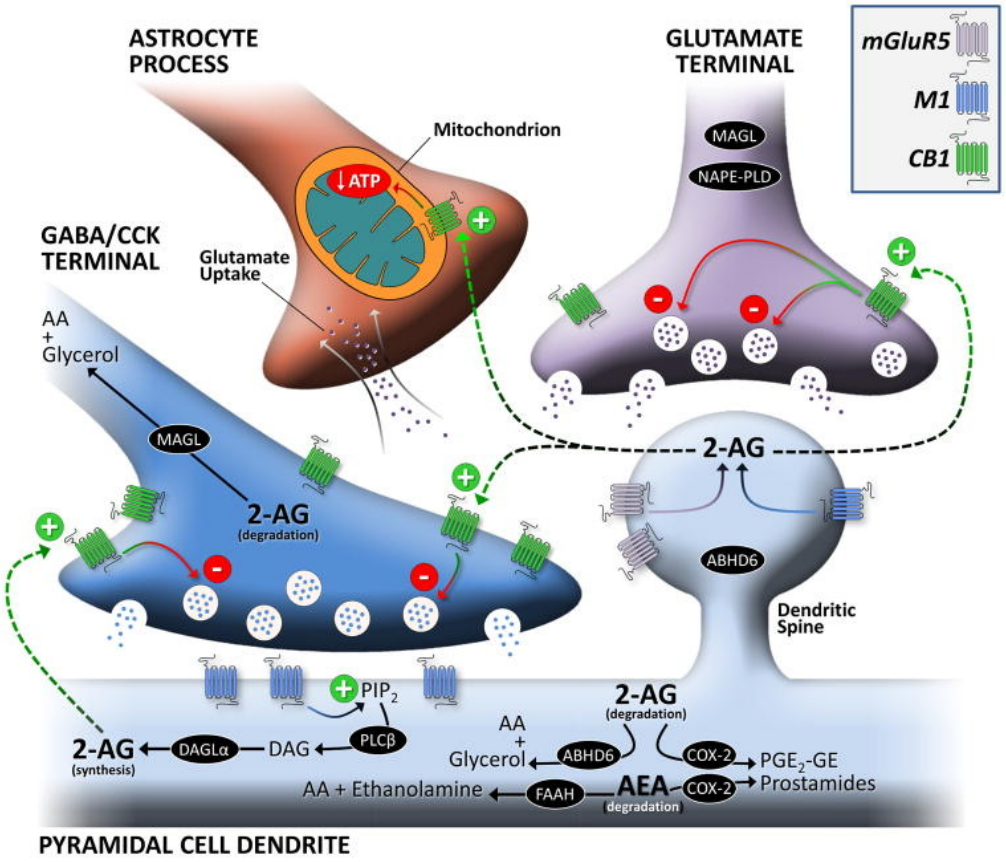
GABBA, GABBA, GABBA





basicmedicalkey.com/sedative-hypnotic-and-anxiolytic-drugs-2/.
Mayo Clinic Proceedings 2019;94:1840-1851.

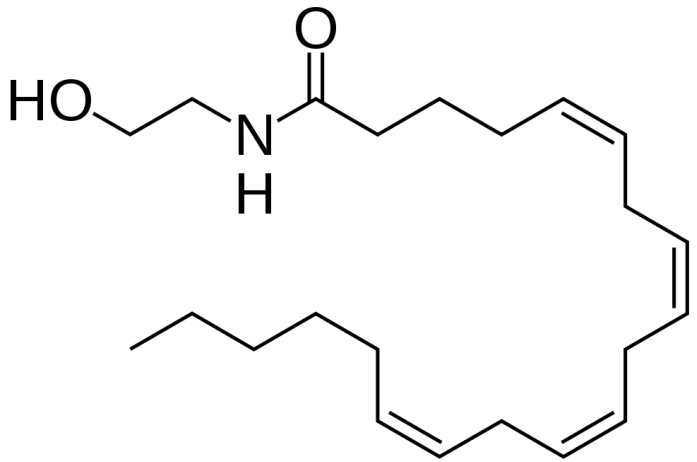
Endocannabinoids

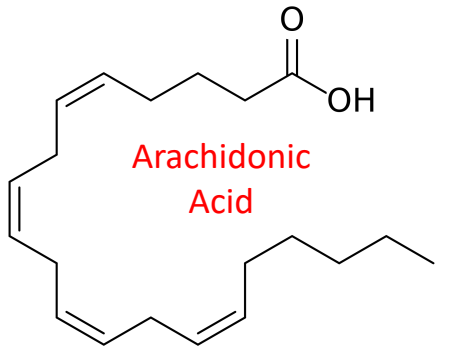


Lu. *Biol Psychiatry*. 2016;79(7):516-525.

Anandamide (AEA)

- Endocannabinoid
- Origin
  - Ananda (Sanskrit for “bliss, joy, delight”)
  - Amide (nitrogen)
- Fatty acid amide hydrolase (FAAH) enzyme
  - Metabolizes anandamide into ethanolamine and arachidonic acid
  - FAAH inhibitors are in clinical development
- 1992: First described and named by Raphael Mechoulam

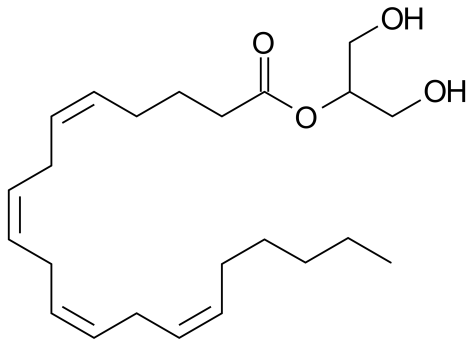




Mayo Clinic Proceedings. 2019;94:1840-1851.

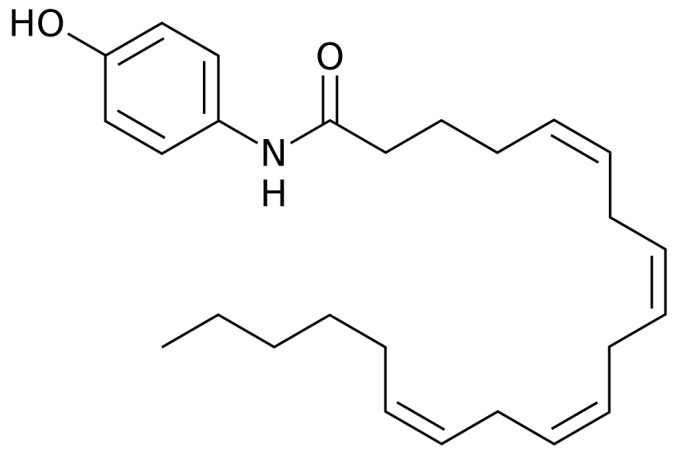
2-Arachidonylglyerol (2-AG)

- CB1 and CB2 agonist
- Ester formed from the omega-6 fatty acid arachidonic acid and di-acyl-glycerol
- Brain 2-AG levels are ~170 times higher than those of anandamide (AEA)
- Synthesized on-demand acting as a retrograde messenger inhibiting neurotransmitter release at both inhibitory and excitatory synapses (mediating plasticity)



Baggelaar. *Prog Lipid Res*. 2018;71:1-17.

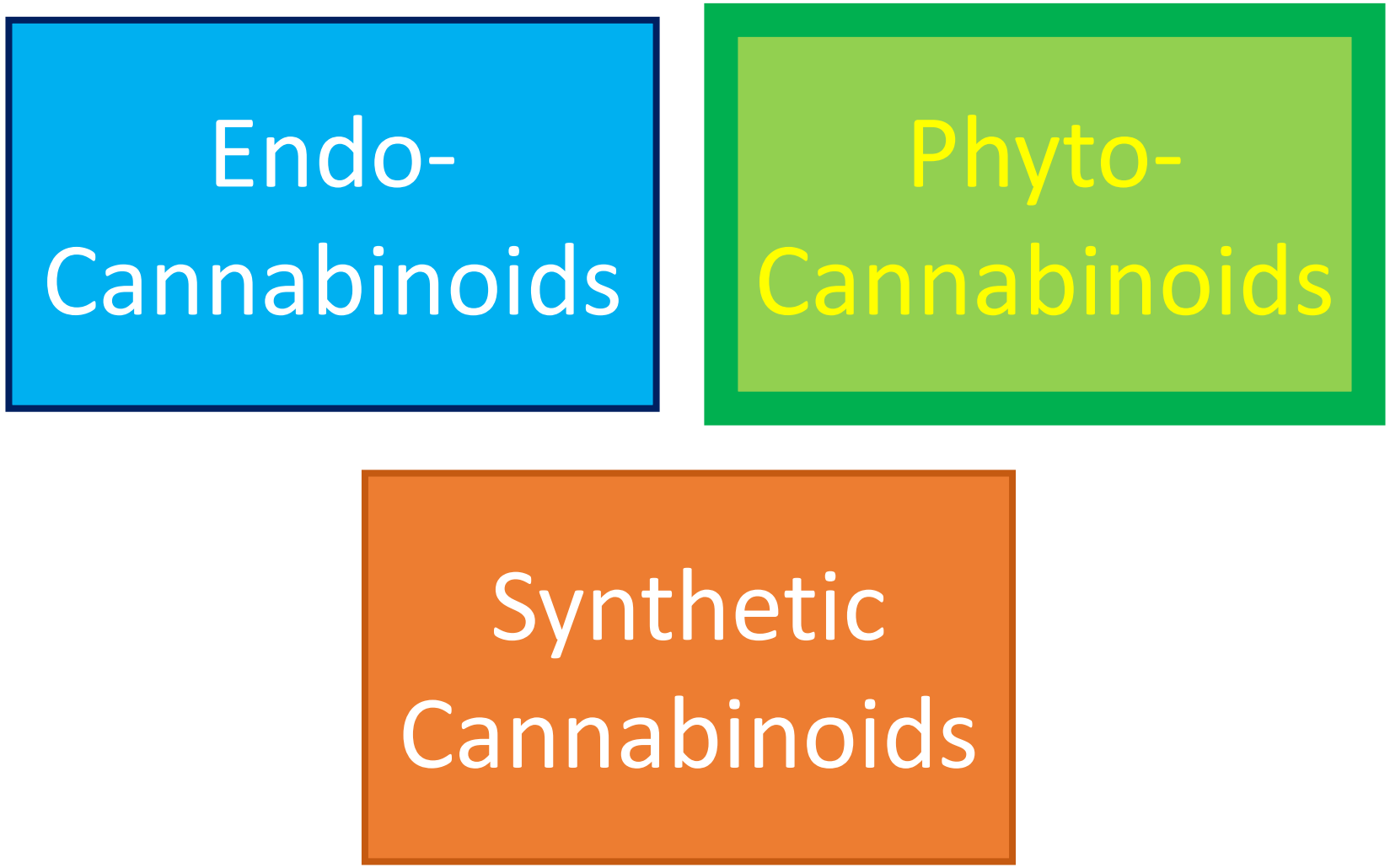
N-Arachidonoylaminophenol (AM-404)



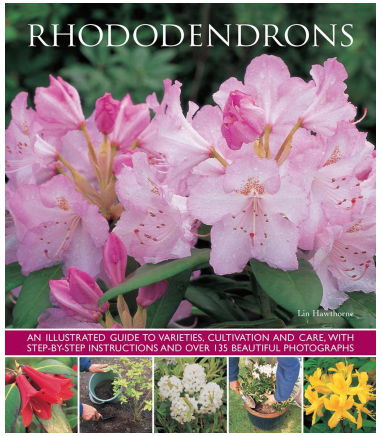
- An active metabolite of acetaminophen
- Mechanisms of action
- Endogenous cannabinoid reuptake inhibitor (ECRI)
  - Think SSRI MoA, but cannabinoid instead of serotonin
- TRPV-1 agonist
- COX-1 and COX-2 inhibitor

Mayo Clinic Proceedings. 2019;94:1840-1851.

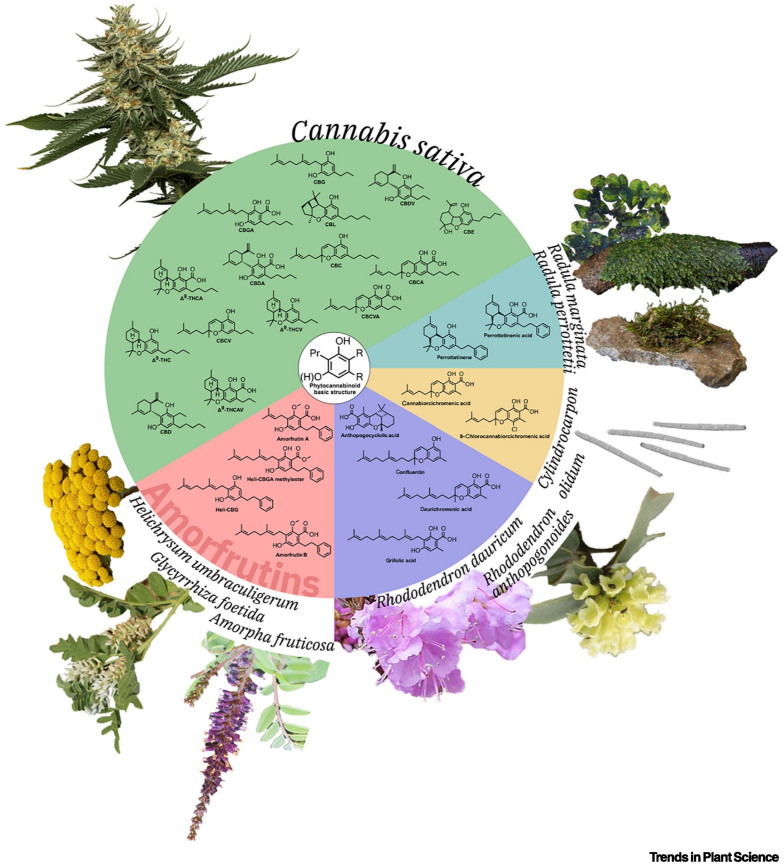
Cannabinoids

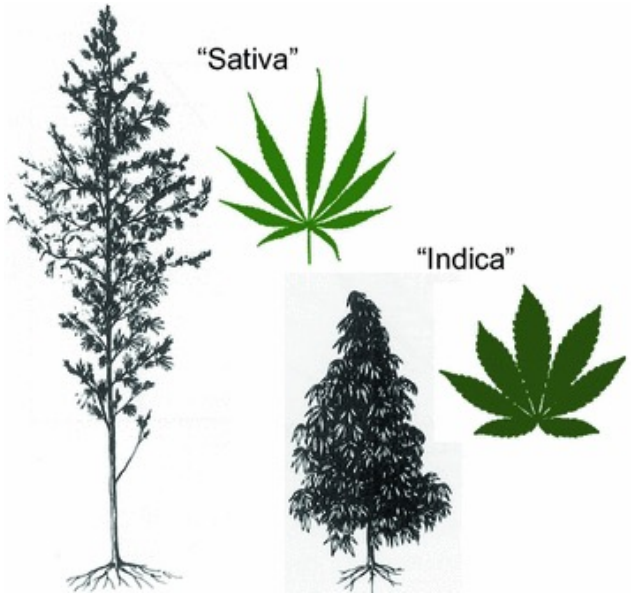


Cannabinoid Natural Sources



Echinacea

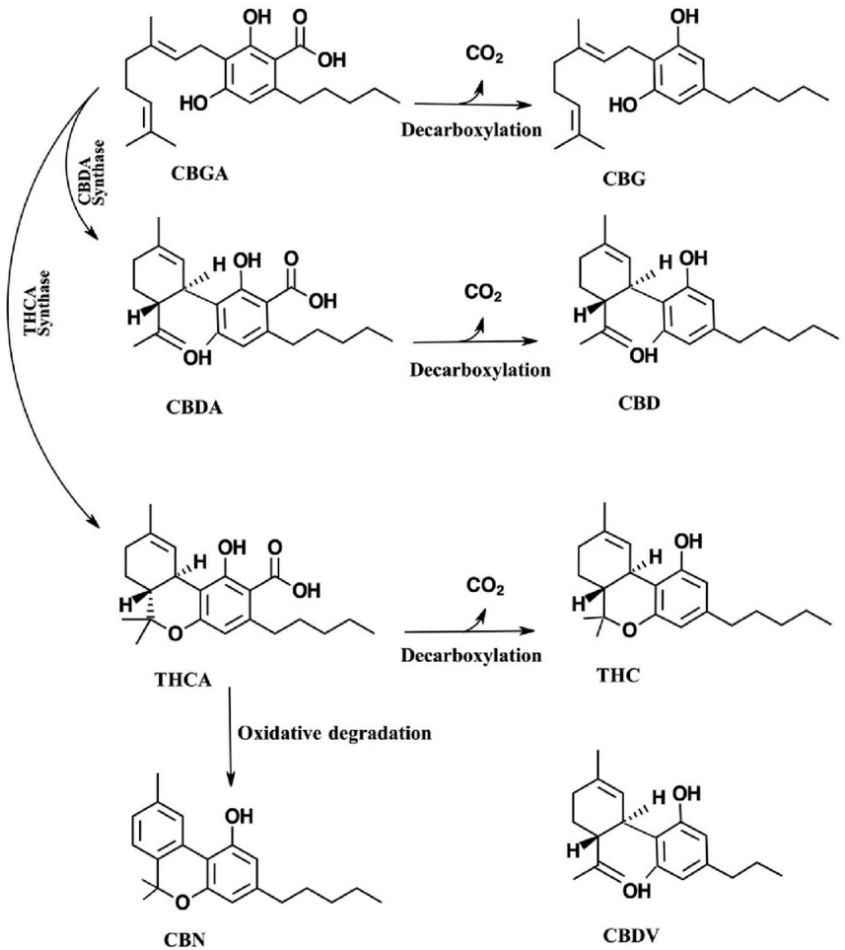




Trends Plant Sci. 2020 25985-1004.
Gertsch. *Br J Pharmacol*. 2010;160:523-529.

A Pot Full of Cannabinoids...

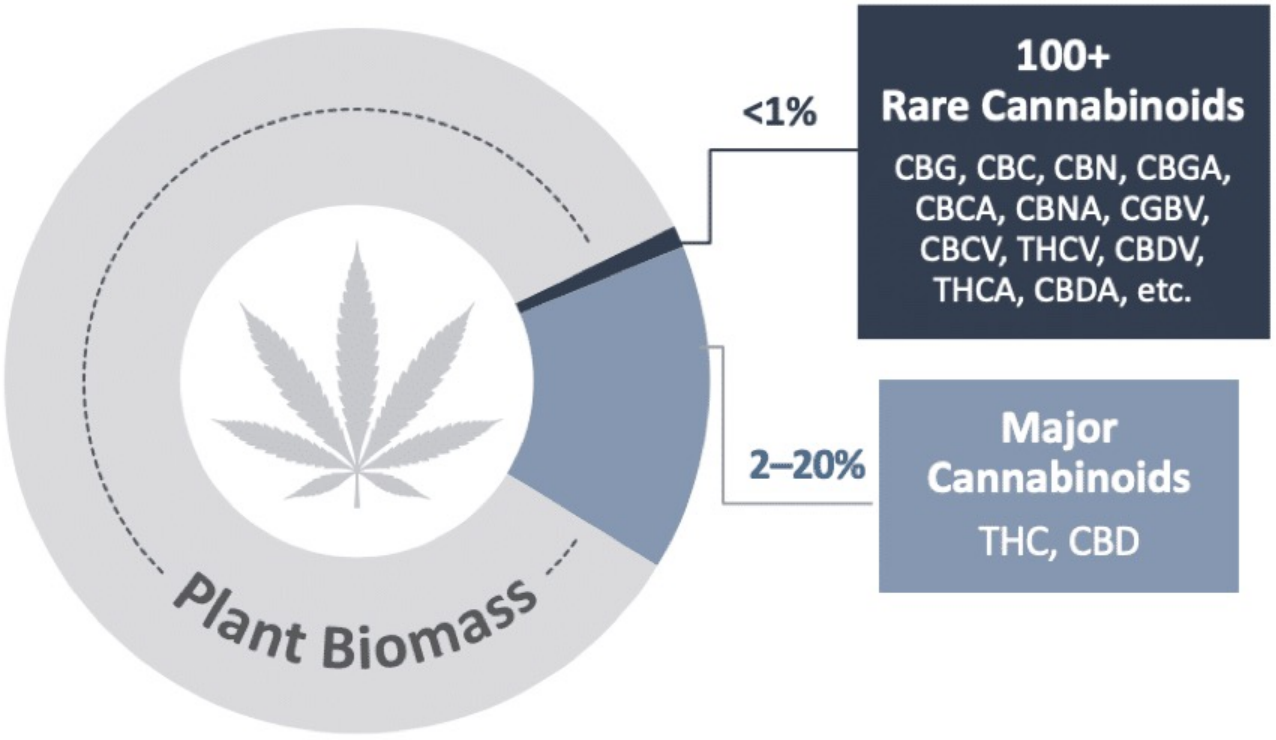
Cannabis Biosynthesis & Conversion of Cannabinoids



- CBGA: Cannabigerolic acid
- CBG: Cannabigerol
- CBDA: Cannabidiolic acid
- CBD: Cannabidiol
- THCA: Tetrahydrocannabinolic acid
- THC: Tetrahydrocannabinol
- CBN: Cannabinol
- CBDV: Cannabidivarin

www.researchgate.net/figure/Major-cannabinoids-present-in-Cannabis-sativa-L-Biosynthesis-and-conversion-pathways_fig1_332566538.

A Pot Full Of Cannabinoids

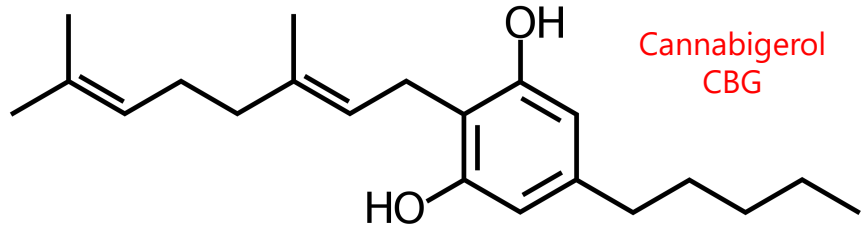


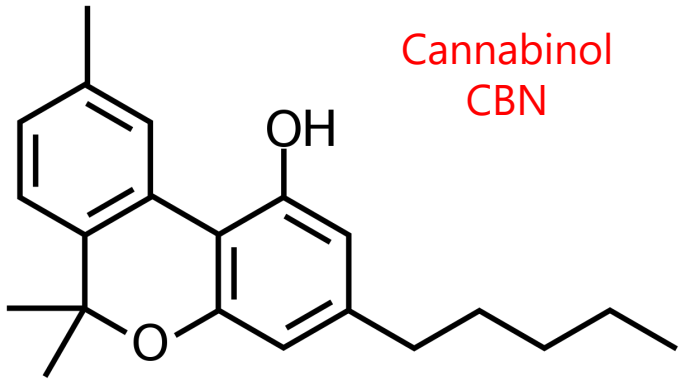
www.inmedpharma.com/media-news/cannabinol-101-the-science-of-cannabinol-cbn/.

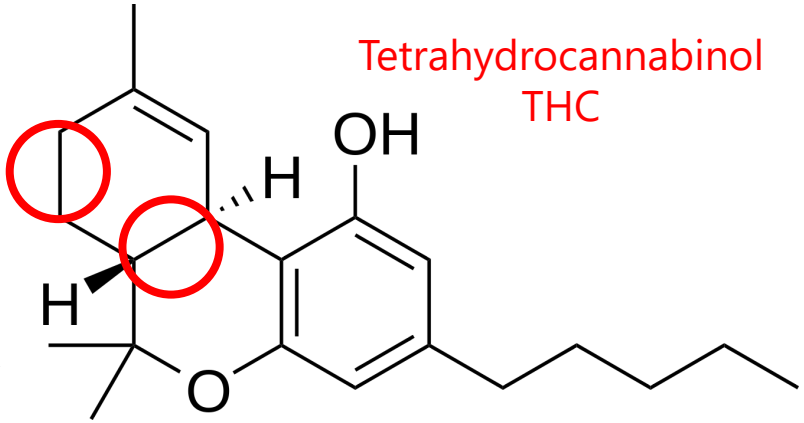
Phytocannabinoids

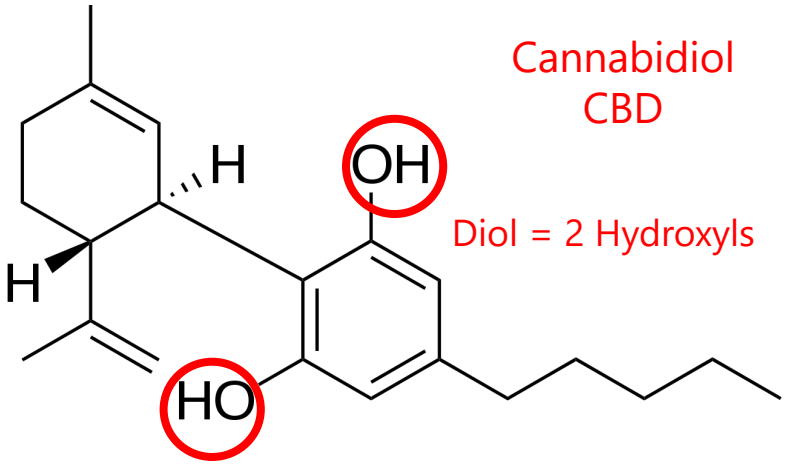
100+ (Highlighting Big 4)

- CBG (Cannabigerol)
- CBN (Cannabinol)
- THC (Tetrahydrocannabinol)
- CBD (Cannabidiol)





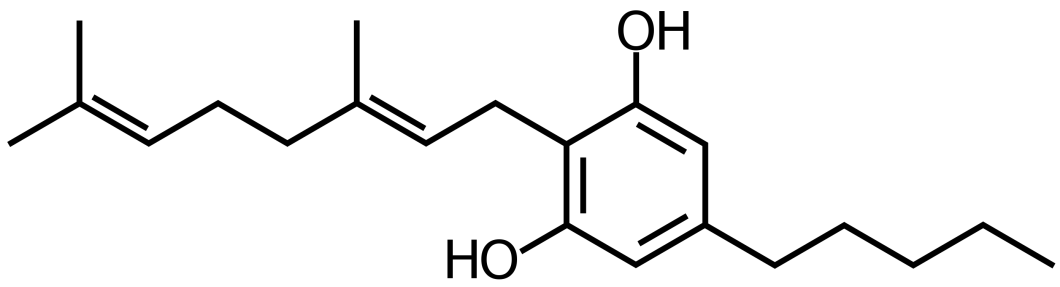




Horn. *Pharmacy Times*. Dec 2014.
www.royalqueenseeds.com/blog-cannabinol-cbn-what-is-it-and-what-are-its-effects-n474.

Cannabigerol (CBG)

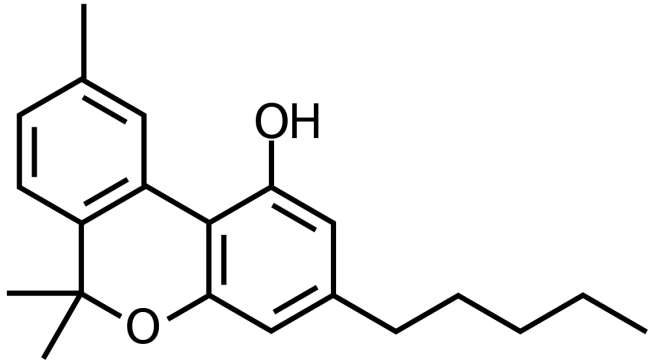
- "Mother of All Cannabinoids"
  - Plant produces 1st, then converted to other cannabinoids
- Constitutes <1% of cannabinoids in plant
- Mechanisms of action
  - Partial CB1 and CB2 agonist
    - Preferential CB2
  - Alpha-2 agonist
  - $5HT_{1A2}$ antagonist
  - TRPV1 agonist
  - Suggested to be a PPAR-gamma agonist

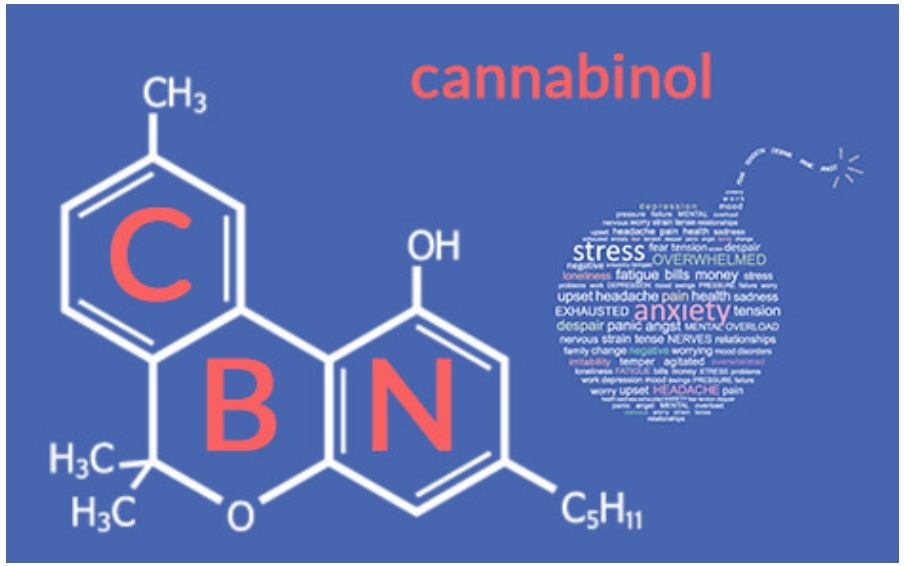


cannigma.com/plant/what-is-cbg/.

Cannabinol (CBN)

- 1st isolated natural cannabinoid (1896)
- Product of the degradation of THC
  - Heat and light
  - Not a THC metabolite
  - Not derived from CBG
- Mechanisms of action
  - CB1 and CB2 partial agonist
    - CB2 > CB1 receptor affinity

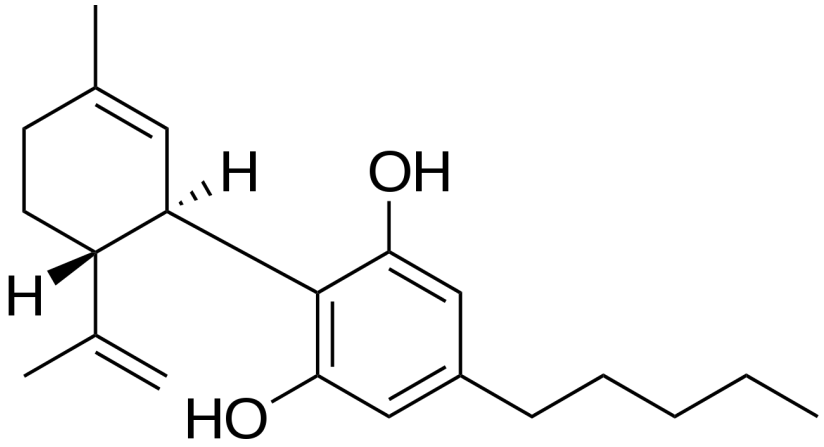




Horn. *Pharmacy Times*. Dec 2014.

Cannabidiol (CBD)

- Discovered in 1940
- 40% of plant cannabinoid extract
- Mechanisms of action
  - Indirect CB1 antagonist
  - GPR18 partial agonist and GPR55 antagonist
  - PPARγ agonist
  - $5HT_{1A}$ agonist
  - Mu and delta opioid modulator
- May reduce THC Clearance
- Bioavailability: oral (6%) and inhalation (11% to 45%)



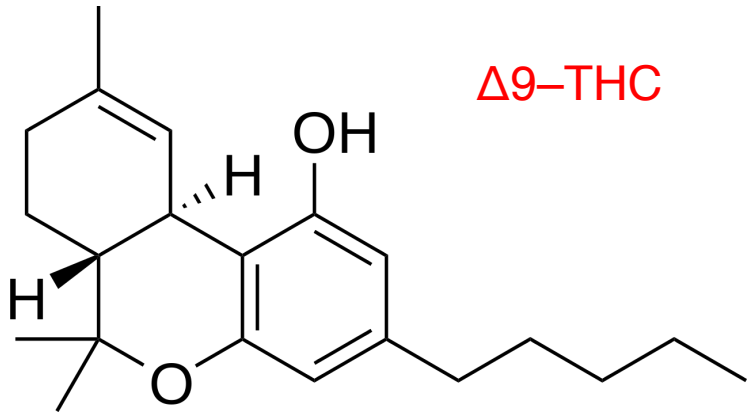
- t ½: 18 to 32 hours

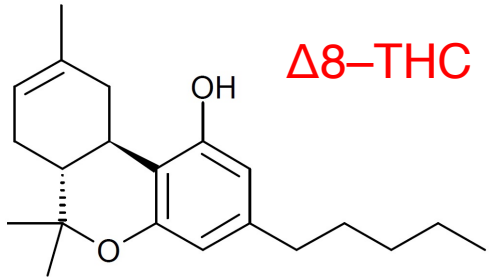
➢ CBD derived from hemp (with 0.3% THC or lower) is legal to sell as a cosmetics ingredient, but cannot be sold under federal law in food or dietary supplements

Horn. *Pharmacy Times*. Dec 2014.
Kathmann. *Naunyn Schmied Arch Pharmacol.* 2006;372:354-361.

Tetrahydrocannabinol (THC)

- Δ9–tetrahydrocannabinol
  - Δ8–tetrahydrocannabinol also exists
- Mechanism of action
  - CB1 partial agonist
- Inhalation
  - Immediate absorption
  - Peak 15 to 30 minutes
  - Taper off in 2 to 3 hours
- Oral ingestion
  - Effects delayed (30 minutes to 1 hour)
  - Peak 2 to 3 hours
  - Taper off in ~12 hours
- Highly lipophilic
  - Distributing rapidly to highly perfused tissues, and later to fat tissue





Horn. *Pharmacy Times*. Dec 2014.
Bridgeman. *P T*. 2017;42(3):180-188.

Cannabinoid Receptor Affinity
CBG, CBN, THC, and CBD

Green: Agonist
Purple: Partial Agonist
Red: Antagonist

Phytocannabinoid	CB1	CB2
CBG	+	+
CBN	+	+
THC	+	
CBD	×	

www.inverse.com/mind-body/thc-cbd-the-science-of-cannabinoids-and-the-brain
Navarro. *Front Pharmacol*. 2018;9:632.

Cannabinoids

Endo-Cannabinoids

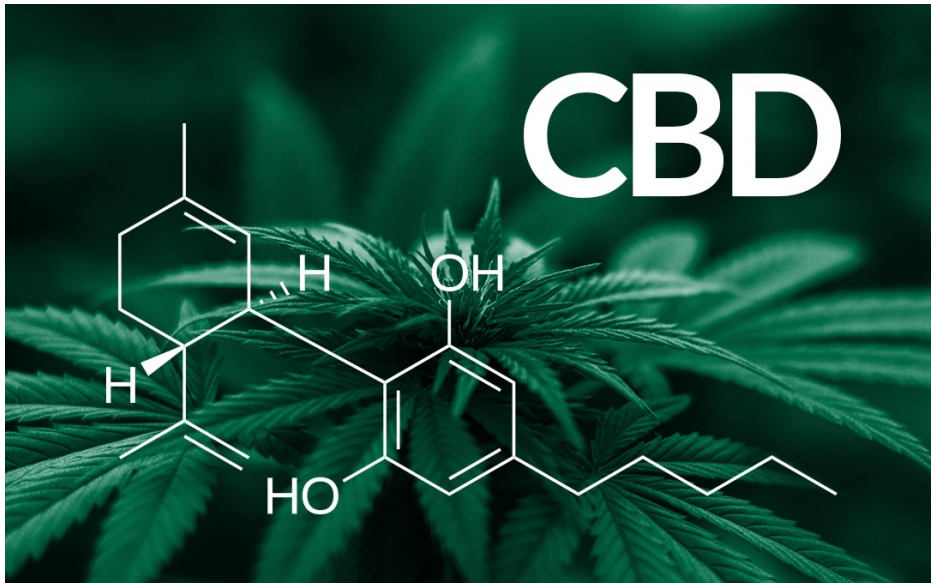
Phyto-Cannabinoids

Synthetic Cannabinoids

Synthetic Cannabinoids
CBD Derivatives

See “Medical” & Recreational Marijuana Course

- Hydrogenated
- Dimethylheptyl (DMH)
- C4′-alkyl chain modifications
- Halogenated (Cl, Br, Fl, & I)
- Hydroxyl
- Diacetylated
- Quinones



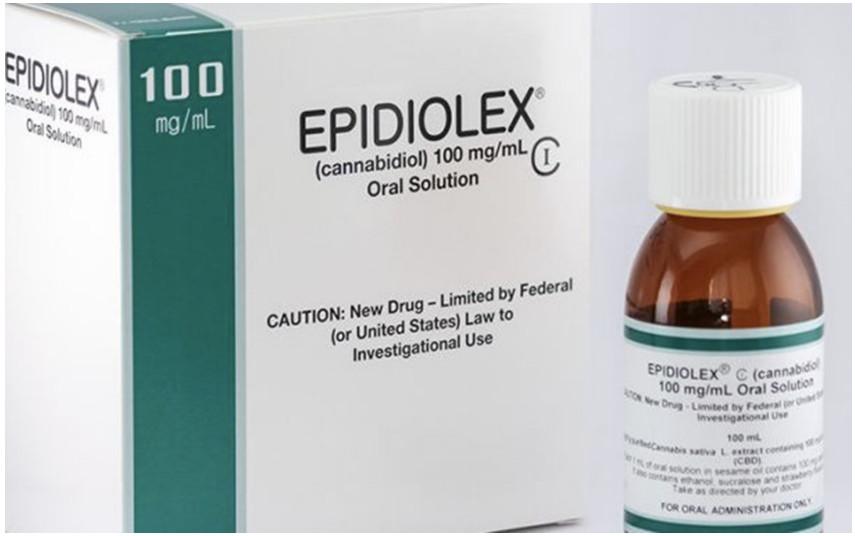
Synthetic Cannabinoids
THC Derivatives

See “Medical” & Recreational Marijuana Course

- 1st generation
  - Sterling-Winthrop Aminoalkylindoles (WIN-X)
  - John Williams Huffman (JWH-X)
  - Hebrew University (HU-X)
  - Charles Pfizer (CP-X)
- 2nd generation
  - Alkyl derivatives
  - N-methylpiperidines
  - Benzoindoles
- 3rd generation
  - Indoles
  - Indazoles

Synthetic Cannabinoids
Cannabidiol (Epidiolex)

- FDA approvals (>/= 2yo)
  - Dravet syndrome
  - Tuberous sclerosis
  - Lennox-Gastaut syndrome (LGS)



Clinical Pharmacology Online Database.

Synthetic Cannabinoids

Tetrahydrocannabinol Products

- Dronabinol (Marinol®) capsules
- Syndros®: liquid, C3
- FDA approvals
  - Chemo-induced N/V
  - Aids-anorexia
- Off-label
  - Cancer-anorexia
  - Intractable pruritus secondary to cholestatic liver disease

Clinical Pharmacology Online Database.

Synthetic Cannabinoids

CBD and THC (Nabiximols)

Approvals and trials

- Approved for MS spasticity in >2 dozen countries (Canada, Mexico, Europe, etc)
- Approved for MS neuropathic pain and cancer pain in Canada
- US Phase 3 clinical trials (MS spasticity and neuropathic pain)

Dosage

- Each 100-microliter spray contains:
  - 2.7 mg delta-9-tetrahydrocannabinol (THC)
  - 2.5 mg cannabidiol (CBD)
- Dose titration (sprays)
  - Starting with 1/day up to 12/day

www.practicalpainmanagement.com/treatments/pharmacological/analgesics-future-potential-endocannabinoid-system.

Synthetic Cannabinoids
Nabilone

- Nabilone capsules
- Controlled Substance Class 2
- FDA approval: chemo-induced N/V (CINV)

Clinical Pharmacology Online Database.

The More Cs, the More Potency

Novel Cannabinoids

Cannabinoids and Carbon Chains

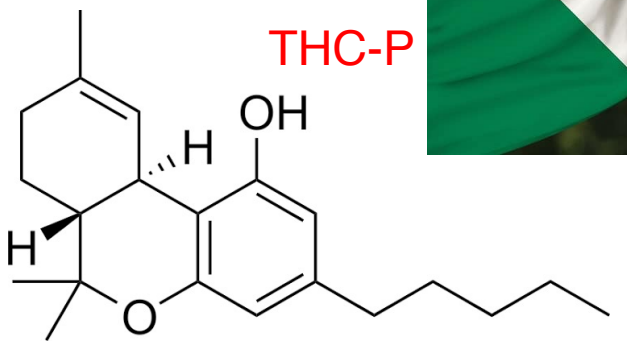
Novel Cannabinoids
Cannabinoids and Carbon Chains

The More Cs, the More Potency

Novel Cannabinoids
THC-P & CBD-P

7C

- 7-carbon chain as compared to 5-carbon chain
- THC-P (tetrahydrocannabiphorol)
  - THC-P is 33x > potent than THC
- CBD-P (cannabidiphorol)



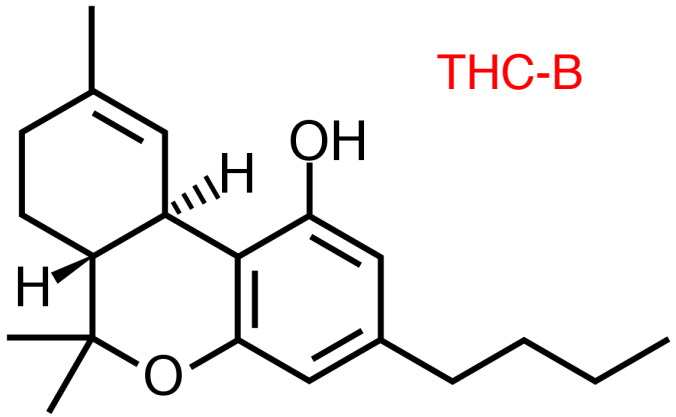
- First observed naturally in an Italian medicinal cannabis variety
  - Italian FM2

weedmaps.com/news/2020/08/an-in-depth-look-at-the-study-that-discovered-thcp-a-cannabinoid-more-potent-than-thc/.
Adams. *J Am Chem Soc.* 1941;63:1971-1973.
Martin. *J. Pharmacol Exp Ther.* 1999;290:1065-1079.
Citti. *Sci Rep.* 2019;9:20335.

Novel Cannabinoids
THC-B & CBD-B

4C

- Butyl 4-carbon chain
- THC-B (tetrahydrocannabutol)
- CBD-B (cannabidibutol)

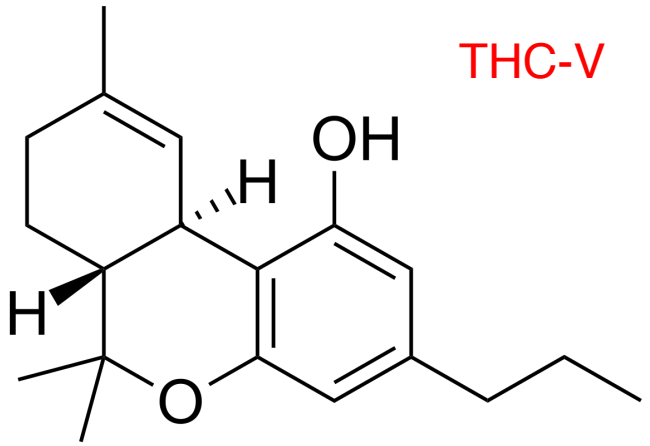


weedmaps.com/news/2020/08/an-in-depth-look-at-the-study-that-discovered-thcp-a-cannabinoid-more-potent-than-thc/.
Adams. *J Am Chem Soc.* 1941;63:1971-1973.
Martin. *J. Pharmacol Exp Ther.* 1999;290:1065-1079.
Citti. *Sci Rep.* 2019;9:20335.

Novel Cannabinoids
THC-V & CBD-V

3C

- Varinoid 3-carbon chain
  - Minimum Cs for CB-receptor binding
- THC-V (tetrahydrocannabivarin)
- CBD-V (cannabidivarin)

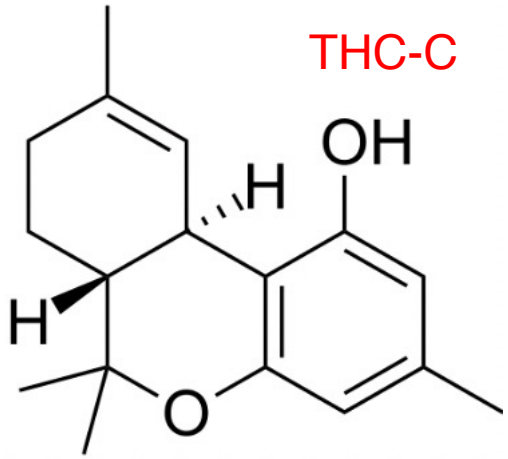


weedmaps.com/news/2020/08/an-in-depth-look-at-the-study-that-discovered-thcp-a-cannabinoid-more-potent-than-thc/.
Adams. *J Am Chem Soc.* 1941;63:1971-1973.
Martin. *J. Pharmacol Exp Ther.* 1999;290:1065-1079.
Citti. *Sci Rep.* 2019;9:20335.

Novel Cannabinoids
THC-C & CBD-C

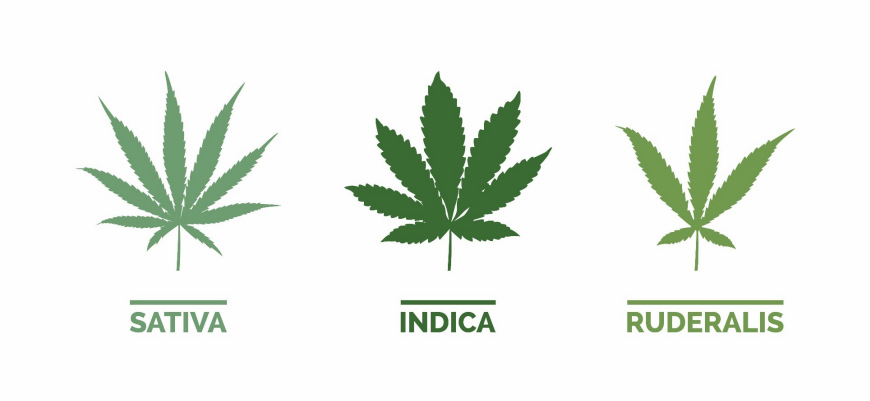
1C

- Orcinoid 1-carbon chain
- THC-C (tetrahydrocannabiorcol)
- CBD-C (cannabidiorcol)



weedmaps.com/news/2020/08/an-in-depth-look-at-the-study-that-discovered-thcp-a-cannabinoid-more-potent-than-thc/.
Adams. *J Am Chem Soc.* 1941;63:1971-1973.
Martin. *J. Pharmacol Exp Ther.* 1999;290:1065-1079.
Citti. *Sci Rep.* 2019;9:20335.

Cannabis & Cannabinoids



Endo-Cannabinoids

Phyto-Cannabinoids

Synthetic Cannabinoids

PainWeek

ADVANCED EDUCATION

CERTIFICATION SERIES

CANNABINOIDS

Cannabis & Cannabinoid Pharmacology

Mark Garofoli, PharmD, MBA, BCGP, CPE