



Why is cannabis broad-spectrum medicine.

Lumír Ondřej Hanuš

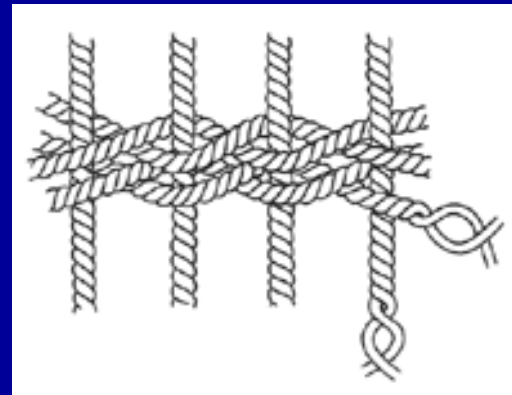
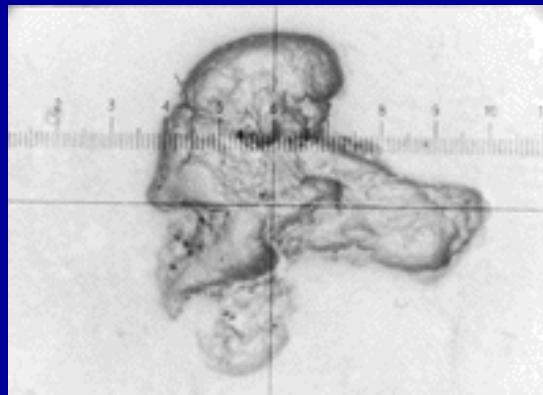
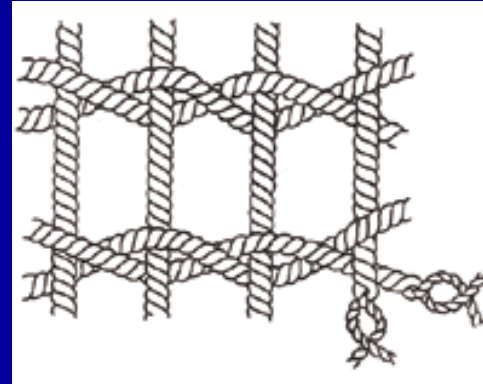
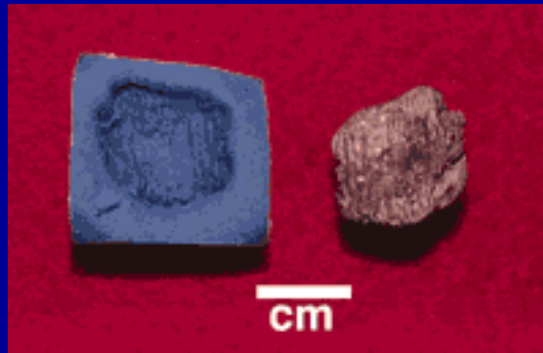
Hebrew University
Jerusalem, Israel

Medical Cannabis Conference 2016
Budapest
Wednesday, June 1th 2016



Siberia, Russia
September 2006

In the Czech Republic



Impressive techniques.

Positive cast and original impression (*image top left*), probably of type of weave illustrated to the right.

Positive cast (*image lower left*) of type of weave shown in lower right.

between 26,980 and 24,870 years ago



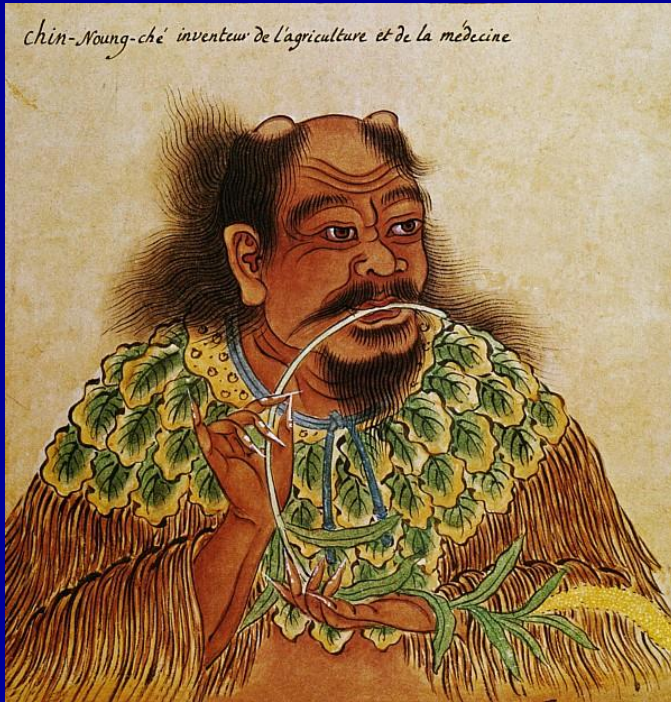
麻

In China
6,000 years ago



In China 4700 years ago during the reign of mythical emperor Shen-Nung the first evidence of the use of hemp (*chu-ma*, female hemp) as medicine to treat:

- malaria
- gout (arthritis urica)
- beri-beri (a nutritional deficit in thiamine)
- constipation
- rheumatism
- absentmindedness
- menstrual problems

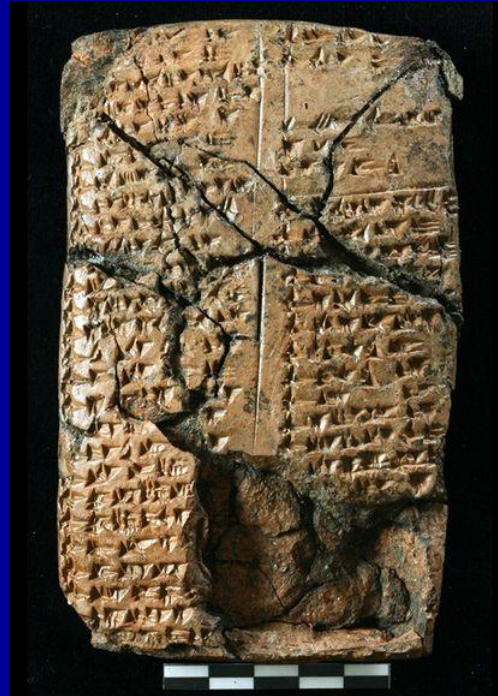


苧麻

He deemed *chu-ma* one of the Superior Elixirs of Immortality

Assyria

3000 – 2000 BC

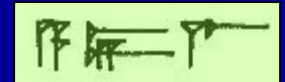


Gur-gur-ru – a ship's cable or rope of hemp

Qu-nu-bu – used in religious rites



A-zal-la – hand of the ghost, poison of all limbs
(nocturnal epilepsy)



Gan-zi-gun-nu – a drug which takes away the mind
(= cannabimimetic)

Egypt

1700 BC

Shm-shm-tu

„medical hemp“



hieroglyphs



demotic script

Ebers papyrus (1500 B.C.)

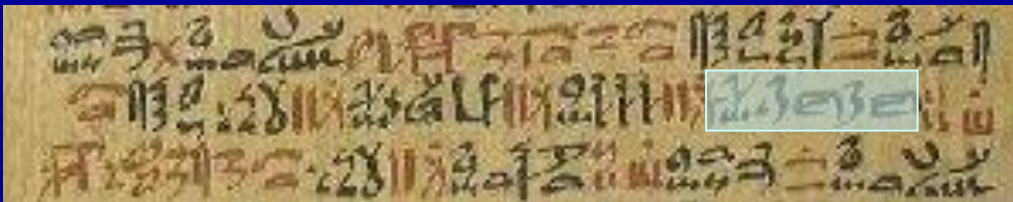
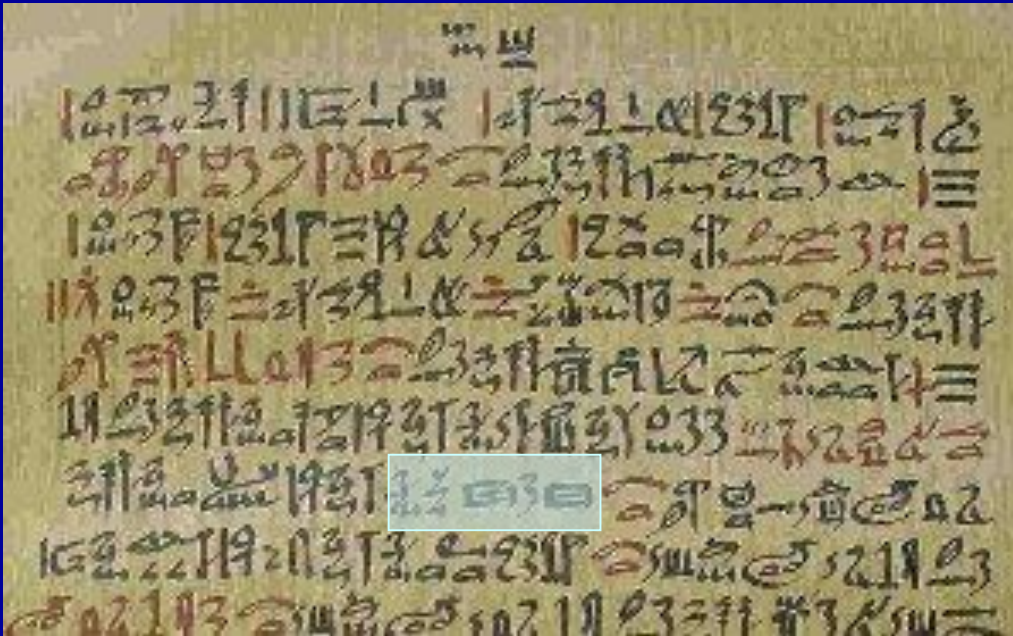
Lines 7 and 8:

„hemp ground in honey;
introduced into her vagina“

Treatment of inflammation

Lines 10 and 11:

Remedy for a toe-nail
(honey with ochre, hemp
and other ingredients)



India

2000 – 1400 BC

“a sacred grass, bhang “



अथर्ववेद
Atharva Veda

"preserve one from disease . . . and
prolong the years we have to live"



Scythians

an ancient Iranian people of horse-riding
nomadic pastoralists



5th century BC
Iron Age

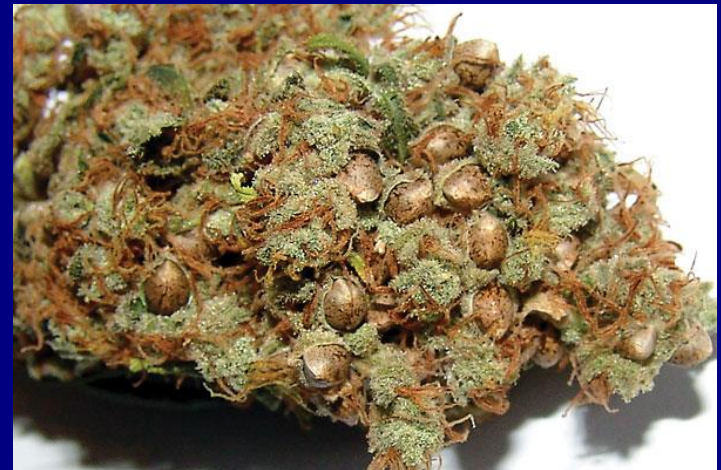


Scythian hemp seeds
Pazyryk, Siberia

Herodotus of Halicarnassus
The History, Book 4 - Melpomene

4.74 Hemp grows in Scythia...

4.75. The Scythians then take the seed of this hemp and creep under the felt coverings, and then they throw the seed upon the stones which have been heated red-hot: and it burns like incense and produces a vapour so thick that no vapour-bath in Hellas would surpass it: and the Scythians being delighted with the vapour-bath howl like wolves.



Treatment of breast cancer 2500 years ago

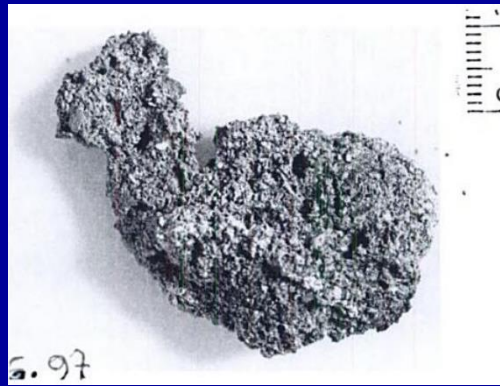


Cannabis and coriander seeds

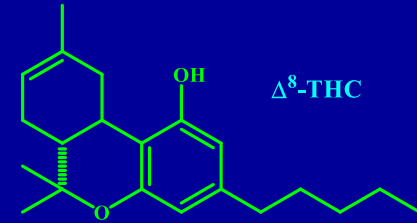
Treatment of breast cancer 2500 years ago



Judea



4th century AD



Were found the skeletal remains of a girl aged about 14 at death in a burial tomb in Beit Shemesh.

Were found the skeletal remains of a full-term fetus in the pelvic area of the girl, apparently in the last stages of pregnancy or giving birth at the time of her death.

In the abdominal area of the skeleton, a grey, carbonized material was recovered and analyzed.

It seems likely that the immature pelvic structure through which full-term fetus was required to pass was the cause of death in this case, due to rupture of the cervix and eventual haemorrhage.

Cannabis administered to the young girl as an inhalant to facilitate the birth process.



Ancient Rome

Pliny, the Elder (79 n.l.)

The roots boiled in water ease cramped joints, gout too and similar violent pain.



Ancient Greece

Pedanius Dioscorides
(90 n.l.)

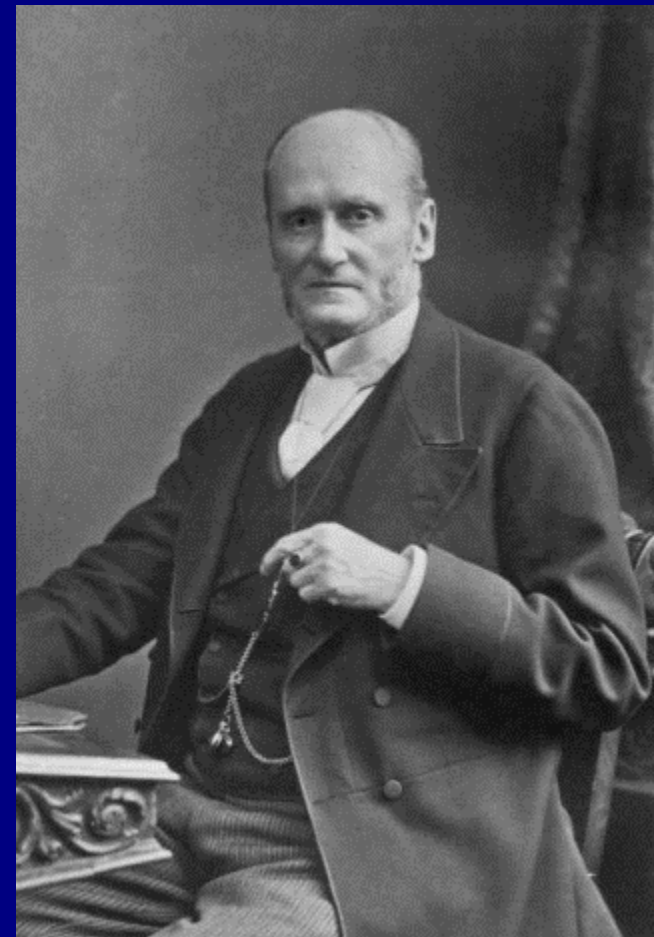
The sodden root when placed on inflammations soothes them, eliminates edema and disperses obdurate matter above inflammed joints.

John Russell Reynolds

British neurologist and physician

For the relief of certain kinds of pain, I believe, there is no more useful medicine than Cannabis within our reach.

Archives of Medicine 2, 154-160 (1859)



Indian hemp, when pure and administered carefully, is one of the most valuable medicines we possess.

Lancet 135, 637-638 (1890)



UNIVERZITA PALACKÉHO
V OLMOUCI

Zdeněk Krejčí

(25.března 1923 – 31.března 1992)





Cannabis extracts



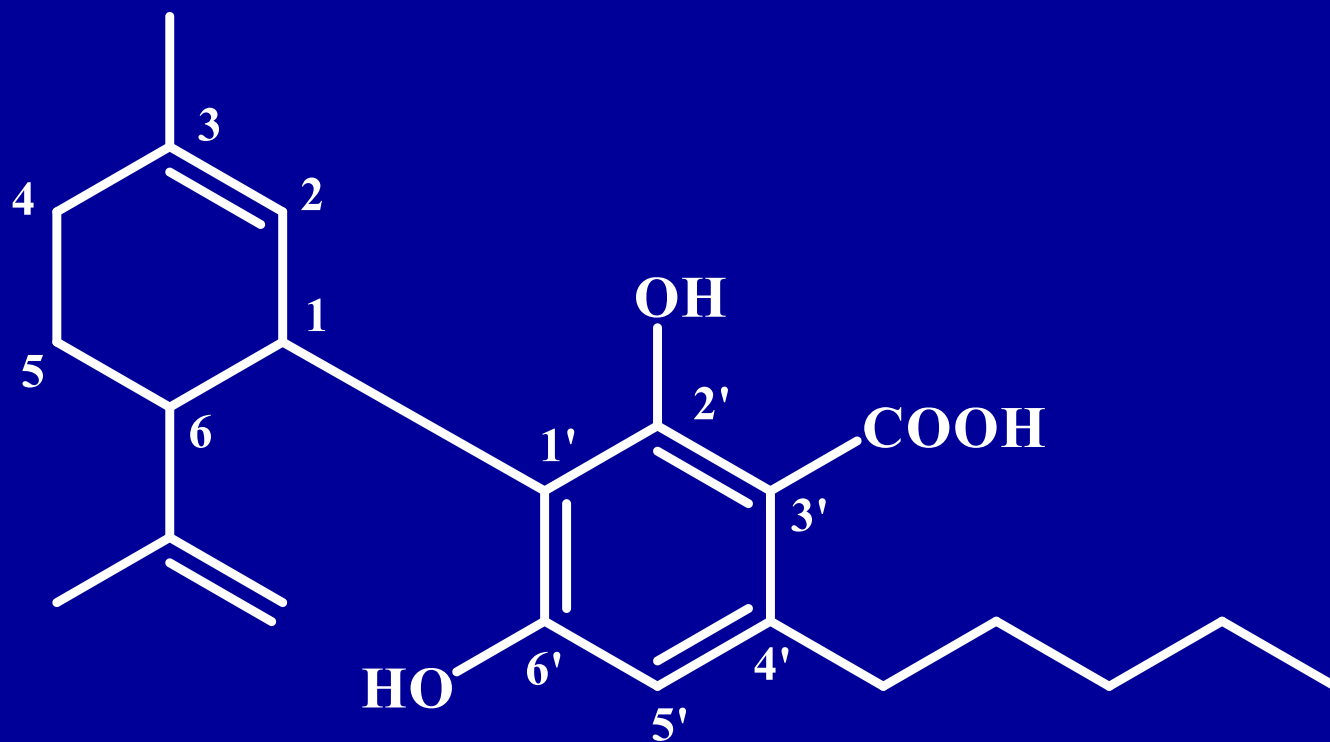
A significant antibacterial effects
(upon gram-positive microorganisms including
some common pathogenic microorganisms)

successfully examined clinically
(stomatology, otorhinolaryngology, gynaecology, dermatology and the like)

Z. Krejčí

7, 500 (1952)

Acta Univ. Olomuc., Fac. Med. 6 (1955)



cannabidiolic acid

Str. 27.-114.

II.

KONOPI JAKO LÉK

*Hygienický ústav lékařské fakulty Palackého university v Olomouci
ve spolupráci s jinými ústavy.*

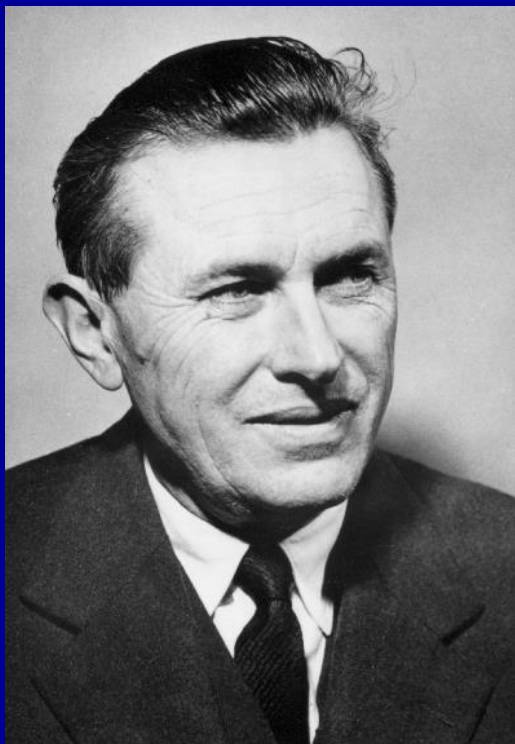
ODBORNÝ REDAKTOR: PROF. DR. JAN KABELÍK



UNIVERZITA PALACKÉHO
V OLMOUCI

František Šantavý

(23.dubna 1915 – 27.března 1983)





Δ^9 -tetrahydrocannabinol (Δ^9 -THC)



Yehiel Gaoni

* 1. září 1928



Y. Gaoni

Raphael Mechoulam

* 5. listopadu 1930



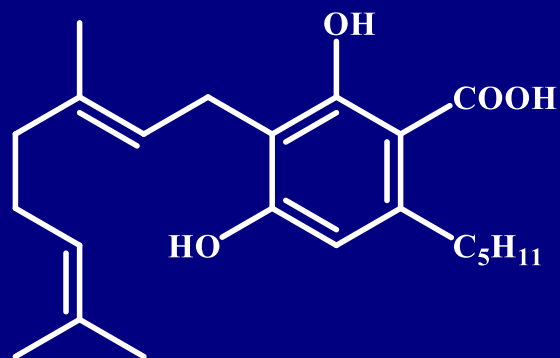
R. Mechoulam

Compounds identified in cannabis up to March 2016

Total in cannabis identified **1232** compounds

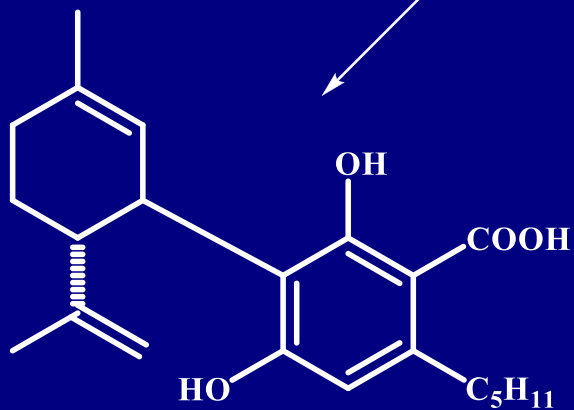
144 are **cannabinoid compounds**, which are typical for this plant and do not occur in any other plant

1088 are all **other identified substances**



cannabigerolic acid (CBGA)

**CBDA
synthase**



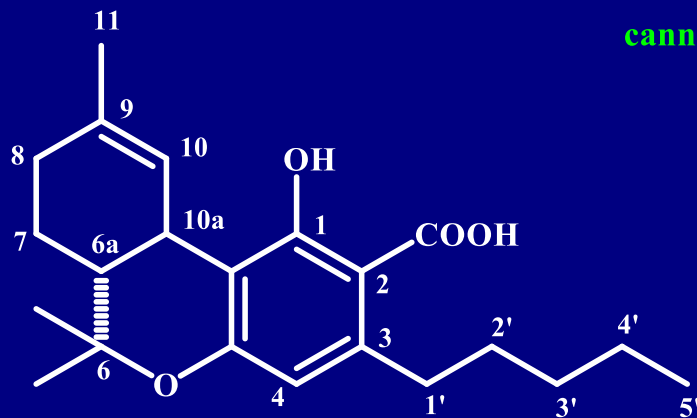
cannabidiolic acid (CBDA)

**CBCA
synthase**

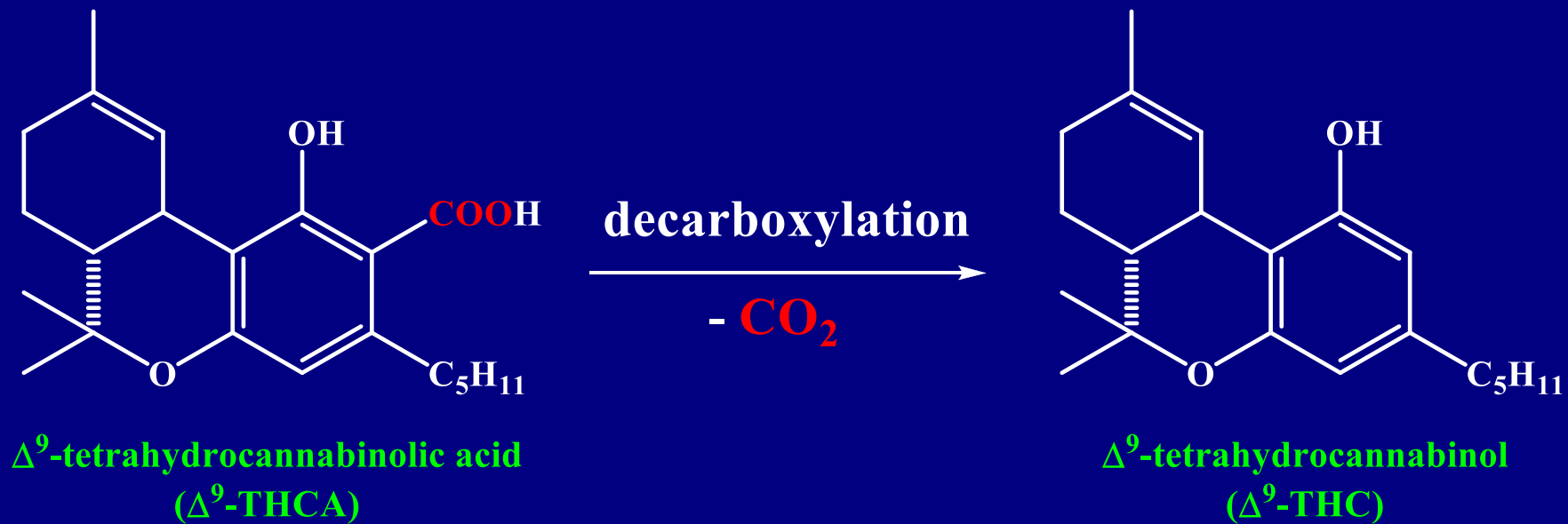


cannabichromenic acid (CBCA)

**Δ^9 -THCA
synthase**



Δ^9 -trans-tetrahydrocannabinolic acid (Δ^9 -THCA)



Cannabinoid receptors

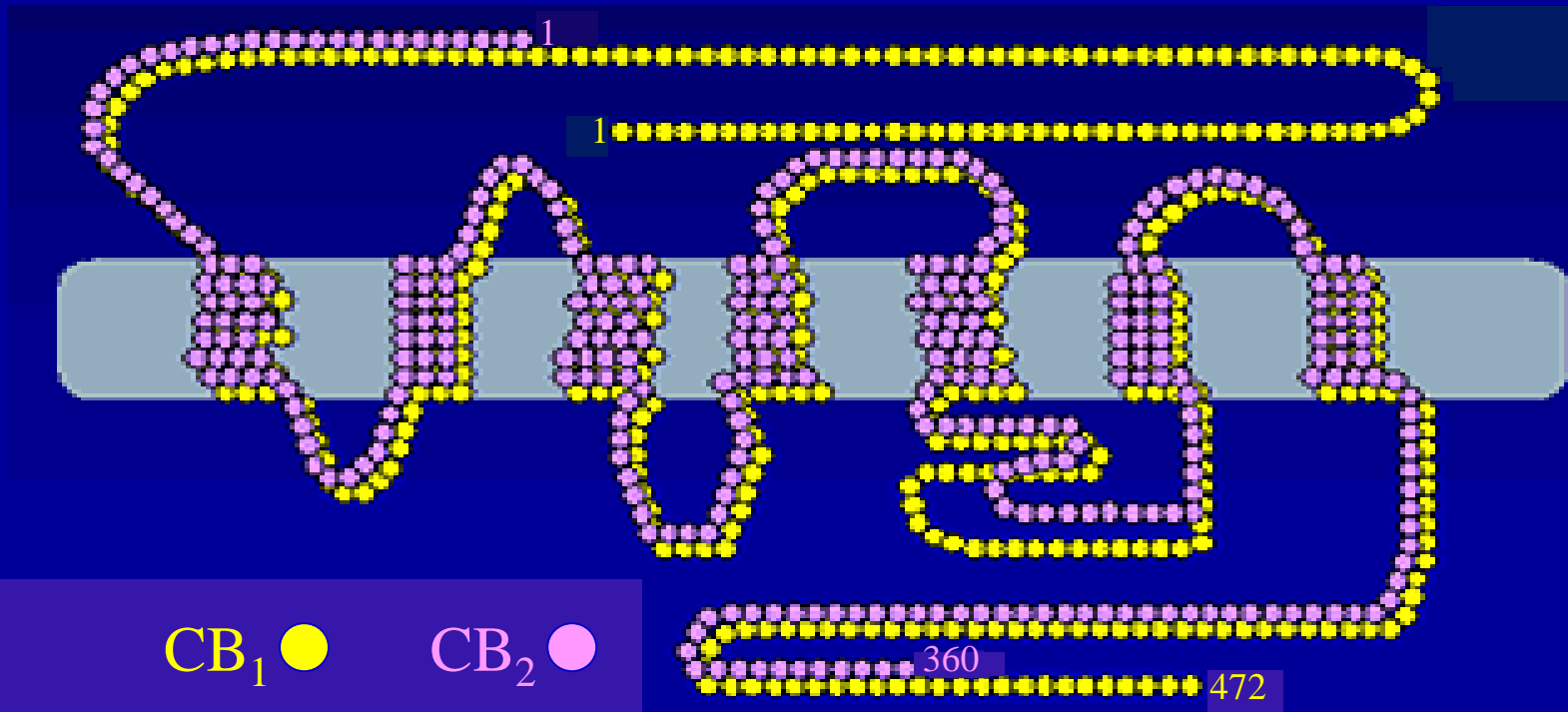
Cannabinoid receptors

* Two types identified (thus far)

CB₁, present in brain and central nervous system, 472 amino acids

CB₂, present in spleen and immune cells, 360 amino acids

* Both types are 7-helix transmembrane spanning receptors. Three extra-cellular and three intra-cellular loops. A glycosylated extra-cellular N-terminal domain, and an intra-cellular C-terminal domain involved in the interaction with the G-protein.



Brain regions in which cannabinoid receptors are abundant.

Brain Region	Functions Associated with Region
Basal ganglia Substantia nigra pars reticulata Entopedunculus nucleus Globus pallidus Putamen	Movement control
Cerebellum Hippocampus Cerebral cortex, especially cingulate frontal, and parietal regions	Body movement, coordination Learning and memory, stress Higher cognitive function
Nucleus accumbens	Reward center

CB₂ receptor:
part of protective system
works in conjunction with the immune
system and with various other
physiological systems.

Cannabinoid receptors distribution

CB₁ receptor

cerebral cortex

hippocampus

basal ganglia

cerebellum

reproductive system

CB₂ receptor

lymphoid organs:

spleen

thymus

tonsils

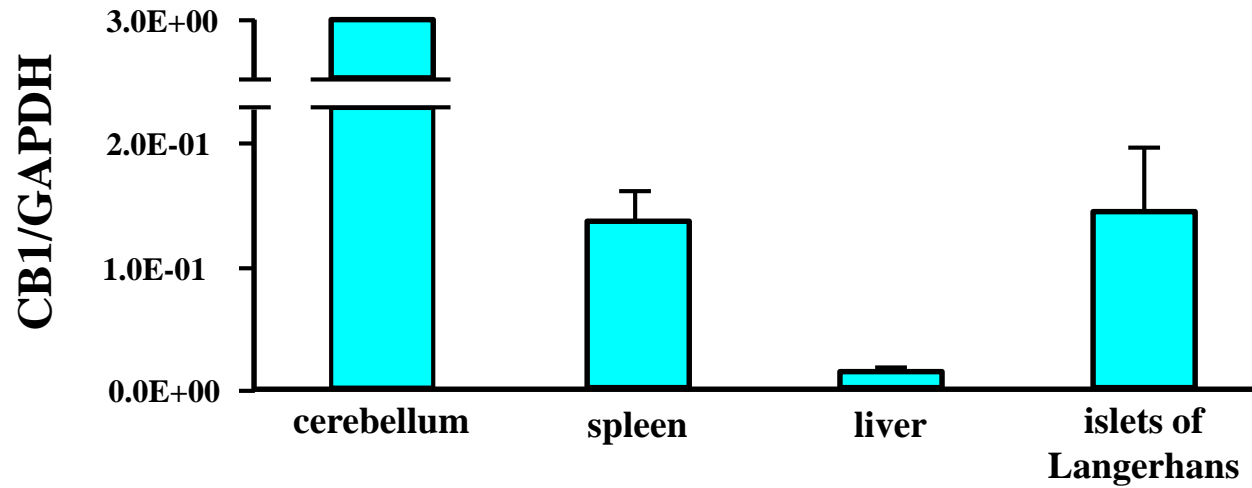
bone marrow

leukocytes

pancreas

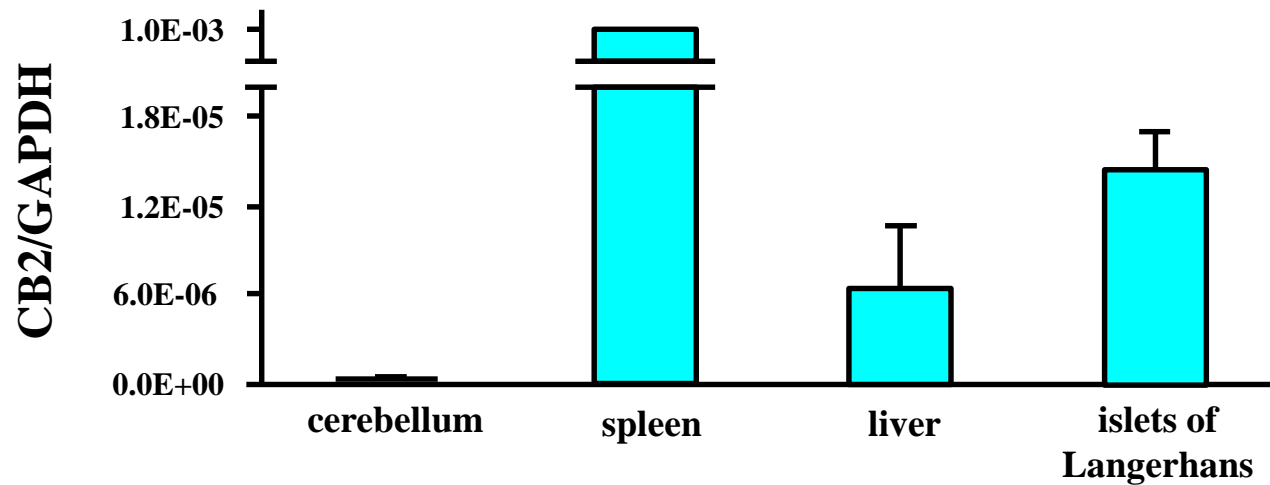
macrophages

CB1 expression



GAPDH =
glyceraldehyde
3-phosphate
dehydrogenase

CB2 expression

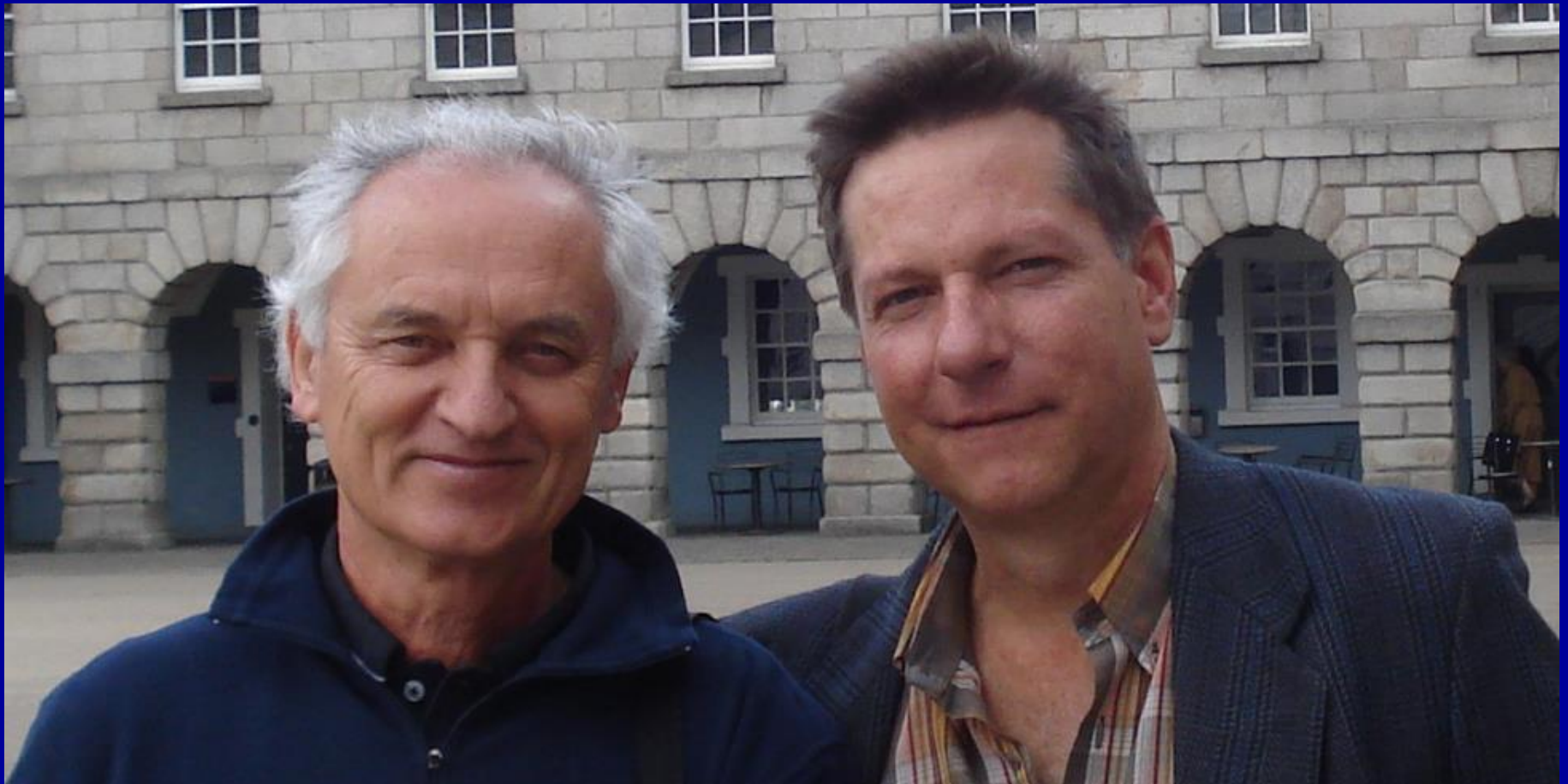


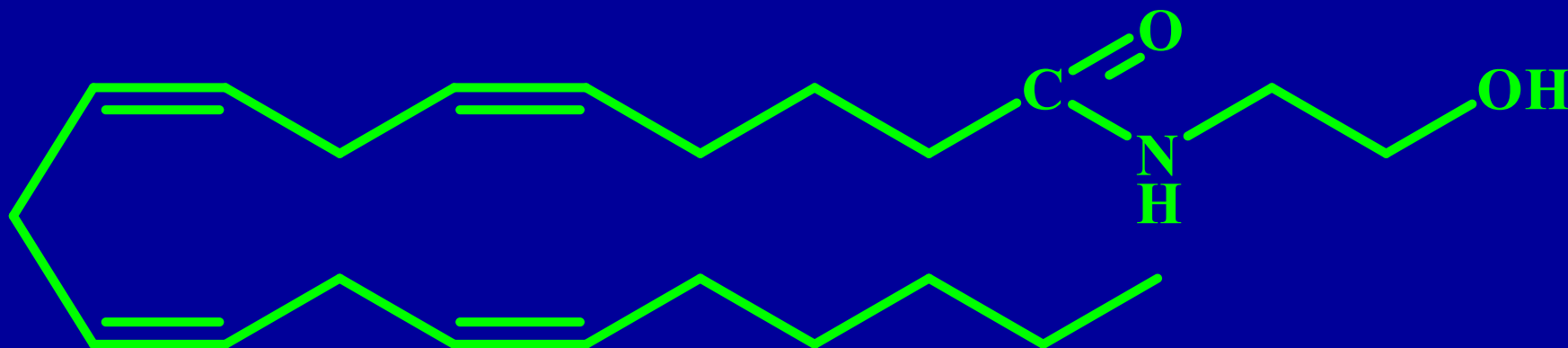
Endocannabinoids

Anandamide



האוניברסיטה העברית בירושלים The Hebrew University of Jerusalem



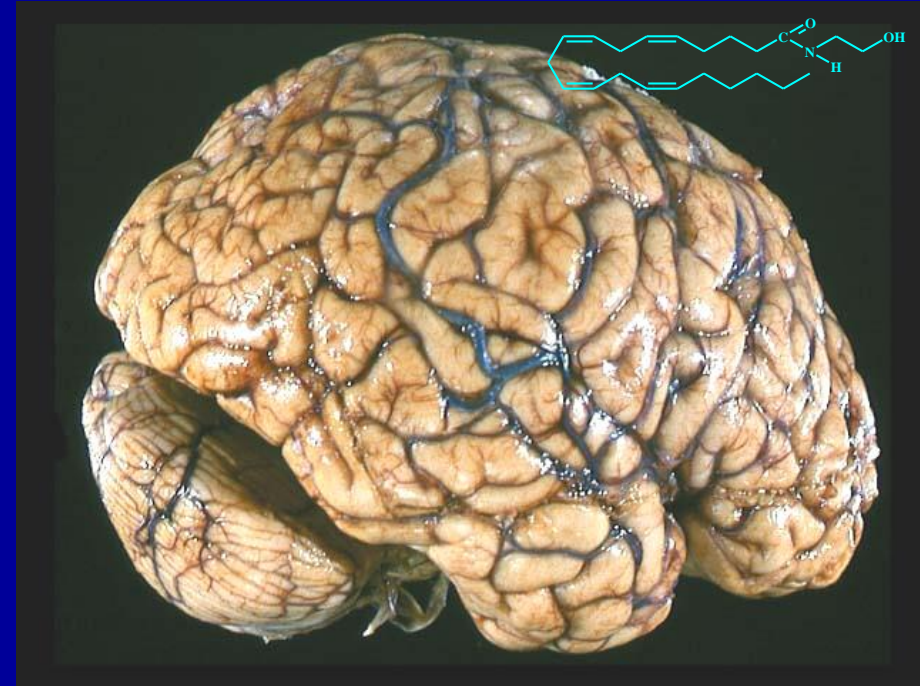


arachidonylethanolamide
(anandamide)

$K_i = 39.2 \pm 5.7 \text{ nM}$ CB1

Anandamide is endogenous cannabinoid neurotransmitter.

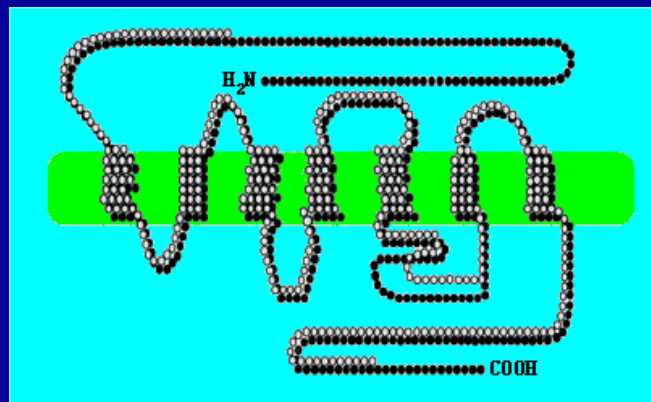
It is molecular „messenger”, which plays a role in pain, depression, appetite, memory, and fertility.



Δ^9 -tetrahydrocannabinol

Anandamide

Cannabinoid receptor



Ester Fride



The first *in vivo* examination of anandamide. After *i.p.* administration in mice caused lowering of activity in an immobility and in an open field test, and produced hypothermia and analgesia (these effects parallel those caused by psychotropic cannabinoids).

E. Fride, R. Mechoulam: Pharmacological activity of the cannabinoid receptor agonist, anandamide, a brain constituent. *Eur. J. Pharmacol.* 231, 313-314(1993)

Physiological systems and conditions affected by endocannabinoids (a partial list)

Appetite/feeding

Blood pressure

Cerebral blood flow

Digestive system

Emesis and nausea

Immune system

Inflammation

Bone formation

Memory

Mood

Movement

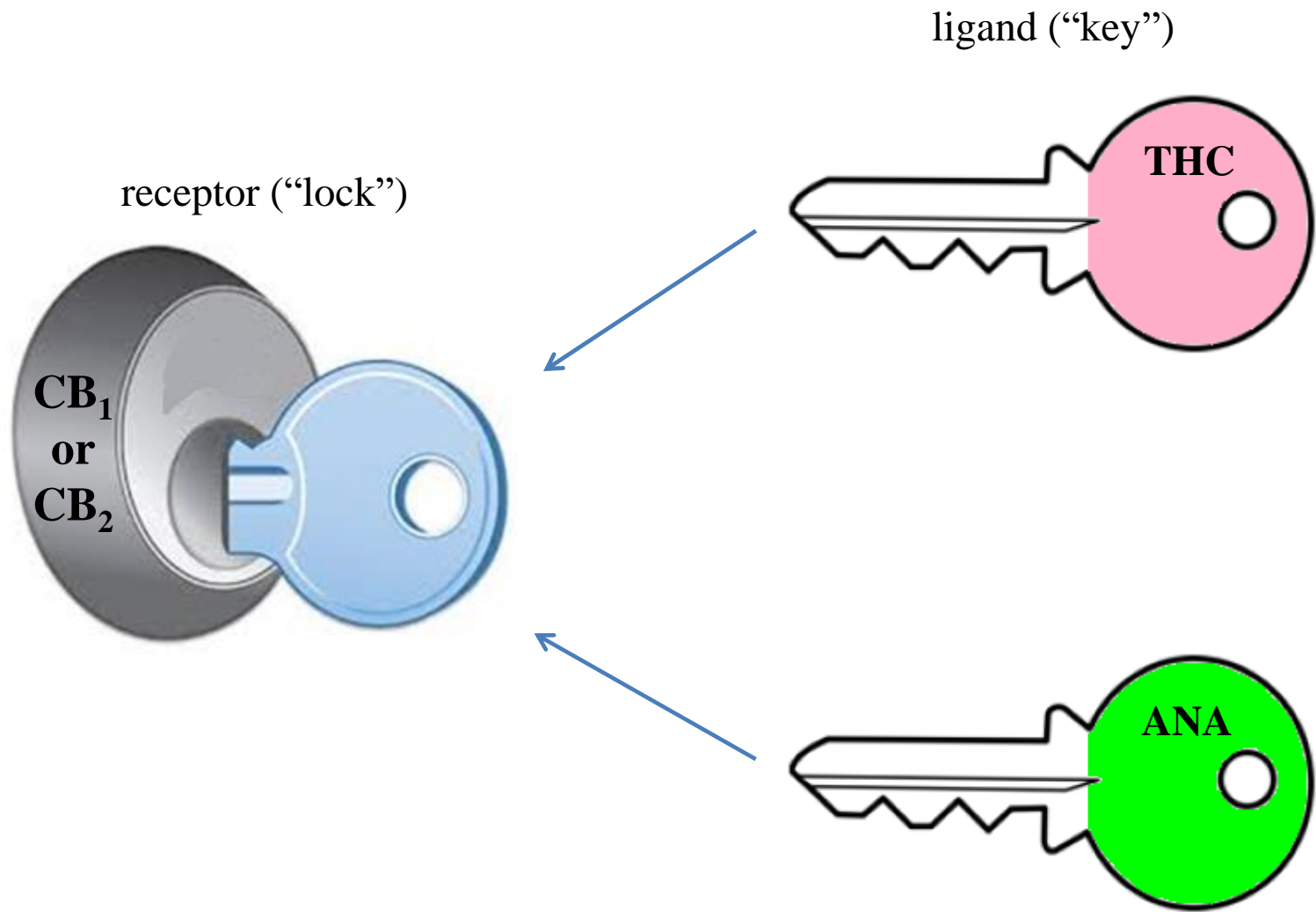
Neuroprotection

Pain

Reproduction

Stress

Endocannabinoid-like molecules are part of numerous protective systems, which work in conjunction with the immune system and with various other physiological systems.



Hermann Emil Fischer, 1894

Paul Ehrlich, 1897

Synaptic transmission

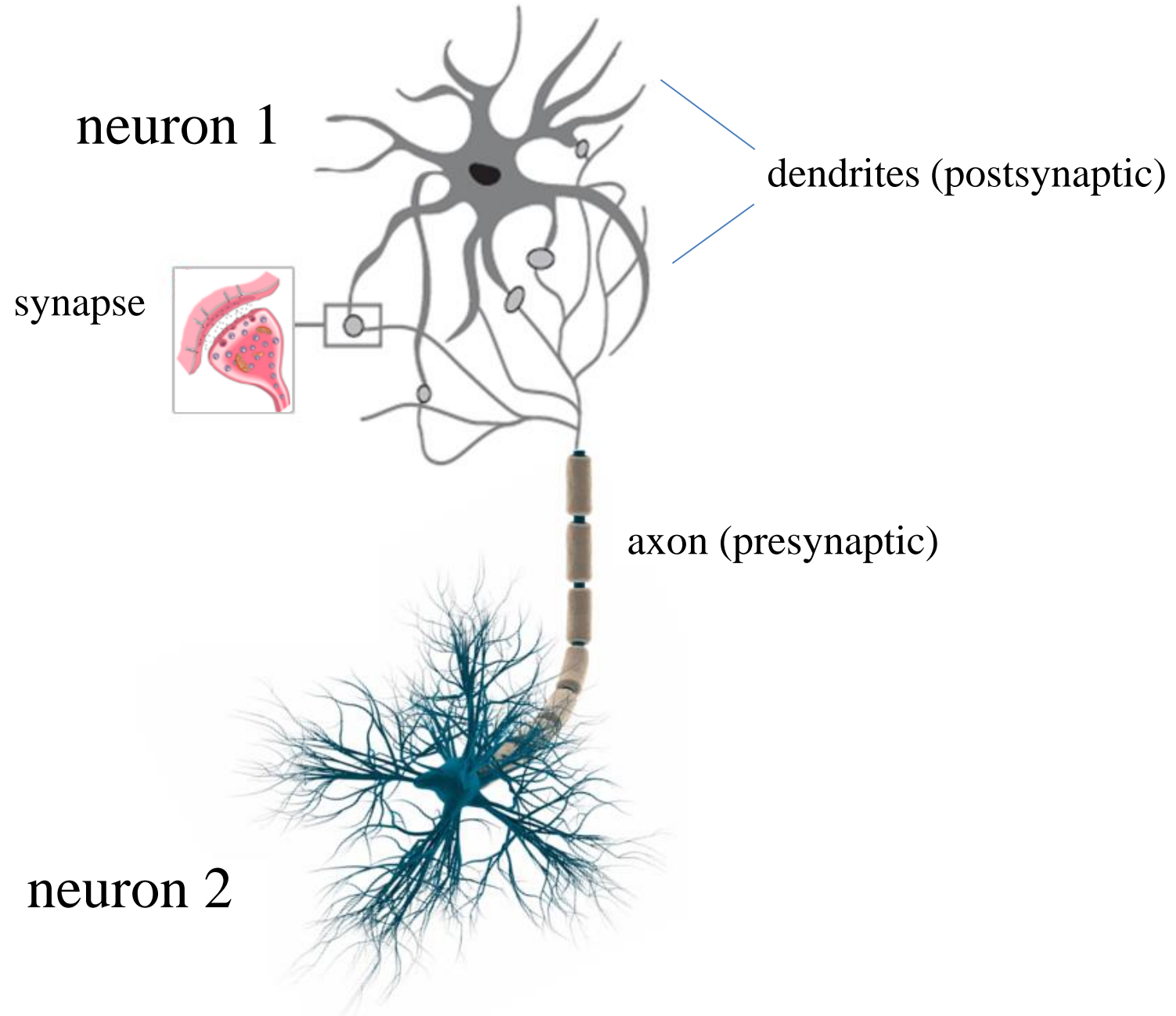
or

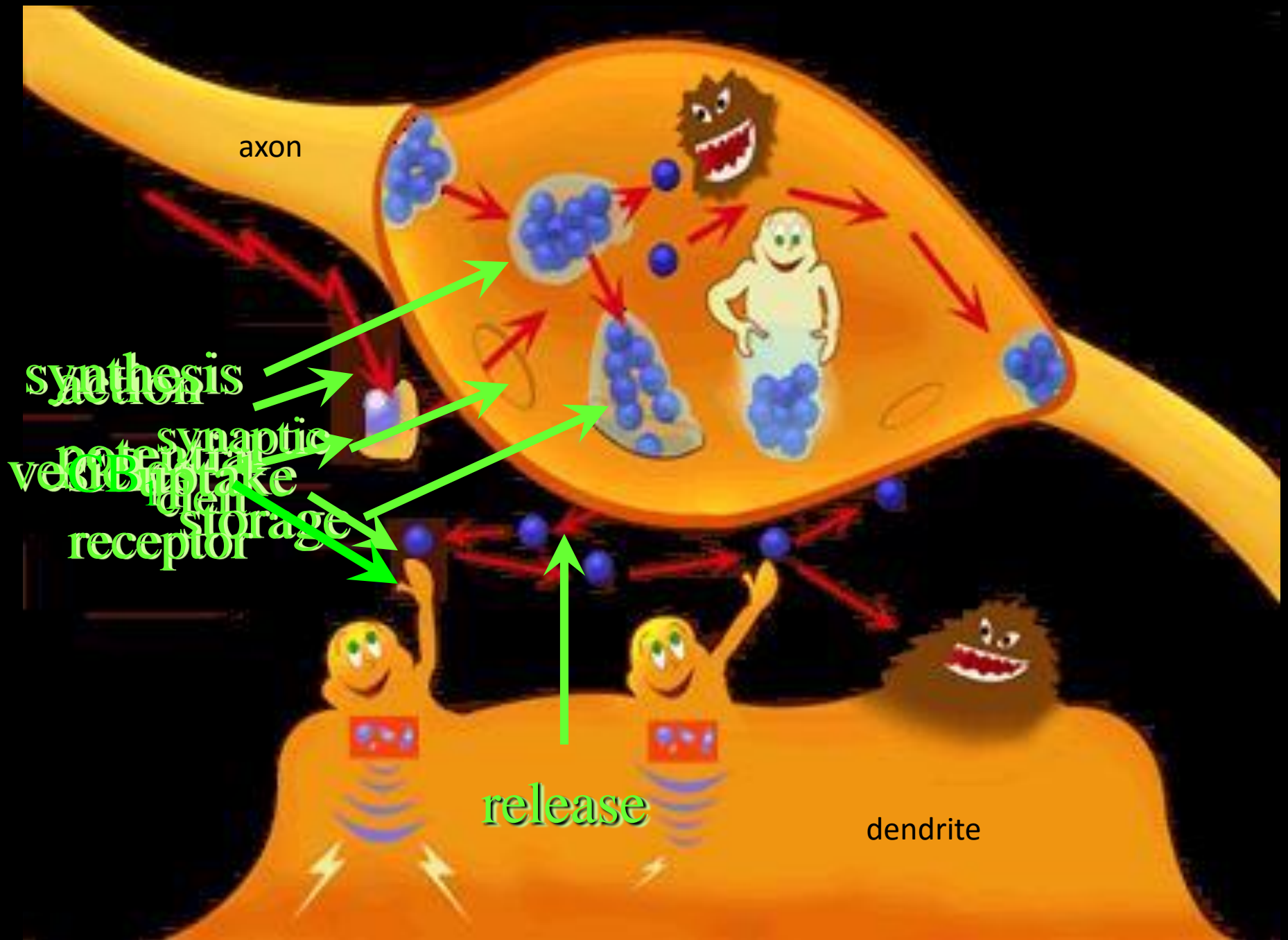
the passage of information
(in the form of a neurotransmitter)
from one nerve cell to another

Synaptic transmission: A four step process

1. Synthesis and Storage of Neurotransmitters (endocannabinoids)
2. Neurotransmitter (endocannabinoid) Release
3. Neurotransmitter (endocannabinoid) Postsynaptic Receptors
4. Inactivation of Neurotransmitters (endocannabinoids)

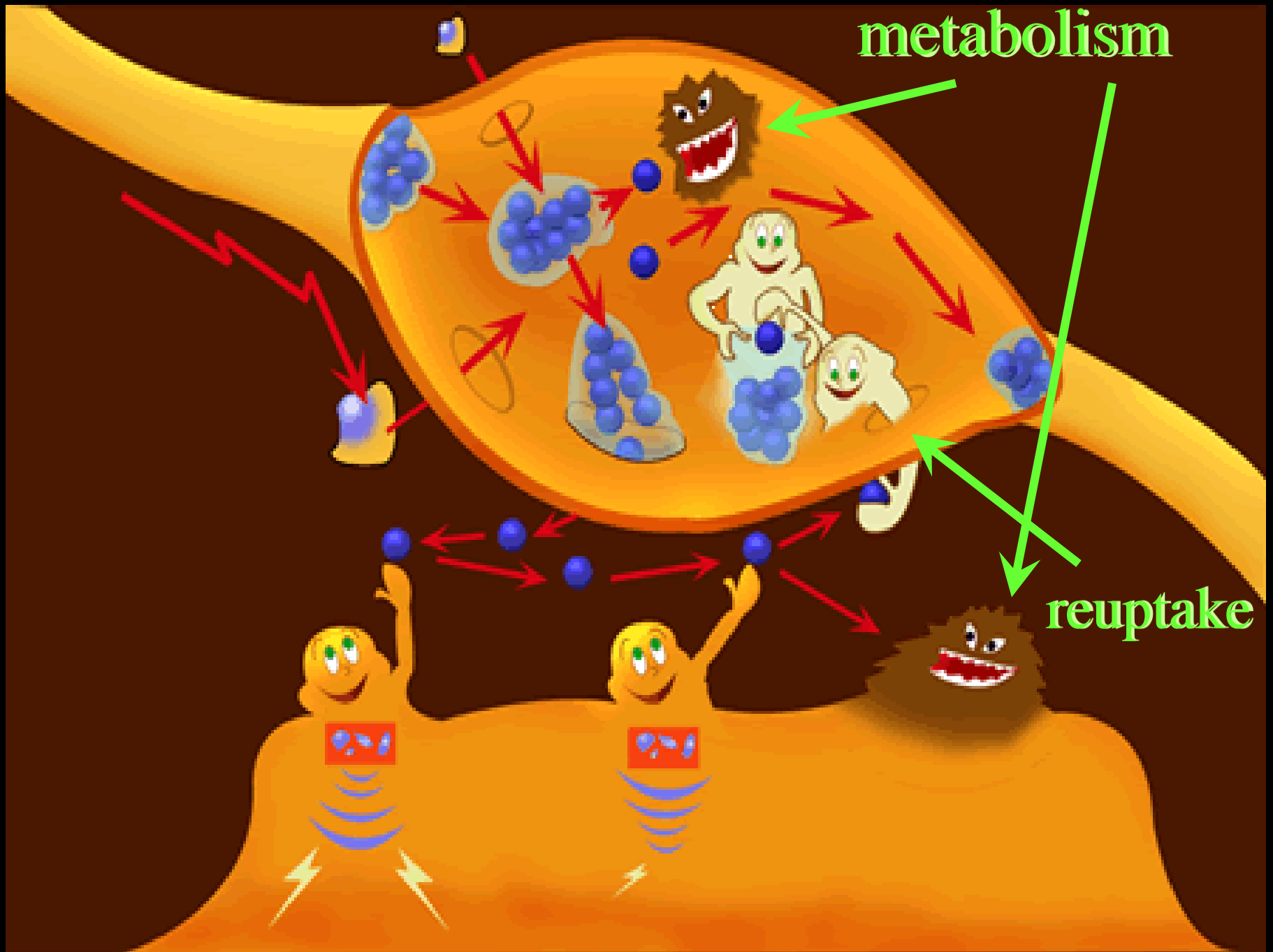
Neurons are connected by synapses



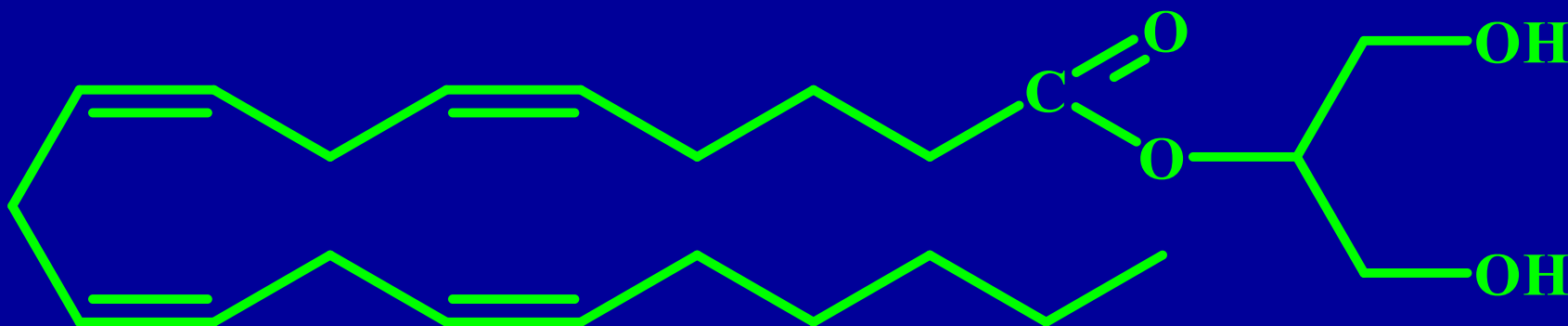


metabolism

reuptake



**2-arachidonoyl
glycerol**



2-arachidonoyl glycerol (2-AG)



anandamide
(Science, 1992)



homo-γ-linolenylethanolamide
(J. Med. Chem., 1993)



7,10,13,16-docosatetraenylethanolamide
(J. Med. Chem., 1993)



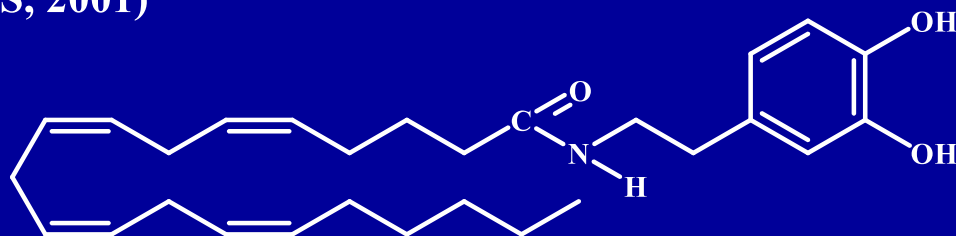
2-arachidonoyl glycerol
(Biochem. Pharmacol., 1995)



noladin ether
(PNAS, 2001)



virodhamine
(Porter, 2002)



arachidonoyl dopamine (NADA)
(Huang, 2002)

What do endocannabinoids?

“Relax, eat, sleep, forget and protect”

Keep in mind that cannabis is a wonderful medicine, but it is no panaceum and therefore it:

1. does not cure every time
2. does not cure everyone
3. does not cure every disease
4. does not cure every stage of the disease

Cannabis is inherently polypharmaceutical and synergy arises from interactions between its multiple components.

Recent study of Pacher and Kunos have suggested that “modulating endocannabinoid system activity may have therapeutic potential in almost all diseases affecting humans, including obesity/metabolic syndrome; diabetes and diabetic complications; neurodegenerative, inflammatory, cardiovascular, liver, gastrointestinal and skin diseases; pain; psychiatric disorders; cachexia; cancer; and chemotherapy-induced nausea and vomiting, amongst many others”. This strong statement supports a long list of examples, although mostly *in vitro* or *in vivo* in animals.

**Results: 123,771***(from All Databases)**(Number of results is approximate)***You searched for: TOPIC:***(Anandamide or hemp or *cannabi* or**marijuana or marihuana or hashish)**...More***Refine Results**

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AMERICAN CRIMINAL LAW REVIEW Volume: 53 Issue: 1 Pages: 215-234 Published: WIN 2016



Times Cited: 0

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