CANNABINOIDS
Cannabis sativa

**Phytocannabinoids**
- Cannabinoids (Δ⁹-THC)
  - marijuana (inflorescence)
  - hashish (resin)

**Endocannabinoids**
- N-arachidonoyl ethanolamine (Anandamide, AEA)
- 2-arachidonoylglycerole (2-AG)
- 2-arachidonyl-glyceryl-ether (noladin ether)
- O-arachidonoyl-ethanolamine (virodhamine)
- N-arachidonoyl-dopamine (NADA)
Plant-derived cannabinoid

Endogenous cannabinoids
Pharmacokinetics of THC in different tissues
Cannabinoid receptors: CB1 and CB2: $G_i$ protein

**CB1:** CNS (hippocampus, Ctx, PG) spinal cord, PNS, endocrine glands, salivary glands, leukocytes, spleen, heart, reproductive, urinary, gastrointestinal system

Terminals: inhibition of neurotransmitter release

**CB2:** leukocytes, spleen, tonsils (immune system)

Pain, spasticity, nausea, appetite

**Drugs**
Dronabinol, nabilone (agonists)
Rimonabant (antagonist)
Density and autoradiographic distribution of CB1 receptors
Cannabis

Main active constituent is Δ⁹-tetrahydrocannabinol (THC), though pharmacologically active metabolites may be important.

Actions on CNS include both depressant and psychotomimetic effects.

Subjectively, subjects experience euphoria and a feeling of relaxation, with sharpened sensory awareness.

Objective tests show impairment of learning, memory and motor performance.

THC also shows analgesic and antiemetic activity, as well as causing catalepsy and hypothermia in animal tests.

Peripheral actions include vasodilatation, reduction of intraocular pressure and bronchodilatation.

Cannabinoid receptors belong to the G-protein-coupled receptor family, linked to inhibition of adenylate cyclase and effects on calcium and potassium channel function, causing inhibition of synaptic transmission. The brain receptor (CB₁) differs from the peripheral receptor (CB₂), which is expressed mainly in cells of the immune system. Selective agonists and antagonists have been developed.

Anandamide, an arachidonic acid derivative, is an endogenous ligand for the CNS cannabinoid receptor; its function has not yet been ascertained.

Cannabinoids are less liable than opiates, nicotine or alcohol to cause dependence but may have long-term psychological effects.

Nabilone, a THC analogue, has been developed for its antiemetic property.

Trials are in progress for symptomatic treatment of multiple sclerosis and AIDS.

Increased heart rate, decreased blood pressure, conjunctiva redness

Dronabinol (Δ⁹-THC). neuropathic pain, anorexia
THC effects

**THC:** euphoria, relaxation, appetite stimulation, hallucinations, delusional ideas, decreases motor control, sleepiness, memory

- Metabolized by oxidases, eliminated via bile
- Tolerance, weak dependence

**Interactions with THC**

Opiates
Ethanol
Glaucoma
it affects the optic nerve and leads to a progressive reduction in vision

For some decades THC has been used in the treatment of glaucoma, in combination with other drugs.
Stabilizing intraocular pressure THC avoids excessive changes in the internal pressure of the eye, which are very risky
The effect is quite short and cause several side effects
Side effects of tetrahydrocannabinol

TACHICARDIA

IPOTENSIONE

ALLUCINAZIONI
Criteri diagnostici per F12.00 Intossicazione da Cannabis [292.89]

A. Uso recente di cannabis.

B. Modificazioni malattive comportamentali o psicologiche clinicamente significative (per es., compromissione della coordinazione motoria, euforia, ansia, sensazione di rallentamento del tempo, deficit della capacità critica, ritiro sociale) che si sviluppano durante, o poco dopo, assunzione di cannabis.

C. Due (o più) dei seguenti segni, che si sviluppano entro due ore dall'assunzione di cannabis:

1) iperemia congiuntivale
2) aumento dell'appetito
3) secchezza delle fauci
4) tachicardia.

D. I sintomi non sono dovuti a una condizione medica generale e non risultano meglio spiegati con un altro disturbo mentale.

Nota per la codificazione: F12.04 se
Con Alterazioni Percettive
HALLUCINOGENS
Chemical structure of principal hallucinogens

- DMT
- Psilocin: R = H; Psilocina
- R = PO₃H; Psilocibina
- 5-Metossi-DMT
- Serotonin; 5-HT
- LSD
- Mescaline
The main types are:
—LSD, psilocybin and mescaline (actions related to 5-HT and catecholamines)
—phencyclidine.

• Their main effect is to cause sensory distortion of a fantastic and hallucianatory nature.
• LSD is exceptionally potent, producing a long-lasting sense of dissociation and disordered thought, sometimes with frightening hallucinations and delusions, which can lead to violence. Hallucinatory episodes can recur after a long interval.
• LSD and phencyclidine precipitate schizophrenic attacks in susceptible patients, and LSD may cause long-lasting psychopathological changes.
• LSD appears to act as an agonist at 5-HT$_2$-receptors, and suppresses electrical activity in 5-HT raphe neurons, an action that appears to correlate with psychotomimetic activity.
• They do not cause physical dependence and tend to be aversive, rather than reinforcing, in animal models.
• The mechanism of action of phencyclidine is complex; it binds to the σ-receptor and also blocks the glutamate-activated NMDA-receptor channel, as well as interacting with other neurotransmitter systems.
Peyote as a supplement for transcendental practices

Ghost Dance

Peyote (mescaline)

Psilocybe (psilocybin)
PET after psilocybin
Most frequently reported positive effects with recreational use of:

<table>
<thead>
<tr>
<th>ecstasy</th>
<th>amphetamine</th>
<th>hallucinogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loquacity</td>
<td>Energy enhancement</td>
<td>Weird thoughts</td>
</tr>
<tr>
<td>Open mind</td>
<td>Loquacity</td>
<td>Open mind</td>
</tr>
<tr>
<td>Intimacy with others</td>
<td>Alertness</td>
<td>Affability</td>
</tr>
<tr>
<td>Happiness</td>
<td>Confidence</td>
<td>Intuition</td>
</tr>
<tr>
<td>Fatigability</td>
<td>Affability</td>
<td>Restlessness</td>
</tr>
<tr>
<td>Euphoria</td>
<td>Attention towards others</td>
<td>Loquacity</td>
</tr>
<tr>
<td>Confidence</td>
<td>Increase in self-estimate</td>
<td>Increase in energy</td>
</tr>
<tr>
<td>Open mind</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Most frequently reported negative effects with recreational use of:

<table>
<thead>
<tr>
<th>ecstasy</th>
<th>amphetamine</th>
<th>hallucinogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of appetite</td>
<td>Loss of appetite</td>
<td>Visual illusions</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>Insonnia</td>
<td>Visual hallucinations</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Tachycardia</td>
<td>Loss of appetite</td>
</tr>
<tr>
<td>Tension in the jaw</td>
<td>Tension in the jaw</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Teeth grinding</td>
<td>Confusion</td>
</tr>
<tr>
<td>Teeth grinding</td>
<td>Dry mouth</td>
<td>Lack of concentration</td>
</tr>
<tr>
<td>Hot and cold sensation variation</td>
<td>Palpitations</td>
<td>Auditory hallucinations</td>
</tr>
<tr>
<td>Sweating / sweaty hands</td>
<td>Irritability</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Lack of concentration</td>
<td>Tremor</td>
<td>Tachycardia</td>
</tr>
</tbody>
</table>
Criteri diagnostici per F16.00 Intossicazione da Allucinogeni [292.89]

A. Uso recente di un allucinogeno.

B. Modificazioni maladattive psicologiche o comportamentali clinicamente significative (per es., rilevante ansia o depressione, idee di riferimento, paura di impazzire, ideazione paranoide, compromissione delle capacità critiche o compromissione del funzionamento sociale o lavorativo) che si sviluppano durante, o poco dopo, l'uso di allucinogeni.

C. Alterazioni percettive ricorrenti in stato di piena consapevolezza e vigilanza (per es., intensificazione soggettiva delle percezioni, de-personalizzazione, derealizzazione, illusioni, allucinazioni, sinestesie) che si sviluppano durante, o poco dopo, l'uso di allucinogeni.

D. Due (o più) dei seguenti segni, che si sviluppano durante, o poco dopo, l'uso di allucinogeni:

1) midriasi
2) tachicardia
3) sudorazione
4) palpitations
5) annebbiamenti del visus
6) tremori
7) incoordinazione.

E. I sintomi non sono dovuti a un'altra condizione medica generale e non risultano meglio spiegati con un altro disturbo mentale.