Medical Marijuana Risk/Benefit Profile: Is it Safe

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Teaching methods

Power point

Return demonstration of knowledge through questions

Feedback from audience of experience of patients with medical cannabis

Post test where 70% is required

Pennsylvania Qualifying Conditions for Medical Marijuana (23 Conditions)

Amyotrophic Lateral Sclerosis

Anxiety disorders

Autism

Cancer

Crohn's Disease

Dyskinetic Disorders

Damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity

Epilepsy

Glaucoma

Terminal Illness

Sickle Cell Anemia

Tourette syndrome

HIV / AIDS

Huntington's Disease

Inflammatory Bowel Disease

Intractable Seizures

Multiple Sclerosis

Neurodegenerative Disorders

Neuropathies

Opioid Use Disorder

Parkinson's Disease

Post-traumatic Stress Disorder

Severe chronic or intractable pain of neuropathic origin or severe chronic or intractable pain in which conventional therapeutic intervention and opiate therapy is contraindicated or ineffective

Objectives

Describe what is endocannabinoid system

Identify common adverse effects of medical cannabis use.

Identify contraindications to medical cannabis use.

Describe medical cannabis drug interactions.

Describe respiratory, cardiovascular, immune, neuropsychiatric, reproductive and other risks associated with medical cannabis use.

Introduction to Cannabis

Cannabis Indica and Cannabis sativa are the best-known species.

A product's chemical profile is more important than the strain of plant from which it originated.

Products should be characterized by analytical chemistry - percentages of cannabinoids or THC:CBD Ratio.

Compounds in Cannabis

Cannabis is a polypharmaceutical substance.

108 cannabinoids have been isolated.

The cannabis-derived cannabinoids of most therapeutic interest are THC and cannabidiol (CBD).
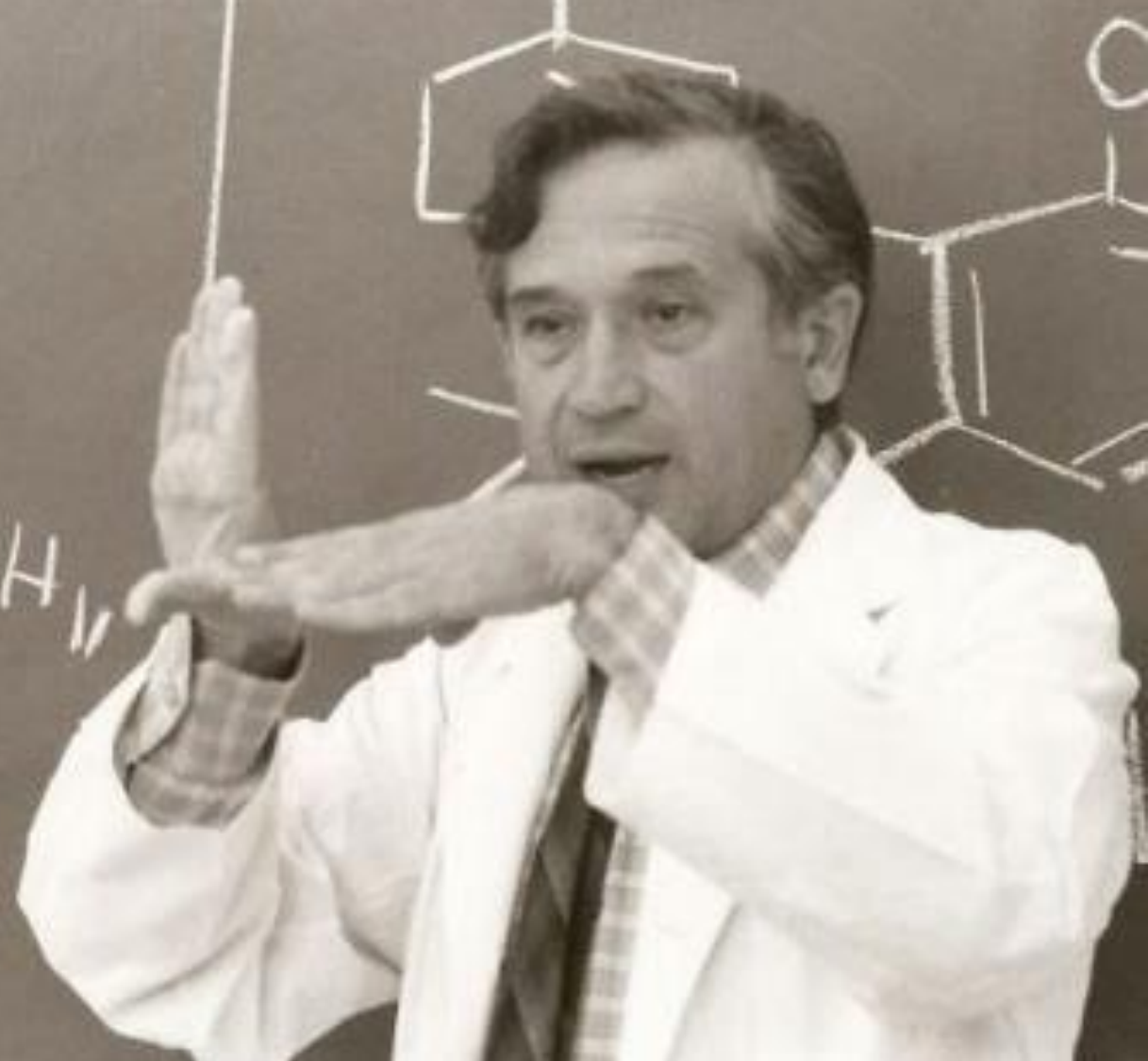
Terpenoids are common, often aromatic, organic compounds found in many plants. Terpenoids found in cannabis include β-caryophyllene, myrcene, limonene, and pinene.
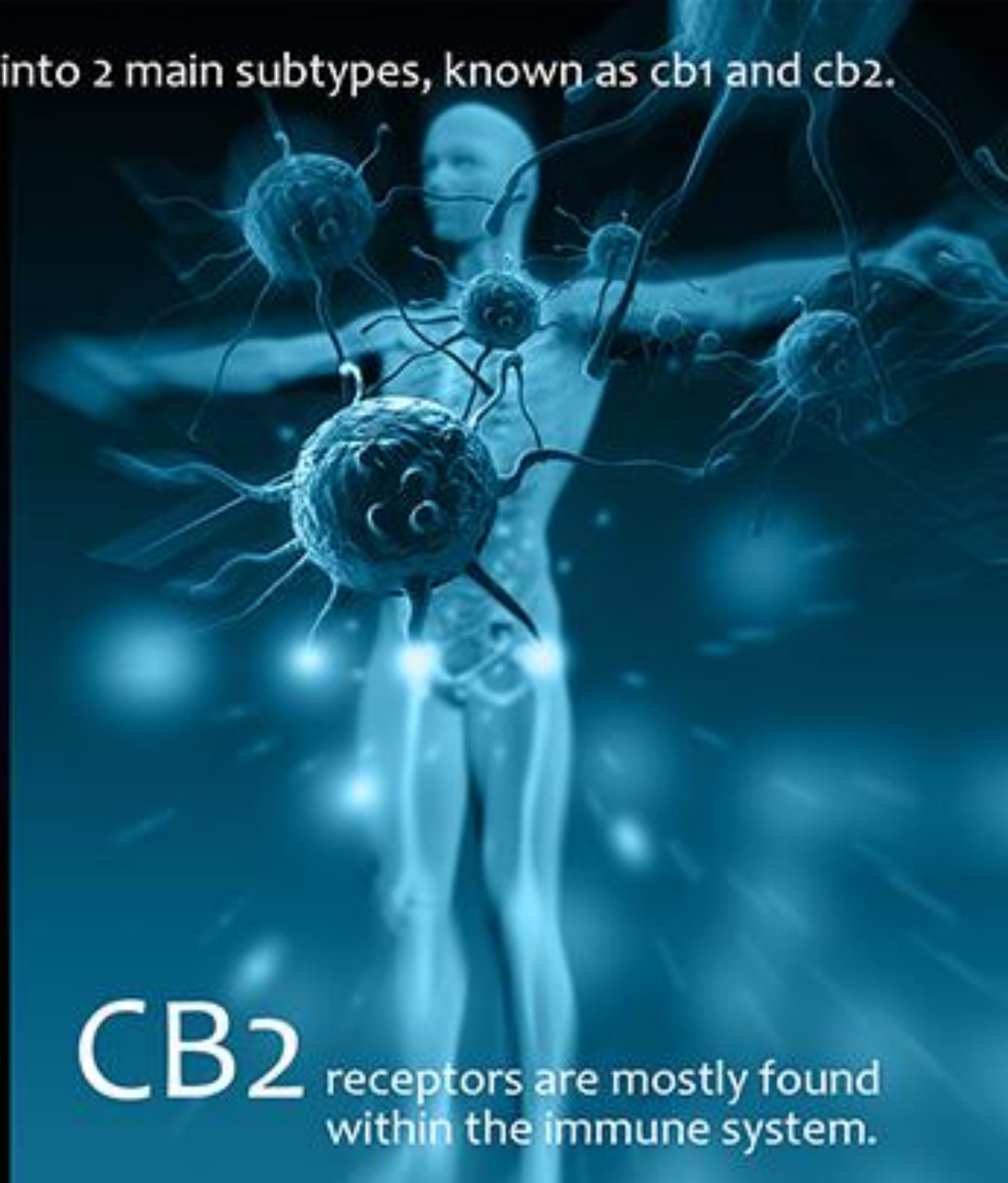
As many as 420 other constituents occur in the plant.
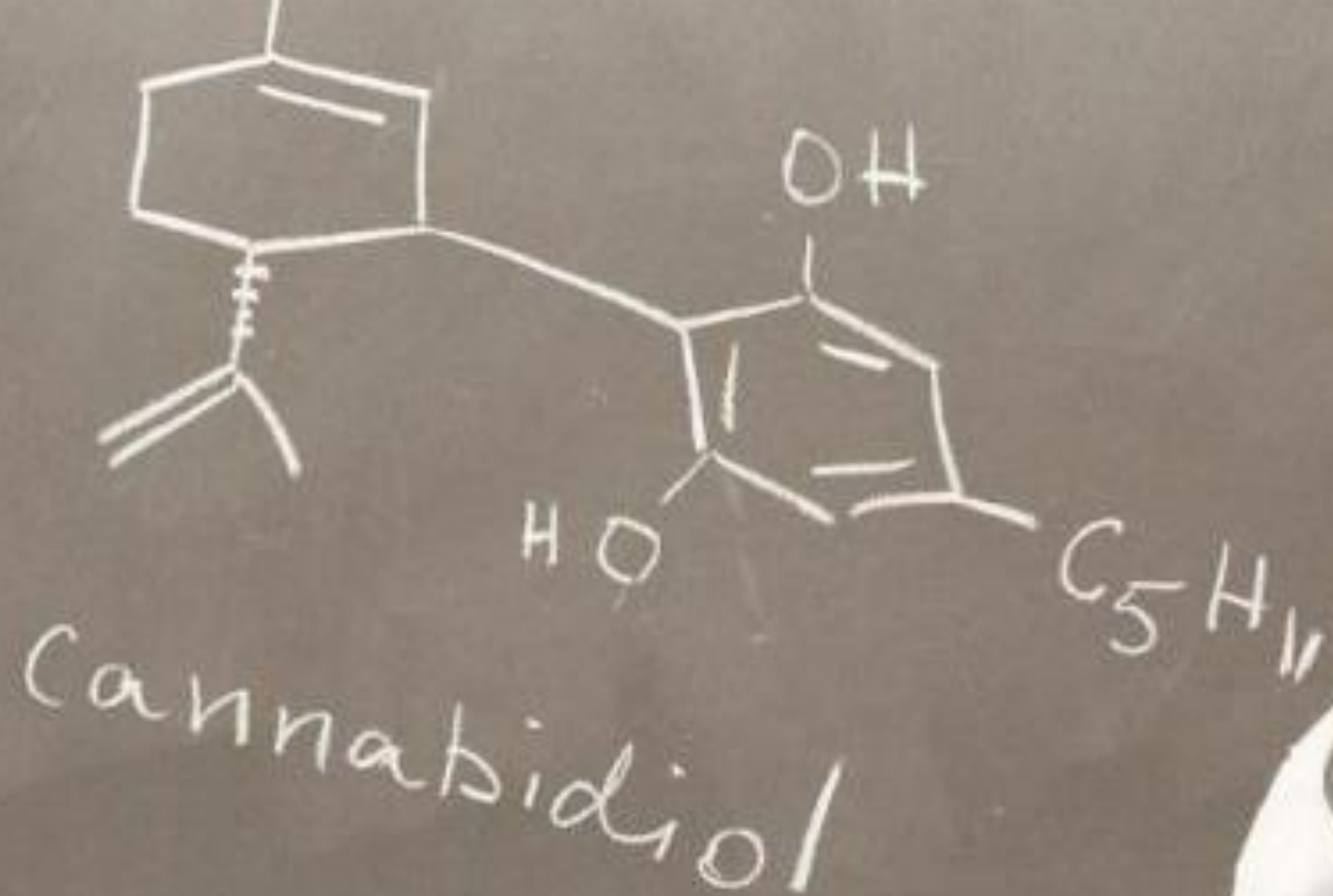
The cannabinoid receptors are further divided into 2 main subtypes, known as cb1 and cb2.

CB1 is found mostly in the brain.

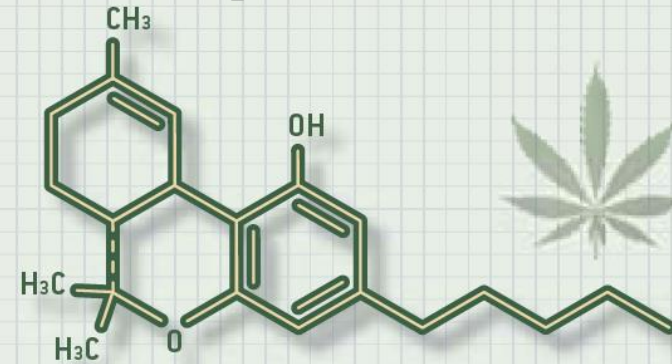CB2 receptors are mostly found within the immune system.

Endocannabinoids: *Bind CB1 > CB 2 structure, related to prostaglandins*

Annandamide

(arachidonyl-ethanolamid)

2-Arachidonoyl - glycerol (2-AG)

more abundant, less potent
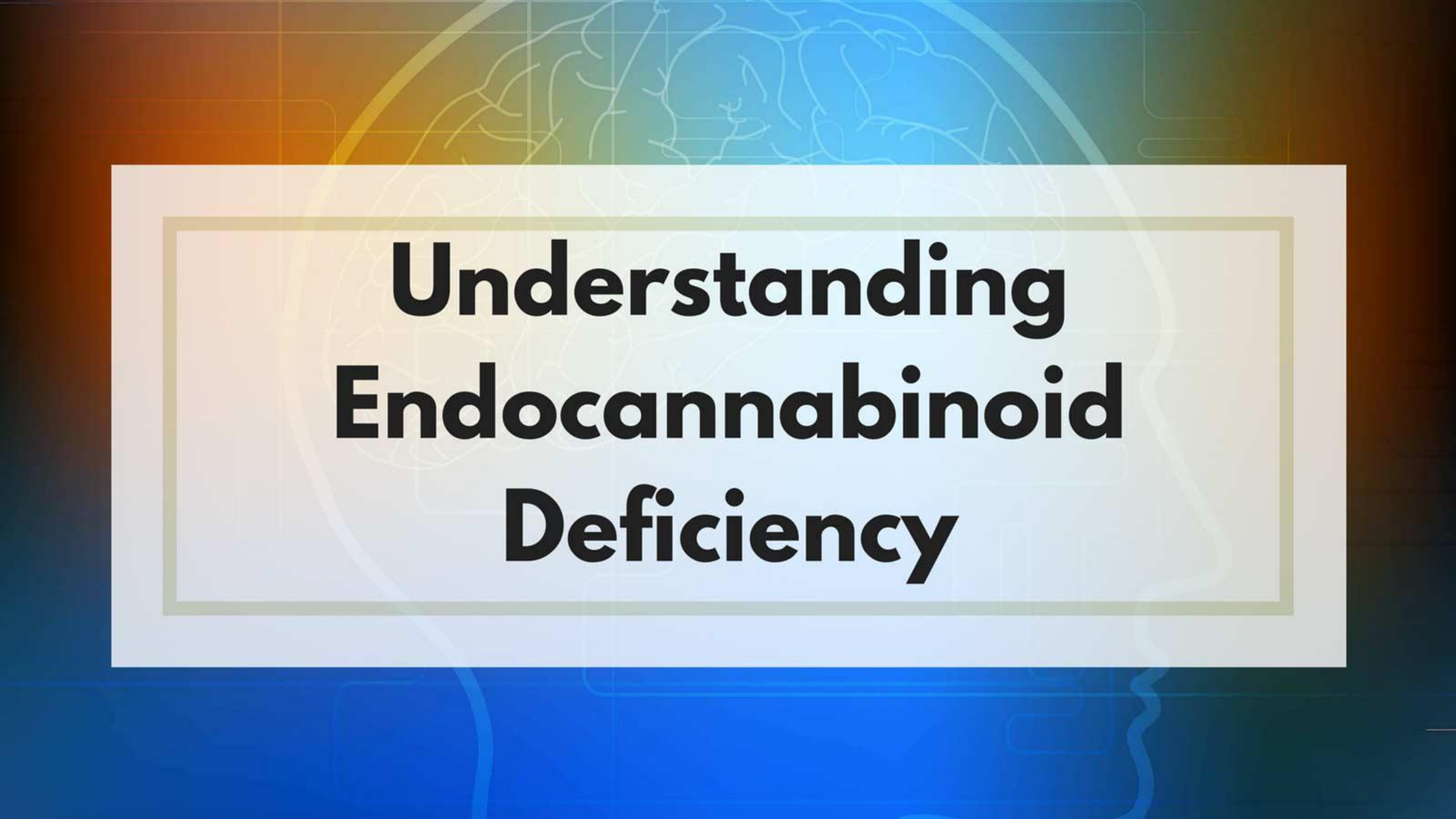
CH₃
OH
H₃C
H₃C
O
Delta-9-Tetrahydrocannabinol (THC)
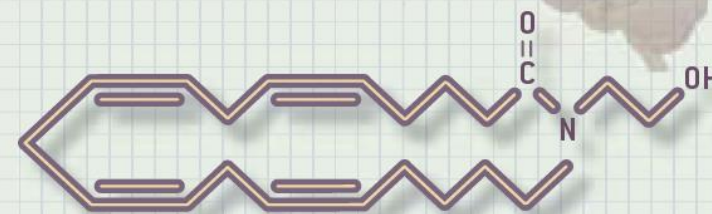
Anandamide
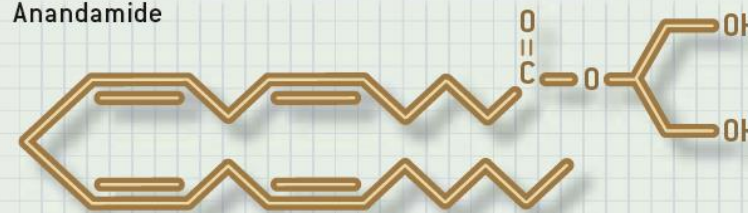
2-Arachidonoyl glycerol (2-AG)

Understanding Endocannabinoid Deficiency

Cannabis Safety Profile

Little is known about the safety of individual compounds. Serious adverse effects are rare with cannabis or its constituents.

Marijuana has low to moderate dependence potential; the active dose is very far below the lethal dose

Active/Lethal Dose Ratio and Dependence Potential of Psychoactive Drugs
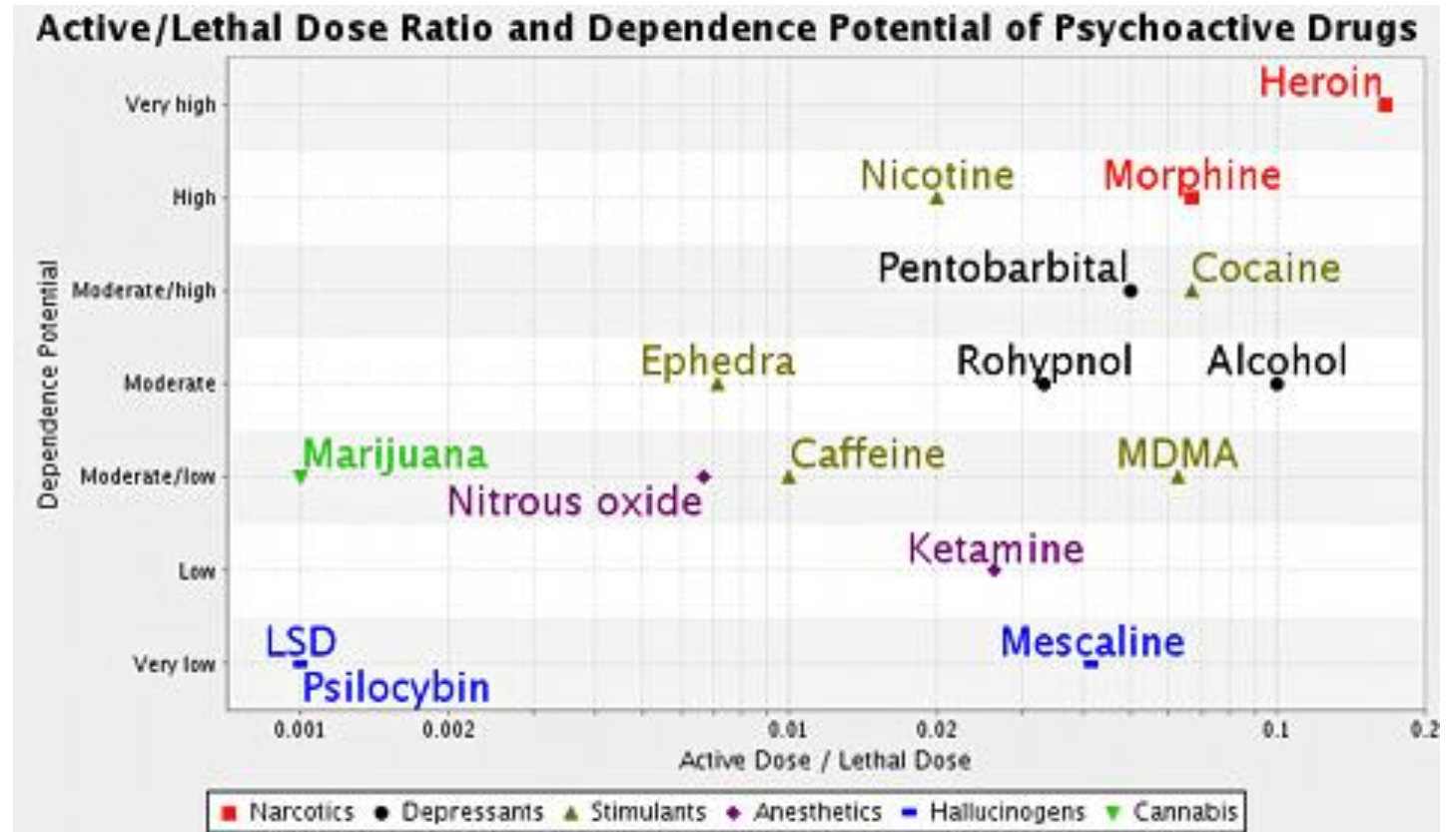
Common Adverse Effects

Anxiety

Dry mouth

Reddened eyes

Bronchitis

Sedation

Changed visual perception

Altered sense of time

Slowed pupillary response to light

Ataxia

Dysphoria

Cough

Decreased sperm count

What is the P450 Enzyme System?

Drug are metabolized in the liver.

The P450 enzyme system is responsible for metabolism of drugs

Either classified as an inhibitor or inducer.

An inducing agent can increase the rate of another drug's metabolism therefore impacting its therapeutic dose

An inhibitor decreases a drugs metabolism and cause an increase in the drug therapeutic level and possibly result in a harmful or adverse effec

THC and CBD are metabolized by CYP3A4 and CYP2C9.

THC can decrease serum concentrations of clozapine, duloxetine, naproxen, cyclobenzaprine, olanzapine, haloperidol, and chlorpromazine

CBD may increase serum concentrations of macrolides, calcium channel blockers, benzodiazepines, cyclosporine, sildenafil (and other PDE5 inhibitors), antihistamines, haloperidol, antiretrovirals, and some statins (atorvastatin and simvastatin, but not pravastatin or rosuvastatin).

CBD may increase serum concentrations of SSRIs, tricyclic antidepressants, antipsychotics, beta blockers and opioids (including codeine and oxycodone).

Drug Interactions Cytochrome P450 Enzymes

Drug Interaction Studies

Warfarin
- ◦ THC and CBD increase warfarin levels
- ◦ Frequent cannabis use has been associated with increased INR.

Alcohol
- ◦ Alcohol may increase THC levels .

Theophylline
- ◦ Smoked cannabis can decrease theophylline levels.

Clobazam in children treated for epilepsy
- ◦ CBD increased clobazam levels.

Drug Interaction Studies

Cannabis has additive CNS depressant effects with alcohol, barbiturates and benzodiazepines.

In a small study, cannabis did not have additive CNS effects when combined with opioids.

Contraindications

Absolute contraindications include acute psychosis and other unstable psychiatric conditions

Relative contraindications severe cardiovascular, immunological, liver, or kidney disease, especially in acute illness

Cannabis may exacerbate arrhythmia or a history of arrhythmias

Lung Function

National Health and Nutrition Examination Survey (NHANES) data found that up to 20 joint-years* of marijuana use caused no adverse changes in lung function

The Coronary Artery Risk Development in Young Adults study, a cohort study found no effect of occasional low marijuana use on pulmonary function.

A Scottish study in 500 adults found evidence of impaired lung function in both cannabis and tobacco smokers (concurrent smoking)

A joint-year is the number of joints per day multiplied by the number of years of usage

Smoked Cannabis

Smoked cannabis is clearly associated with symptoms of bronchitis, which resolve after cessation of use.

At least 200 compounds occur in cannabis smoke: these include carbon monoxide, acetaldehyde, ammonia, nitrosamines, and polycyclic aromatic hydrocarbons ("tars").

Combining tobacco and cannabis appears to have synergistic adverse effects, increasing respiratory symptoms over tobacco use alone.

Vaporization

A survey of 6,883 cannabis users found that vaporizing, compared with smoking, causes fewer respiratory symptoms (coughing, wheezing, shortness of breath, mucus production).

Analysis of vapor from a vaporizer recovered 89.1% THC and 9.5% smoke toxins

In contrast, cannabis smoke from a pipe recovered 10.8% THC and about 87% smoke toxins.

Vaporization generates less carbon monoxide.

Chronic Obstructive Pulmonary Disease

Most studies have found that cannabis is not associated with COPD.

A survey of 878 adults older than 40 in Vancouver found that cannabis smokers had no more COPD or respiratory symptoms than non-smokers.

Lung Cancer

Cannabis does not appear to increase lung cancer risk.

A pooled meta-analysis of 6 case-control studies in the US, Canada, UK, and New Zealand that included data on 2,159 lung cancer cases and 2,985 controls found "little evidence for an increased risk of lung cancer among habitual or long-term cannabis smokers"

Pneumonia

It is unclear whether cannabis is associated with an increased risk of pneumonia.

Some case series and studies in immunocompromised patients have noted a link

Some effects of smoked cannabis could predispose to pneumonia. Delta-9 tetrahydrocannabinol suppresses alveolar macrophage function and causes replacement of ciliated bronchial epithelium with hyperplastic mucus-secreting bronchial epithelial cells.

Contamination in Cannabis

Fungal contamination (*Aspergillus* and *Penicillium* species) in marijuana samples has been demonstrated. Contamination with fungal or bacterial pathogens could increase risk of pneumonia and other respiratory problems. Lack of ventilation and high humidity increase the likelihood of mold growth in indoor growing operations .

While medical cannabis may be safer than unregulated cannabis, testing for fungal or bacterial contamination varies by jurisdiction.

There are concerns that pesticides may pose risks in cannabis products

Cardiovascular Effects

THC can cause tachycardia; chronic users may develop bradycardia.

Cannabis can cause changes in blood pressure. High doses can cause orthostatic hypotension and syncope.

Cannabis can cause an acute increase in blood pressure.

Cannabis can increase the risk of angina.

Rarely marijuana can trigger an acute myocardial infarction.

In patients who have had a myocardial infarction, an 18-year follow up study showed no conclusive evidence that smoking marijuana increased mortality.

Case reports have associated cannabis use with acute coronary syndrome, arrhythmias, sudden cardiac death, and cardiomyopathy.

Allergies and Hypersensitivity

Cannabis pollen inhalation has been associated with allergic rhinitis, conjunctivitis, and asthma.

Skin exposure to plant material has been associated with urticaria, generalized pruritus, and periorbital angioedema.

Anaphylaxis has been reported after intravenous use of cannabis and ingestion of hemp seed-encrusted seafood (patient tolerated a subsequent oral seafood challenge).

Industrial hemp dust exposure has been implicated in byssinosis, an occupational obstructive lung disease associated with organic textile dust exposure.

Cognitive Function

Long-term cannabis users exhibit deficits in prospective memory and executive function.

In depressed and non-depressed regular marijuana users, there was an inverse association between marijuana use and verbal learning function

Adolescent marijuana users demonstrated significantly smaller medial orbitofrontal and inferior parietal volumes (regions of the brain associated with higher order cognition); smaller medial orbitofrontal volumes were associated with poorer complex attention.

A study looked at the impact of cannabis use during adolescence on subsequent cognitive function. Use of cannabis before age 18 lowered IQ 20 years later.

Anxiety and Depression

Although cannabis acts as an anxiolytic in low doses, high doses can be anxiogenic and can elicit panic reactions.

CBD exerts anti-anxiety effect

Chronic use may increase the risk of depression, although studies are mixed. A meta-analysis of 14 studies showed a weak risk (HR 1.17, 95% CI 1.05-1.30).

Psychosis/Schizophrenia

Whether or not cannabis can cause psychosis is debated.

Studies suggest that people at risk for schizophrenia run a higher risk of psychosis outcomes after cannabis use.

Smoking cannabis with a significant proportion of CBD may produce fewer psychotic symptoms.

Cochrane systematic review of cannabis and schizophrenia noted that studies were limited, and that "currently evidence is insufficient to show cannabidiol has an antipsychotic effect".

Dependence

Cannabis dependence may occur: the estimated global prevalence is 0.23% in males and 0.14% in females.

Prevalence peaks in the 20-24 years age group and decreases steadily with age.

In a survey of 6,917 marijuana users, 15% met the criteria for a marijuana use disorder. People who met the criteria for marijuana use disorder also were correlated with weekly marijuana use, early marijuana use, other substance use disorders, substance abuse treatment, and serious psychological distress.

Marijuana usage goes up in states that pass medical marijuana laws. However, the dependence rate among marijuana users does not differ between states with or without medical marijuana laws.

Driving Under the Influence

THC alters perception and psychomotor performance and may contribute to an increased risk of causing a traffic accident.

A systematic review and meta-analysis of nine observational studies found that acute cannabis consumption is associated with an increased risk of motor vehicle crashes, especially for fatal collisions.

A case-control study comparing alcohol and cannabis use on driving.

THC with a 29% increase in unsafe driving

101% for alcohol increase in unsafe driving

Exposure During Pregnancy

Cannabis use during pregnancy is not recommended.

Heavy use of cannabis during pregnancy may cause adverse effects on early neurodevelopment, including subtle cognitive impairment and decrements in executive functioning later in life.

Cannabis use has not been shown to increase the risk of congenital anomalies.

Some studies have shown a decrease in fetal growth.

There is a possible increased risk of preterm birth.

Lactation and Fertility

Cannabis use during lactation is not recommended.

THC and its metabolites are excreted in breast milk.

Infants exposed to marijuana during lactation had lower scores on the Psychomotor Developmental Index compared to non-exposed infants (effects could not be separated from prenatal exposure).

Some studies indicate that chronic use of marijuana may decrease plasma testosterone and decreases sperm count, concentration, and motility.

Cannabinoid Hyperemesis Syndrome

Chronic cannabis use may be associated with Cannabinoid Hyperemesis Syndrome (also called Cyclic Vomiting Syndrome).

It is characterized by episodes of nausea and vomiting, abdominal pain, and sometimes polydipsia.

Obsessive hot-water bathing may be observed, as it alleviates symptoms.

The syndrome can lead to weight loss or acute renal failure from dehydration.

The etiology of CHS is thought to be activation of CB1 receptors that can reduce gastric emptying.

Summary

Cannabis is generally well-tolerated, and serious adverse effects, including increased risk of cardiovascular events, are rare.

Adverse changes in cognitive function, especially executive function, may occur, especially with fetal or adolescent exposure.

Cannabis should be avoided by adolescents, pregnant women, and nursing mothers.

Cannabis should be avoided in those at risk of psychosis.

Many studies show driving impairment, but on a much lower scale than alcohol.

Drug interactions are a concern.

Cannabis enhances CNS depressant effects when combined with alcohol, barbiturates and benzodiazepines, but probably not opioids

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