



APIRx Pharmaceuticals, BV

CPhI Worldwide, October 9-11, 2018

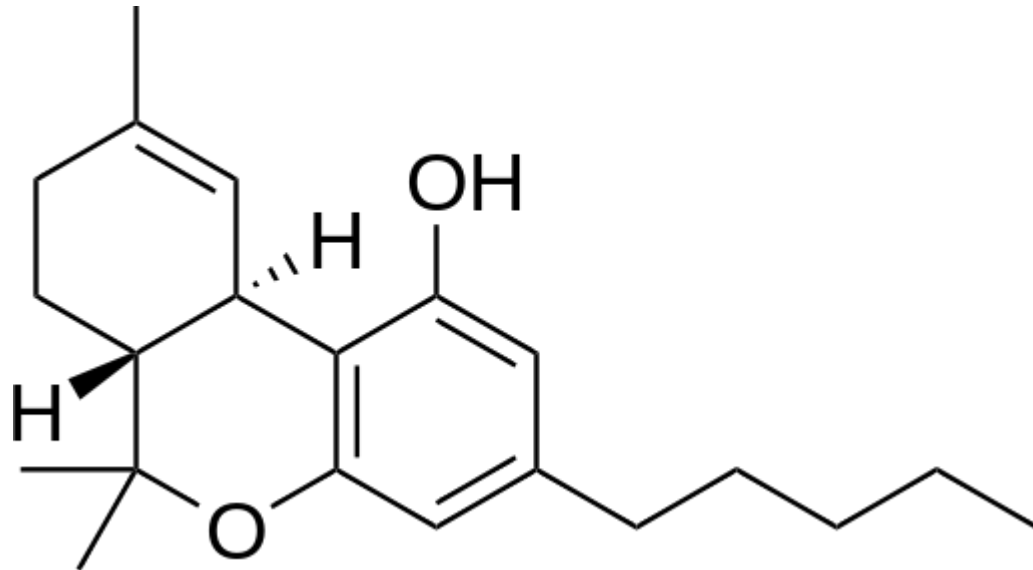
Madrid, Spain

APIRx Pharma



- Cannabis sativa contains 145 identified chemical compounds known as cannabinoids. Several of these compounds demonstrate biological activities.
- APIRx is the world' first manufacturer of pharma-quality cGMP cannabinoid API's from cannabis plant:
 - THC (tetrahydrocannabinol)
 - CBD (cannabidiol)
 - CBG (cannabigerol)
- We use cannabis supplied by Bedrocan BV, which cultivates the plant according to GMP conditions.
- We are in a process of filing DMF's in the US, Canada, as well as CEP in Europe.

Tetrahydrocannabinol (THC)



THC was first isolated from cannabis plant in 1964 by Raphael Mechoulam and Yechiel Gaoni at the Weizman Institute of Science in Israel.

THC is scheduled by the UN Convention on Psychotropic Substances. It was listed under Schedule I in 1971, but reclassified to Schedule II in 1991.

In the US THC is listed as a Sch I controlled substance by US federal law under the Controlled Substance Act.

Synthetic THC is used in the US in an antiemetic drug; *Marinol* and its generic versions (dronabinol), and natural THC is used in a drug *Nabiximols (Sativex)*, which has been registered in a number of countries to treat spasticity in MS.

THC CoA



Certificate of Analysis

Product	THC (10% w/w in ethanol)
Name	Delta-9-tetrahydrocannabinol (10% w/w solution in ethanol)
Origine	Plant derived
Batch number	250844-A
Quality regimen	GMP Pharmaceutical grade
Specification	THC-001 v0.1

Test	Test method	specification	Result (%)	complies
Assay	LC-THC-001	For information but around 10% w/w	>13.2	Y
Purity*	LC-THC-001	98-100%	>99.4	Y
Impurities***	LC-THC-001	Report each impurity >0.05%		
		THCV (C3)**	<0.24	n.a.
		THC-C4**	<0.16	n.a.
		THC-A**	<0.21	n.a.
		Others	none	n.a.

* Purity based on the peak areas

* Compounds were identified by means of the PDA and MS-data. A CBN-reference standard was used

** THCv(C3), THC C-4 and THC-A are typical constituents of plant derived material indicating the origin of the source.

QA-statement: the data were collected in agreement with GMP-regulations as laid down in EU-regulations. The reported data adequately reflect the raw data

Conclusion: this batch of THC is approved

Stability: This product is stable for at least 1 year when stored at 2-8°C in the absence of light and the original container

This certificate is approved by the Manager QA

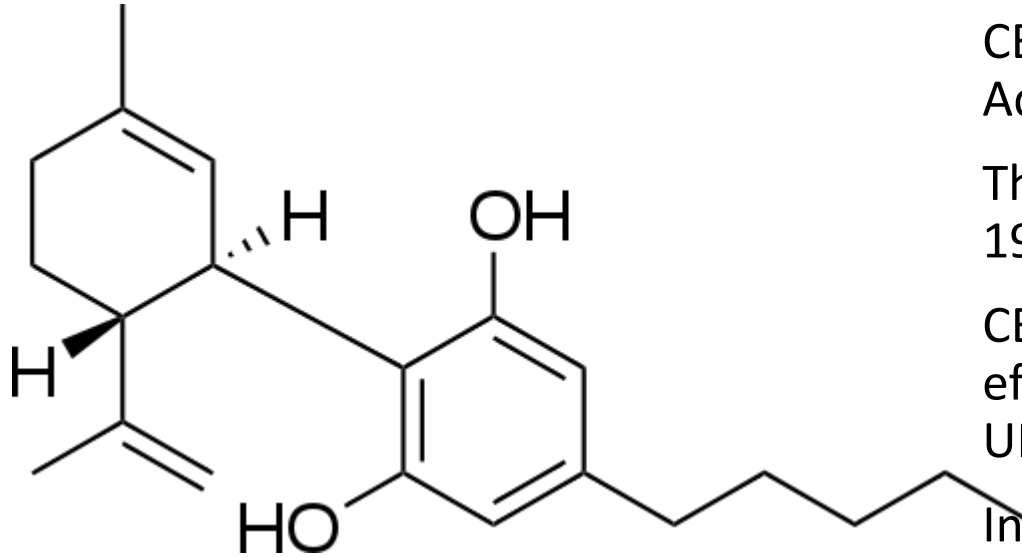
Signature and date

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Cannabidiol (CBD)



CBD was isolated from cannabis in 1940 independently by Adams and Todd and their colleagues.

The chemical structure of CBD was fully established in 1963 by Mechoulam and Shvo.

CBD does not appear to have any psychotropic ("high") effects such as those caused by THC and is not listed in the UN Convention on Psychotropic Substances.

In the US CBD is schedule I (CI) controlled substance, while outside the US its legal status varies from country to country.

CBD is one of two active ingredients in a drug *Sativex* and was recently approved by the USFDA as *Epidolex* for rare types of childhood epilepsy (Dravet, Lennox-Gastaut, Tuberous Sclerosis) as a sole API. DEA scheduled *Epidolex* as CV controlled drug.

CBD CoA



Certificate of Analysis

Product Name	CBD, crystalline
Origin	Plant derived
Batch number	1801002.1572
Quality regimen	GMP Pharmaceutical grade
Specification	CBD-001 v0.1

Test	Test method	specification	Result (%)	complies
Assay	LC-CBD-001	96-100%	>99.8	Y
Purity*	LC-CBD-001	96-100%	>99.8	Y
Impurities**	LC-CBD-001	Report each impurity >0.05%		
		CBDV**	<0.05	n.a.
		CBD C4**	<0.06	n.a.
		Unassigned	<0.07	n.a.
		Others	None	n.a.

* Purity based on the peak areas

** Compounds were identified by means of the PDA and MS-data.

** CBDV and CBD C4 are typical constituents of plant derived material indicating the origin of the source.

QA-statement: the data were collected in agreement with GMP-regulations as laid down in EU-regulations. The reported data adequately reflect the raw data.

Conclusion: this batch of CBD is approved

Stability: This product is stable for at least 1 year when stored at 2-8°C in the absence of light and in the original container

This certificate is approved by the Manager QA

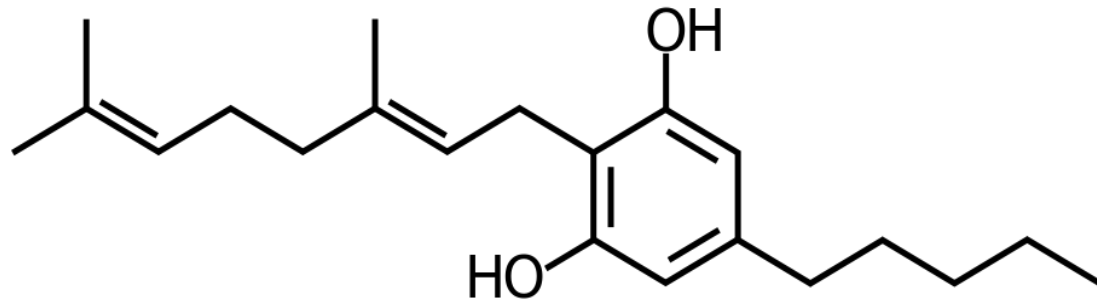
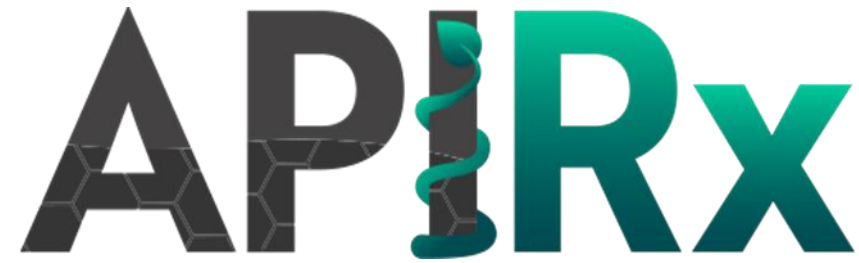
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Cannabigerol (CBG)



Cannabigerol is a minor constituent of cannabis. During plant growth, most of the CBG is converted into other cannabinoids, primarily THC and CBD, usually leaving below 1% CBG in the plant.

CBG is not listed in the UN Convention on Psychotropic Substances.

Research is limited, including laboratory models of colitis, neurodegeneration, cancer, infectious diseases (MRSA, MDRB), dermatological conditions and feeding behavior as well as some other diseases and conditions where it demonstrated promising results.

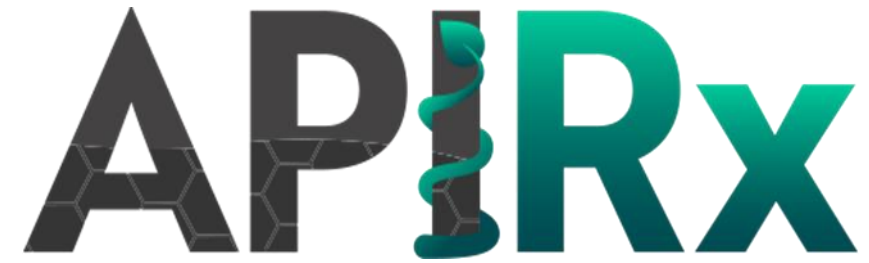
CBG has been shown to promote apoptosis in cancer cells (Colon CA) and inhibit tumor growth in vivo and in vitro.

Cannabinoids



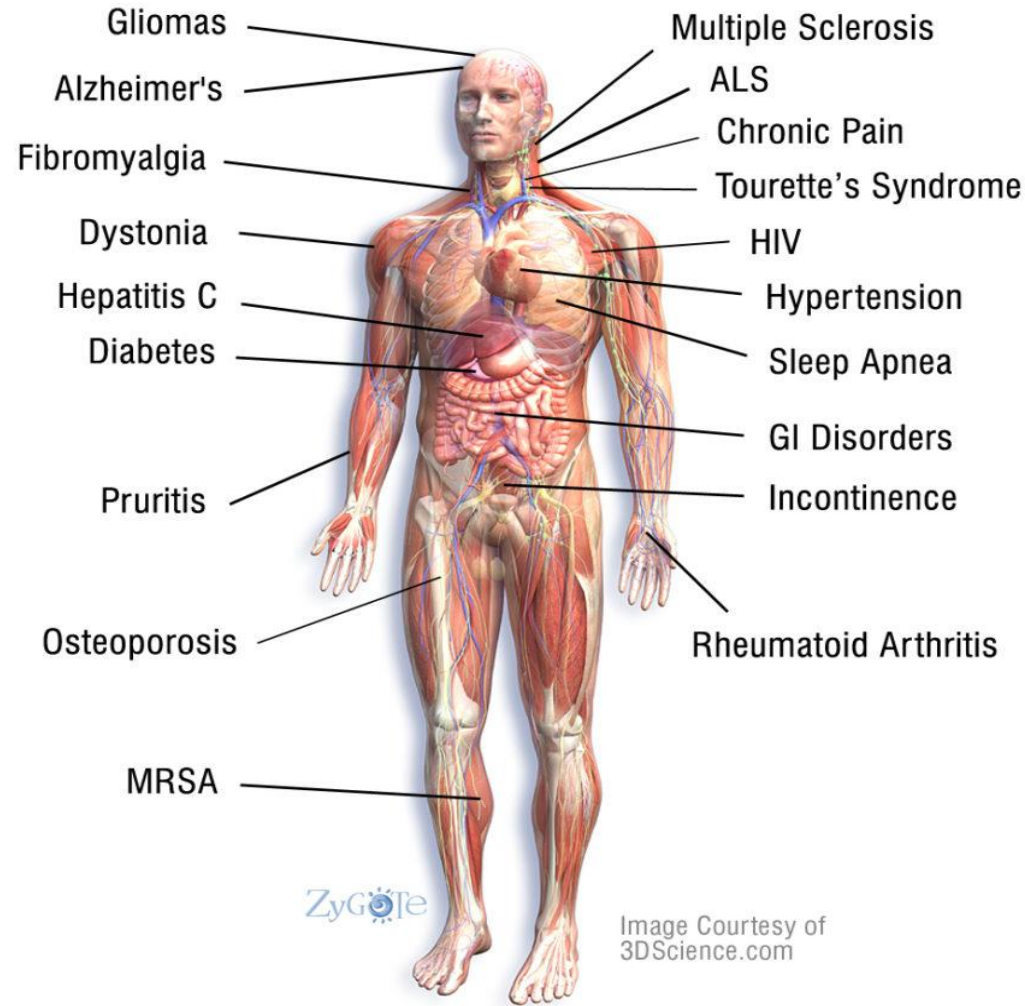
- Cannabis have been used for medical purposes for over 4000 years; first in China and India then in Egypt and Mediterranean region and since the 16th century in Europe.
- Individual cannabinoids were first isolated and characterized in Israel in mid 1960's by Professor Raphael Mechoulam (Hebrew University, Jerusalem).
- In 1990's Professor Mechoulam and his colleagues discovered and identified the endocannabinoid system which participates in all physiological processes in human, animal and primitive organisms.
- This opened up an opportunity of using cannabinoids for treating multiple disorders and symptoms.

The Endocannabinoid System



- Endocannabinoids and their receptors are found throughout the body: in the brain, all organs, connective tissues, glands, immune cells, etc. In each tissue, the ECS performs different tasks, but the goal is always the same: homeostasis, the maintenance of a stable internal environment despite fluctuations in the external environment.
- Cannabinoids promote homeostasis at every level of biological life; from the sub-cellular, to the organism, and beyond. Endocannabinoids and cannabinoids are found at the intersection of the body's various systems allowing communication and coordination between different cell types.
- At the site of an injury, cannabinoids can be found decreasing the release of activators and sensitizers from the injured tissue, stabilizing the nerve cell to prevent excessive firing, and calming nearby immune cells to prevent release of pro-inflammatory substances, thus being neuroprotective.

Cannabinoid' Potential Therapeutic Applications



APIRx

Potential Therapeutic Use of Cannabinoids

Glioma

Osteoporosis

Tourette's Syndrome

Alzheimer's

ALS

HIV

Fibromyalgia

MRSA

Hypertension

Dystonia

MS

Sleep Apnea

Hepatitis C

Chronic Pain

Incontinence

Diabetes

IBS

Rheumatoid Arthritis

Pruritus

IBD

Reproductive



Cannabinoids in USA



- The very first cannabinoid drug (*Marinol*) was approved in the USA in 1985. This drug product and its generic versions are soft gelatin capsules containing synthetic THC dissolved in sesame oil. The drug is used predominantly as an antiemetic in cancer patients to suppress nausea and vomiting resulting from chemotherapy and loss of appetite/ weight loss in HIV/ AIDS.
- *Syndros*, a synthetic THC oral solution (in sesame oil) has also been approved for the same indication.
- Several drug candidates containing synthetic CBD are being developed in the US.

Cannabinoids in USA and Beyond

- In April of 2018 FDA approved the first drug which contained plant derived CBD – *Epidolex*.
- In the countries outside the US which include Israel, Canada, Spain, Germany, etc. plant-derived cannabinoids are used in drug development projects.
- The first drug which contains THC and CBD (*Sativex*) has been approved by the EMA and in more than 30 countries worldwide.
- So far, cGMP plant-derived cannabinoids were not commercially available on the market.

Inquiries, Samples and Shipment



Should you need a sample or supply of cannabinoid API's which we offer, APIRx can ship the samples or commercial quantities of the material after a customer provides an original import permit issued in the country where the material needs to be shipped.

Visit our website: WWW.APIRXPHARMA.COM