



CÂMARA DOS DEPUTADOS
COMISSÃO ESPECIAL - PL 0399/15 - MEDICAMENTOS
FORMULADOS COM CANNABIS

Indicações terapêuticas dos canabinóides & Diferenças entre canabinóides naturais e sintéticos

Sidarta Ribeiro, Ph.D.





き 多文化共生フェスティバル 2010







Non-psychotropic plant cannabinoids: new therapeutic opportunities from an ancient herb

Angelo A. Izzo^{1,4}, Francesca Borrelli^{1,4}, Raffaele Capasso^{1,4}, Vincenzo Di Marzo^{2,4} and Raphael Mechoulam³

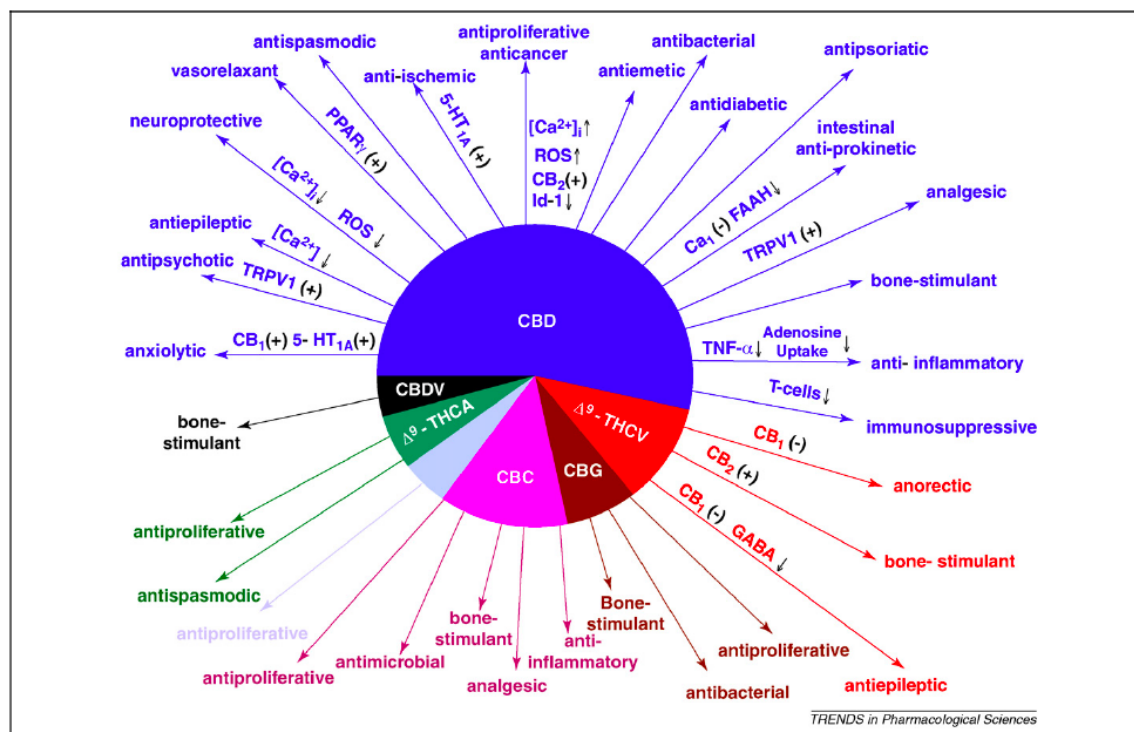


Figure 1. Pharmacological actions of non-psychotropic cannabinoids (with the indication of the proposed mechanisms of action).

Abbreviations: Δ⁹-THC, Δ⁹-tetrahydrocannabinol; Δ⁸-THC, Δ⁸-tetrahydrocannabinol; CBN, cannabino; CBD, cannabidiol; Δ⁹-THCV, Δ⁹-tetrahydrocannabivarin; CBC, cannabichromene; CBG, cannabigerol; Δ⁹-THCA, Δ⁹-tetrahydrocannabinolic acid; CBDA, cannabidiolic acid; TRPV1, transient receptor potential vanilloid type 1; PPAR_γ, peroxisome proliferator-activated receptor γ; ROS, reactive oxygen species; 5-HT_{1A}, 5-hydroxytryptamine receptor subtype 1A; FAAH, fatty acid amide hydrolase. (+), direct or indirect activation; ↑, increase; ↓, decrease.

Non-psychotropic plant cannabinoids: new therapeutic opportunities from an ancient herb

Angelo A. Izzo^{1,4}, Francesca Borrelli^{1,4}, Raffaele Capasso^{1,4}, Vincenzo Di Marzo^{2,4} and Raphael Mechoulam³

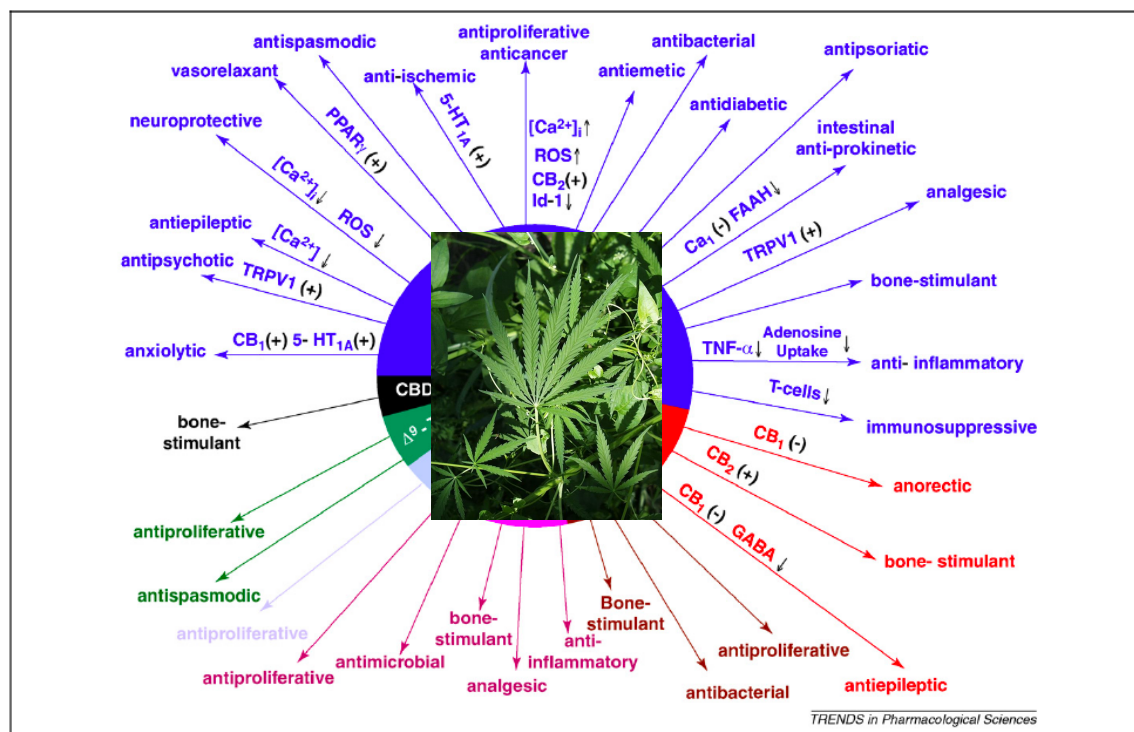


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Abbreviations: Δ^9 -THC, Δ^9 -tetrahydrocannabinol; Δ^8 -THC, Δ^8 -tetrahydrocannabinol; CBN, cannabino; CBD, cannabidiol; Δ^9 -THCV, Δ^9 -tetrahydrocannabivarin; CBC, cannabichromene; CBG, cannabigerol; Δ^9 -THCA, Δ^9 -tetrahydrocannabinolic acid; CBDA, cannabidiolic acid; TRPV1, transient receptor potential vanilloid type 1; PPAR γ , peroxisome proliferator-activated receptor γ ; ROS, reactive oxygen species; 5-HT $_{1A}$, 5-hydroxytryptamine receptor subtype 1A; FAAH, fatty acid amide hydrolase. (+), direct or indirect activation; \uparrow , increase; \downarrow , decrease.



Why I changed my mind on weed

By **Dr. Sanjay Gupta**, CNN Chief Medical Correspondent

August 9, 2013 – Updated 0044 GMT (0844 HKT)

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GONE TO POT

'I HAVE TRIED IT'

Sanjay Gupta's special 'Weed' premieres on CNN Sunday at 8pm

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GE imagination at work

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The Marijuana

Será a Cannabis
um Santo Graal
para a medicina?



Epilepsia

Envelhecimento

Câncer

Epilepsia

PROVINCIAL MEDICAL JOURNAL

And Retrospect of the Medical Sciences.

No. 123.]

LONDON, SATURDAY, FEBRUARY 4, 1843.

PRICE SIXPENCE.
[Stamped Edition Sevenpence.]

ON THE PREPARATIONS OF THE INDIAN HEMP, OR GUNJAH,* (*Cannabis Indica*)

Their Effects on the Animal System in Health, and their Utility in the Treatment of Tetanus and other Convulsive Diseases.

By W. B. O'SHAUGHNESSY, M.D., Bengal Army,
Late Professor of Chemistry and Materia Medica in the
Medical College of Calcutta.

[Concluded from p. 347.]

Experiments by the Author—Inferences as to the Action of the Drug on Animals and Man.

Such was the amount of preliminary information before me, by which I was guided in my subsequent attempts to gain more accurate knowledge of the action, powers, and possible medicinal applications of this extraordinary agent.

There was sufficient to show that hemp possesses, in small doses, an extraordinary power of stimulating the digestive organs, exciting the cerebral system, of acting also on the generative apparatus. Larger doses, again, were shown by the historical statements to induce insensibility or to act as a powerful sedative. The influence of the drug in allaying pain was equally manifest in all the memoirs referred to. As

twenty minutes was ridiculously drunk; in four hours his symptoms passed away, also without harm.

Expts. 3, 4, and 5.—Three kids had ten grains each of the alcoholic extract of *gunjah*. In one no effect was produced; in the second there was much heaviness, and some inability to move; in the third a marked alteration of countenance was conspicuous, but no further effect.

Expt. 6.—Twenty grains were given, dissolved in a little spirit, to a dog of very small size. In a quarter of an hour he was intoxicated; in half an hour he had great difficulty of movement; in an hour he had lost all power over the hinder extremities, which were rather stiff but flexible; sensibility did not seem to be impaired, and the circulation was natural. He readily acknowledged calls by an attempt to rise up. In four hours he was quite well.

In none of these or several other experiments was there the least indication of pain, or any degree of convulsive movement observed.

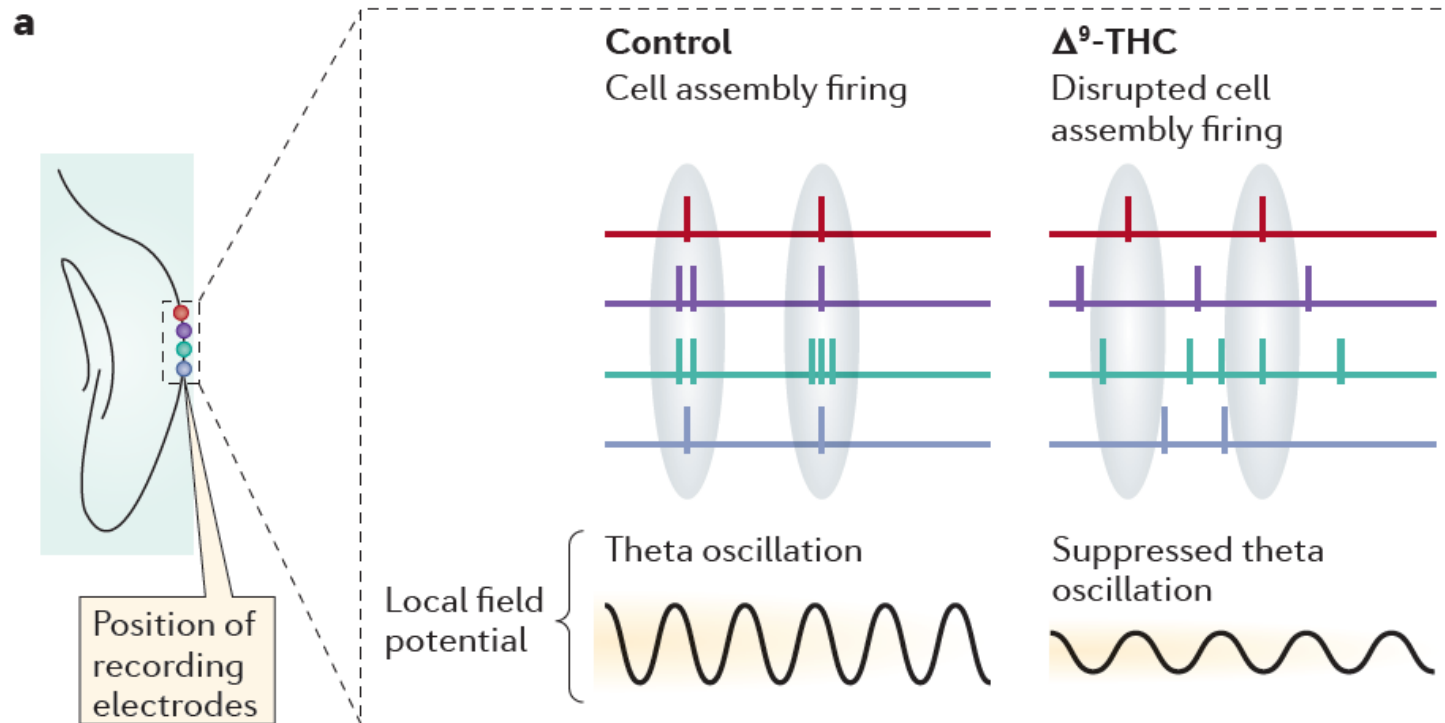
It seems needless to dwell on the details of each experiment; suffice it to say that they led to one remarkable result—that while carnivorous animals and fish, dogs, cats, swine, vultures, crows, and adjutants, invariably exhibited the intoxicating influence of the drug, the graminivorous, such as the horse, deer, monkey, goat, sheep, and cow, experienced but

Cannabinoids reveal importance of spike timing coordination in hippocampal function

David Robbe¹, Sean M Montgomery¹, Alexander Thome², Pavel E Rueda-Orozco¹, Bruce L McNaughton² & György Buzsáki¹

1526

VOLUME 9 | NUMBER 12 | DECEMBER 2006 NATURE NEUROSCIENCE



Ensaio clínico com CBD

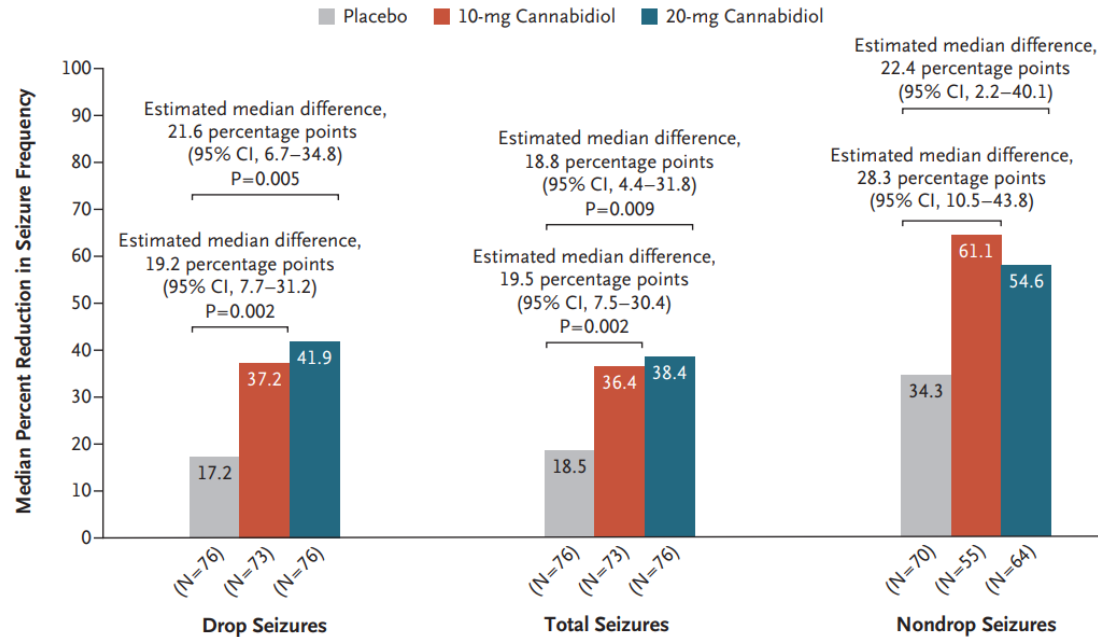
Table 2. Primary Efficacy End Point of Percentage Change in Convulsive-Seizure Frequency in Each Trial Group.*

Variable	Cannabidiol	Placebo	Adjusted Median Difference (95% CI)	P Value†
<i>percentage points</i>				
No. of convulsive seizures per mo — median (range)				
Baseline	12.4 (3.9 to 1717)	14.9 (3.7 to 718)		
Treatment period	5.9 (0.0 to 2159)	14.1 (0.9 to 709)		
Percentage change in seizure frequency — median (range)	-38.9 (-100 to 337)	-13.3 (-91.5 to 230)	-22.8 (-41.1 to -5.4)	0.01

* CI denotes confidence interval.

† The P value was calculated with the use of a Wilcoxon rank-sum test with the Hodges–Lehmann approach.

**Devinsky et al.,
The New
England
Journal, 2017**



**Devinsky et al.,
The New
England
Journal, 2018**

RESEARCH ARTICLE

A prospective open-label trial of a CBD/THC cannabis oil in dravet syndrome

Bláthnaid McCoy^{1,2}, Laura Wang³, Maria Zak¹, Sameer Al-Mehmadi¹, Nadia Kabir¹, Kenda Alhadid¹, Kyla McDonald⁴, Grace Zhang⁴, Rohit Sharma¹, Robyn Whitney^{1,2}, Katia Sinopoli⁴ & O. Carter Snead III¹

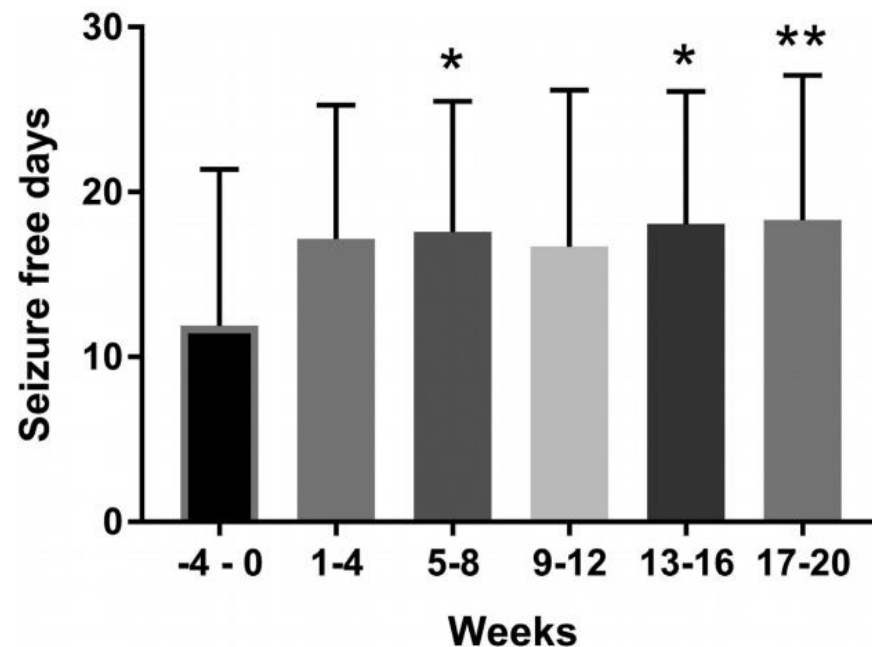
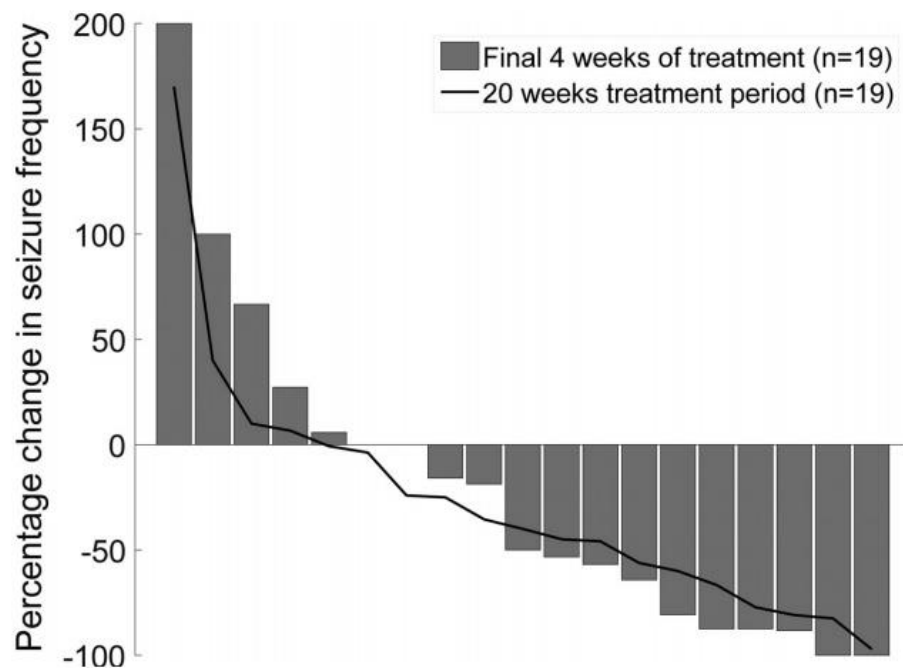
¹Division of Neurology, the Hospital for Sick Children, Toronto, Canada

²Department of Pediatrics, University of Toronto, Toronto, Canada

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Ensaio clínico
com óleo de
Cannabis





ANNUAL MEETING ABSTRACTS: VIEW

[« Back to Search Results](#)**(Abst. 2.233), 2018****CANNABIDIOL TOLERANCE IN CHILDREN AND ADULTS WITH TREATMENT-RESISTANT EPILEPSY**

Authors: Shimrit Uliel-Sibony, Tel-Aviv Sourasky Medical Center, Dana Children's Hospital; Moran Hausman-Kedem, Tel-Aviv Sourasky Medical Center, Dana Children's Hospital; and Uri Kramer, Tel-Aviv Sourasky Medical Center, Dana Children's Hospital

Content:RATIONALE:

The aim of this study is to assess the tolerance rate of cannabinoids in the treatment of epilepsy in the pediatric and adults population.

METHODS:

Prospective review of the tolerance to cannabinoids of 92 consecutive patients aged 1-37 years (mean 11.8 years) with treatment-resistant epilepsy during the period of 1.3.2014 to 31.9.2017. Tolerance was defined as either the necessity to increase dose in 30% or more following reduction of efficacy, or response reduction of more than 30%.

RESULTS:

Ninety-two patients with treatment-resistant epilepsy of various etiologies were treated with cannabis oil extract (CBD/THC ratio of 20:1) for an average of 19.8 months. Tolerance was seen in 30 (32.6%) of the patients. It was reported on an average dose of 12.6 mg/kg/d and the mean time till appearance of tolerance was 7.3 months (range: 1-24 months). Out of these patients 58% (17 patients) showed > 50% reduction in mean monthly seizure frequency. While trying to resist the tolerance effect, CBD dose was increased in most patients with observed tolerance. This led to achieving previous response level in 12 and satisfying but less than prior response level in 15 patients. Of the patients with observed tolerance, in nine it was concomitant with drug's tapering.

CONCLUSIONS:

Our findings suggest that cannabidiol tolerance exists and it limits the efficacy of this antiseizure treatment in the long-term clinical management of epilepsy in the pediatric and adults population

FUNDING:

No funding was received.

CBD puro
deixa de
funcionar
depois de 7
meses
(tolerância)

Envelhecimento



In vivo Evidence for Therapeutic Properties of Cannabidiol (CBD) for Alzheimer's Disease

Georgia Watt¹ and Tim Karl^{1,2*}

¹ Karl Group, Behavioural Neuroscience, Western Sydney University, Penrith, NSW, Australia, ² Research Australia, Randwick, NSW, Australia

TABLE 1 | Summary of the effects of CBD and CBD-THC combinations on AD models.

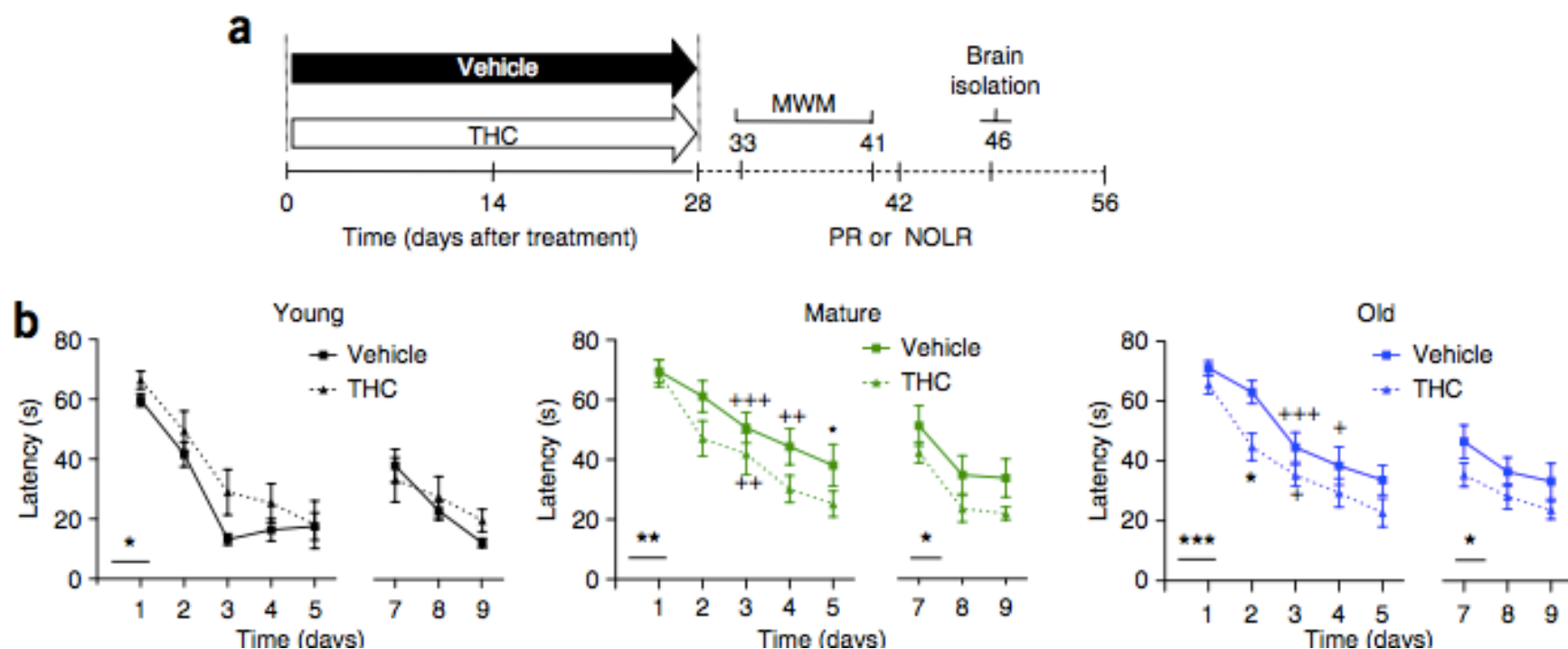
Effect of Cannabidiol on AD-like Pathology		
Model	Effect	References
IN VITRO STUDIES USING CBD		
PC12 Neuronal Cells	Protected against A β neurotoxicity and oxidative stress, increased cell survival and decreased ROS production and lipid peroxidation Inhibited tau hyperphosphorylation Prevented transcription of pro-inflammatory genes	Iuvone et al., 2004 Esposito et al., 2006a Esposito et al., 2006b
Glutamate Neuronal Toxicity Model	Antioxidant properties	Hampson et al., 1998
Primary Rat Microglia	Increased microglial migration and prevented ATP-induced intracellular calcium increase	Martin-Moreno et al., 2011
PC12 and SH-SY5Y Cells	Improved cell viability after treatment with tert-butyl hydroperoxide treatment	Harvey et al., 2012
SH-SY5Y Cells	Protected against A β neurotoxicity and microglial-activated neurotoxicity	Janežford et al., 2014
SH-SY5Y ^{APP+} Cells	Induced APP ubiquitination and subsequently A β production and increased cell survival by reducing apoptotic rate	Scuderi et al., 2014
IN VIVO STUDIES USING CBD		
Mice inoculated with human A β ₄₂ peptide	Attenuated A β induced neuroinflammatory responses by decreasing expression of pro-inflammatory gene and mediators Reduced reactive gliosis	Esposito et al., 2007 Esposito et al., 2011
Mice intraventricularly injected with fibrillar A β	Decreased microglial activation and reversed a spatial reference memory deficit in the MWM	Martin-Moreno et al., 2011
APPxPS1 transgenic mice (mixed background)	Reversed social and object recognition memory deficits in the CB task Prevented development of social recognition memory deficits. No effect on A β load but subtle effects on inflammatory markers, cholesterol and dietary phytosterol retention	Cheng et al., 2014a Cheng et al., 2014b
IN VIVO STUDIES USING CBD-THC		
Young APPxPS1 transgenic mice (mixed background)	Improved memory deficits in the two-object recognition task and the active avoidance task. Decreased soluble A β ₄₂ levels and changed plaque composition and reduced astrogliosis, microgliosis and inflammatory related molecules	Aso et al., 2015
Aged APPxPS1 transgenic mice (mixed background)	Restored cognition in the two object recognition task but had no effects on A β load or related glial reactivity	Aso et al., 2016
Transgenic tauopathy mouse model	Reduced A β and tau deposition in the hippocampus and cerebral cortex, increased autophagy, decreased gliosis, increased the ratio of reduced/oxidized glutathione and reduced levels of iNOS	Casarejos et al., 2013

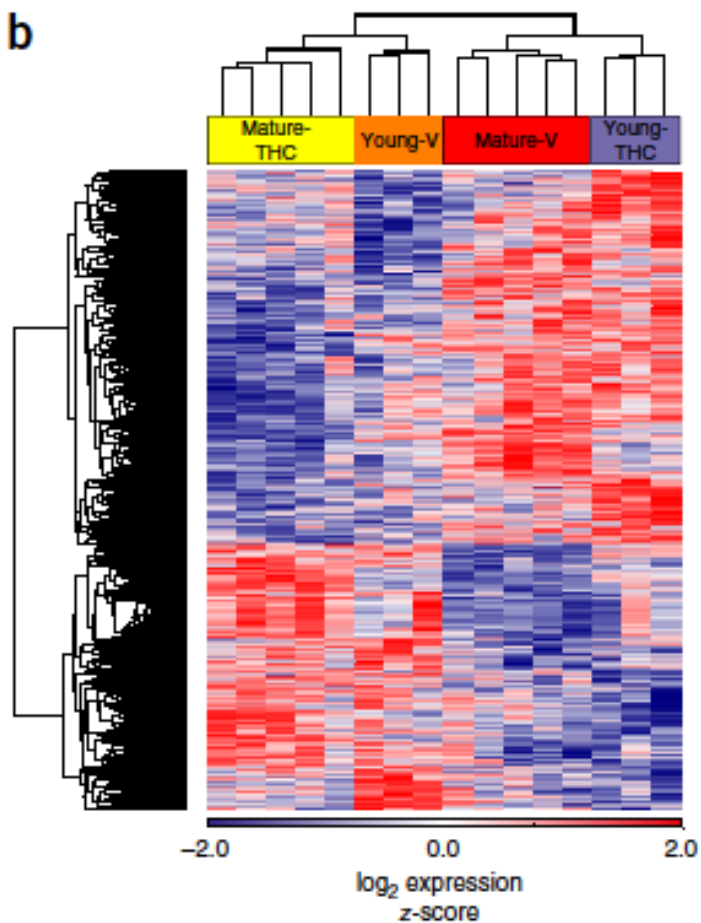
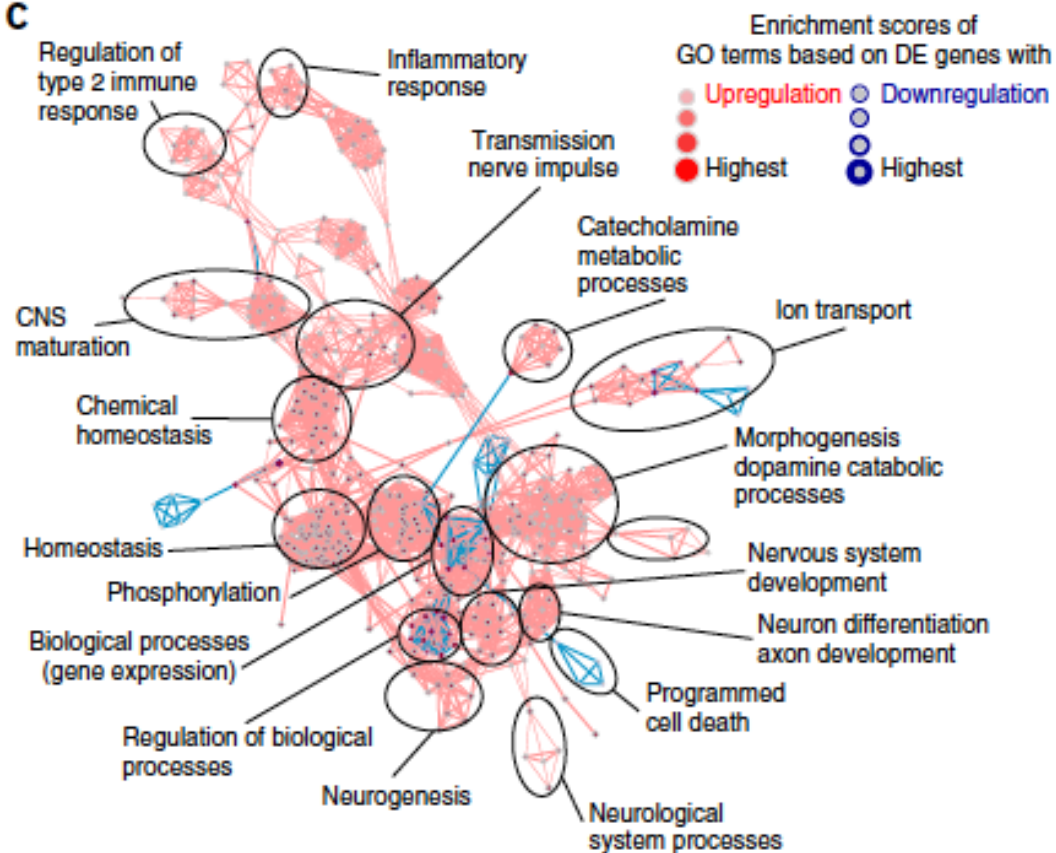
A chronic low dose of Δ^9 -tetrahydrocannabinol (THC) restores cognitive function in old mice

Andras Bilkei-Gorzo^{1,4}, Onder Albayram^{1,4}, Astrid Draffehn², Kerstin Michel¹, Anastasia Piyanova¹, Hannah Oppenheimer³, Mona Dvir-Ginzberg³, Ildiko Rácz¹, Thomas Ulas², Sophie Imbeault¹, Itai Bab³, Joachim L. Schultze² & Andreas Zimmer¹

¹Institute of Molecular Psychiatry, University of Bonn, Bonn, Germany. ²Genomics and Immunoregulation, LIMES Institute, Bonn, Germany. ³Institute of Dental Sciences, Hebrew University, Jerusalem, Israel. ⁴These authors contributed equally to this work. Correspondence should be addressed to A.Z. (neuro@uni-bonn.de).

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b**c**

Câncer



Preclinical and Clinical Assessment of Cannabinoids as Anti-Cancer Agents

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¹ Department of Pharmacology and Toxicology, Brody School of Medicine, East Carolina University, Greenville, NC, USA,

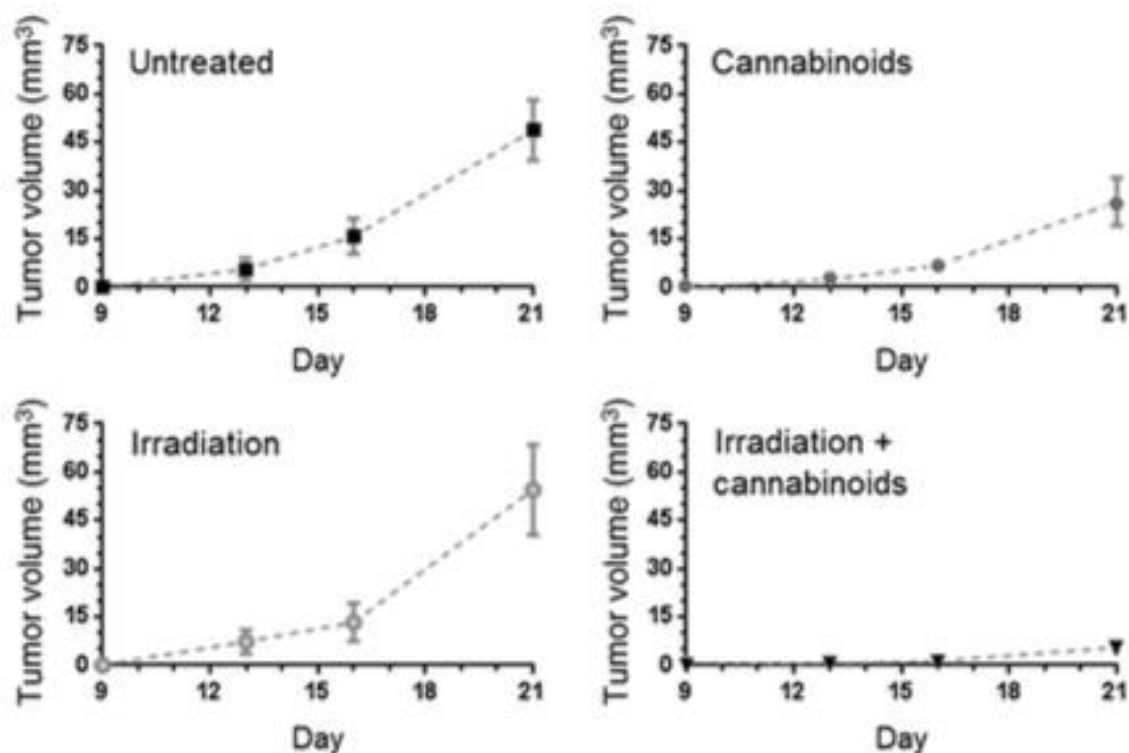
² Department of Pharmacology and Toxicology, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt, ³ Center for Health Disparities, East Carolina University, Greenville, NC, USA

Tipo de câncer	Publicações
Glioma	18
Seio	11
Pulmão	9
Intestino	7
Fígado	5
Melanoma	3
Próstata	2
Tiróide	2
Câncer de pele (não-melanoma)	2
Pâncreas	1

Small Molecule Therapeutics

The Combination of Cannabidiol and Δ^9 -Tetrahydrocannabinol Enhances the Anticancer Effects of Radiation in an Orthotopic Murine Glioma Model

Katherine A. Scott, Angus G. Dalgleish, and Wai M. Liu



The Horizon for Medical Cannabis:

Epilepsia

Envelhecimento

Câncer

Dor neuropática

Esclerose múltipla

Autismo

Mal de Parkinson

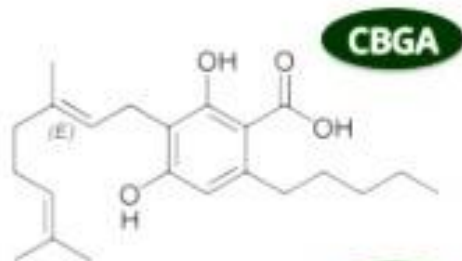
Doença de Alzheimer

Depressão

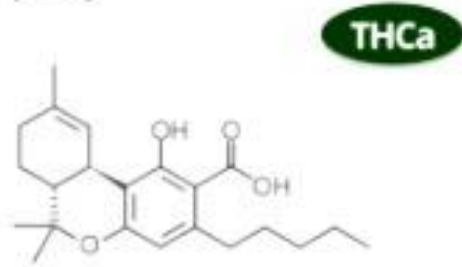
Ansiedade

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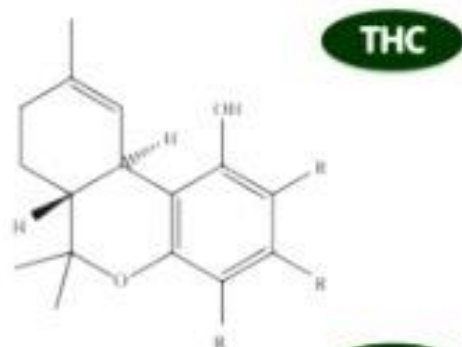
NATURAL CANNABINOIDS



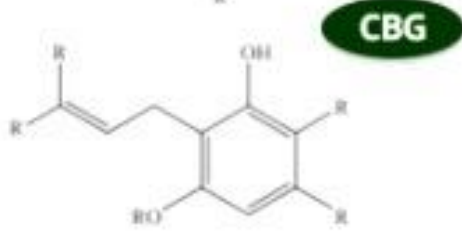
CBGA



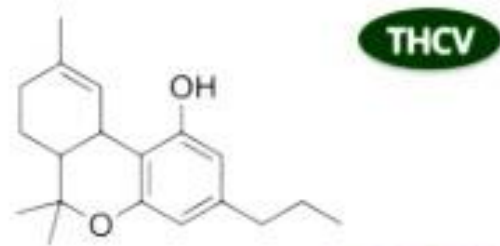
THCa



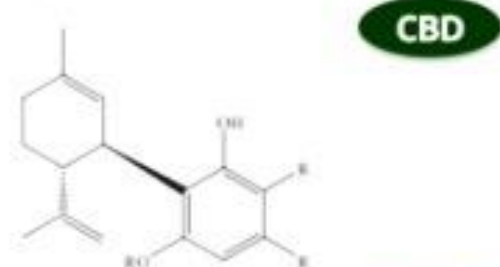
THC



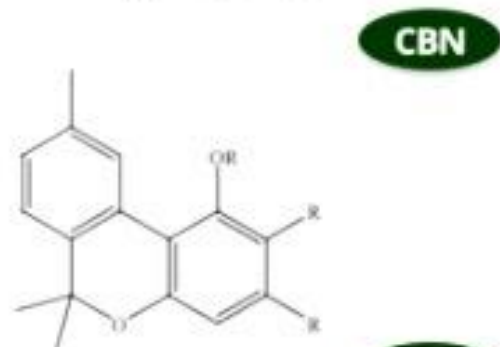
CBG



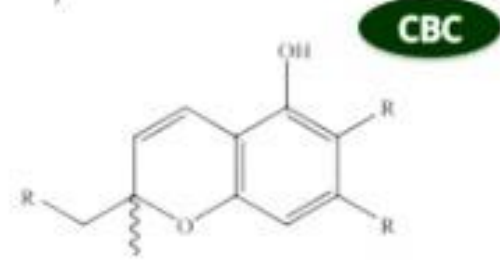
THCV



CBD



CBN



CBC



REVIEW

Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects

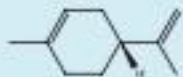

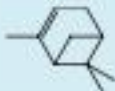









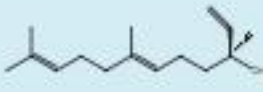

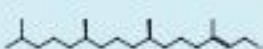

Ethan B Russo

GW Pharmaceuticals, Salisbury, Wiltshire, UK

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Keywords
cannabinoids; terpenoids;
essential oils; THC; CBD;
limonene; pinene; linalool;
caryophyllene; phytotherapy

Received
19 November 2010
Revised
29 December 2010
Accepted
12 January 2011

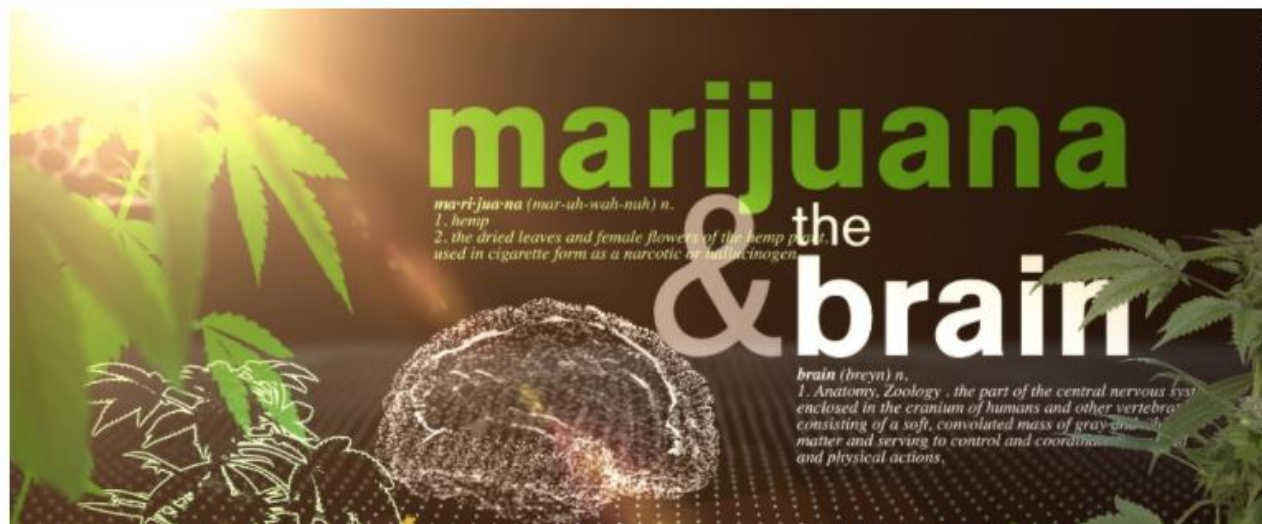
Terpenoid	Structure	Commonly encountered in	Pharmacological activity (Reference)	Synergistic cannabinoid
Limonene		 Lemon	Potent AD/immunostimulant via inhalation (Komori et al., 1995) Anxiolytic (Carvalho-Freitas and Costa, 2002; Pultrini Ade et al., 2006) via 5-HT _{2A} (Komiya et al., 2006) Apoptosis of breast cancer cells (Vigushin et al., 1998) Active against acne bacteria (Kim et al., 2008) Dermatophytes (Sanguineti et al., 2007; Singh et al., 2010) Gastro-oesophageal reflux (Harris, 2010)	CBD CBD CBD, CBC CBD CBC THC
α -Pinene		 Pine	Anti-inflammatory via PGE-1 (Gi et al., 1989) Bronchodilatory in humans (Falk et al., 1990) Acetylcholinesterase inhibitor, aiding memory (Petry et al., 2000)	CBD THC THC?, CBD
β -Myrcene		 Hops	Blocks inflammation via PGE-2 (Lorenzetti et al., 1991) Analgesic, antagonized by naloxone (Rao et al., 1990) Sedating, muscle relaxant, hypnotic (do Vale et al., 2002) Blocks hepatic carcinogenesis by aflatoxin (de Oliveira et al., 1997)	CBD CBD, THC THC CBD, CBC
Linalool		 Lavender	Anti-anxiety (Russo, 2001) Sedative on inhalation in mice (Buchbauer et al., 1993) Local anesthetic (Ile et al., 2000) Analgesic via adenosine A _{2A} (Peana et al., 2006) Anticonvulsant/anti-glutamate (Elisabetsky et al., 1995)	CBD, CBC? THC THC CBD CBD, THC, CBDV
β -Caryophyllene		 Pepper	Potent anti-leishmanial (do Socomo et al., 2003) AI via PGE-1 compatible phenylbutazone (Basile et al., 1988) Gastric cytoprotective (Tamise et al., 1996) Anti-malarial (Campbell et al., 1997) Selective CB ₂ agonist (100 nM) (Gertsch et al., 2008) Treatment of pruritus? (Karsak et al., 2007) Treatment of addiction? (Xi et al., 2010)	CBD THC ? THC THC CBD
Caryophyllene Oxide		 Lemon balm	Decreases platelet aggregation (Lin et al., 2005) Antifungal in onychomycosis comparable to ciclopiroxolamine and sulconazole (Yang et al., 1999) Insecticidal/anti-feedant (Bettarini et al., 1993)	THC CBC,CBG THCA, CBGA
Nerolidol		 Orange	Sedative (Binet et al., 1972) Skin penetrant (Cornwell and Barry, 1994) Potent antimalarial (Lopes et al., 1999; Rodrigues Goulart et al., 2004) Anti-leishmanial activity (Arnuda et al., 2005)	THC, CBN - ? ?
Phytol		 Green tea	Breakdown product of chlorophyll Prevents Vitamin A teratogenesis (Arnhold et al., 2002) TCASA via SSADH inhibition (Bang et al., 2002)	- - CBD



Medical marijuana and 'the entourage effect'

By Dr. Sanjay Gupta, CNN chief medical correspondent

🕒 Updated 1:58 PM ET, Tue March 11, 2014



Synthetic Cannabinoids (K2/Spice)

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What are synthetic cannabinoids?

Synthetic cannabinoids are human-made mind-altering chemicals that are either sprayed on dried, shredded plant material so they can be smoked or sold as liquids to be vaporized and inhaled in e-cigarettes and other devices. These products are also known as herbal or liquid incense.

These chemicals are called *cannabinoids* because they are similar to chemicals found in the marijuana plant. Because of this similarity, synthetic cannabinoids are sometimes misleadingly called "synthetic marijuana" (or "fake weed"), and they are often marketed as safe, legal alternatives to that drug. In fact, they are not safe and may affect the brain much more powerfully than marijuana; their actual effects can be unpredictable and, in some cases, more dangerous or even life-threatening.

Additional Drug Facts



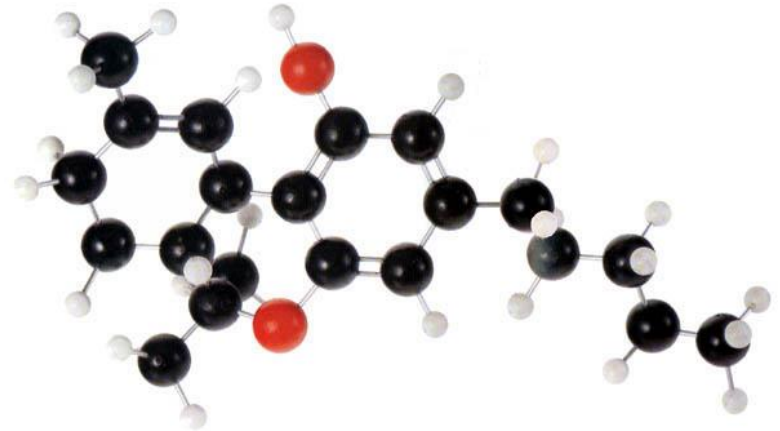
easyread.drugabuse.gov

Qual é melhor?

Planta inteira?



Molécula isolada?

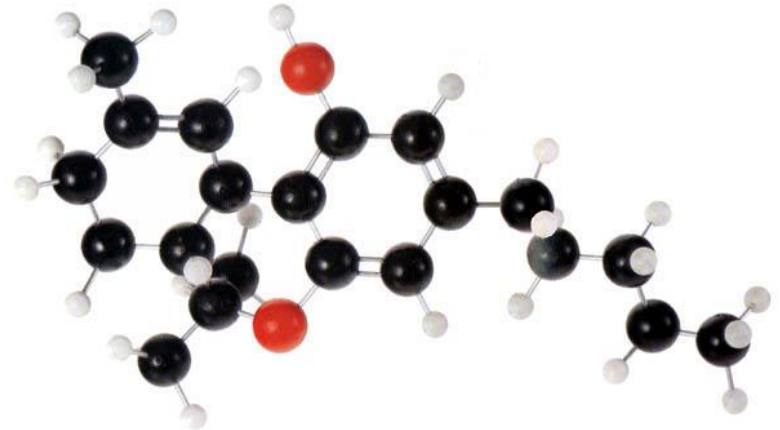


Qual é melhor?

Planta inteira?



Molécula isolada?



Depende!

A Cannabis está para a medicina do século XXI como os antibióticos estiveram para a medicina do século XX:

Uma grande revolução

A Cannabis está para a medicina do século XXI como os antibióticos estiveram para a medicina do século XX:

Uma grande revolução

Será acessível para todos?



O que deseja encontrar?



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[Início](#) /

~R\$ 2.800 por 30 ml

10ml Frasco Spray - Contém 3 Frascos
TETRAIDROCANABINOL,CANABIDIOL

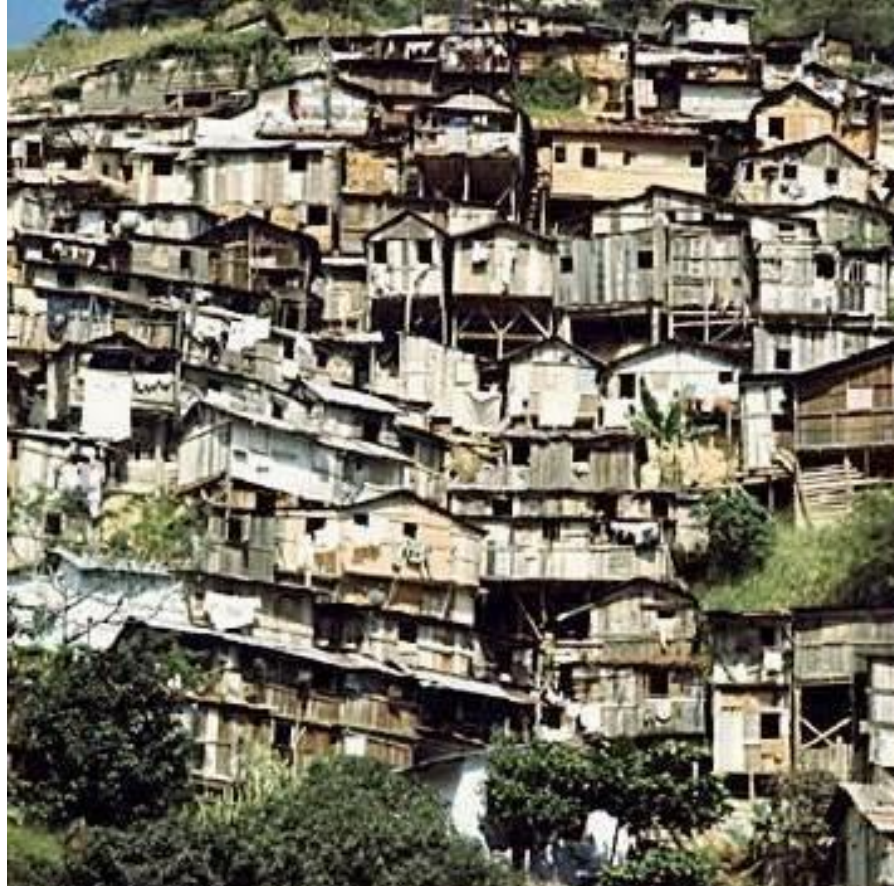
0 de 5 ★★★★★ (0)

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SEU USO PODE TRAZER RISCOS. PROCURE UM
MÉDICO OU UM FARMACÊUTICO. LEIA A BULA.**

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Comer frutas e vegetais provê nutrição pior do que a ingestão de vitaminas?



A maconha é benéfica? A maconha é perigosa?
Devemos legalizar a maconha?



A maconha é benéfica? A maconha é perigosa?
Devemos legalizar a maconha?



A maconha é benéfica? A maconha é perigosa?
Devemos legalizar a maconha?



A maconha é benéfica? A maconha é perigosa?
Devemos legalizar a maconha?



Assim como a maconha, os cães foram criados por nossos ancestrais para satisfazer diversas necessidades humanas através da seleção artificial de raças com diferentes utilidades





A maconha é benéfica? A maconha é perigosa?
Devemos legalizar a maconha?



O cão é benéfico? O cão é perigoso?
Devemos legalizar o cão?

Para atender a população da forma mais ampla é preciso garantir:

- 1) Auto-cultivo e Cooperativismo para produção de extratos de maconha;
- 2) Suporte tecnológico de universidades e institutos de pesquisas para dosagem de canabinóides e controle de qualidade;
- 3) Eco-sistema empresarial de medicina canábica com alta diversidade e livre de oligopólios;
- 4) Inclusão na economia canábica das comunidades vulneráveis mais afetadas pela guerra às drogas