



*La «Letteratura»  
CBD come funzione e perché funziona*



Emilio Russo  
Science of Health Department  
University of Catanzaro  
[erusso@unicz.it](mailto:erusso@unicz.it)  
Nothing to Disclose

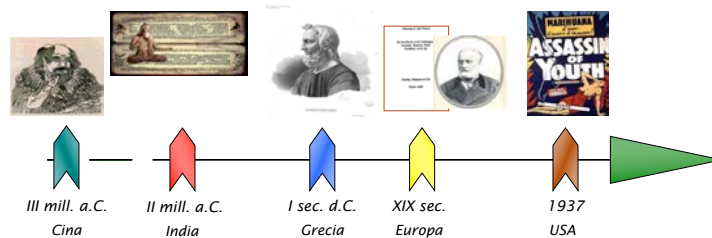


Marijuana - Cannabis - Droga

# History

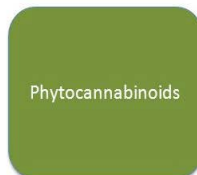
- 1937- Marijuana Tax Act: Cannabis becomes illegal in USA and in the world after being used for 38 million years by humans as a therapy, to enjoy and to pray (Harry Anslinger)
- Before prohibition 1% of population have been using Marijuana, today 50% (12-35) has used it at least once
- In USA and in the world Cannabis has engaged its own revenge
- Too much has been said without proper background knowledge and too much prejudgement

• Gianluigi Gessa – Professore Emerito Università di Cagliari



In your brain and body

Anandamide, 2-AG,  
Noladin ether  
etc.



In plants

THC, CBD, CBG, CBDV,  
THCV, CBC, CBN, THCVA  
etc.

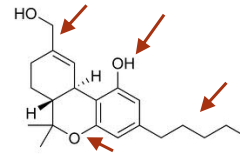


From the lab

Nabilone, HU-210, AB-  
PINACA, JWH-018,  
etc

## More than just $\Delta^9$ -THC

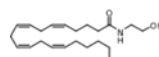
- In addition to THC, cannabis also contains:
  - >100 other 'cannabinoids'
    - Plant cannabinoids are chemical entities that are structurally similar to THC.
    - THC is characterised by an alkyl chain, phenol ring, central pyran ring and mono-unsaturated cyclohexyl ring.
    - Not found in any other plant
  - >400 other non-cannabinoids.
    - Cannot rule out specific effects of these non-cannabinoids.
    - e.g. Eugenol: acts at similar receptors in the brain as other drugs (e.g. alcohol; GABA<sub>A</sub>R).



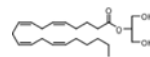
Elsohly MA, Slade D (2005) Chemical constituents of marijuana: the complex mixture of natural cannabinoids Life Sci. 78(5):539-48

## The endocannabinoid system in a nutshell

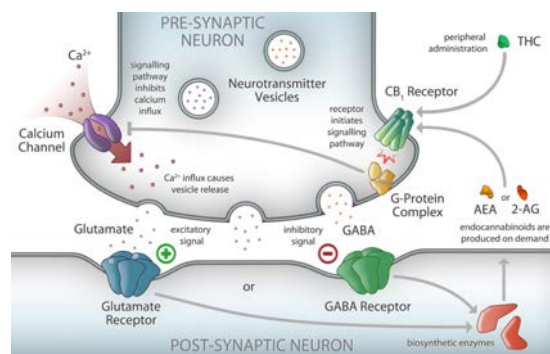
- The endocannabinoid system was first described in the late 1980s/early 1990s
- Comprises endogenous ligands, receptors, synthetic and degradation enzymes
- Cannabinoid receptors:
  - cell surface receptors
  - present on a wide variety of cell types.
  - two CBR types:
    - CB1: principally in the CNS, affect neuronal excitability by modulating neurotransmitter release
    - CB2: principally in non-brain areas and linked to immune response
- Endocannabinoids:
  - Two principal ECs thus far identified:
    - anandamide
    - 2-arachidonoyl glycerol

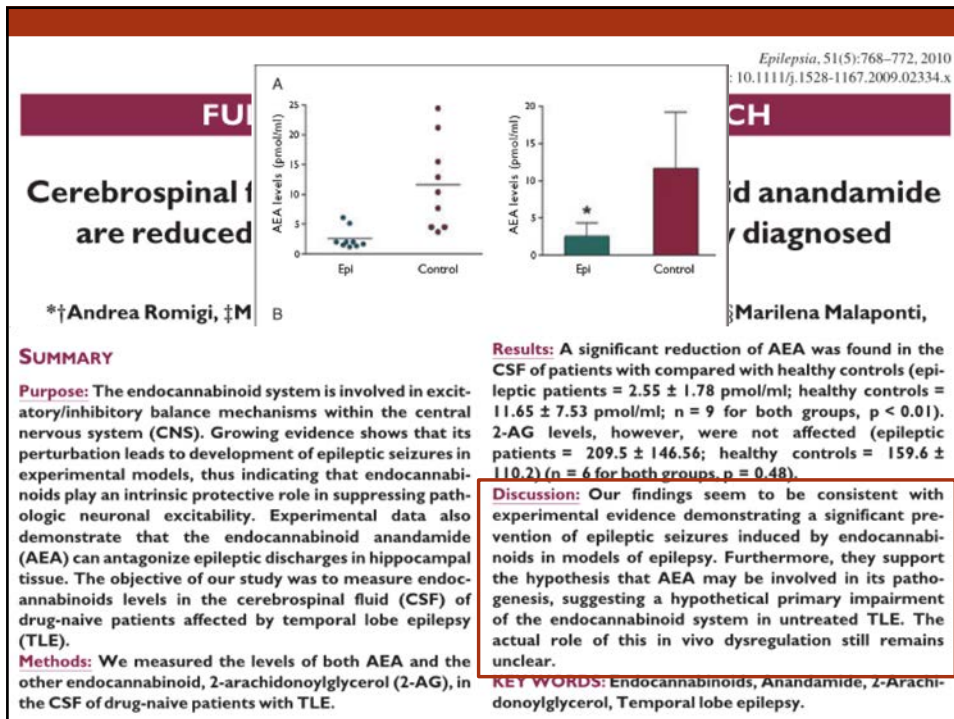
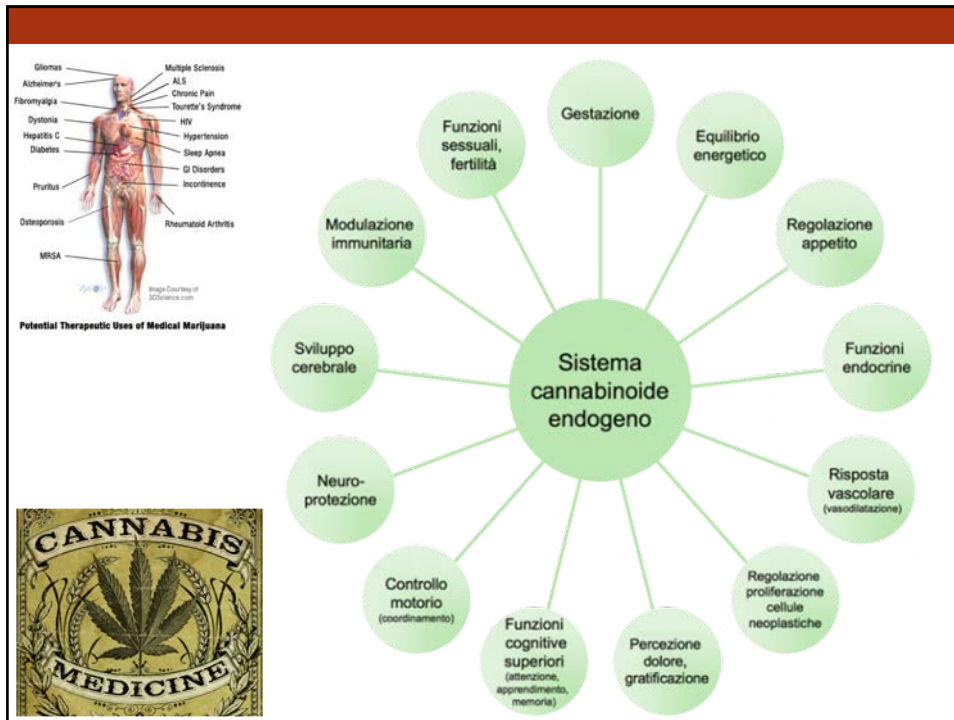


Anandamide



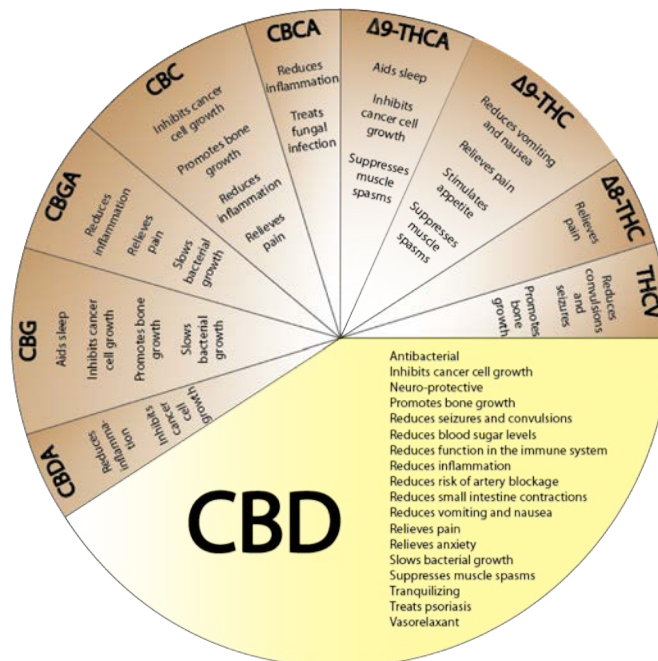
2-arachidonoyl glycerol (2-AG)





## But it's got 'cannab-' in the name...

- The endocannabinoid system was so named because the CB1 receptor is the target for  $\Delta^9$ -THC.
  - **This does not mean that all cannabinoids act via the endocannabinoid system!**
- Numerous synthetic ligands for CB1Rs and CB2Rs have also been developed
  - e.g. WIN55-212,2, CP55-940, HU-210 (agonists) and AM251, SR141716A (antagonists)
- Most were developed as research compounds to probe the endocannabinoid system
  - Now notorious as constituents of 'spice blends' ('legal highs')
- Importantly, of the ~100 plant cannabinoids, only 3 act via CB1R/CB2R ligands (<3%):
  - **$\Delta^9$ -THC (tetrahydrocannabinol)**
    - principal psychoactive component
    - Partial agonist at CB1R and CB2R
  - **CBN (cannabinol)**
    - Agonist
    - ~50x times less potent than  $\Delta^9$ -THC
  - **THCV (tetrahydrocannabivarin)**
    - Competitive antagonist at CB1R and CB2R





Review  
**Therapeutic effects of cannabinoids in animal models of seizures, epilepsy, epileptogenesis, and epilepsy-related neuroprotection**  
 Evan C. Rosenberg <sup>a,1</sup>, Pabitra H. Patra <sup>b,1</sup>, Benjamin J. Whalley <sup>b,\*</sup>

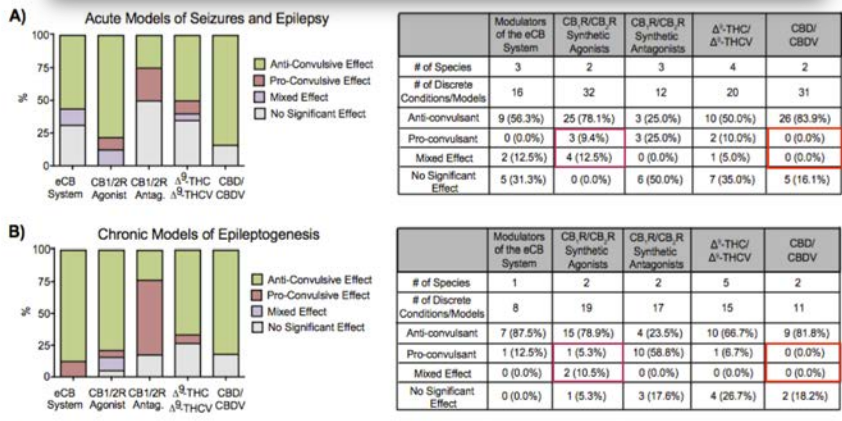


Fig. 1. Pre-clinical animal models of seizures, epilepsy, and epileptogenesis. Compiled data from synthetic and phytocannabinoids in 181 total animal models of A. Acute models of seizures and epilepsy. B. Chronic models of epileptogenesis. Pre-clinical interventions were subdivided into (1) Modulators of the Endocannabinoid System ("eCB System"), (2) CB<sub>1</sub>/CB<sub>2</sub>R Agonists, (3) CB<sub>1</sub>/CB<sub>2</sub>R Antagonists, (3) Δ<sup>1</sup>-THC/THCV, and (4) CBD/CBDV. See Suppl. Tables 1, 2 for further description of analyzed studies.

Studies were evaluated based on their scientific rigor and use of physiologically relevant drug concentrations to in vivo studies

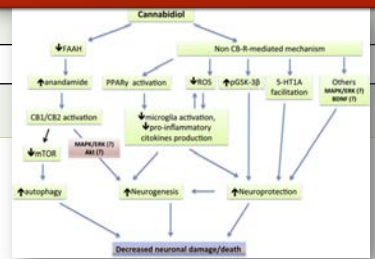
## CBD and CBDV pharmacology

CBD	CBDV
5HT <sub>1A</sub> agonist (PMID 16258853)	TRPV1 agonism (PMID 25029033)
GPR55 antagonist (PMID 17876302)	DAGL-alpha inhibition (PMID 21175579)
Adenosine reuptake inhibition (PMID 26218440)	

## Drug-Drug Interactions?

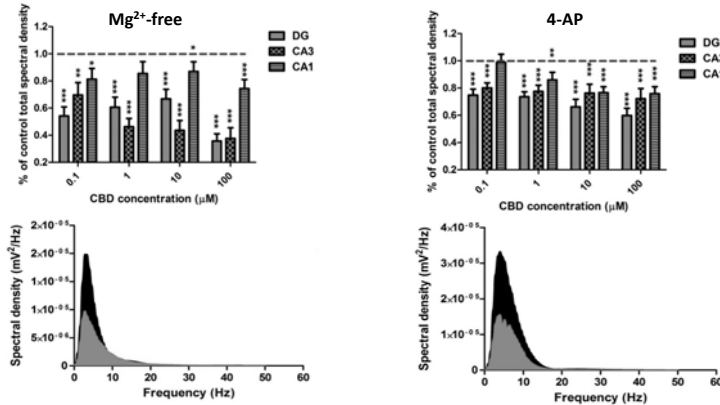
VGSC blockade (PMID 24642454)
mTOR inhibition (PMID: 26283212)
CB1 negative allosteric modulator (PMID: 26218440)

- Caveats:
  - All are *in vitro* and have not been definitively linked to functional effects in whole animals/humans.
  - Often employ physiologically irrelevant (high μM/mM) concentrations



## CBD vs Mg<sup>2+</sup>-free & 4-AP epileptiform activity

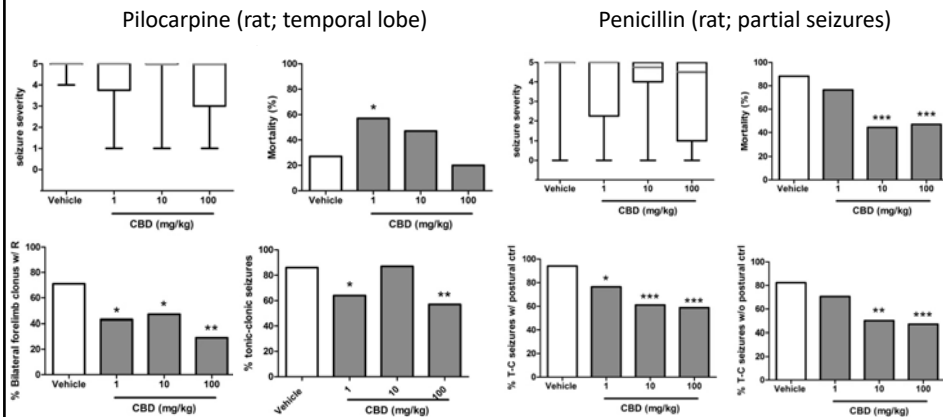
- Multi-electrode array recording from two, validated *in vitro* models of epileptiform activity in acute, rat hippocampal slices.



- Total signal power was significantly reduced at concentrations >0.1 μM
- Effects were comparable to felbamate and phenobarbital

Hill *et al.*, 2010. *J Neurosci Methods* **185**: 246-256  
Hill *et al.*, 2012. *BJP* DOI: 10.1111/j.1476-5381.2012.02207.x

## CBD vs pilocarpine- and penicillin-induced convulsions



- CBD exhibited modest anti-convulsant effects, significantly lowering the incidence of the most severe seizures, indicative of effects *vs status*.

Model of temporal lobe convulsion. Animals (Wistar rats) received vehicle (2:1:17 cremophor:ethanol:saline) or CBDV (50-200 mg/kg; i.p.), 60 min prior to a high dose of pilocarpine (90 mg/kg; i.p.). Seizure activity recorded for 60 min.

- CBD had significant anti-convulsant effects, lowering the incidence of the most severe seizures and mortality.

Animals (Wistar rats) received vehicle (2:1:17 cremophor:ethanol:saline) or CBDV (1-200 mg/kg; i.p.), 60 min prior to a high dose of penicillin (525 IU; i.c.v). Seizure activity recorded for 120 min.

Hill *et al.*, 2012. *Seizure* **21**: 348-357

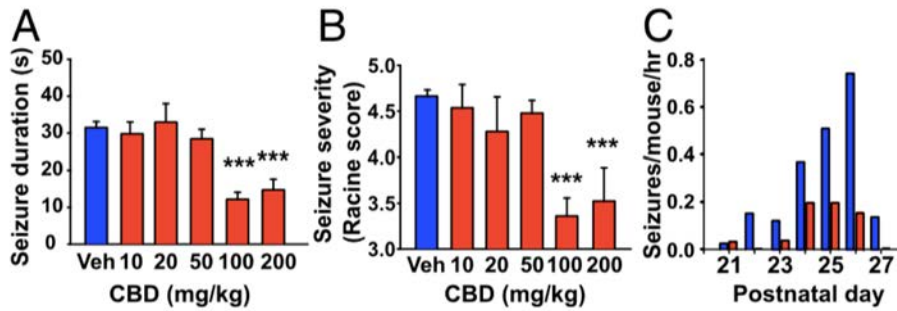
# Cannabidiol attenuates seizures and social deficits in a mouse model of Dravet syndrome

Joshua S. Kaplan<sup>a</sup>, Nephi Stella<sup>a,b,1</sup>, William A. Catterall<sup>a,1,2</sup>, and Ruth E. Westenbroek<sup>a,1</sup>

<sup>a</sup>Department of Pharmacology, University of Washington, Seattle, WA 98195; and <sup>b</sup>Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA 98195

Contributed by William A. Catterall, September 7, 2017 (sent for review July 3, 2017; reviewed by Lori L. Isom, Daniele Piomelli, and Peter C. Ruben)

Worldwide medicinal use of cannabis is rapidly escalating, despite (17). Previous work showed that DS symptoms result from the loss-



## La Cannabis Flos del "Bureau olandese"

Varietà'	contenuto THC	contenuto CBD
Bedrocan	~ 19%	<1%
Bedrobinol	~ 12%	<1%
Bediol	~ 6%	~ 7,5%



**Forma farmaceutica**

infiorescenze di *Cannabis Sativa* L.

**Paese importazione**

Olanda

**Indicazioni**

- nausea e vomito associato a chemioterapia in pazienti che non rispondono agli antiemetici convenzionali
- sindrome di Gilles de La Tourette
- glaucoma resistente alla terapia convenzionale
- sindromi correlate a perdita di peso (es. cachessia in AIDS)
- dolore neuropatico cronico

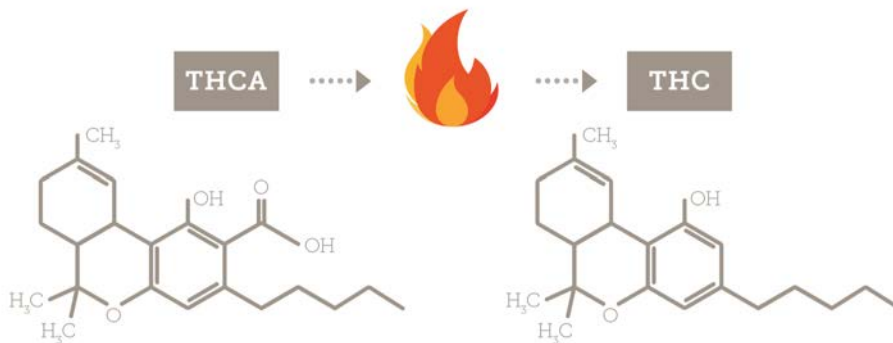
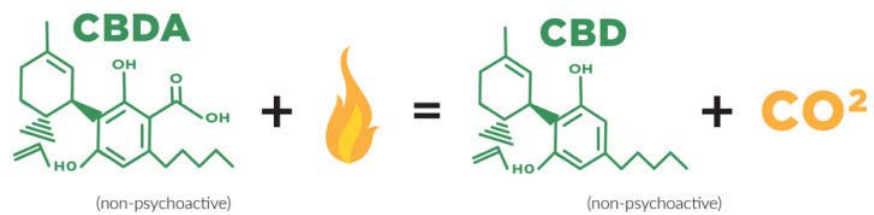




## Modalità somministrazione Cannabis Flos (1)

### Decotto

- Bollire 200 mL circa in acqua in un tegame con coperchio.
- Aggiungere la busta filtro di Cannabis prescritta dal medico.
- Abbassare il fuoco e lasciare a sobbollire dolcemente per 15' con il coperchio sul tegame.
- Bere il decotto caldo (attenzione che il THC precipita o aderisce alle pareti se si fa raffreddare la soluzione...).



HOME > SHOP

ENDOCA Prima pagina Su di noi Tutto sul CBD Vendita all'ingrosso di CBD Fondazione FAQ Shop

KANALIFE AZIENDA CBD CATALOGO SHOP NEWS FAQ B2B CONTATTI

Home > shop online

SHOP ONLINE

CBD Supposte

CBD Dried Flowers

CBD Dab/Wax


CBD Cristalli


CBD Capsule


CBD Hemp Oil

CBD Eliquid

ordina per

 CBD Hemp Oil 2% (300mg) in 15ml  
€ 40,00

 CBD Capsule 600mg - 30 pezzi  
€ 90,00

 CBD Capsule 300mg - 30 pezzi  
€ 60,00

ACQUISTA

ACQUISTA

ACQUISTA



Article

## Quality Traits of “Cannabidiol Oils”: Cannabinoids Content, Terpene Fingerprint and Oxidation Stability of European Commercially Available Preparations

**Abstract:** Cannabidiol (CBD)-based oil preparations are becoming extremely popular, as CBD has been shown to have beneficial effects on human health. CBD-based oil preparations are not unambiguously regulated under the European legislation, as CBD is not considered as a controlled substance. This means that companies can produce and distribute CBD products derived from non-psychoactive hemp varieties, providing an easy access to this extremely advantageous cannabinoid. This leaves consumers with no legal quality guarantees. The objective of this project was to assess the quality of 14 CBD oils commercially available in European countries. An in-depth chemical profiling of cannabinoids, terpenes and oxidation products was conducted by means of GC-MS and HPLC-Q-Exactive-Orbitrap-MS in order to improve knowledge regarding the characteristics of CBD oils. Nine out of the 14 samples studied had concentrations that differed notably from the declared amount, while the remaining five preserved CBD within optimal limits. Our results highlighted a wide variability in cannabinoids profile that justifies the need for strict and standardized regulations. In addition, the terpenes fingerprint may serve as an indicator of the quality of hemp varieties, while the lipid oxidation products profile could contribute in evaluation of the stability of the oil used as milieu for CBD rich extracts.

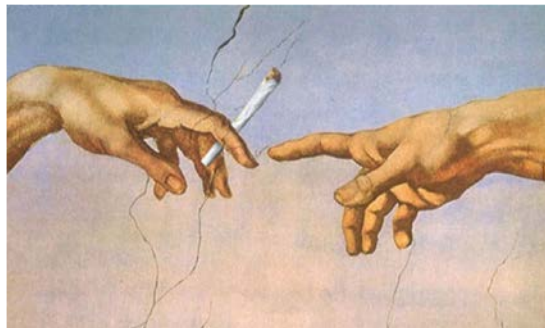
## Conclusioni

- I cannabinoidi sono una nuovo pianeta da scoprire
- Ulteriori studi sono necessari per determinare l'esatto meccanismo d'azione di queste molecole
- Non tutto è sistema endocannabinoide ... abbandonato?
- Il CBD ha risultati positivi in RCTs per Dravet e LGS
  - Conferma definitiva in giugno da FDA
  - Approvazione Europa
- Determinare lo spettro d'azione
- Aumentare le conoscenze sull'efficacia e la tollerabilità di CBD
- CBDV..... Altri in futuro



**Cannabis As Medicine**

Proven Research Creates A Solid Foundation



**GRAZIE PER L'ATTENZIONE**