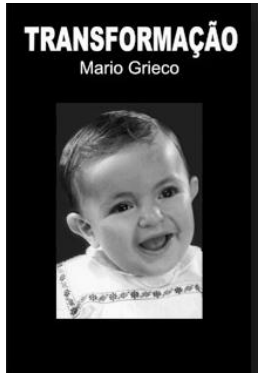
# CANNABIS MEDICINAL BRASIL

MARIO GRIECO - PRESIDENTE DA KNOX MEDICAL BRASIL/AMÉRICA LATINA





- **Médico com pós-graduação em Medicina da Família pela Universidade da Florida e MBA em Administração de Empresas**

- **30 anos de experiência na indústria farmacêutica**

- **Atualmente presidente Brasil e América Latina da Knox Medical/Fluent, uma empresa voltada à Canabis Medicinal.**

- **Presidiu:**

BAYER SEARLE Pfizer MONSANTO Bristol-Myers Squibb moksha8 LIFE DIAGNÓSTICOS KNOX Cannabis Dispensaries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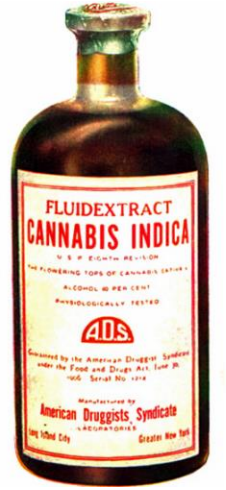
# CONTEXTO HISTÓRICO

- Cultivada para fibras desde 4000 a.C.
- Uso medicinal desde 2.900 a.C. ( China)
- Introduzida na medicina ocidental pelo Dr. William Brooke O'Shaughnessy, em torno de 1840
- Século XIX e XX: componente comum em medicamentos patenteados
- Prescrita para a Rainha Vitoria a fim de avaliar cólicas menstruais
- Proibida na América do Norte nas décadas de 1920 e 1930, interrompendo as pesquisas para seu uso medicinal.

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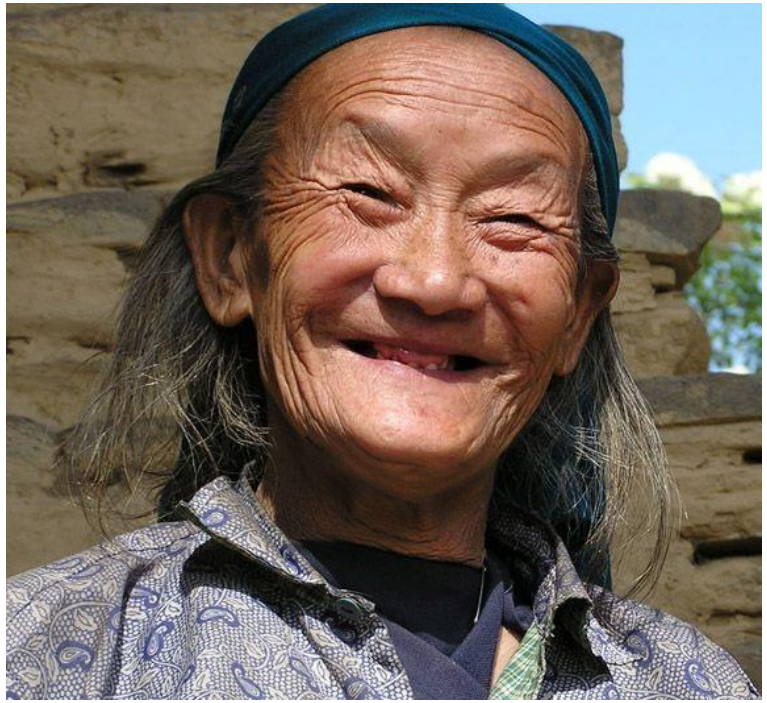
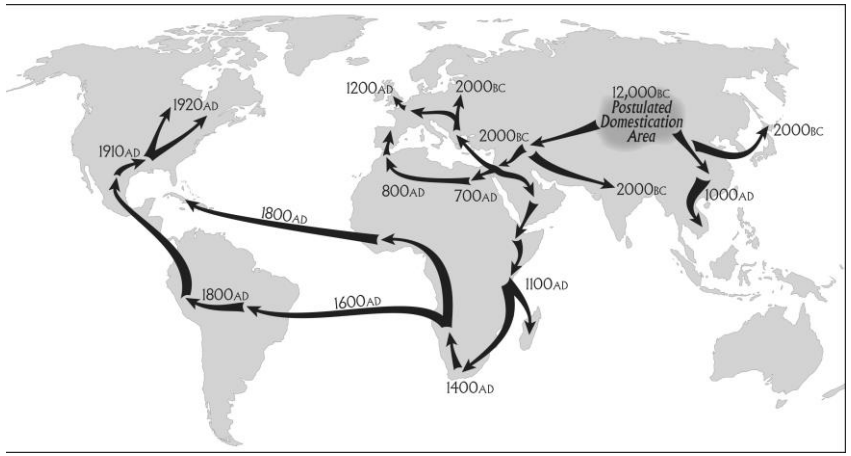





Shen Neng, 2727 a.C

# CONSAGRADO ANALGÉSICO

DOR
Neuropatias crônicas

ESPASMOS
Esclerose múltipla

The Siberian Times

*'I've grown fat, got a tan & now look like a Siberian'*

***Vladimir Lenin, 1897, in Siberian exile***





# Iconic 2,500 year old Siberian princess 'died from breast cancer', reveals MRI scan

By Anna Liesowska

14 October 2014

Preserved by ice, the 25 year old ancient woman covered in tattoos used cannabis to cope with her ravaging illness.

'Princess Ukok' mummy in Anokhin museum, Gorno-Altaisk. Picture: Alexander Tyryshkin

## Features

### 5,000 year old battle between mountain sheep comes back to life in new rock art discovery

But how did ancient artists create prehistoric masterpieces on sheer cliffs today only accessible by sophisticated modern climbing equipment?

Comments (2) | Add to My Stories

### Mountainside gallery where all civilisations added their own art from Bronze Age to medieval times

On the border between Russia and Mongolia, we reveal awe-inspiring Kara-Turug petroglyphs, and they contain a BIG secret about ancient Siberia.

Comments (3) | Add to My Stories

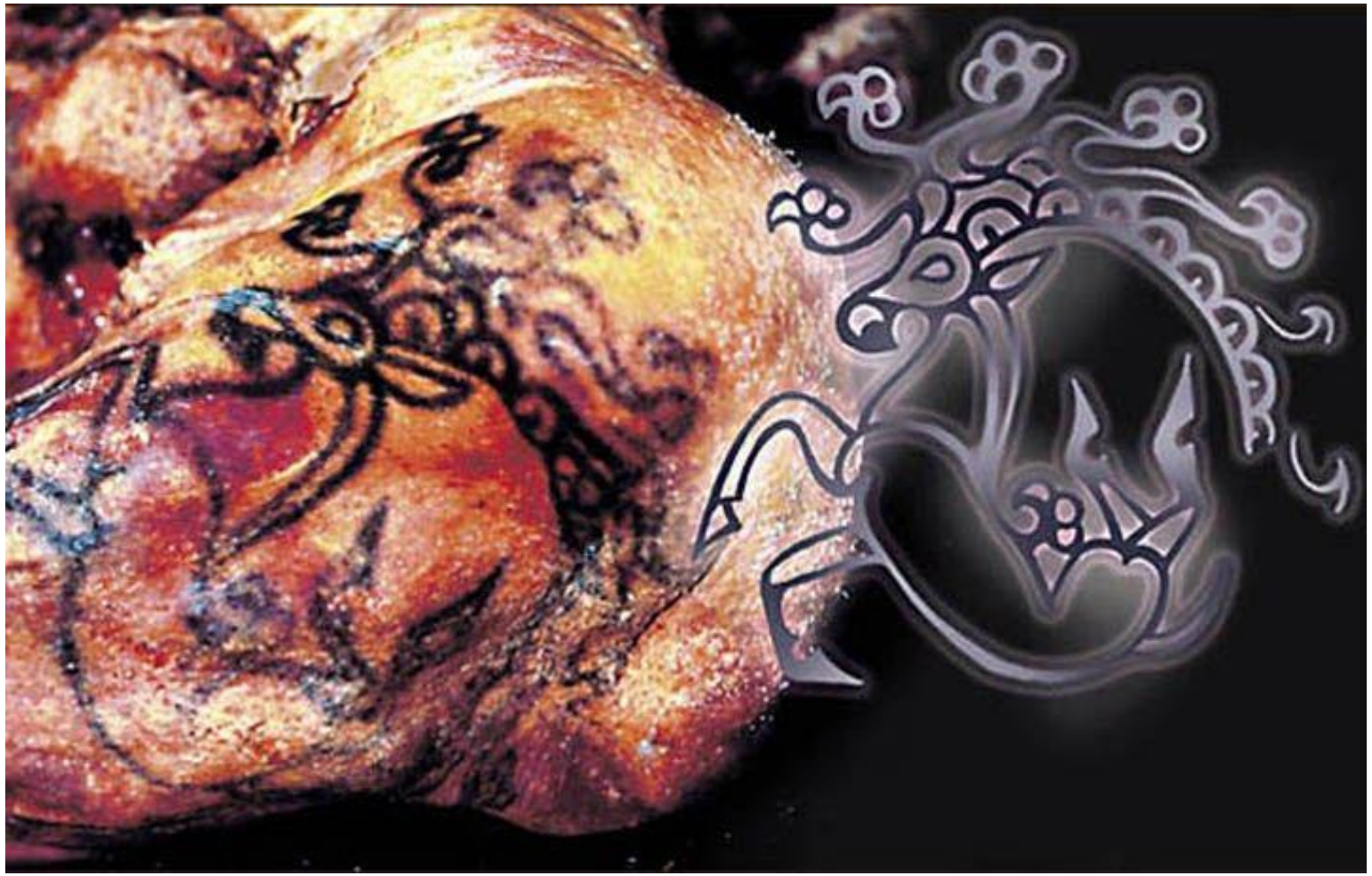
### Lake Baikal to become a new ocean - but not for 20 million years, say scientists

Eurasia will split in two, dividing the world's largest land mass in southern Siberia.

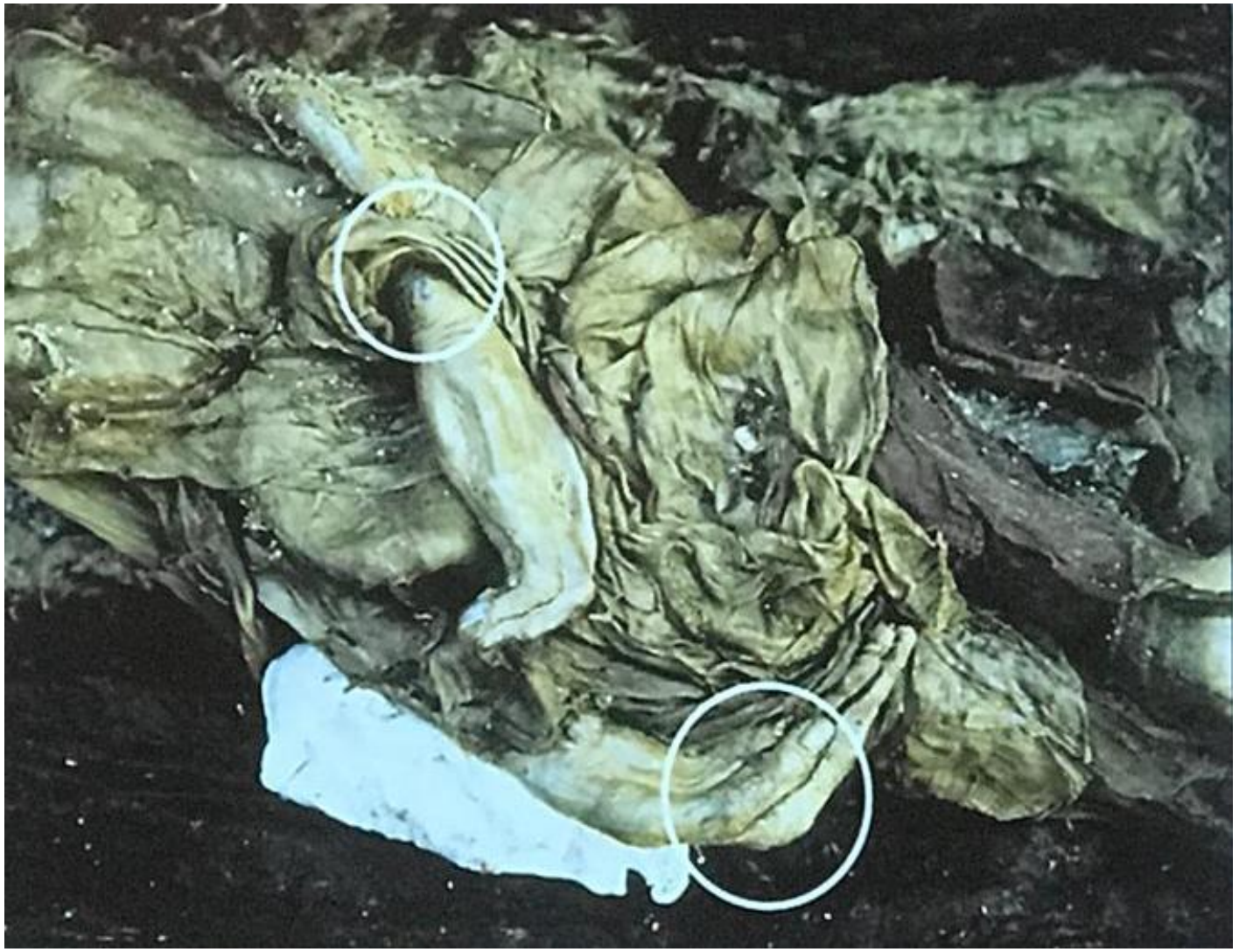
Comments (3) | Add to My Stories

### Grave of medieval 'infant

Canabinoides – Câncer de mama



pictures: institute of archeology and ethnography, Siberian Branch of Russian Academy of science



pictures: institute of archeology and ethnography, Siberian Branch of Russian Academy of science


Asthma

Catarrhos

Insomnia

# CIGARROS INDIOS, Cannabis Indica

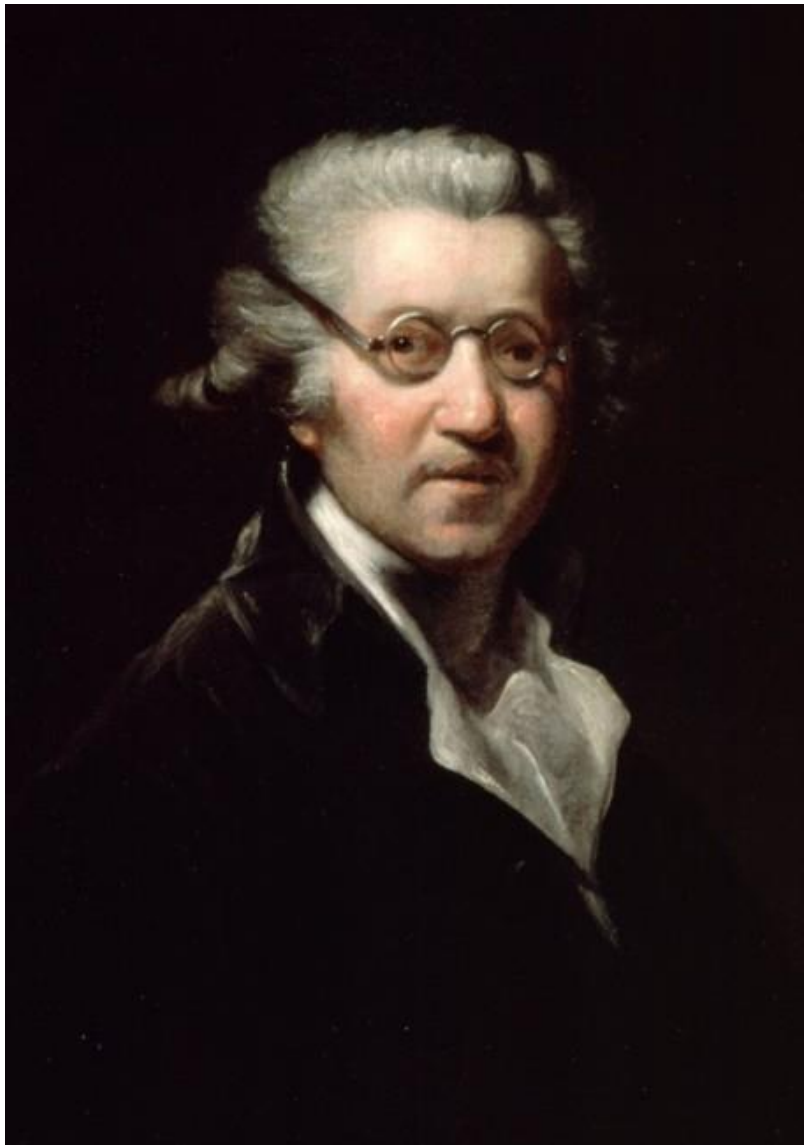
*De GRIMAULT e Cia*

A difficuldade em respirar, a roncadura, os flatos, a aspiração sibilante acabam quasi logo, produz-se uma expectoração abundantissima quasi sempre em pouco tempo, torna-se mais facil, a respiração, mais branda a tosse e um dormir reparatorio afasta todos os symptomas assustadores que se tinham manifestado.

1834

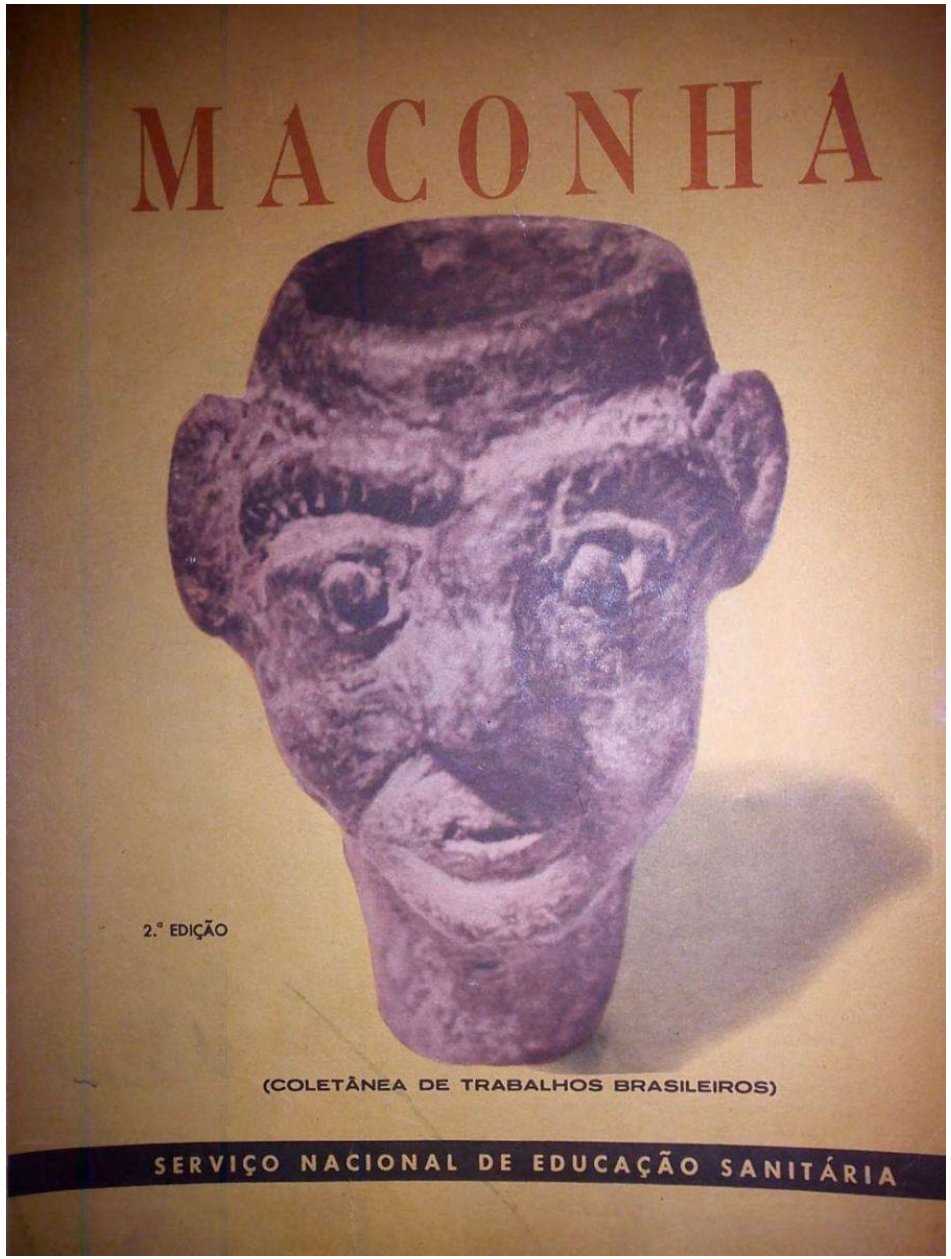
WILLIAM O’ SHAUGHNESSY

1889

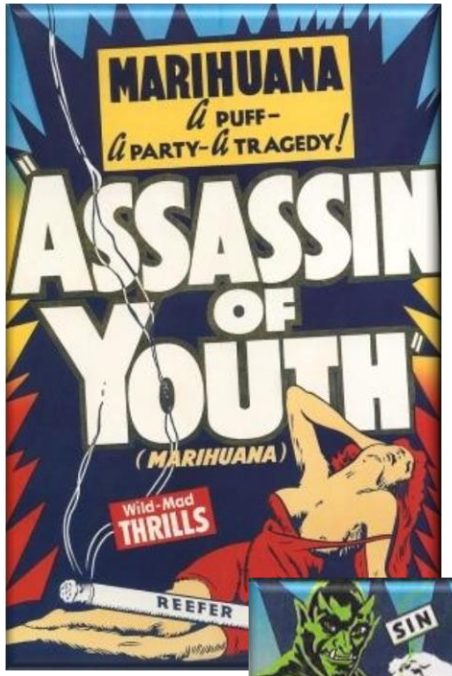


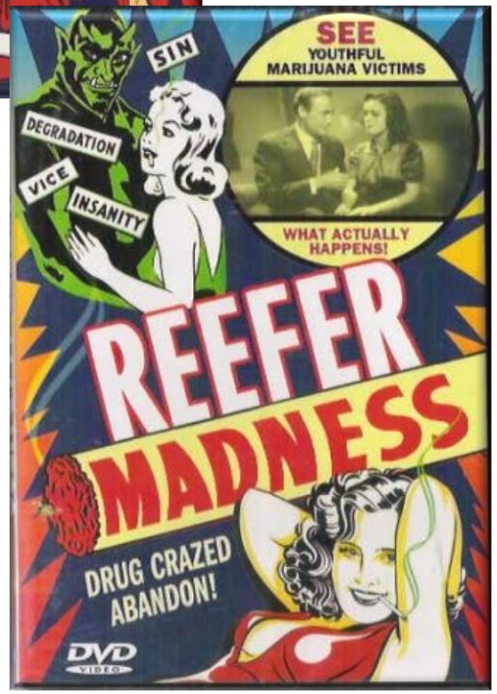
E.A BIRCH LANCET

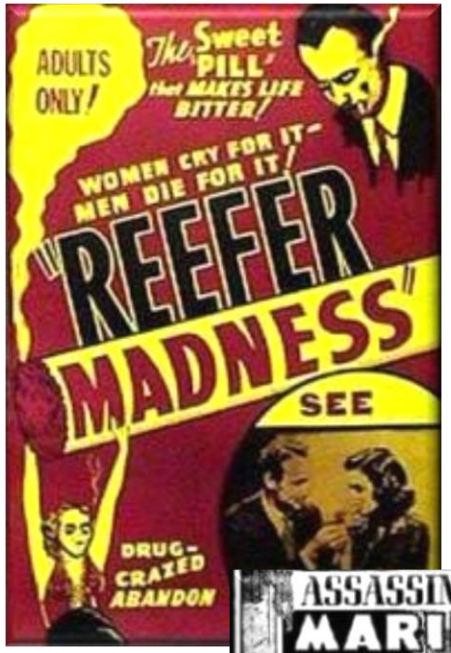
Os "brabos" do Recife. (De "Maxambombas e Maracatus", de Mário Sette, em desenho de Nestor Silva)



# 1925 – DROGA PERIGOSA






# Tricomas da Cannabis

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# Cannabis

## C.ruderalis (cânhamo)

- Não é psicoativo ( Não dopa)
- THC ≤ 0,3%
- Alta % de CBD

## C.sativa – C.indica (maconha)

- Psicoativo ( Dopa)
- THC : 5% - 35%
- Mínima % de CBD

# O que há na Cannabis?

**C. sativa - C. indica - C.ruderalis**
A maioria das variedades são híbridas

Compostos puros isolados
Mais de 500 compostos químicos

**Não canabinoides**
Terpenos e Flavonoides

**Fitocanabinoides**
Foram identificados mais de 120

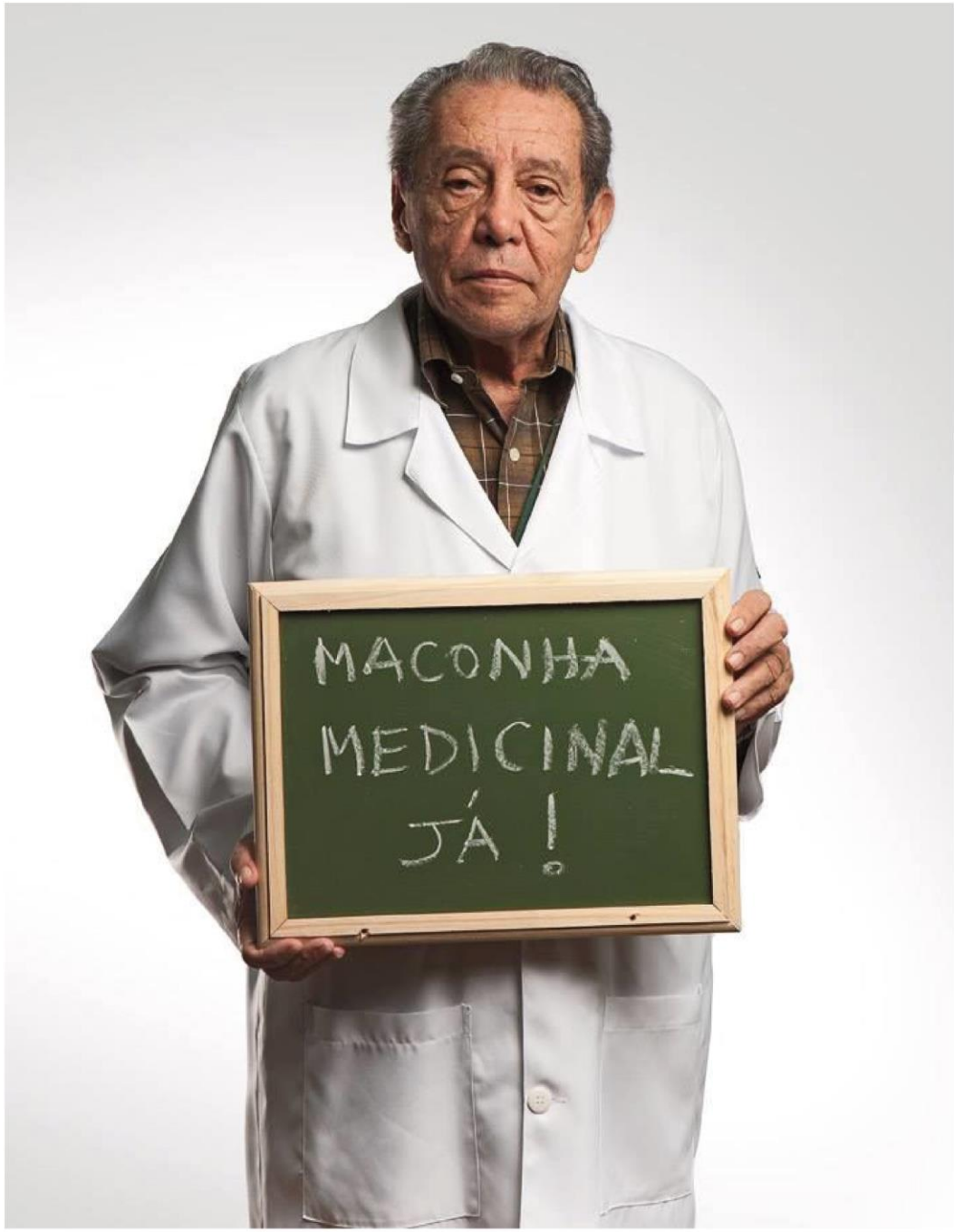
Psicoativo
**THC**

Psicoativo mas não eufórico
**CBD**

Mais de 60 outros compostos

Efeito Entourage ou Comitiva


1960

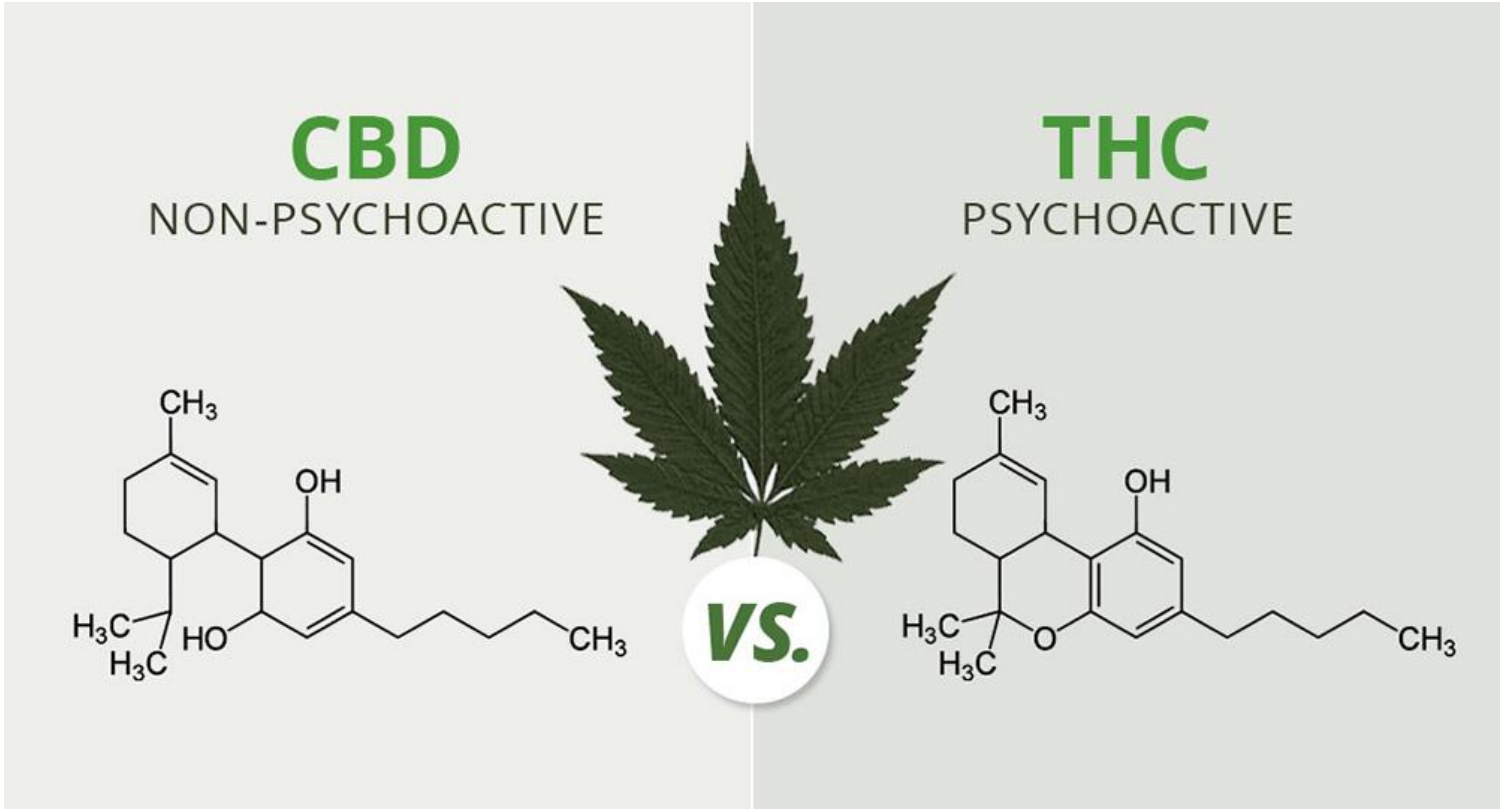



# PROF. ELISALDO CARLINI

Aos 88 anos, dedicou 50 deles pesquisando na Unifesp (Universidade Federal de São Paulo), em especial os benefícios medicinais da Cannabis.

Suas descobertas foram tantas que foi 12 mil vezes citado em artigos internacionais e recebeu grandes prêmios.

# Cannabis
## Dois principais compostos

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- **Responsável por muitos dos efeitos farmacológicos da Cannabis, incluindo o seu efeito psicoativo.**

- **Interagem com receptors canabinoides para induzir:**

**Analgesia**
**Atividade antiespasmódica**
**Redução das nauseas e vômitos**
**Estimulação do apetite**

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- **Efeitos indiretos nos receptores CB1 e CB2**
- **Afeta a atividade de um número significativo de outros sistemas, incluídos os canais iônicos, os receptores e as enzimas**

**A pesquisa indicou que o CBD tem ação:**

**Analgésico**
**Ansiolítico**
**Antiemético**
**Antipsicótico**
**Anticonvulsivo**
**Antiinflamatórios**

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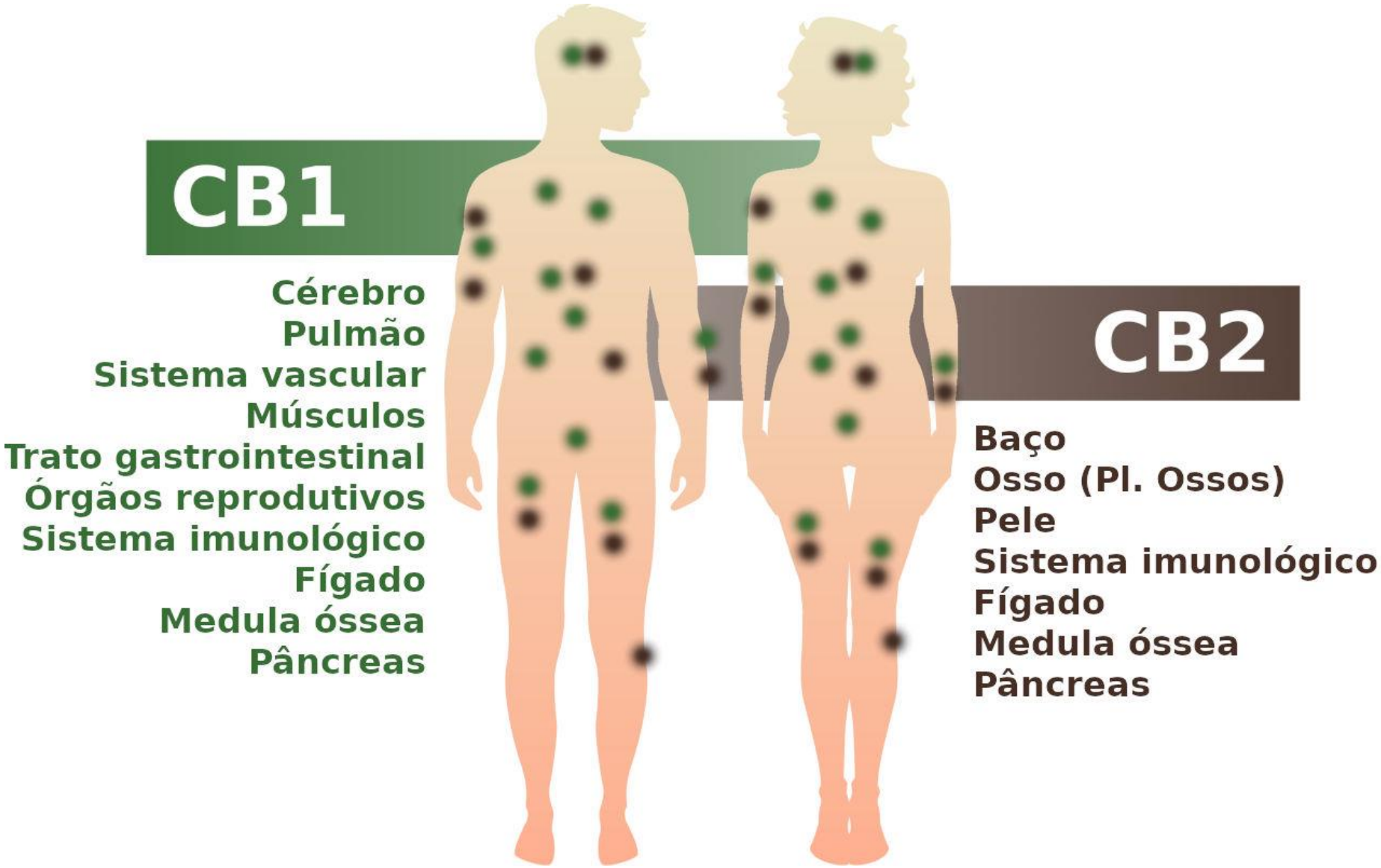
# Receptores canabinoides

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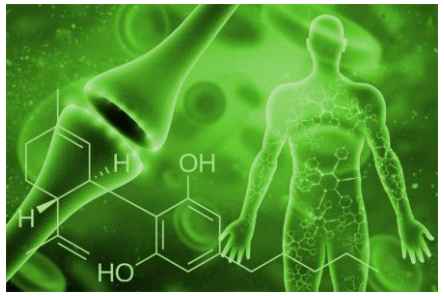
# Canabinoides

- Três categorias de moléculas que interagem com os receptores canabinoides
  Endocanabinoides
- Produzidos naturalmente no corpo ( Anandamida – 2-AG )
- Parte do Sistema Endocanabinoide

- Fitocanabinoides
- Estrutura típica
- Encontra-se em muitas plantas, mas as concentrações mais altas estão na Cannabis

- Canabinoides sintéticos

* Produtos farmacêuticos como o análogo THC conhecido como nabilona

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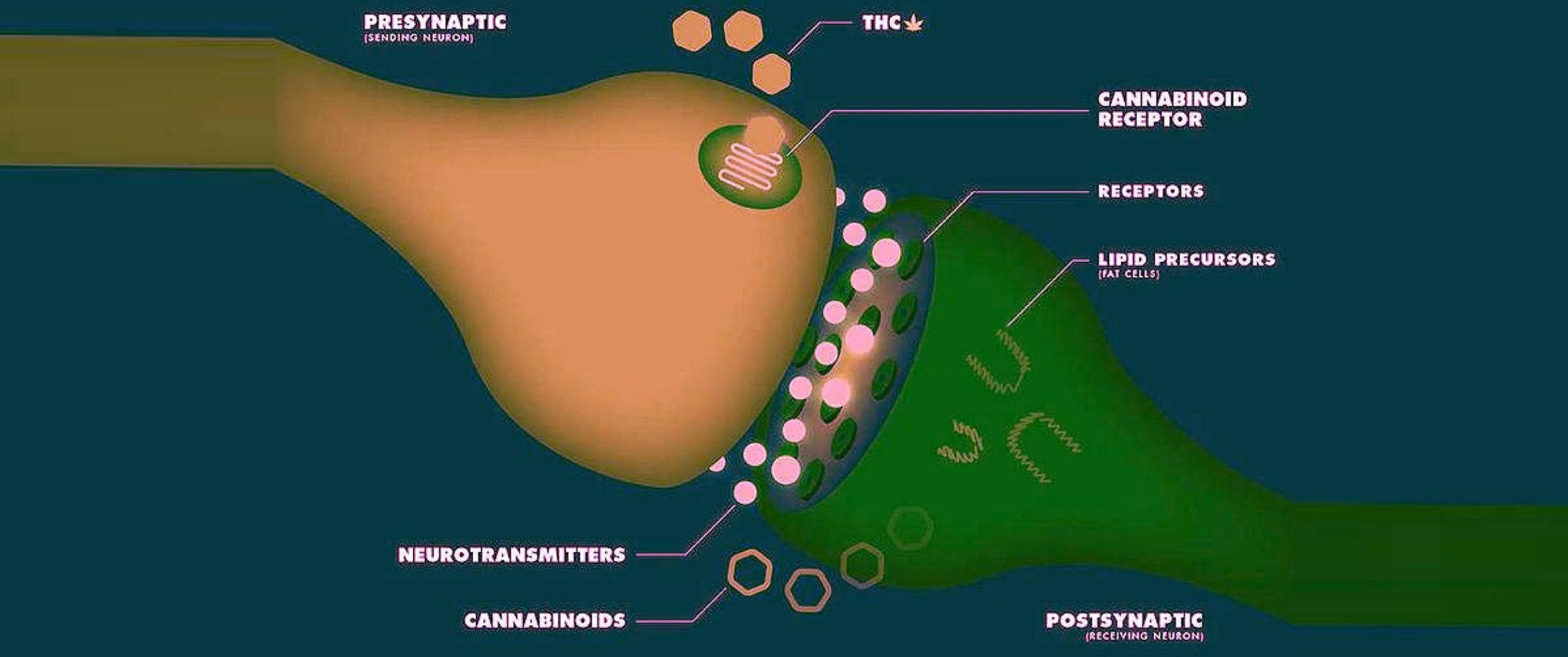
# SISTEMA ENDOCANABINOIDE



# Os canabinoides como “ Interruptores sinápticos”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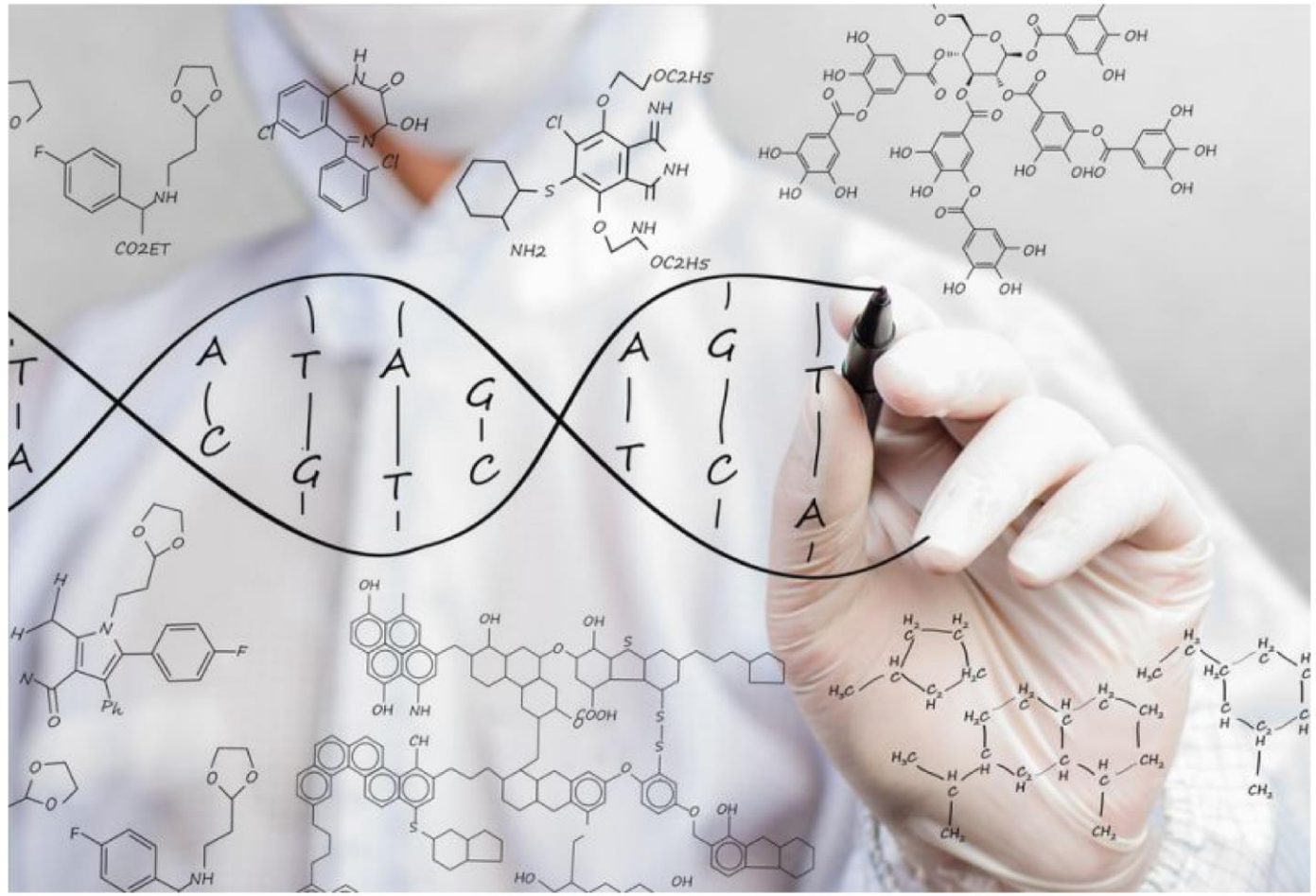
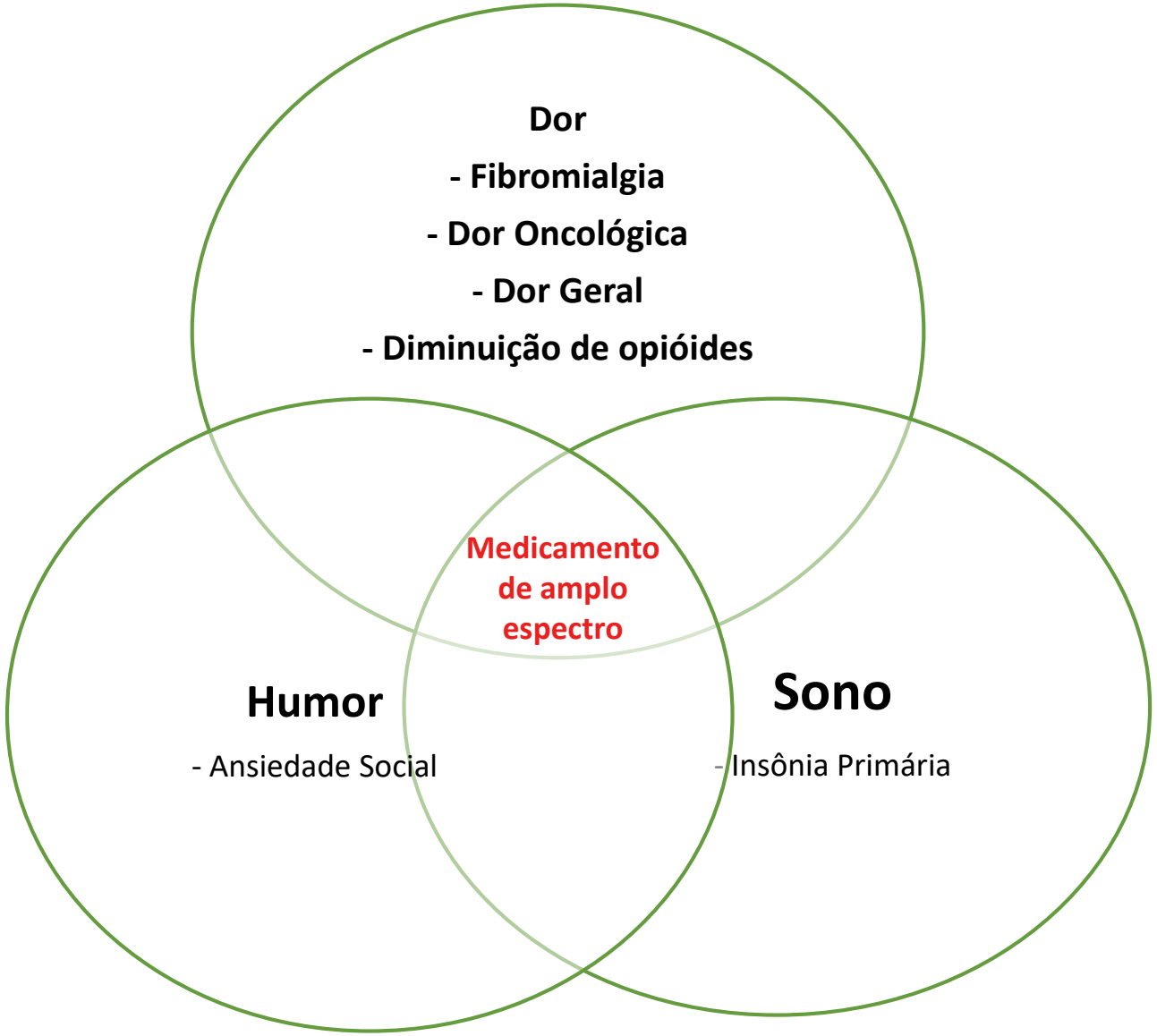
# COMO A CANNABIS ALTEROU O NOSSO GENOMA



# Cannabis na Pratica Clinica

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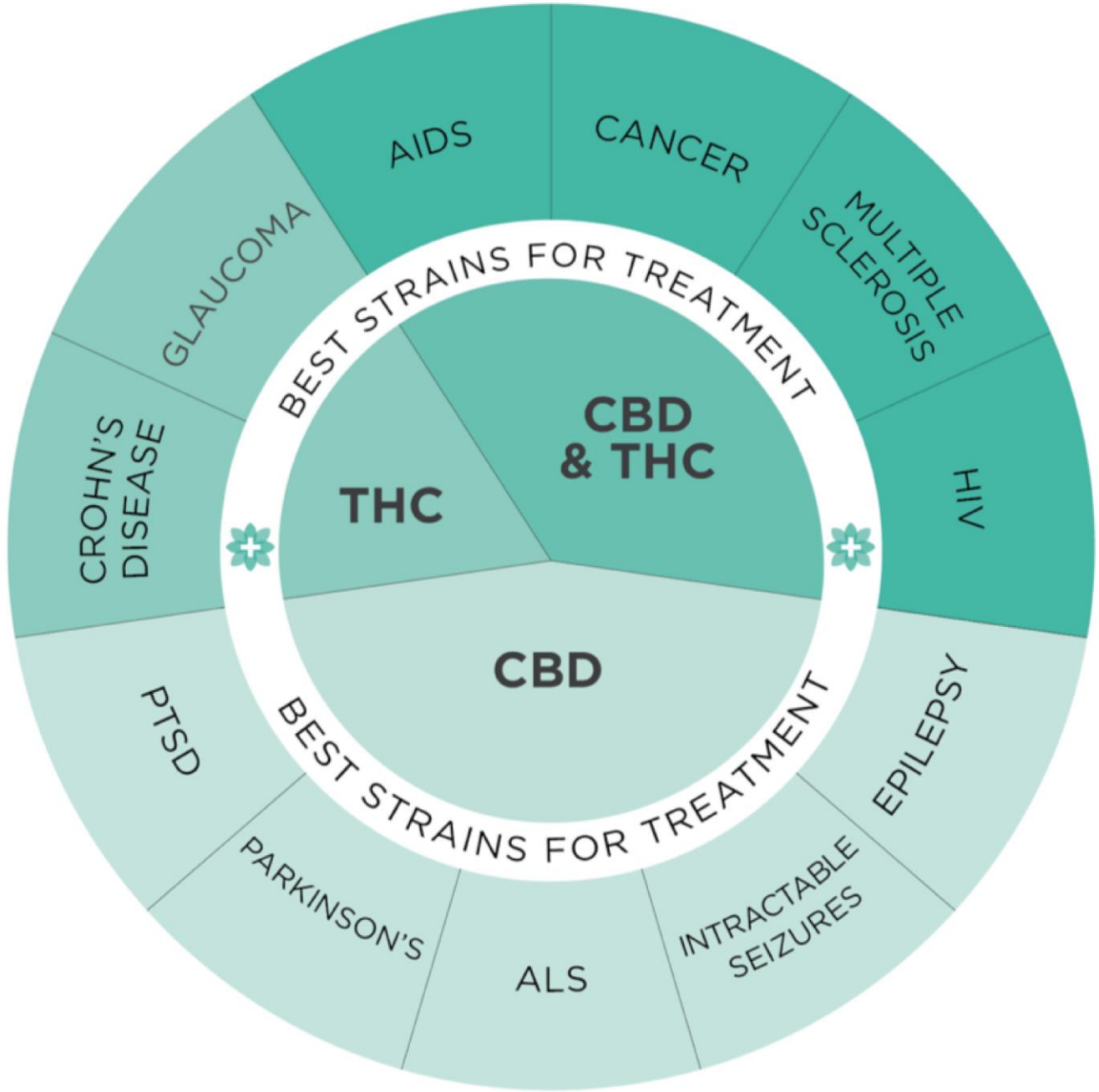
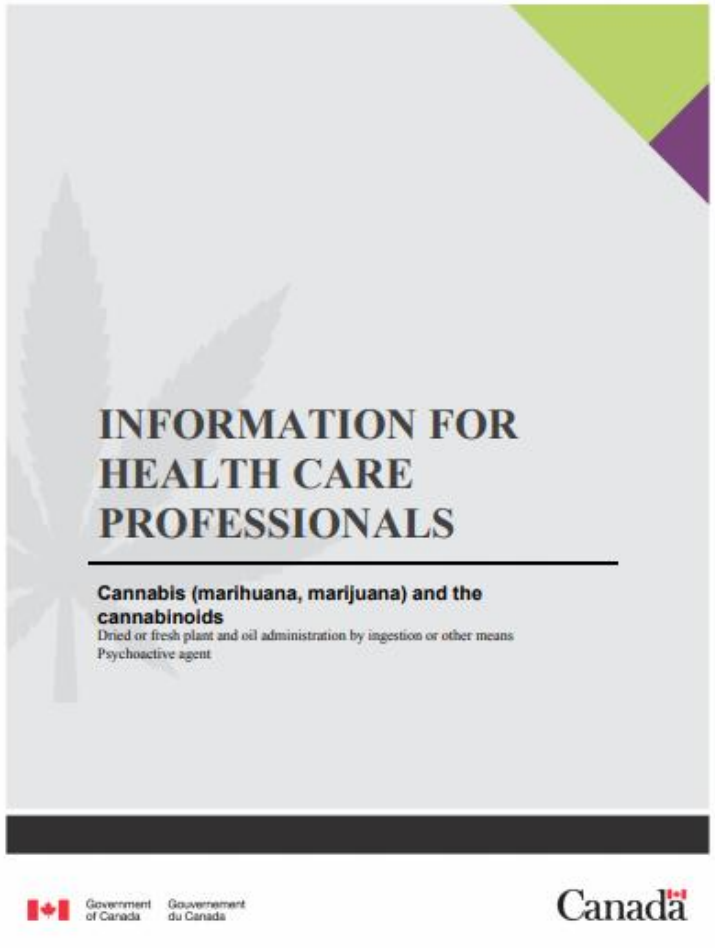
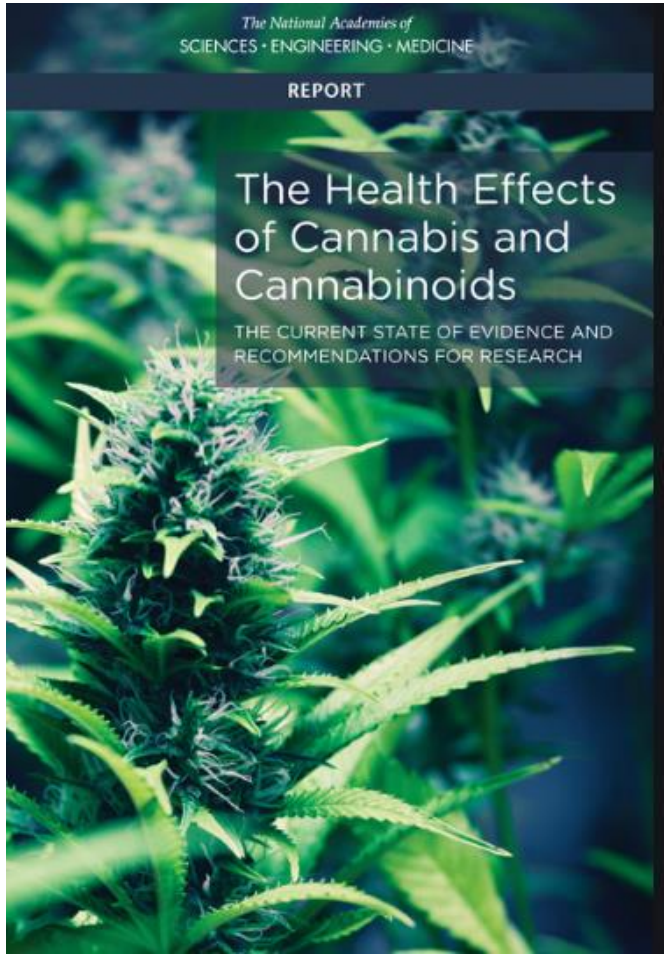

AIDS
CANCER
MULTIPLE SCLEROSIS
HIV
EPILEPSY
INTRACTABLE SEIZURES
ALS
PARKINSON'S
PTSD
CROHN'S DISEASE
GLAUCOMA
BEST STRAINS FOR TREATMENT
THC
CBD & THC
BEST STRAINS FOR TREATMENT
CBD


No ano passado, a The National Academies of Sciences, Engineering and Medicine anunciou que havia revisado mais de 10.700 estudos relevantes sobre os efeitos da Cannabis de um total de mais de 24.000 pesquisas publicadas

# As revisões sistemáticas apoiam os canabinoides para a dor crônica




“ Há provas mais constantes da eficácia dos canabinoides ( Cannabis fumado/ vaporizado, nabiximol) no tratamento da dor crônica de diversas etiologias, especialmente nos casos em que os tratamentos convencionais foram testados e fracassaram”.




**Evidência substancial ou concludente**

“ Nos adultos com dor crônica, os pacientes que foram tratados com Cannabis ou canabinoides tem mais probabilidades de experimentar uma redução clinicamente significativa nos sintomas da dor”.

# A Cannabis poderia ajudar a reduzir as doses de opióides na dor crônica

- Meta-analyses de 19 estudos pré-clínicos e 9 clínicos.
- A media da dose efetiva ( DE50) de morfina administrada em combinação com delta- 9- THC é 3,6 vezes menor ( 95% (IC) 1.95, 6.76) que a DE50 de morfina sozinha.
- A ED50 para codeina administrada em combinação com delta-9- THC foi 9.5 vezes menor ( IC de 95% 1.6, 57.5) que a ED50 de codeine sozinha.

Neuropsychopharmacology (2017) 42, 1752–1766
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www.neuropsychopharmacology.org

Review

## Opioid-Sparing Effect of Cannabinoids: A Systematic Review and Meta-Analysis

Suzanne Nielsen[A,1,2], Pamela Sabioni[3], Jose M Trigo[3], Mark A Ware[4], Brigid D Betz-Stablein[5], Bridin Murnion[A,7], Nicholas Lintzeris[1,8], Kok Eng Khor[9], Michael Farrell[1], Andrew Smith[9] and Bernard Le Foll[3]

[1]The National Drug and Alcohol Research Centre, The University of New South Wales, Sydney, NSW, Australia; [2]Drug and Alcohol Services, South Eastern Sydney Local Health District, Surry Hills, NSW, Australia; [3]Translational Addiction Research Laboratory, Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto, ON, Canada; [4]Departments of Anaesthesia and Family Medicine, McGill University, Montreal, QC, Canada; [5]School of Public Health and Community Medicine, The University of New South Wales, Sydney, NSW, Australia; [6]Discipline of Addiction Medicine, University of Sydney, Sydney, NSW, Australia; [7]Pain Management Centre, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [8]Department of Pain Management, Prince of Wales Hospital, Randwick, NSW, Australia; [9]Pain and Addiction Medicine, Centre for Addiction and Mental Health, Toronto, ON, Canada

Cannabinoids, when co-administered with opioids, may enable reduced opioid doses without loss of analgesic efficacy (ie, an opioid-sparing effect). The aim of this study was to conduct a systematic review to determine the opioid-sparing potential of cannabinoids. Eligible studies included pre-clinical and clinical studies for which the outcome was either analgesia or opioid dose requirements. Clinical studies included controlled studies and case series. We searched Scopus, Cochrane Database of Systematic Reviews, Medline, and Embase. Nineteen pre-clinical and nine clinical studies met the search criteria. Seventeen of the 19 pre-clinical studies provided evidence of synergistic effects from opioid and cannabinoid co-administration. Our meta-analysis of pre-clinical studies indicated that the median effective dose ($ED_{50}$) of morphine administered in combination with delta-9-tetrahydrocannabinol (delta-9-THC) is 3.6 times lower (95% confidence interval (CI) 1.95, 6.76; $n=6$) than the $ED_{50}$ of morphine alone. In addition, the $ED_{50}$ for codeine administered in combination with delta-9-THC was 9.5 times lower (95% CI 1.6, 57.5, $n=2$) than the $ED_{50}$ of codeine alone. One case series ($n=3$) provided very low quality evidence of a reduction in opioid requirements with cannabinoid co-administration. Larger controlled clinical studies showed some clinical benefits of cannabinoids; however, opioid dose changes were rarely reported and mixed findings were observed for analgesia. In summary, pre-clinical studies provide robust evidence of the opioid-sparing effect of cannabinoids, whereas one of the nine clinical studies identified provided very-low-quality evidence of such an effect. Prospective high-quality-controlled clinical trials are required to determine the opioid-sparing effect of cannabinoids.

Neuropsychopharmacology (2017) 42, 1752–1765; doi:10.1038/npp.2017.51; published online 5 April 2017

### INTRODUCTION

Chronic pain is associated with enormous personal, social, and economic burden and is the largest contributor to years lived with disability globally (Rice *et al*, 2015). Despite this, existing medications provide only modest relief. Opioids in particular have considerable side effects, including constipation, impaired sleep, and respiratory depression (Chou *et al*, 2015). The last two decades have seen an increase in the prescription of opioids, which has been associated with an increase in opioid use disorders and opioid-related mortality (Chou *et al*, 2015; Volkow and McLellan, 2016; Zedler *et al*, 2016). This has been termed as an 'opioid crisis', and has caused regulators, health professionals, and the public to begin seeking means to reduce problems associated with high-dose opioid use. Consequently, there is a need for evidence-based strategies for reducing reliance on high-dose opioids without compromising pain management.

Using combinations of medications to harness complementary but distinct mechanisms of action can maximise the analgesic response, enabling the use of a lower dose of each medication and resulting in an improved side effect profile. One promising area for medication combinations is the use of opioid-sparing medications. Opioid-sparing medications, when co-administered with opioids, enable a reduced opioid dose without loss of analgesic efficacy. Cannabinoid medications are increasingly being studied for their analgesic- and opioid-sparing potential. The endocannabinoid system represents an ideal target because it is a key endogenous system in modulating pain-processing pathways (Woodhams *et al*, 2015).

The endocannabinoid system is composed of the cannabinoid CB1 and CB2 receptors, the endocannabinoid ligands

*Correspondence: Dr S Nielsen, The National Drug and Alcohol Research Centre, The University of New South Wales, Sydney, NSW 2052, Australia, Tel: +61 2 99360317, Fax: +61 2 9385 0222, E-mail: s.nielsen@unsw.edu.au

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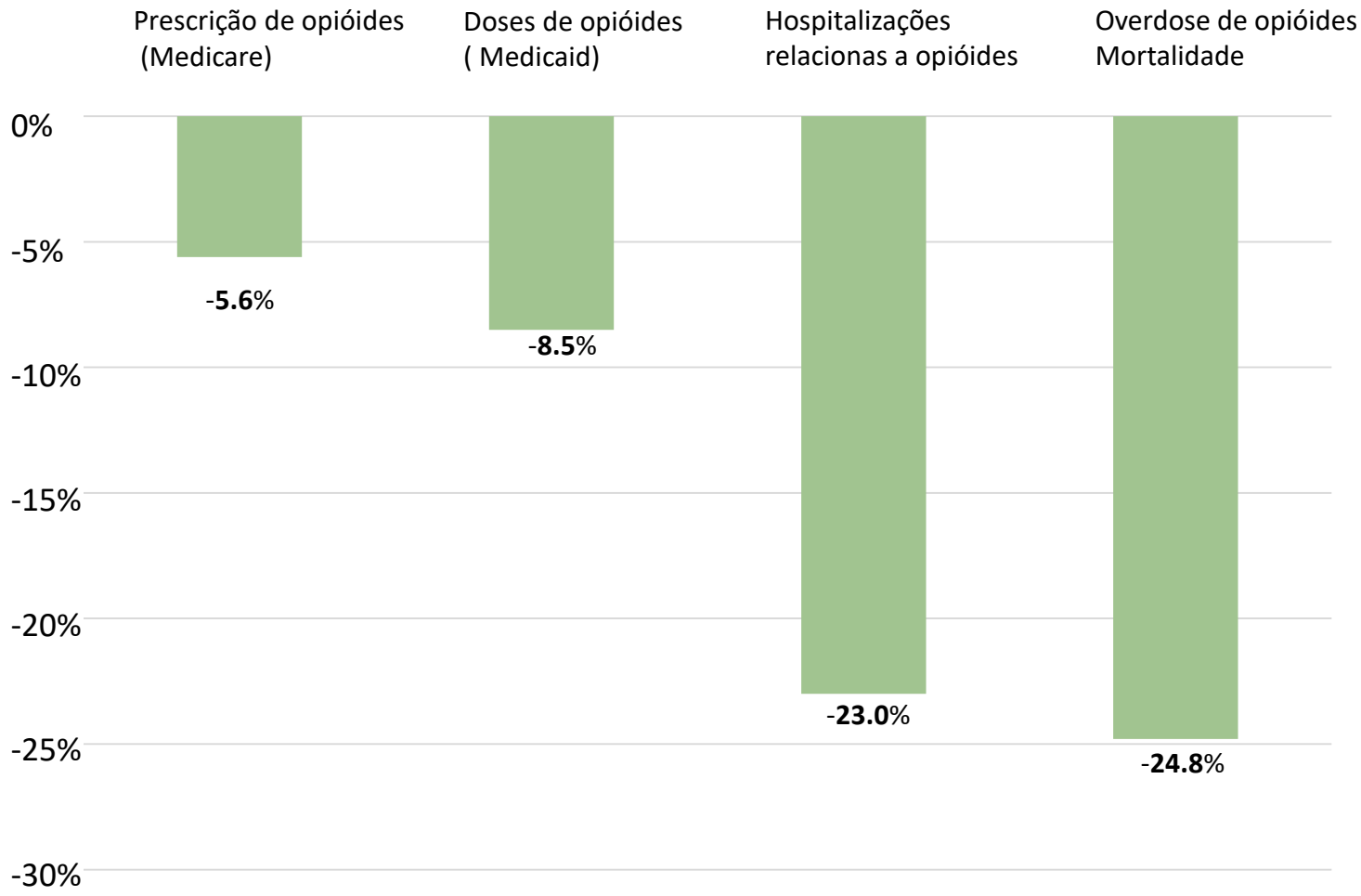
# Estudos Norte Americanos: impacto da Cannabis medicinal no uso de opióides

Os estados com leis da Cannabis medicinal tem reduções em:




CANNABIS
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MAN WITH SEVERE PARKINSON'S DISEASE

TRIES MARIJUANA FOR THE FIRST TIME

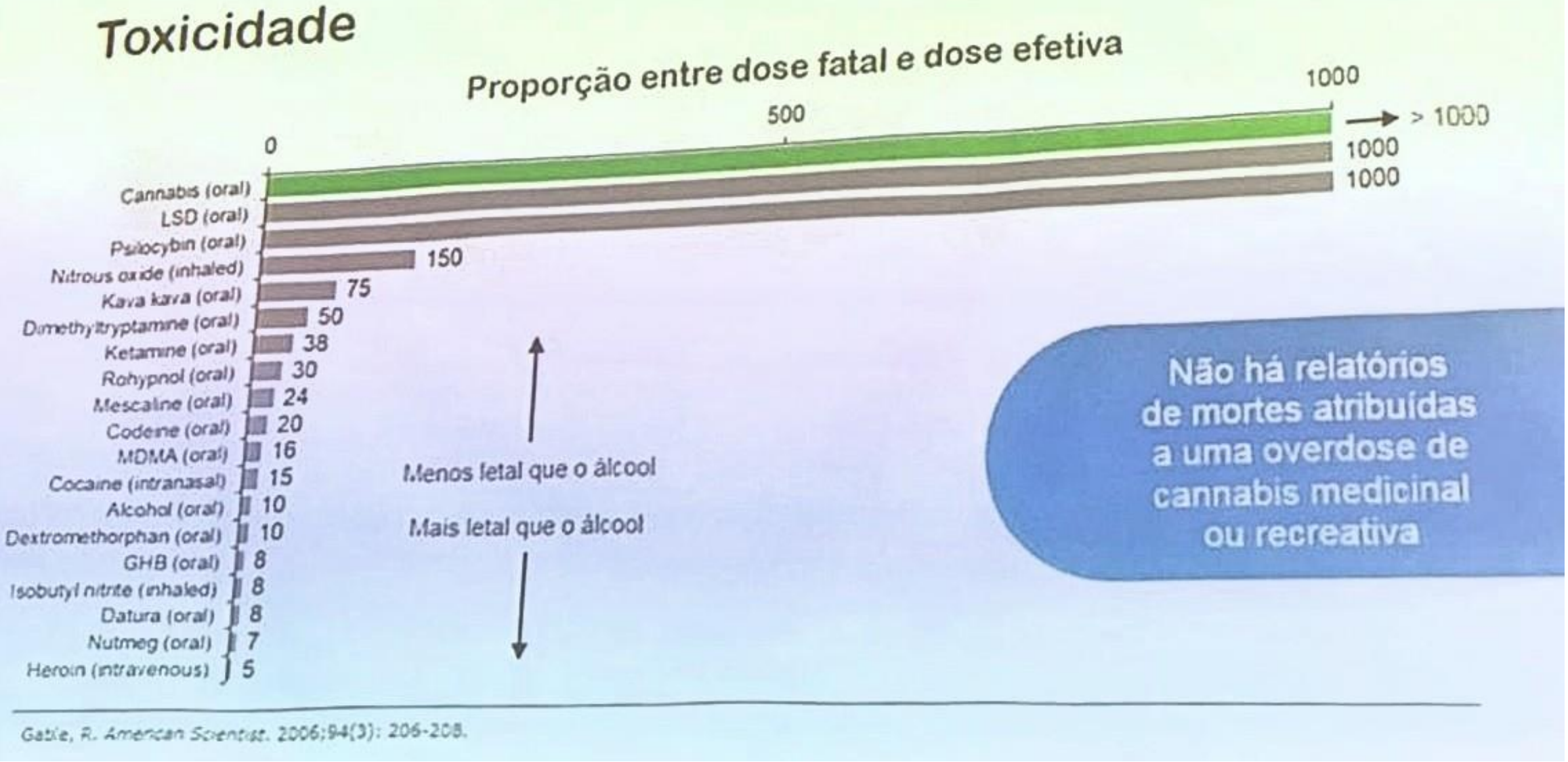

NDC 0051-0022-21
60 Capsules
5 mg
MARINOL®
(DRONABINOL)
Capsules
Each capsule contains:
Dronabinol 5 mg
MARINOL® is a registered trademark of Unimed Pharmaceuticals, Inc.
℞ only
UNIMED


Sativex
Spray zur Anwendung in der Mundhöhle
2,7 mg Delta-9-Tetrahydrocannabinol / 2,5 mg Cannabidiol
3 x 10-ml-Sprühflaschen
Zur Anwendung in der Mundhöhle
GW pharmaceuticals
Almirall


NDC 0037-1221-50
Cesamet®
(Nabilone Capsules)
1 mg
MEDA


EPIDIOLEX®
100 mg/mL
(cannabidiol) 100 mg/mL
Oral Solution
CAUTION: New Drug – Limited by Federal (or United States) Law to Investigational Use

# Toxicidade




Gable, R. American Scientist. 2006;94(3): 206-208.

# Cannabis: Eventos Adversos (EA)

- Sonolência/fadiga
- Tontura
- Boca seca
- Tosse, catarro, bronquites ( somente fumando)
- Ansiedade
- Nauseas
- Efeitos cognitivos
- A maioria dos EA estão associados ao THC
- dependem da dose
- “Começar com doses baixas, ir devagar” para mitigar os efeitos.

**Combinar CBD com THC para reduzir ainda mais os EA relacionados do THC (efeito entourage)**

CANNABIS MEDICINAL

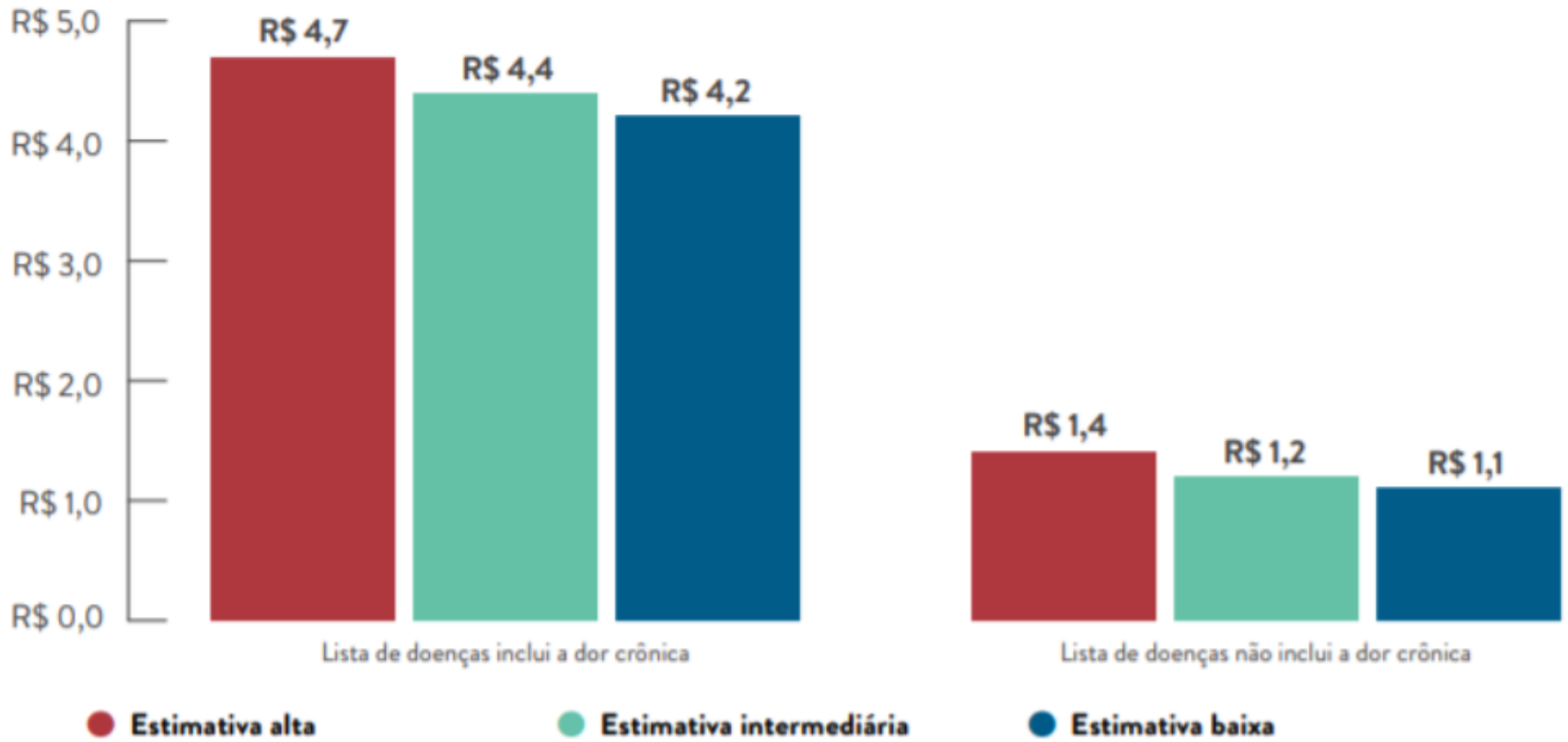
# Grupos nos quais a Cannabis deve ser usada com precaução

Grupos nos quais a Cannabis deve ser usada com precaução

- Pessoas com mais de 25 anos de idade
- Transtorno de uso de substâncias
- Esquizofreniza, psicoses, transtorno de saúde mental não administrado
- Doença cardiaca instável
- Doença respiratória instável ( se inalado)
- Gravidez e lactação

CANNABIS
MEDICINAL

## RECEITA POTENCIAL DE *CANNABIS* MEDICINAL NO BRASIL:
### 36 MESES APÓS O INÍCIO DA VENDA LEGAL (EM BILHÕES DE REAIS - R$)



# JUDICIALIZAÇÃO

# O GOVERNO AMERICANO CONTROLA A  PATENTE

US006630507B1

(12) **United States Patent**
**Hampson et al.**

(10) **Patent No.: US 6,630,507 B1**
(45) **Date of Patent: Oct. 7, 2003**

(54) **CANNABINOIDS AS ANTIOXIDANTS AND NEUROPROTECTANTS**


(75) Inventors: **Aidan J. Hampson**, Irvine, CA (US); **Julius Axelrod**, Rockville, MD (US); **Maurizio Grimaldi**, Bethesda, MD (US)

(73) Assignee: **The United States of America as represented by the Department of Health and Human Services**, Washington, DC (US)


( * ) Notice: Subject to any disclaimer, the term of this

OTHER PUBLICATIONS


Windholz et al., The Merck Index, Tenth Edition (1983) p. 241, abstract No. 1723.*

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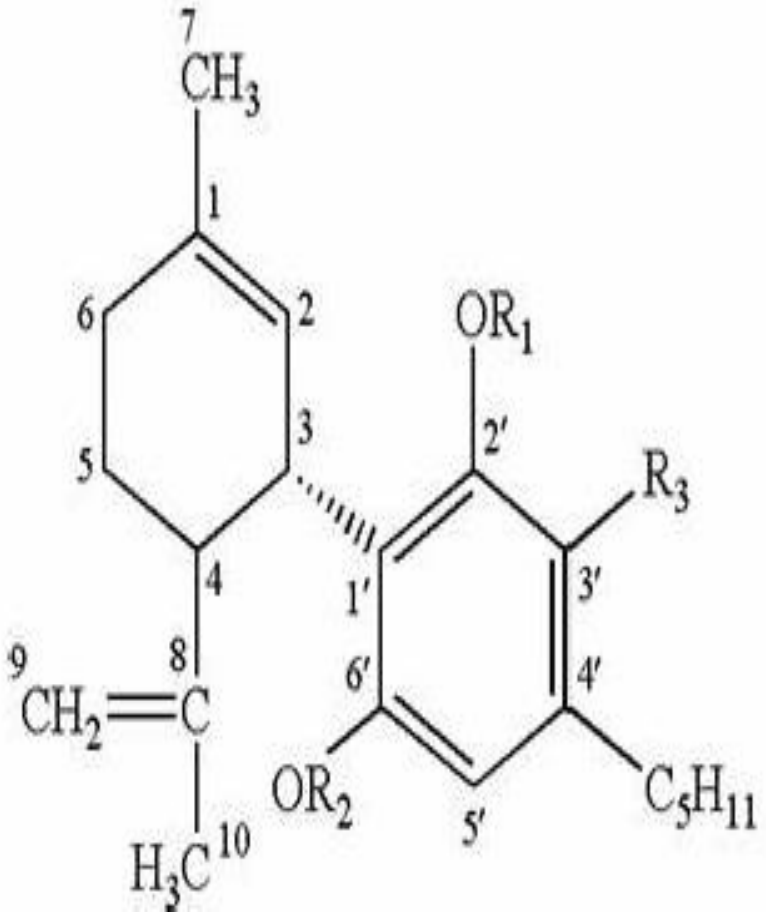
Ottersen et al., "The Crystal and Molecular Structure of Cannabidiol," *Acta Chem. Scand. B 31*, 9:807-812 (1977).

Cunha et al., "Chronic Administration of Cannabidiol to Healthy Volunteers and Epileptic Patients[1]," *Pharmacology*,

# OBRIGADO!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