CURSO DE AVANCES EN GASTROENTEROLOGÍA

PERSPECTIVAS FUTURAS EN GASTROENTEROLOGÍA

17 - 19 Julio 2024 - Hotel InterContinental, Stgo.

SChGE

Cannabinoides: Uso en Patología Digestiva

Disclaimer

Sin financiamiento ni influencias de:

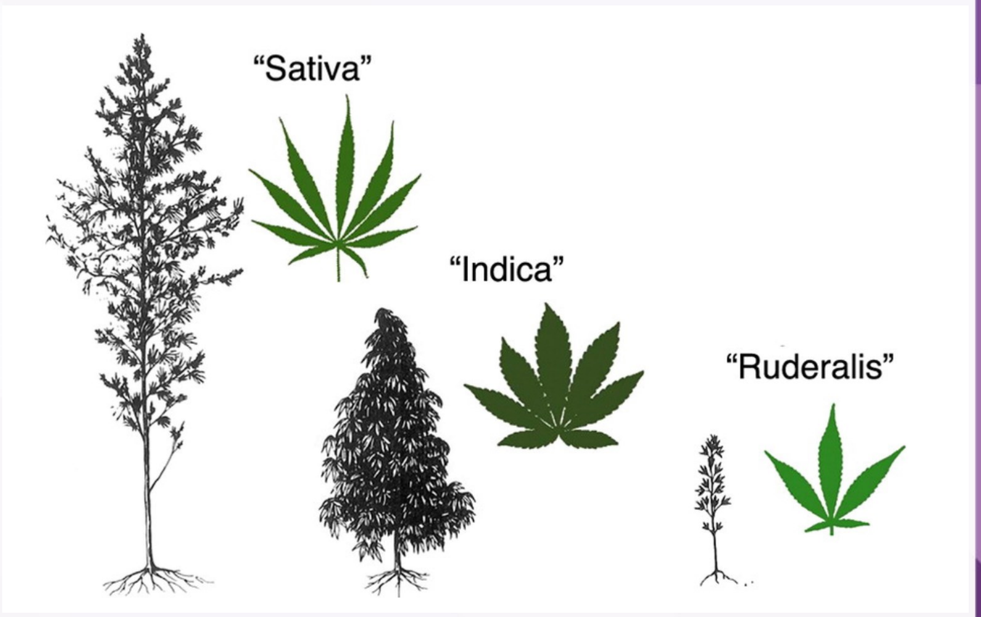
- Industria farmacéutica
- Narcotráfico

Cannabis sativa

Origen en Asia central

C. sativa *indica*
sativa
ruderalis

+ 560 fitocompuestos identificados
+120 cannabinoides (THC, CBD)

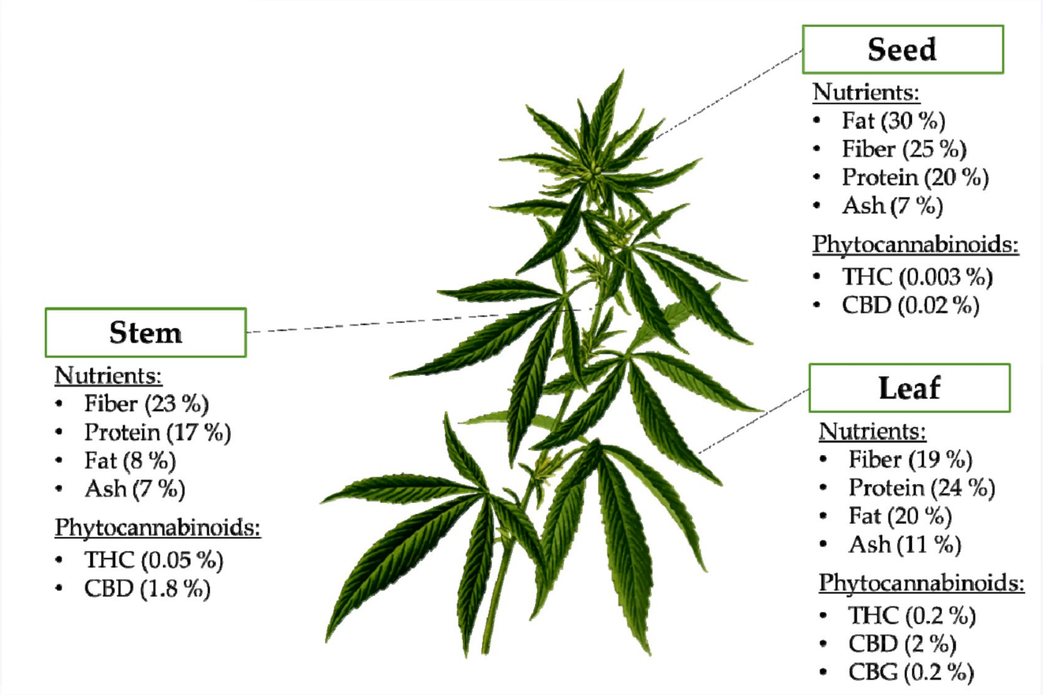


Historia

12.000 años de convivencia

Usos:

- fibra: vestuario - redes
- alimento
- resina
- medicinal
- religioso
- recreativo

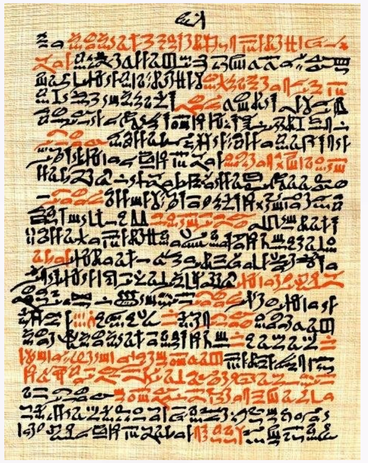


Int. J. Mol. Sci. 2020, 21, 3067

Uso Medicinal

China: 2000 ac, compendio hierbas medicinales
Egipto: 1500 ac, anti-inflamatorio tópico

Herodoto: V ac, escitas quemando κάνναβις
Plinio: I dc, usos analgésicos y anti-inflamatorios
Galeno: II dc, sensación de calor, psicoactivo



ON THE

THERAPEUTICAL USES AND TOXIC EFFECTS OF CANNABIS INDICA.

By J. RUSSELL REYNOLDS, M.D., F.R.S., &c.,

PHYSICIAN IN ORDINARY TO HER MAJESTY'S HOUSEHOLD.

THE LANCET,] DR. J. RUSSELL REYNOLDS ON CANNABIS INDICA. [MARCH 22, 1890. 637

Años oscuros

1914: Ley de Narcóticos de Harrison de 1914 → Delito

1937: Marihuana Taxt Act

1970: Lista 1 de Drogas de los EEUU
"no aceptado su uso médico".

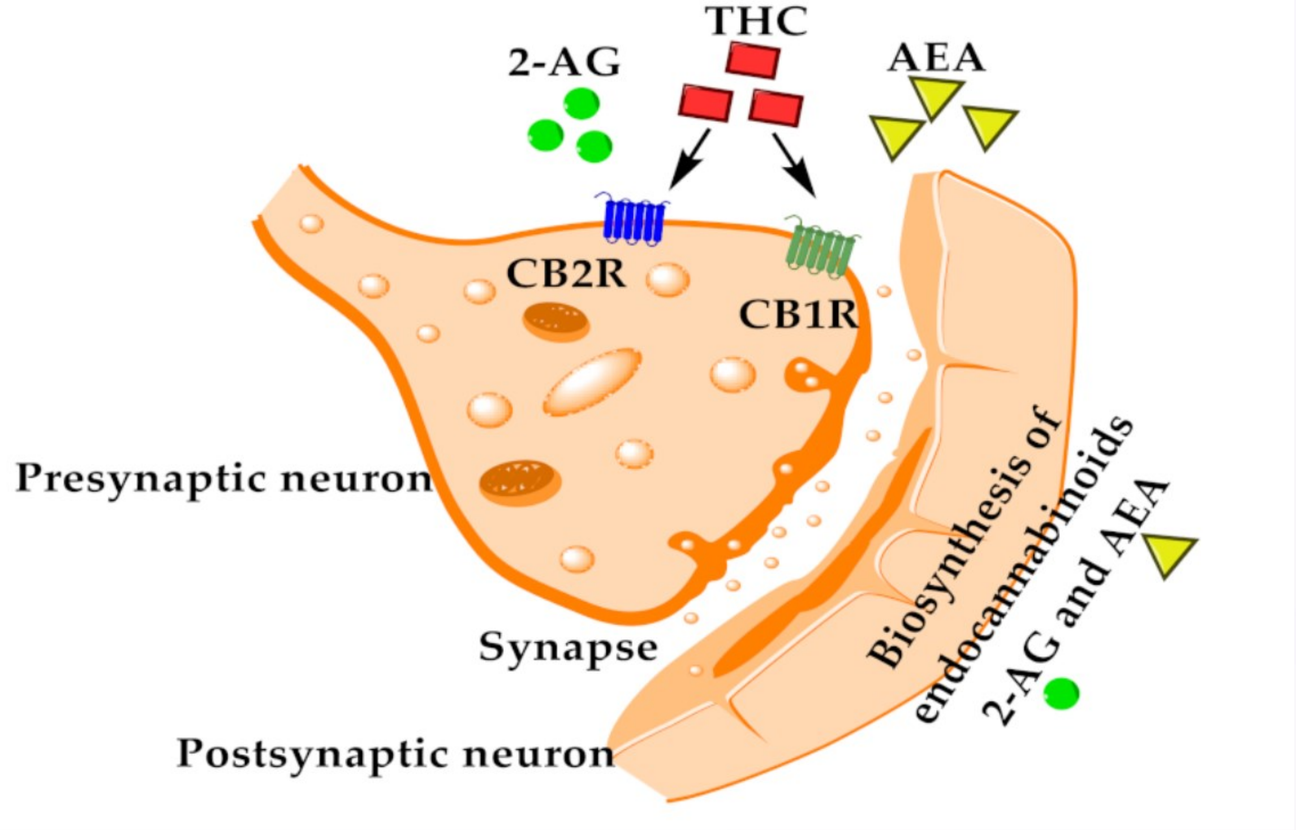
Uso Medicinal v2.0

Fitocannabinoides: CBD (1963) – THC (1964)

1988 → CB1-R
1992 → Anandamida (AEA)
1993 → CB2-R
1995 → 2-Arachidonoylglycerol (2-AG)

Sistema Endocannabinoide

Sistema Endocannabinoide



Toxins 2021, 13, 117

Sistema Endocannabinoide

CB1

SNC – SNP – SNE
Corazón
Pulmón
Piel
Ojos
Huesos

CB2

Células inmunes
Intestino
SNC
Corazón
Tejido adiposo
Hígado
Huesos
Gónadas

Receptores de cannabinoides

Δ^9-TETRAHYDROCANNABINOL
Molecular Targets
CB1 partial agonist
CB2 partial agonist
GPR55 agonist
GPR18 agonist
$5HT_{3A}$ antagonist
PPARγ agonist
TRPA1 agonist
TRPV2 agonist
TRPV3 agonist
TRPV4 agonist
TRPM8 antagonist
μ and δ opioid allosteric modulator
GlyR α_1 and α_3 positive allosteric modulator
AEA uptake inhibition by targeting FABPs
Adenosine reuptake inhibitor

CANNABIDIOL
Molecular Targets
CB1 inverse agonist and negative allosteric modulator
CB2 partial agonist and negative allosteric modulator
GPR55 antagonist
GPR18 antagonist
GPR3 inverse agonist
GPR6 inverse agonist
GPR12 inverse agonist
A_{1A}agonist
$5HT1_A$ agonist
$5HT_{2A}$ partial agonist
$5HT_{3A}$ antagonist
PPARγ agonist
TRPA1 agonist
TRPV1 agonist
TRPV2 agonist
TRPV3 agonist
TRPM8 antagonist
$GABA_A$ positive allosteric modulator
μ and δ opioid allosteric modulator
GlyRα_1 and α_3 positive allosteric modulator
AEA uptake inhibition by targeting FABPs
Adenosine reuptake inhibitor

CANNABICHROMENE
Molecular Targets
CB2 agonist
TRPA1 agonist
TRPV1 agonist
TRPV3 agonist
TRPV4 agonist
TRPM8 weak antagonist
AEA uptake inhibitor
MAGL inhibitor

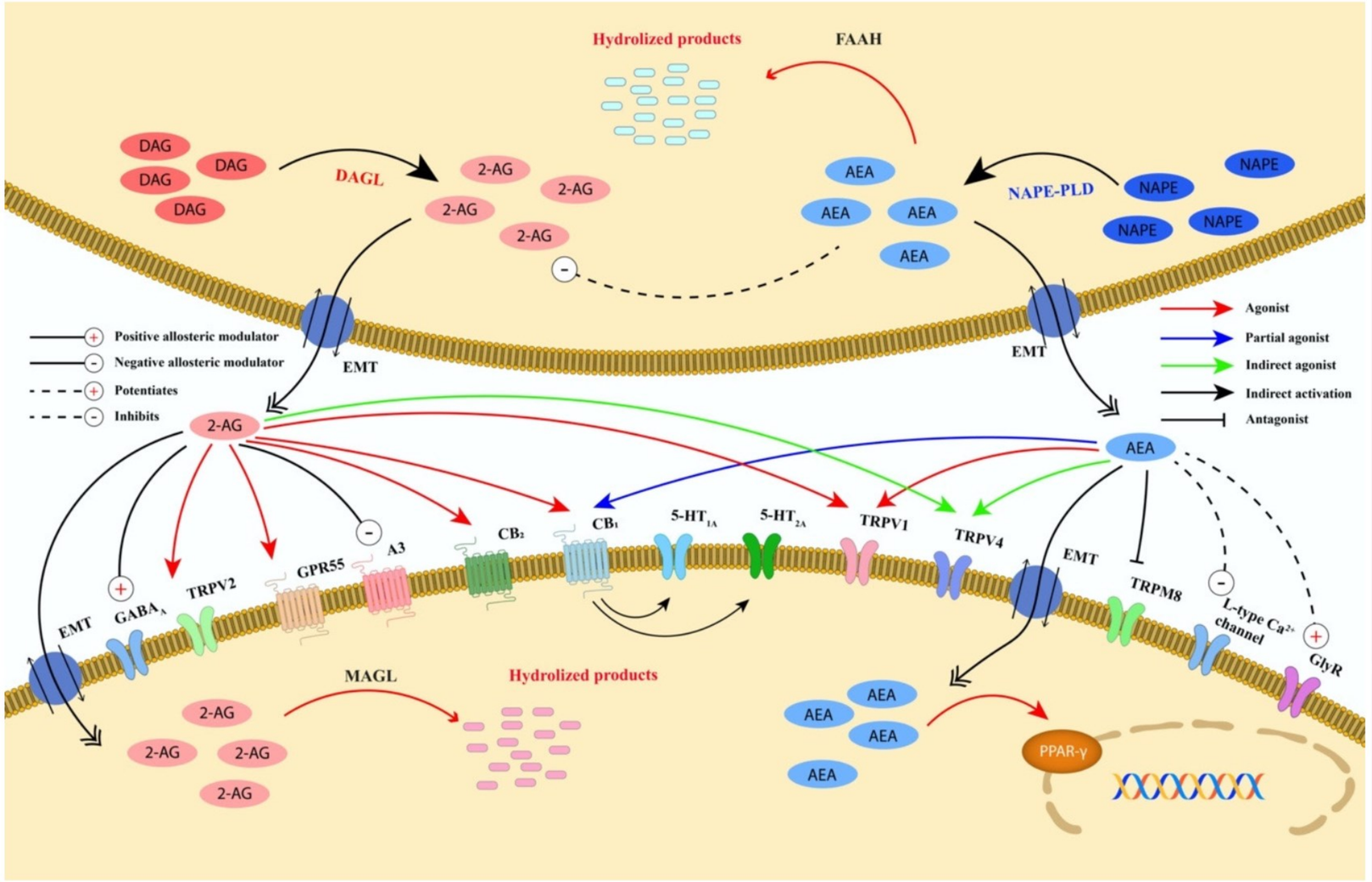
CANNABIDIVARIN
Molecular Targets
GPR55 antagonist
TRPA1 agonist
TRPV1 agonist
TRPV2 agonist
TRPV3 agonist
TRPV4 agonist
TRPM8 antagonist
DAGL inhibitor
AEA uptake inhibitor

Int. J. Mol. Sci. 2020, 21, 3067

Cannabinoides

Fitocannabinoides	Endocannabinoides	Sintéticos
Delta-9-Tetrahidrocannabinol (Δ9-THC)	**Anandamida (AEA)**	**Dronabinol**
Cannabidiol (CBD)	**2-Arachidonoylglycerol (2-AG)**	**Nabilona**
Cannabinol (CBN)	N-Arachidonoyl Dopamine (NADA)	Levonantradol
Cannabigerol (CBG)	O-Arachidonoyl Ethanolamine (Virodamina)	HU-210
Cannabicromeno (CBC)	Palmitoylethanolamide (PEA)	CP 55,940
Cannabicromeno (CBC)	Oleoylethanolamide (OEA)	WIN 55,212-2
Tetrahidrocannabivarina (THCV)		Rimonabant (SR141716A)
Cannabidivarina (CBDV)		JWH-018
Delta-8-Tetrahidrocannabinol (Δ8-THC)		AM-2201

Sistema Endocannabinoide



Toxins 2021, 13, 117

Int. J. Mol. Sci. 2020, 21, 3067

Efectos Digestivos

Efecto inhibitorio – modulador

Disminuye motilidad
Disminuye secreción
Disminuye inflamación
Disminuye dolor

Enfermo >>> Sano

	RECEPTORS	
COMPONENT	**LOCATION**	**FUNCTION**
CB1 (binds AEA, 2-AG)	ENS: cholinergic neurons Mucosa: epithelial and plasma cells Vascular smooth muscle cells Lamina propria: macrophages and plasma cells	Reduces GI motility and secretion Modulates immune function
CB2 (binds AEA, 2-AG)	ENS (under inflammatory conditions) Mucosa: epithelial cells, macrophages > plasma cells Lamina propria: macrophages and plasma cells	Reduces GI motility and secretion Modulates immune function
TRPV1 (binds AEA > OEA)	Extrinsic afferent fibers, running through the muscle layers Immune cells adjacent to blood vessels.	Visceral hypersensitivity signaling Increase in intestinal contractility (under inflammatory conditions)
PPAR-α (binds AEA, 2-AG, OEA, PEA, others)	Enterocytes of the small intestine ENS Vagal afferent fibers Enteric glial cells	
GPR55 (binds PEA)	Epithelial cells and ENS of the small intestine	
GPR119 (binds OEA, PEA > AEA)	Villi: enteroendocrine L cells	Regulates the release of GLP-1

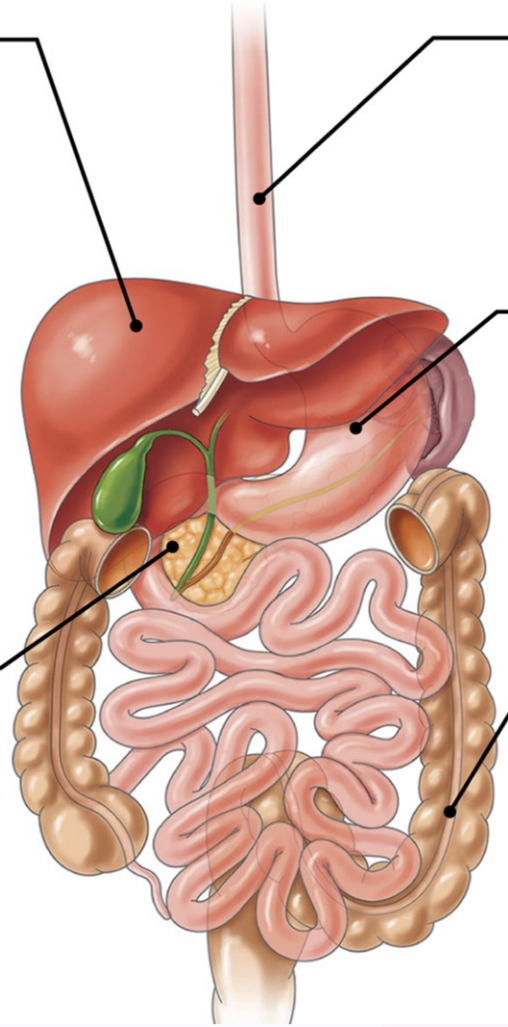
Int. J. Mol. Sci. 2020, 21, 3067

Liver & metabolism

- Increases expression of cannabinoid receptors in acute and chronic liver injury
- May play role in fibrogenesis (although possible protective role?)
- Increases short term energy intake
- Probable long term weight loss through CB2 pathways
- CBD: alters enzymatic pathways (Cyt P-450)

Pancreas

- Mitigates inflammatory response in pancreatitis
- Could be causative agent of pancreatitis
- May improve pain in chronic pancreatitis



Esophagus

- Decreases LES pressure
- Decreases TLESR frequency

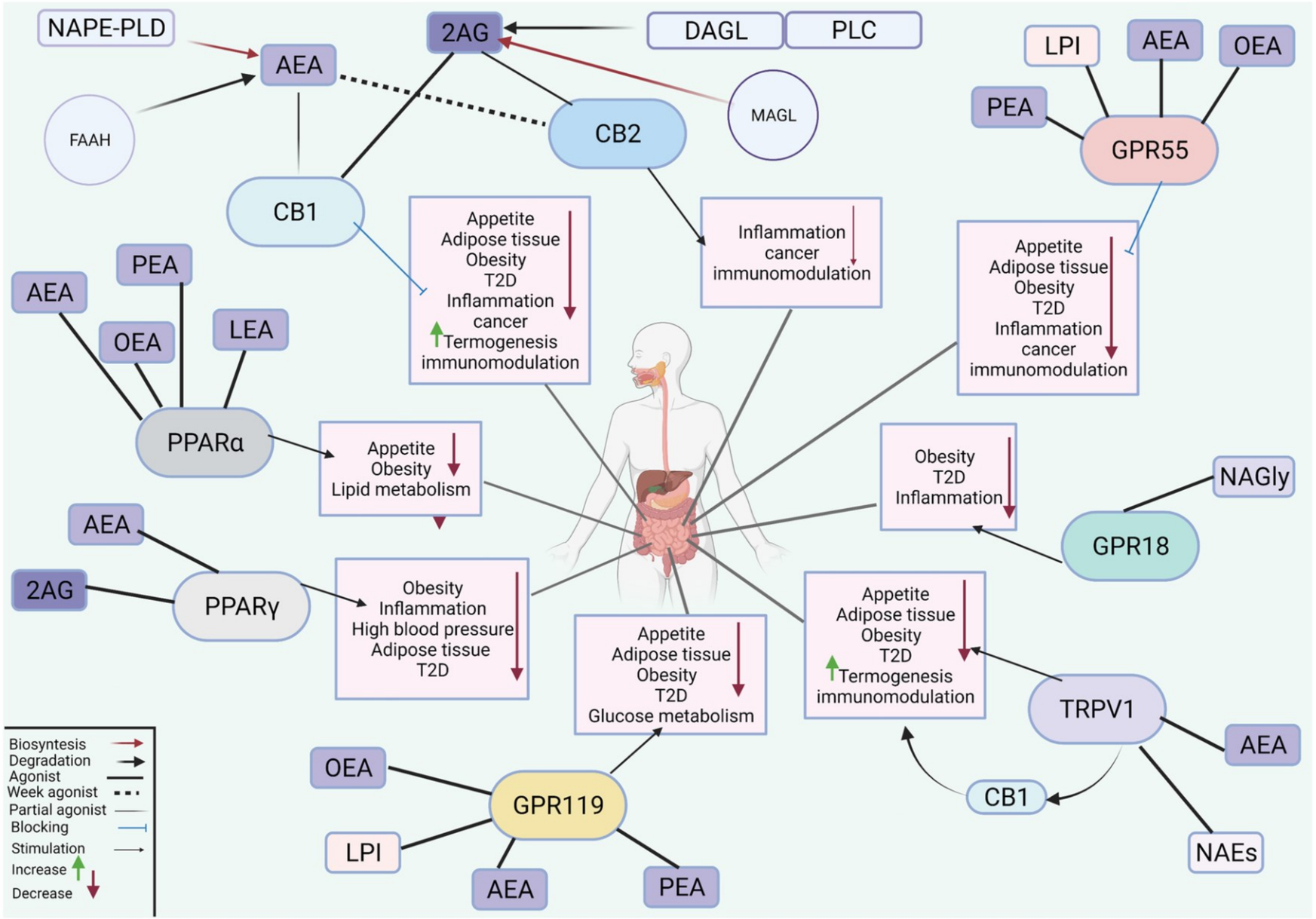
Stomach

- Decreases gastric emptying
- May improve nausea (in gastroparesis and CINV)

Colon

- Decreases motility
- Increases compliance to distension
- May improve abdominal pain associated with IBS

Gastroenterology. 2020;159(1):62-80



Pharmacological Research 175 (2022) 106025

Efectos en Patologías Digestivas

Cannabis for the treatment of ulcerative colitis (Review)

Kafil TS, Nguyen TM, MacDonald JK, Chande N

2 RCT

Irving 2018: CBD vs placebo (n=60)

remisión clínica: 24% vs 26% (RR 0.94, 95% IC 0.39-2.25)

respuesta clínica: 31% vs 22%(RR 1.37, 95% IC 0.59-3.2)

Naftali 2018: THC cigarrillos 23mg/d vs placebo (n=32)

score actividad: MD -4.00, 95% CI -5.98 to -2.02

pcr: D -0.30, 95% CI -1.35-0.75

Cochrane Database of Systematic Reviews 2018, Issue 11. Art. No.: CD012954

Cannabis for the treatment of Crohn's disease (Review)

Kafil TS, Nguyen TM, MacDonald JK, Chande N

3 RCT

Naftali 2013: cig THC 115mg vs placebo (n=21)
remisión clínica: 5/11 vs 1/10 (RR 4.55, 95% CI 0.63-32.56)
respuesta clínica: 10/11 vs 4/10 (RR 2.27, 95% CI 1.04-4.97)

Naftali 2017: aceite CBD 5% vs placebo (n=22)
remisión clínica: 4/10 vs 3/9 (RR 1.20, 95% CI 0.36-3.97)

Naftali 2017: Aceite 15% + CBD 4% THC vs placebo (n=55)
QOL: 96.3 vs 79.9 (MD 16.40, 95% CI 5.72-27.08)
CDAI: 118.6 vs 212.6 (MD -94.00, 95%CI -148.86 a -39.14)

Cochrane Database of Systematic Reviews 2018, Issue 11. Art. No.: CD012853

Enfermedad Inflamatoria Intestinal

Cannabis for the treatment of ulcerative colitis (Review)

Kafil TS, Nguyen TM, MacDonald JK, Chande N

The effects of cannabis and cannabidiol on UC are uncertain, thus no firm conclusions regarding the efficacy and safety of cannabis or cannabidiol in adults with active UC can be drawn.There is no evidence for cannabis or cannabinoid use for maintenance of remission in UC. Further studies with a larger number of patients are required to assess the effects of cannabis in UC patients with active and quiescent disease. Different doses of cannabis and routes of administration should be investigated. Lastly, follow-up is needed to assess the long term safety outcomes of frequent cannabis use.

Cannabis for the treatment of Crohn's disease (Review)

Kafil TS, Nguyen TM, MacDonald JK, Chande N

The effects of cannabis and cannabis oil on Crohn's disease are uncertain. Thus no firm conclusions regarding the efficacy and safety of cannabis and cannabis oil in adults with active Crohn's disease can be drawn. The effects of cannabis or cannabis oil in quiescent Crohn's disease have not been investigated. Further studies with larger numbers of participants are required to assess the potential benefits and harms of cannabis in Crohn's disease. Future studies should assess the effects of cannabis in people with active and quiescent Crohn's disease. Different doses of cannabis and delivery modalities should be investigated.

Enfermedad Inflamatoria Intestinal

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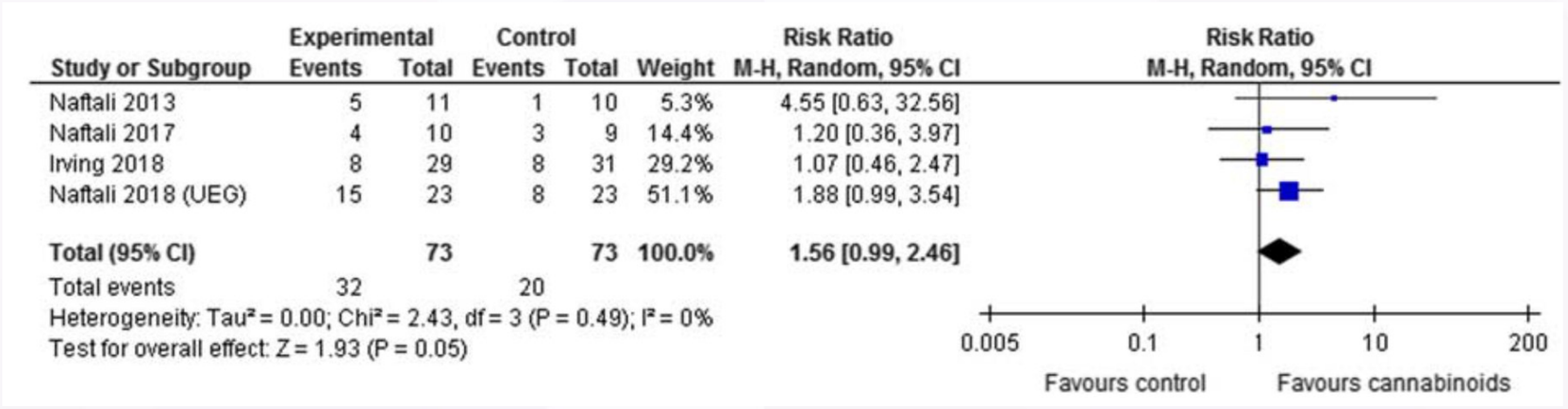
A Systematic Review With Meta-Analysis of the Efficacy of Cannabis and Cannabinoids for Inflammatory Bowel Disease

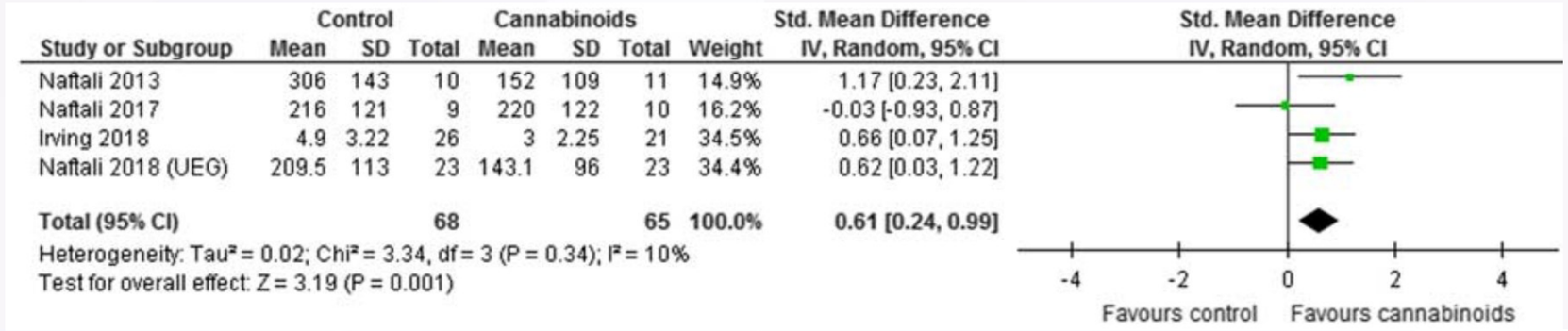
Inducción remisión



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Naftali 2013	5	11	1	10	5.3%	4.55 [0.63, 32.56]
Naftali 2017	4	10	3	9	14.4%	1.20 [0.36, 3.97]
Irving 2018	8	29	8	31	29.2%	1.07 [0.46, 2.47]
Naftali 2018 (UEG)	15	23	8	23	51.1%	1.88 [0.99, 3.54]
Total (95% CI)		**73**		**73**	**100.0%**	**1.56 [0.99, 2.46]**
Total events	32		20			

Heterogeneity: Tau² = 0.00; Chi² = 2.43, df = 3 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.93 (P = 0.05)

Score actividad



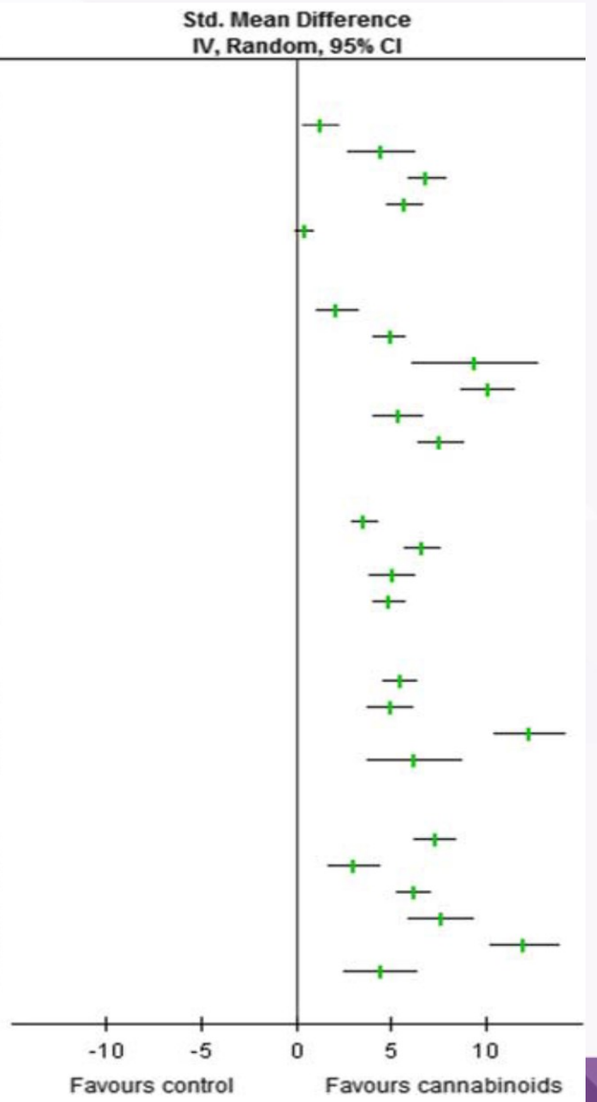
Study or Subgroup	Control Mean	Control SD	Control Total	Cannabinoids Mean	Cannabinoids SD	Cannabinoids Total	Weight	Std. Mean Difference IV, Random, 95% CI
Naftali 2013	306	143	10	152	109	11	14.9%	1.17 [0.23, 2.11]
Naftali 2017	216	121	9	220	122	10	16.2%	-0.03 [-0.93, 0.87]
Irving 2018	4.9	3.22	26	3	2.25	21	34.5%	0.66 [0.07, 1.25]
Naftali 2018 (UEG)	209.5	113	23	143.1	96	23	34.4%	0.62 [0.03, 1.22]
Total (95% CI)			**68**			**65**	**100.0%**	**0.61 [0.24, 0.99]**

Heterogeneity: Tau² = 0.02; Chi² = 3.34, df = 3 (P = 0.34); I² = 10%
Test for overall effect: Z = 3.19 (P = 0.001)

J Clin Gastroenterol 2021;55:798–809

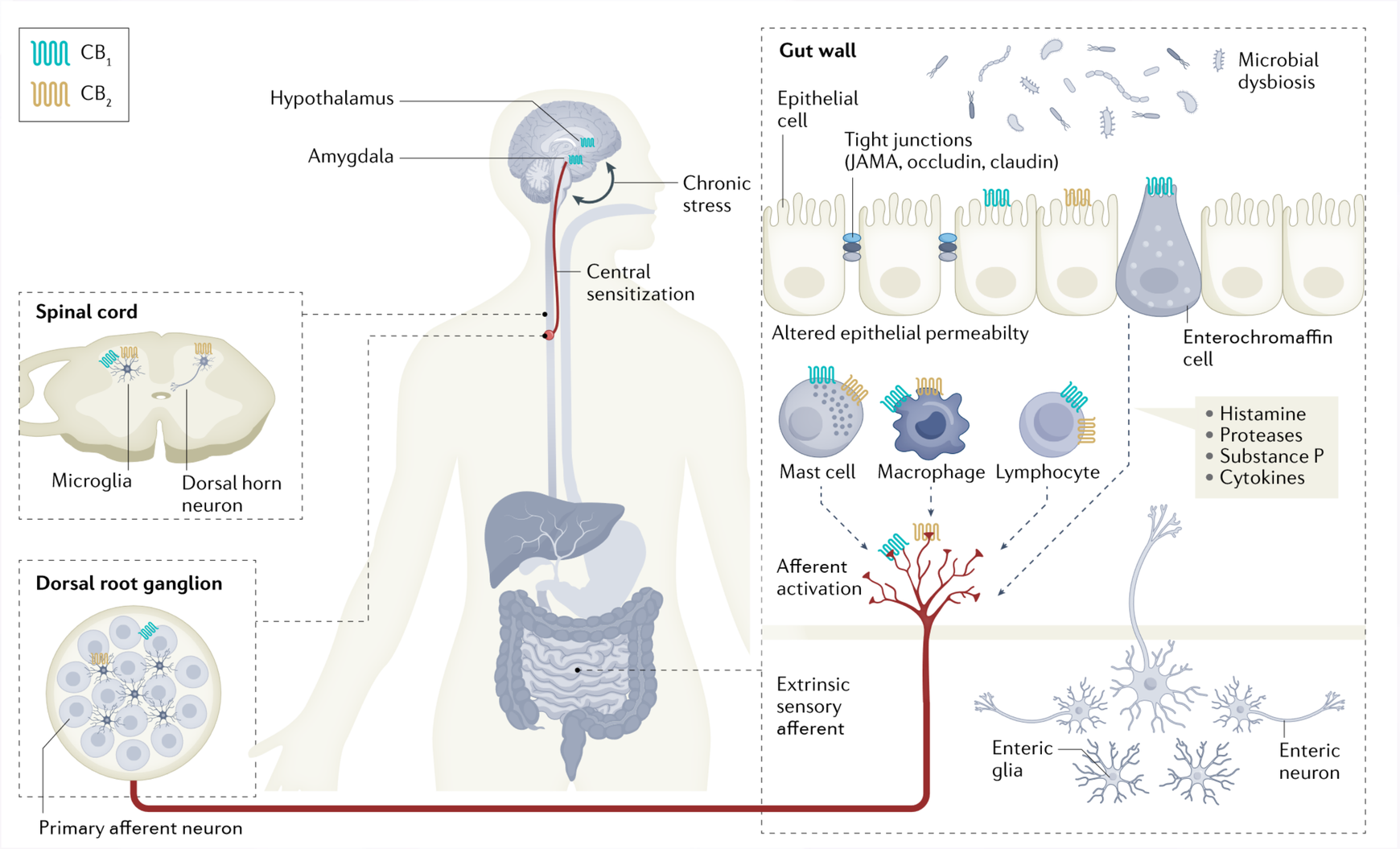
A Systematic Review With Meta-Analysis of the Efficacy of Cannabis and Cannabinoids for Inflammatory Bowel Disease

	Cannabinoids			Control			Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
1.6.1 General well-being							
Naftali 2011	7.3	0	30	3.1	0	30	Not estimable
Lahat 2012	0.81	0.87	11	0	0.0001	11	1.27 [0.33, 2.20]
Naftali 2013	6.18	0.75	11	2.1	1	10	4.46 [2.74, 6.19]
Storr 2014	3.9	0.8	56	0	0.0001	56	6.85 [5.86, 7.83]
Sexton 2016	4.19	1.0318	45	0	0.0001	45	5.69 [4.75, 6.64]
Irving 2018	5.38	1.32	29	4.76	1.64	31	0.41 [-0.10, 0.92]
1.6.2 Abdominal pain							
Lahat 2012	1.09	0.7	11	0	0.001	11	2.12 [1.03, 3.20]
Allegretti 2013	3.86	1.1	48	0	0.0001	48	4.92 [4.11, 5.74]
Naftali 2013	6.73	0.25	11	4.28	0.25	10	9.41 [6.14, 12.68]
Storr 2014	4.3	0.6	56	0	0.0001	56	10.07 [8.67, 11.46]
Phatak 2017	3.77	0.98	24	0	0.0001	24	5.35 [4.10, 6.60]
Merker 2018	3.29	0.61	47	0	0.0001	47	7.57 [6.39, 8.74]
1.6.3 Diarrhea							
Allegretti 2013	3.25	1.28	48	0	0.0001	48	3.56 [2.91, 4.21]
Storr 2014	3.3	0.7	56	0	0.0001	56	6.62 [5.66, 7.58]
Phatak 2017	3.35	0.92	24	0	0.0001	24	5.07 [3.87, 6.26]
Merker 2018	3.02	0.87	47	0	0.0001	47	4.87 [4.05, 5.69]
1.6.4 Nausea							
Allegretti 2013	4	1.03	48	0	0.0001	48	5.45 [4.57, 6.33]
Phatak 2017	3.43	0.97	24	0	0.0001	24	4.92 [3.75, 6.09]
Merker 2018	3.42	0.39	47	0	0.0001	47	12.30 [10.46, 14.14]
Hoffenberg 2019	2.44	0.53	9	0	0.0001	9	6.20 [3.73, 8.67]
1.6.5 Poor appetite							
Allegretti 2013	4.21	0.81	48	0	0.0001	48	7.29 [6.16, 8.42]
Naftali 2013	5.73	0.75	11	4	0.0001	10	3.05 [1.72, 4.39]
Storr 2014	4.4	1	56	0	0.0001	56	6.18 [5.28, 7.08]
Phatak 2017	4.06	0.74	24	0	0.0001	24	7.63 [5.94, 9.32]
Merker 2018	3.42	0.4	47	0	0.0001	47	11.99 [10.20, 13.79]
Hoffenberg 2019	2.33	0.71	9	0	0.0001	9	4.42 [2.54, 6.30]



J Clin Gastroenterol 2021;55:798–809

Síndrome de Intestino irritable



Nature Reviews Gastroenterology & Hepatology **volume 20**, pages5–25 (2023)

Síndrome de Intestino irritable

Muy escasa evidencia

No hay más reingresos hospitalarios por SII

J Clin Gastroenterol. 2022;56(3):257-265

IBS Without Cannabis	IBS With Cannabis
Enterocolitis because of *Clostridioides difficile* 5.6%	Cyclical vomiting 16.2%
IBS without diarrhea 3.8%	IBS with diarrhea 10.6%
Sepsis 3.0%	Endometriosis 7.4%
Noninfective gastroenteritis and colitis 3.0%	Right upper quadrant abdominal pain 7.4%
Acute kidney failure 2.8%	Nausea with vomiting 6.3%

80% de riesgo de SII en pacientes con TUS-C

European Journal of Gastroenterology & Hepatology 2019, 31:756–765

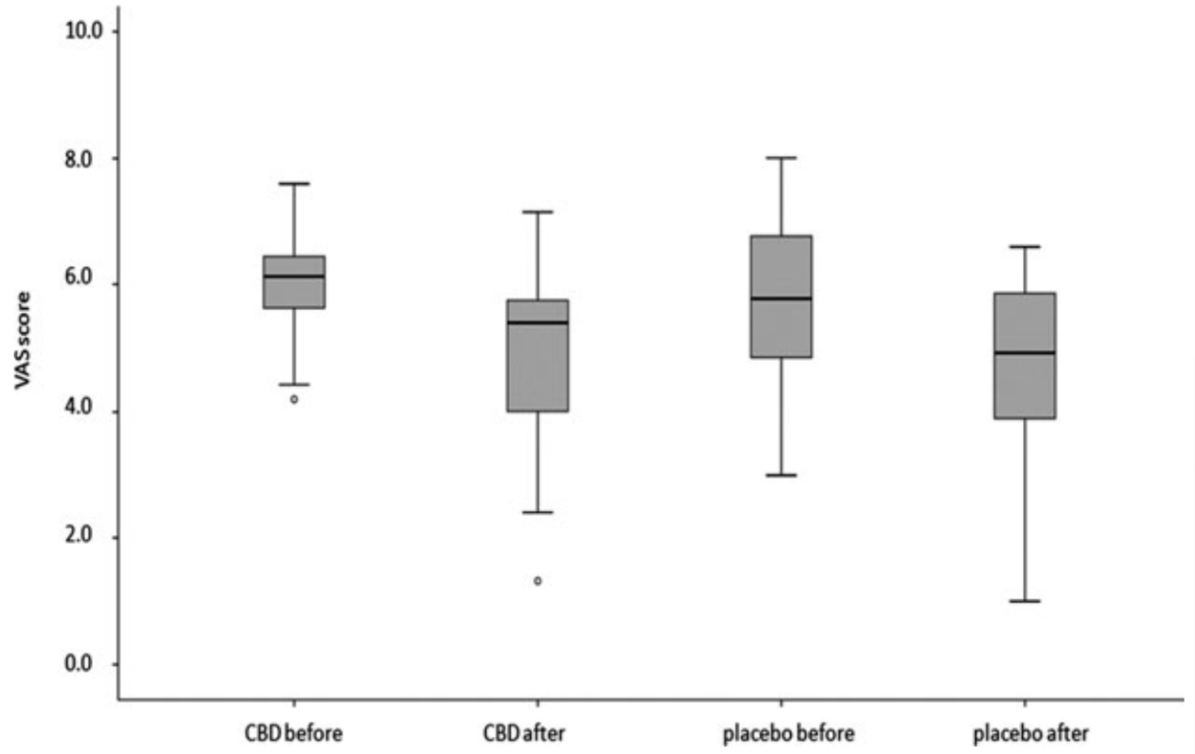
Síndrome de Intestino irritable

Effects of Cannabidiol Chewing Gum on Perceived Pain and Well-Being of Irritable Bowel Syndrome Patients: A Placebo-Controlled Crossover Exploratory Intervention Study with Symptom-Driven Dosing

Anne-Claire B. van Orten-Luiten,[1] Nicole M. de Roos,[1] Soumia Majait,[1] Ben J.M. Witteman,[1,2] and Renger F. Witkamp[1,*]

CBD 50mg
Goma de mascar a demanda, con dolor EVA>4
30 minutos

32 mujeres
No diferencia dolor ni QOL



Cannabis and Cannabinoid Research 7:4, 436–444

Síndrome de Intestino irritable

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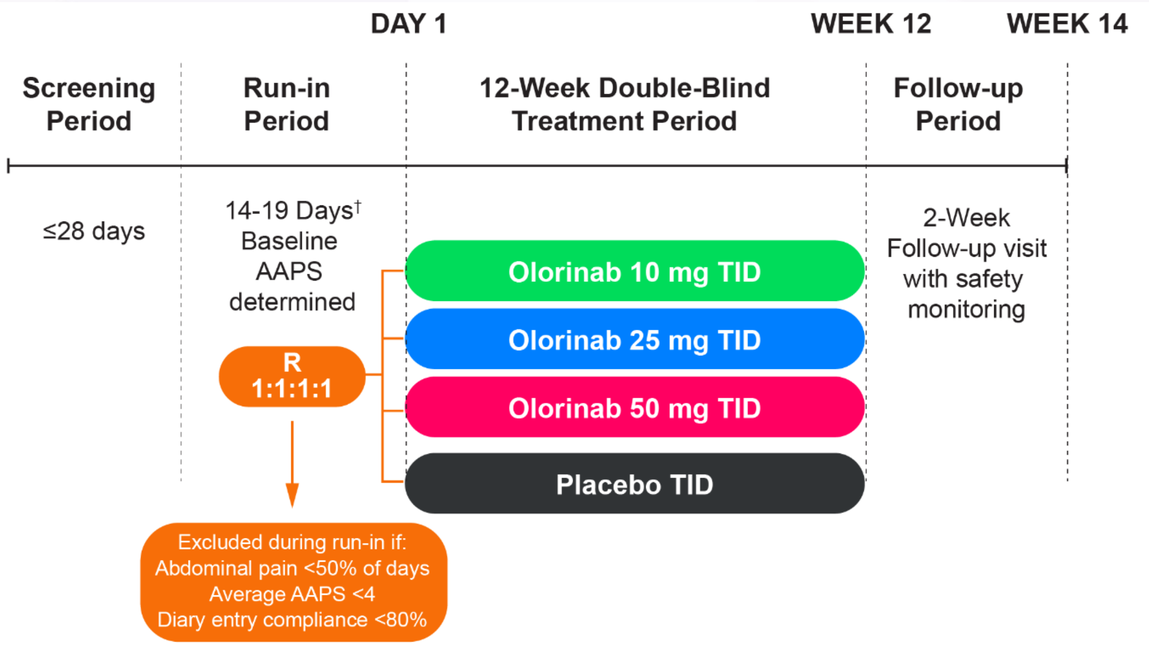
Olorinab (APD371) : agonista selectivo CB2R
Efecto inhibidor TRPV1

273 pacientes
RCT

Dolor abdominal

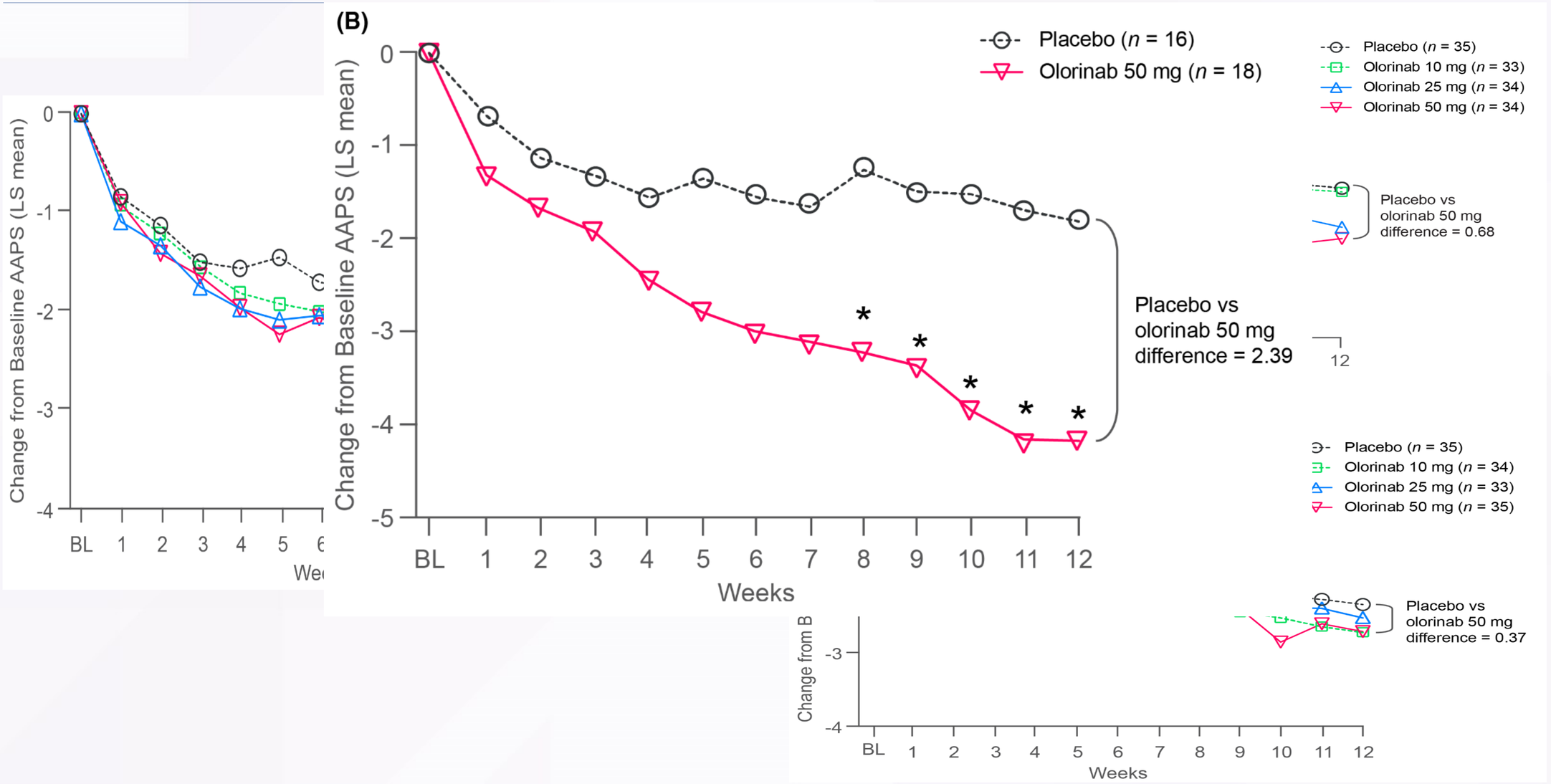
Efficacy and safety of olorinab, a full agonist of the cannabinoid receptor 2, for the treatment of abdominal pain in patients with irritable bowel syndrome: Results from a phase 2b randomized placebo-controlled trial (CAPTIVATE)

Lin Chang[1] | Brooks D. Cash[2] | Anthony Lembo[3] | David C. Kunkel[4] | Brett A. English[5] | Beatriz Lindstrom[5] | Guibao Gu[5] | Sharon Skare[5] | Kye Gilder[5] | Stewart Turner[5] | Fabio Cataldi[5] | Donald Lipkis[6] | Jan Tack[7]



Neurogastroenterology & Motility. 2023;35:e14539

Síndrome de Intestino irritable: Olorinab



Neurogastroenterology & Motility. 2023;35:e14539

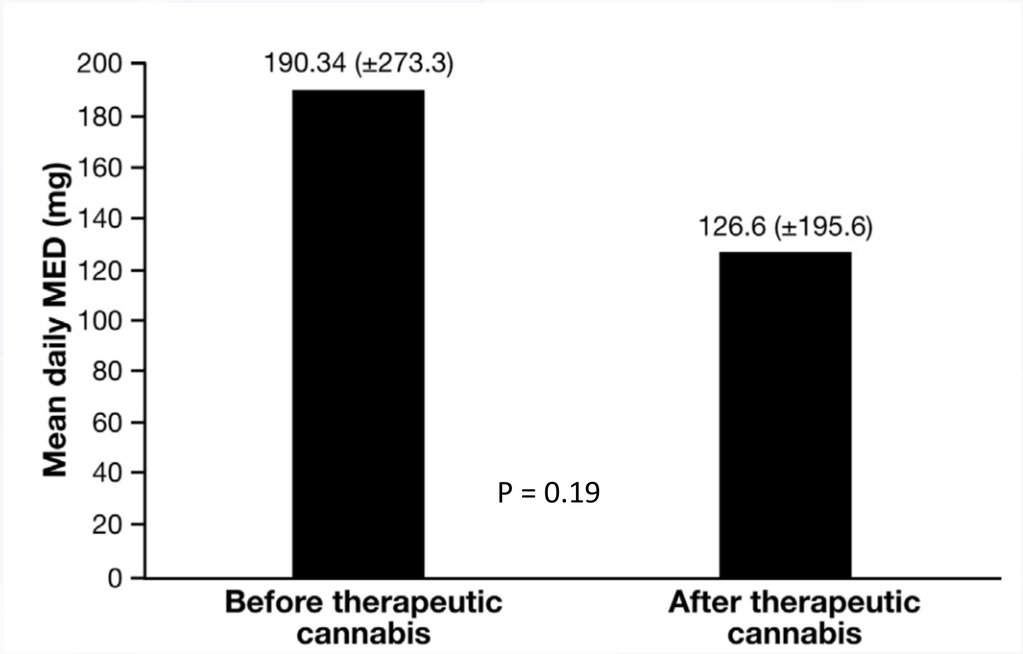
Pancreatitis crónica

Retrospectivo

Dolor
Dosis opiáceos

Effects of Medical Cannabis on Use of Opioids and Hospital Visits by Patients With Painful Chronic Pancreatitis

Trevor S. Barlowe, Jenna L. Koliani-Pace, Kerrington D. Smith, Stuart R. Gordon, and Timothy B. Gardner



Clinical Gastroenterology and Hepatology 2019;17:2608–2609

Dispepsia

48 pacientes
CBD hasta 20 mg/kg
4 semanas

Cannabidiol for Functional Dyspepsia With Normal Gastric Emptying: A Randomized Controlled Trial

Jessica Atieh, MD[1,*], Daniel Maselli, MD[1,*], Margaret Breen-Lyles, BS[1], Monique Torres[1], David Katzka, MD[1], Michael Ryks[1], Irene Busciglio, BS[1], Duane Burton, MHA[1], Paula Carlson, BS[1], W. Scott Harmsen, MS[1,2] and Michael Camilleri, MD, MACG[1]

Parameter (data show median and IQR, or %)	Cannabidiol	Placebo	*P*
4 wk of treatment: patient response outcomes			
Weekly adequate relief ≥2/4 wk (0 = no, 1 = yes)	12/24 (50.0)	11/19 (57.9)	0.61
The mean daily symptom score (UAP, B, and N) (range 0–4)	1.2 (0.9–2.0)	1.1 (0.8–2.0)	0.48
The mean of all symptoms daily on Leuven Postprandial Distress Scale	0.9 (0.7–1.6)	0.9 (0.7–1.4)	0.62
The mean daily epigastric pain on Leuven Postprandial Distress Scale	0.7 (0.1–1.3)	0.8 (0.3–1.1)	0.57
The mean of all daily symptoms (on FDSD) over 28 d	19.3 (12.2–36.6)	19.1 (12.0–39.7)	0.91
Mean Nepean Dyspepsia Index score at 28 d	4.4 (3.2–5.0)	3.6 (3.0–4.7)	0.53

Am J Gastroenterol 2022;117:1296–1304

Dispepsia

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48 pacientes
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4 semanas

Cannabidiol for Functional Dyspepsia With Normal Gastric Emptying: A Randomized Controlled Trial

Jessica Atieh, MD[1,*], Daniel Maselli, MD[1,*], Margaret Breen-Lyles, BS[1], Monique Torres[1], David Katzka, MD[1], Michael Ryks[1], Irene Busciglio, BS[1], Duane Burton, MHA[1], Paula Carlson, BS[1], W. Scott Harmsen, MS[1,2] and Michael Camilleri, MD, MACG[1]

Parameter (data show median and IQR, or %)	Cannabidiol	Placebo	*P*
End of the 4-wk treatment: pharmacodynamics			
Gastric emptying of solids t-lag, min	46.0 (34.3–60.0)	52.1 (30.0–64.2)	0.60
Gastric emptying of solids $T_{1/2}$, min	128.7 (112.3–150.5)	125.8 (120.2–142.2)	0.72
Agg. symptoms at 240 min post-GE meal	23.0 (9.0–75.0)	34.5 (6.0–86.0)	0.56
Fasting gastric volume, mL	179.0 (161.1–212.0)	214.5 (173.7–263.8)	0.11
Gastric accommodation (mL) post-300 mL Ensure	410.2 (324.9–451.1)	417.5 (318.7–473.6)	0.73
Volume to fullness Ensure, mL (30 mL/min)	373.3 (373.3–559.9)	622.1 (373.3–746.6)	0.10
Maximum tolerated volume (MTV) Ensure, mL	808.8 (435.8–995.4)	871.0 (497.7–1,119.8)	0.66
Symptom score (N, F, B, and P) 30 min post-MTV (0–400)	182.5 (132.5–253.0)	219.0 (184.0–250.0)	0.31

Am J Gastroenterol 2022;117:1296–1304

Dispepsia

48 pacientes
CBD hasta 20 mg/kg
4 semanas

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Table 6. Adverse events (*P* value based on the Fisher exact test)

Adverse event	Cannabidiol (n = 25)	Placebo (n = 23)	*P*
Elevated liver enzymes, %	16	4.3	0.35
Abdominal distension, %	24	8.7	0.25
Nausea, %	20	4.3	0.19
Headache, %	12	4.3	0.61
Diarrhea, %	28	4.3	0.05
Dizziness, %	8	0	0.49
Fatigue, %	8	13	0.66
Loss of appetite, %	8	0	0.49

Am J Gastroenterol 2022;117:1296–1304

Gastroparesia

44 pacientes con GP

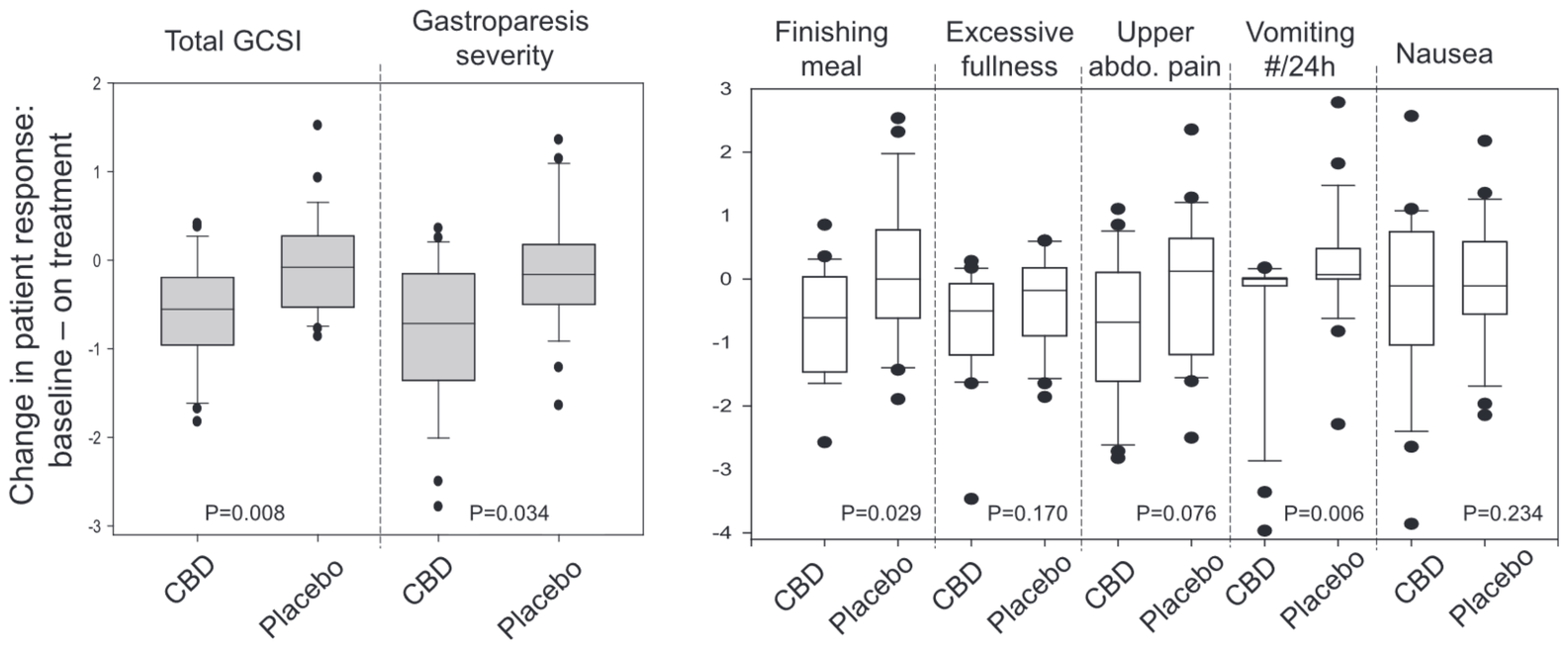
CBD hasta 20mg/kg/d

4 semanas

* Aumento VG 2-4h

A Randomized, Controlled Trial of Efficacy and Safety of Cannabidiol in Idiopathic and Diabetic Gastroparesis

Ting Zheng,[1] Joelle BouSaba,[1] Ann Taylor,[1] Saam Dilmaghani,[1] Irene Busciglio,[1] Paula Carlson,[1] Monique Torres,[1] Michael Ryks,[1] Duane Burton,[1] William Scott Harmsen,[2] and Michael Camilleri[1]



Clinical Gastroenterology and Hepatology 2023;21:3405–3414

Vómitos y náuseas

Efecto CB1 en núcleo tracto solitario, núcleo motor dorsal vago, área postrema

Inhibición receptor 5-HT3

Dronabinol – Nabilona → vómitos refractarios por qmt

Paradoja : síndrome de vómitos por cannabinoides

Hígado

Reportes de FHA

Aumento / disminución fibrosis en HCV

Mejoría encefalopatía hepática (animales)

Sin cambios en mortalidad post trasplante

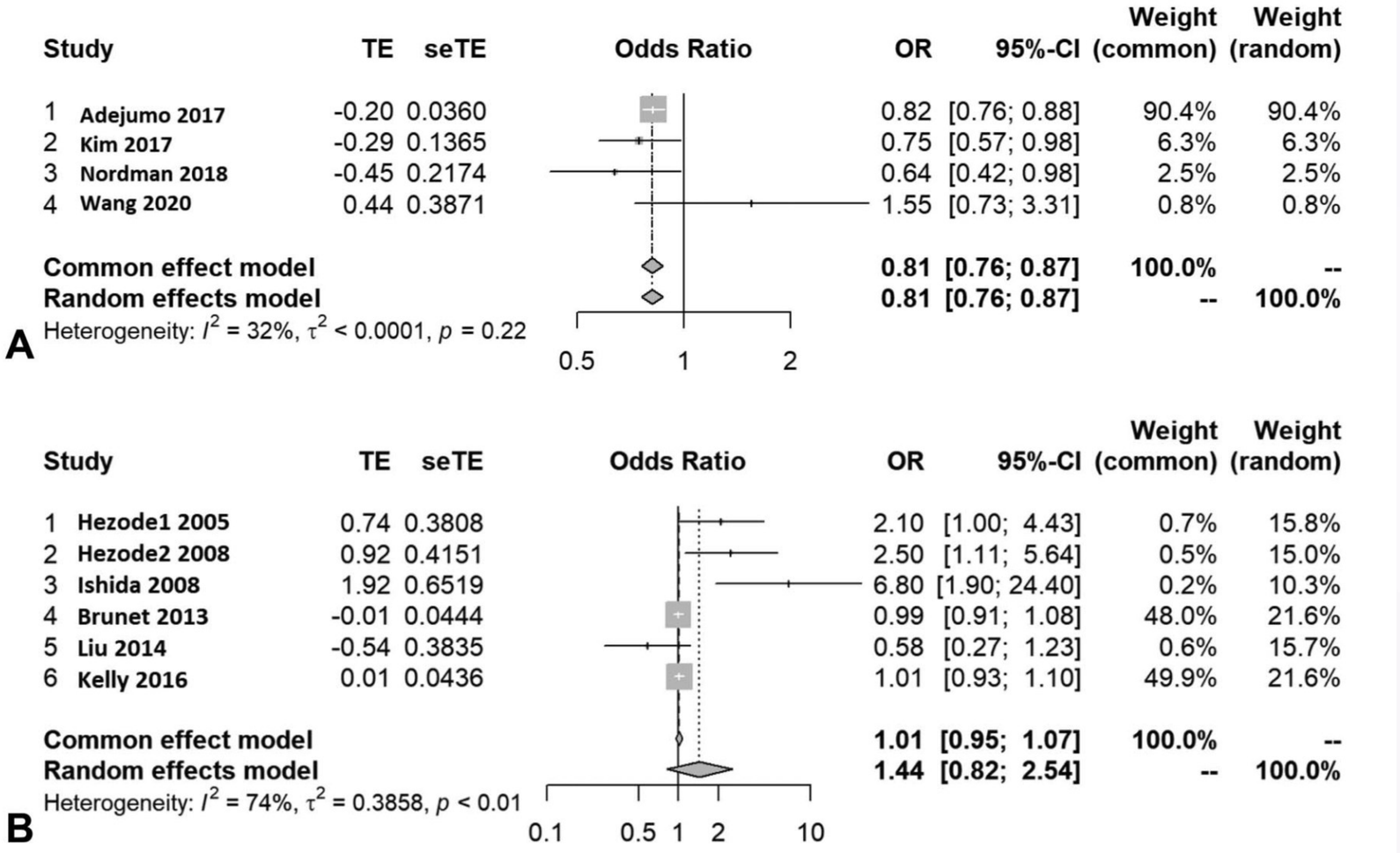
Efecto protector injuria post reperfusión (animales)

Hígado

Alteración CB1:CB2

Sobre-expresión CB2

Respuesta alterada en etapa de fibrosis



American Journal of Therapeutics (2024) 31(2)

Efectos adversos

Adicción 9%
Sd privación – TUS – Intoxicación

Alteraciones en desarrollo de áreas cerebrales
Psicosis – Crisis de pánico – Suicidio

Alteraciones motrices

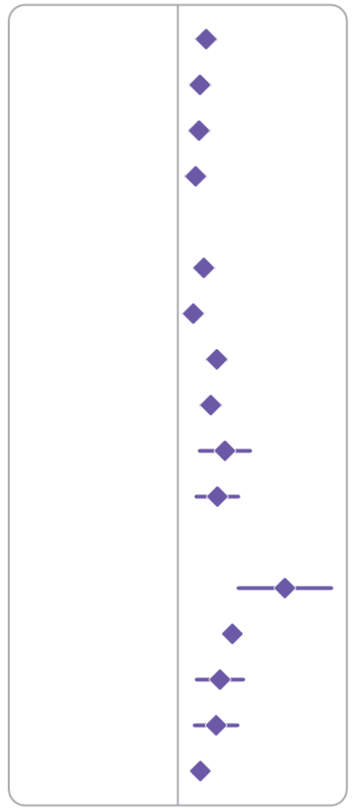
Alteraciones pulmonares

Síndrome de hiperemesis por cannabinoides

Interacciones CYP3A4 ?

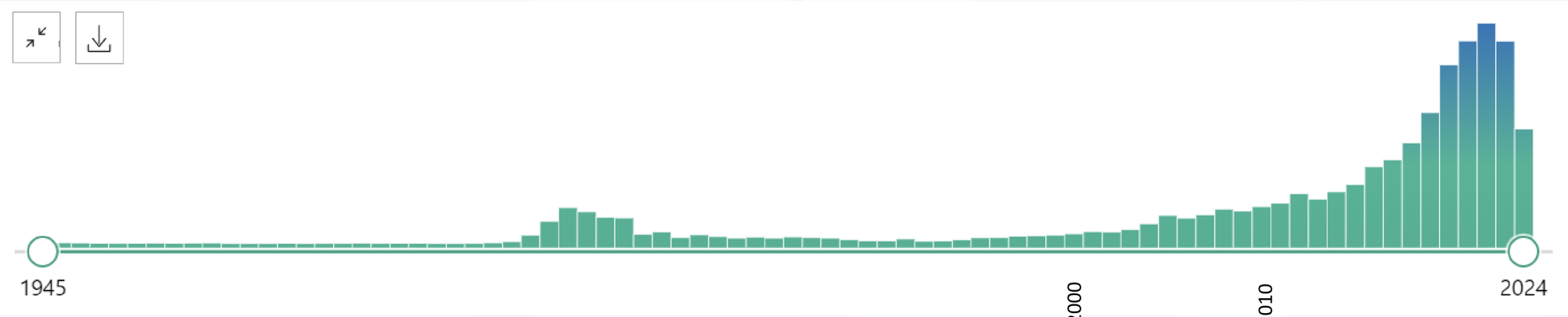
Efectos adversos

Author, year	Cannabinoid specific exposure	Outcome	Studies (k)	Studies n/No	CE/CES	eOR (95% CI)	eOR (95% CI)
Pregnant women							
Marchant 2022	Marijuana use	Small for gestational age	6	2078/22 921	I/I		1.61 (1.41 to 1.83)
Conner 2016	Marijuana use	Low birth weight	12	6204/57 438	I/I		1.43 (1.27 to 1.62)
Marchant 2022	Marijuana use	Neonatal ICU admission	6	1315/18 615	III/III		1.41 (1.15 to 1.71)
Conner 2016	Marijuana use	Pre-term delivery	14	8060/81 326	III/III		1.32 (1.14 to 1.54)
Drivers							
Rogeberg 2019	THC positive	Car crash, culpability	13	NR/78 025	IV/I		1.53 (1.39 to 1.67)
Rogeberg 2019	THC positive	Car crash	13	NR/78 025	IV/I		1.27 (1.21 to 1.34)
Hostiuc 2018	Cannabis use	Car unfavourable traffic events	23	NR/245 021	IV/II		1.89 (1.58 to 2.26)
Hostiuc 2018	Cannabis use	Car death after car crash	5	NR/66 705	IV/II		1.72 (1.40 to 2.10)
Hostiuc 2018	Cannabis use	Car injury	12	NR/95 441	IV/III		2.15 (1.42 to 3.28)
Hostiuc 2018	Cannabis use	Car collision	6	NR/82 875	IV/III		1.91 (1.34 to 2.72)
Psychosis							
Foglia 2017	Cannabis current use	Adherence to antipsychotic treatment	3	NR/259	IV/III		5.78 (2.68 to 12.46)
Foglia 2017	Cannabis any use	Adherence to antipsychotic treatment	11	NR/3055	IV/III		2.46 (1.97 to 3.07)
Bogaty 2018	Cannabis current use	Premorbid IQ	7	NR/515	IV/III		1.99 (1.34 to 2.96)
Schoeler 2016	Cannabis continued use	Psychosis relapse	24	NR/16 257	IV/III		1.88 (1.34 to 2.71)
Schoeler 2016	Cannabis use	Working memory	19	NR/2468	IV/III		1.44 (1.21 to 1.71)



BMJ2023;382:e072348

Perspectivas



Neuro-Gastro-Cannabinology: A Novel Paradigm for Regulating Mood and Digestive Health

Fabio Turco[a] Viola Brugnatelli[a] Raquel Abalo[b, c, d]

Med Cannabis Cannabinoids 2023;6:130–137

Conclusiones

Base teórica prometedora, estudio clínico inicial

Modulación de la inflamación y alivio del dolor

Actualmente: no es mejor que lo disponible

Efecto en bienestar y calidad de vida

Aumento oferta / demanda → DESINFORMACIÓN

Efectos adversos reales

Muchas gracias