Confused about CBD?

Australian retail, regulations and managing growing consumer demand

Despina Lord
Wellbeing Empowered Collective
Natural Health and Nutrition Business Agency

AGENDA

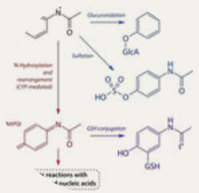
- Cannabis
- Cannabinoids and CBD
- The endocannabinoid system
- CBD regulations
- Alternatives to CBD

Cannabis, like other Plants, has many constituents...

Cannabis sativa

Cannabis sativa extract

Hemp seeds



Cannabinoids

Terpenes

Hemp seed oil:
Vegan source of PUFAs including omega 3, 6, 9 & essential vitamins

Hemp protein

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CANNABIS HEMP SEED IS RICH IN OMEGAs and PROTEIN

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Standard 1.4.4 Prohibited and restricted plants and fungi

1.4.4—6 Exception relating to *Cannabis sativa* seeds and seed products

(1) *Cannabis sativa* seeds may be a food for sale or used as an ingredient in a food for sale if:

(a) the seeds:

(i) are seeds of low THC *Cannabis sativa*; and

(ii) contain not more than 5 mg/kg of total THC; and

(iii) if the food is for retail sale – are non-viable and hulled; and

(b) the only cannabinoids in or on the seeds are naturally present.

(2) Subject to subsection (3), all or any of the following seed products may be a food for sale or used as an ingredient in a food for sale:

(a) oil extracted from seeds of low THC *Cannabis sativa* if the oil contains not more than 10 mg/kg of total THC;

(b) a beverage derived from seeds of low THC *Cannabis sativa* if the beverage contains not more than 0.2 mg/kg of total THC;

(c) any other product that is extracted or derived from seeds of low THC *Cannabis sativa* and contains not more than 5 mg/kg of total THC.

(3) The only cannabinoids in the product must be those that were naturally present in or on the seeds from which the product was extracted or derived.

(4) In subsection (2):

***seeds of low THC* Cannabis sativa** includes viable and unhulled seeds.

(5) In this section:

hulled seeds means seeds from which the outer coat or hull of seeds has been removed.

***low THC* Cannabis sativa** has the meaning given by subsection (6).

non-viable seeds means seeds that are not able to germinate.

seeds includes a part of a seed.

total THC means the total amount of delta 9-tetrahydrocannabinol and delta 9-tetrahydrocannabinolic acid.

(6) *Cannabis sativa* is low THC *Cannabis sativa* if the leaves and flowering heads of the *Cannabis sativa* do not contain more than 1% delta 9-tetrahydrocannabinol.

1.4.4—7 Restriction on claims and representations about foods that are or which contain hemp food products

(1) This section applies to a food for sale that consists of, or has as an ingredient, a hemp food product.

(2) The food for sale must not be labelled or otherwise presented for sale in a form which expressly or by implication suggests that the product has a psychoactive effect.

(3) The label for the food for sale must not include:

(a) a nutrition content claim about cannabidiol; or

(b) a *health claim about cannabidiol; or

(c) an image or representation of any part of the *Cannabis sativa* plant (including the leaf of that plant) other than the seed; or

(d) the words 'cannabis', 'marijuana' or words of similar meaning.

(4) The label for the food for sale may include the word 'hemp'.

(5) In this section:

Hemp food product means *Cannabis sativa* seeds and/or a seed product that are permitted by section 1.4.4—6 to be a food for sale or used as an ingredient in a food for sale.

Psychoactive effect means:

(a) stimulation or depression of a person's central nervous system, resulting in hallucinations or in a significant disturbance in, or significant change to, motor function, thinking, behaviour, perception, awareness or mood; or

(b) causing a state of dependence, including physical or psychological addiction.

1.4.4—8 Level of cannabidiol in food for sale

Cannabidiol must not be present in any food for sale at a level greater than 75 mg/kg.

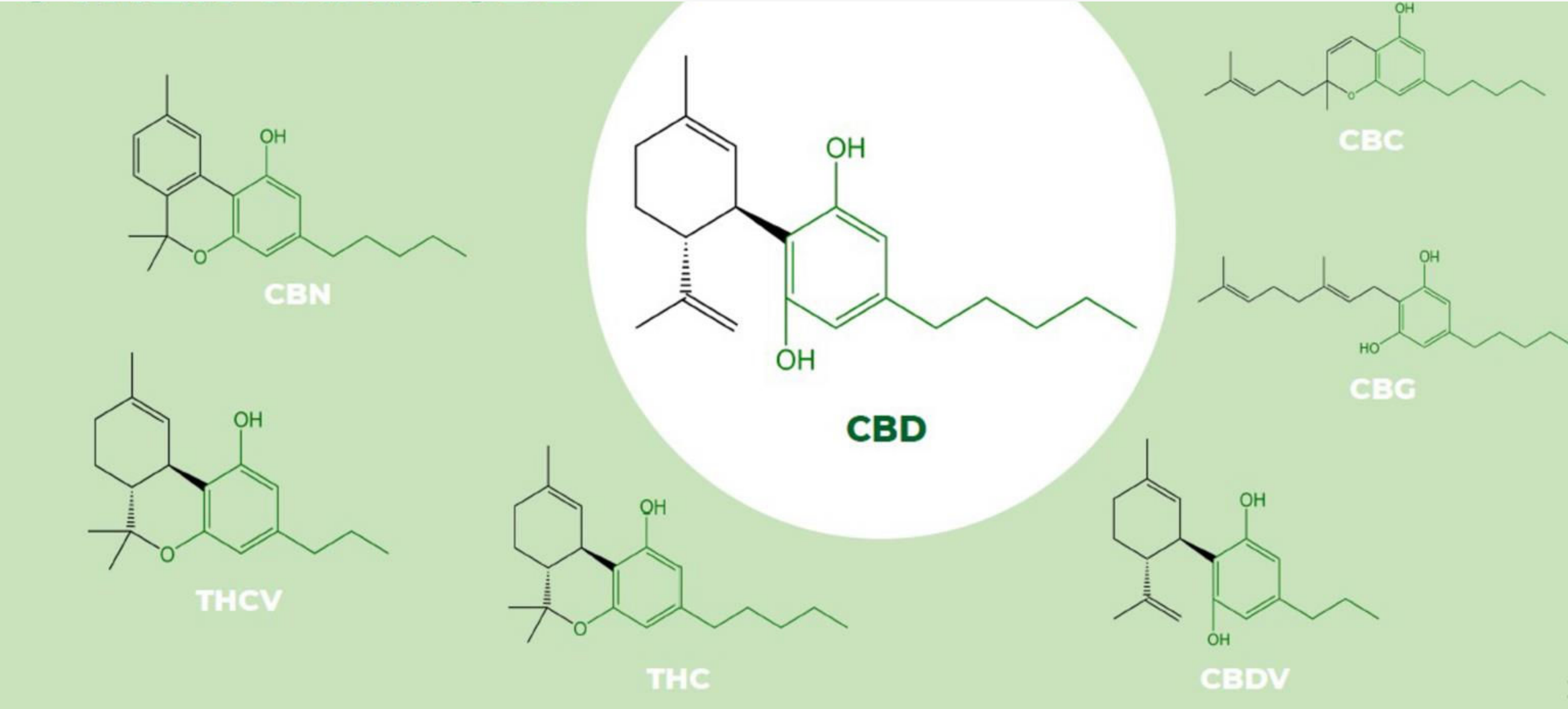
MEDICINAL CANNABIS & CANNABINOIDS

The richest and most consistent source of cannabinoids is the female plant inflorescence

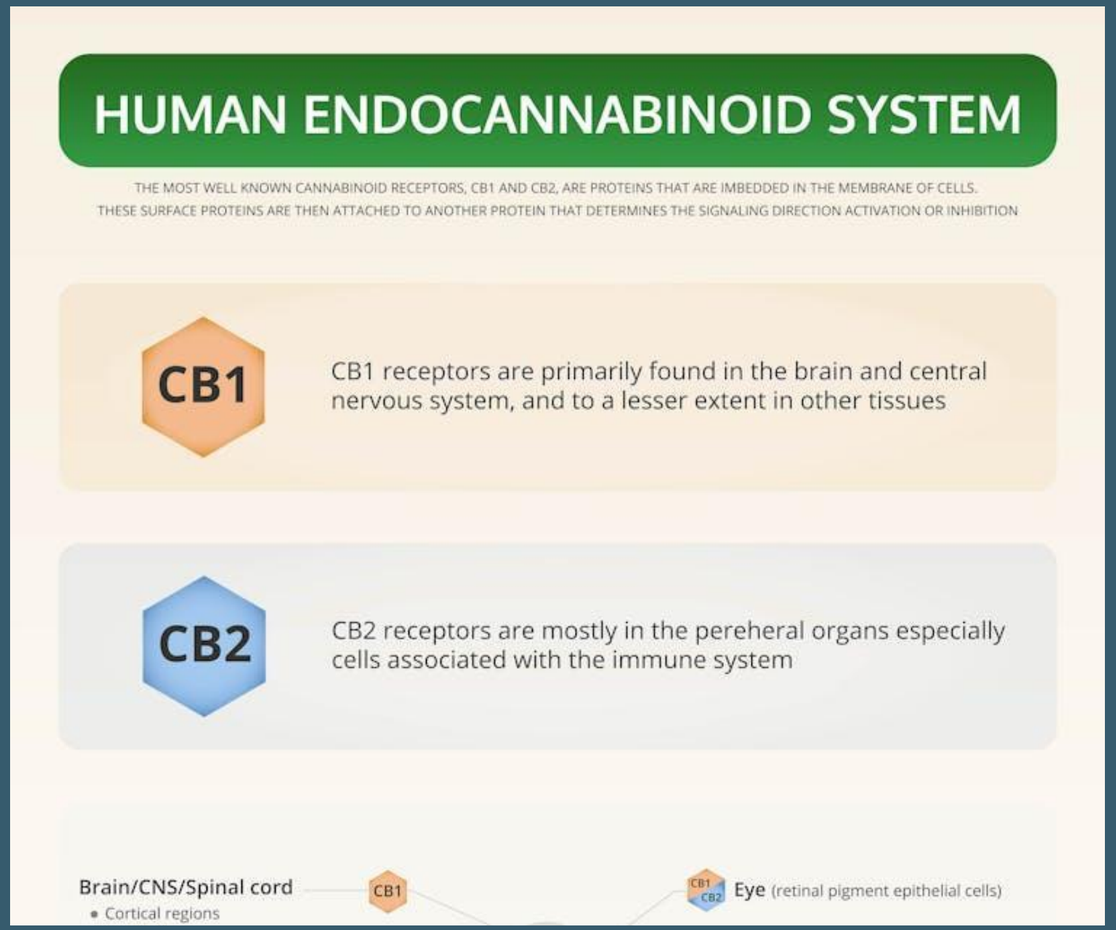
The trichomes produce a cannabinoid and terpene rich resin

There are hundreds of cannabinoids, CBD & THC being the most researched

Cannabinoids of cannabis



Cannabinoids



- Cannabinoids are a class of biological compounds that bind to cannabinoid receptors.
- The cannabinoid receptors are found in the endocannabinoid system
- The most well known are CB1 and CB2 receptors, proteins imbedded onto the surface membranes of certain cells.

Three types of cannabinoids

1

Endocannabinoids

2

Phytocannabinoids

3

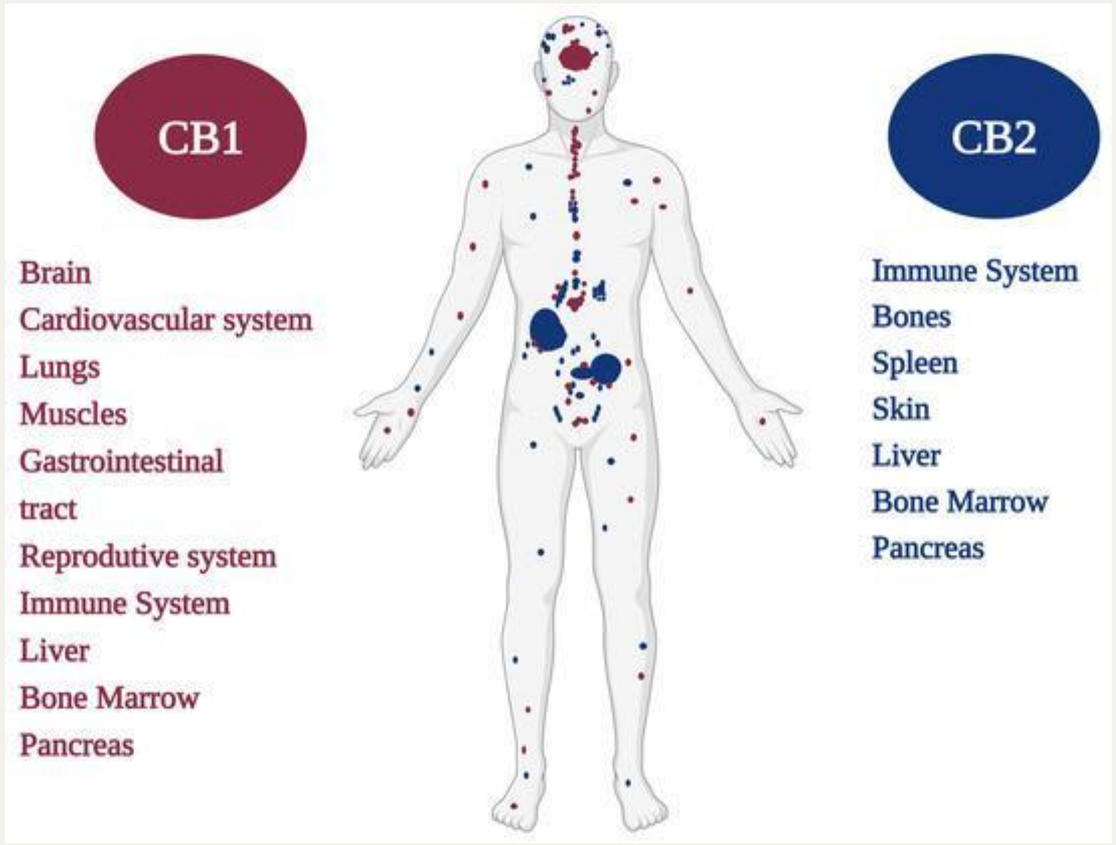
Synthetic cannabinoids

ENDOcannabinoids

- Found in all vertebrate animal species
- Discovered in 1992
- Critical for regulating many bodily functions
- Imbalances lead to major clinical disorders – including neurodegeneration, CV and inflammatory diseases
- Part of the endocannabinoid system

Phytocannabinoids

- Cannabinoids found in plants
- Cannabis most famous for cannabinoids
- THC first identified in 1964
- 100s of cannabinoids found in cannabis
- Acts on the endocannabinoid system



The endocannabinoid system restores balance

Cannabinoid receptors of the endocannabinoid system

This is a ubiquitous system homeostatic and regulatory control of many physiological processes and systems

High abundance in the brain.

Implicated in:

- energy metabolism
- cardiovascular and
- reproductive functions
- inflammation
- cognition
- mood
- neural control and rejuvenation

Image source and reference: Rezende, B.; Alencar, A.K.N.; de Bem, G.F.; Fontes-Dantas, F.L.; Montes, G.C. Endocannabinoid System: Chemical Characteristics and Biological Activity. Pharmaceuticals 2023, 16, 148. https://doi.org/10.3390/ph16020148

Endocannabinoid System (eCB)

Receptors:
CB1 and CB2(Gi/0); vanilloid receptors,
Other GPCRs (GPR55, GPR3, GPR6, GPR12 and GPR19)

↓

Physiological effects

Endogenous ligands:
Anandamide (AEA)
2-arachidonoylglycerol (2-AG)

↓

Most studied endogenous ligands

Cannabinoid compounds:
Delta nine tetrahydrocannabinol (Δ9 –THC)
Delta eight tetrahydrocannabinol (Δ 8 –THC)
Cannabidiol (CBD)
Cannabinol (CBN)

Novel selective ligands → cannabinoid-like

The deficiency theory of eCB might explain some diseases:
Migraine
Fibromyalgia
Irritable bowel syndrome
Neurodegenerative disorders

There is a correlation between eCB with chronic pain and mood disorders. The eCB may be a target for pain, depression, bipolar disorder, anxiety treatment.

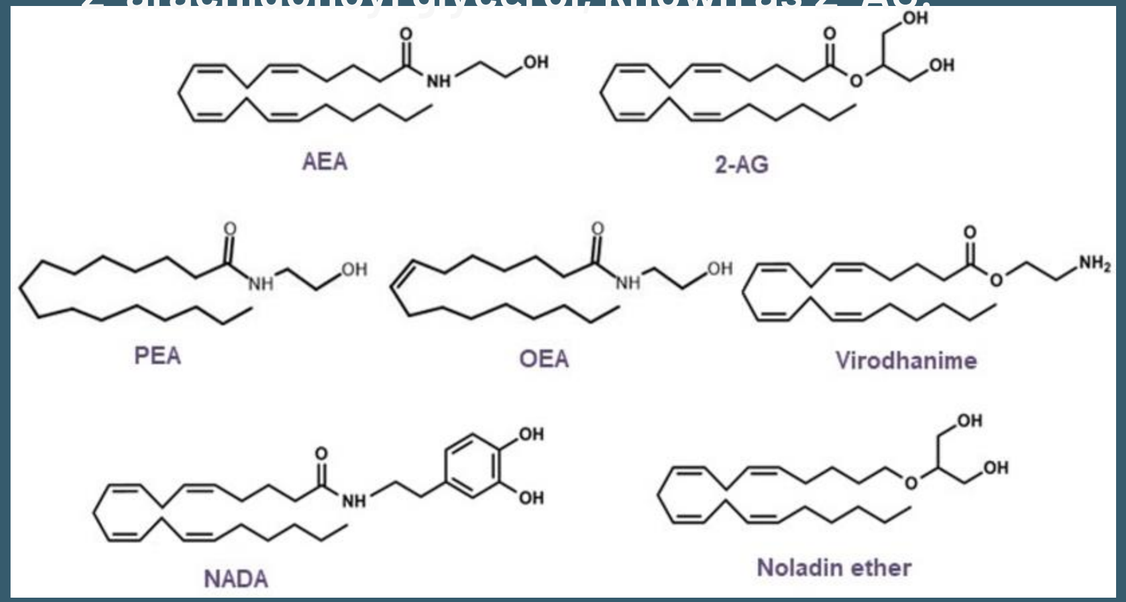
Integrative and complementary health practices (ICHP) improve the eCB

Rezende, B.; Alencar, A.K.N.; de Bem, G.F.; Fontes-Dantas, F.L.; Montes, G.C. Endocannabinoid System: Chemical Characteristics and Biological Activity. *Pharmaceuticals* **2023**, *16*, 148. https://doi.org/10.3390/ph16020148

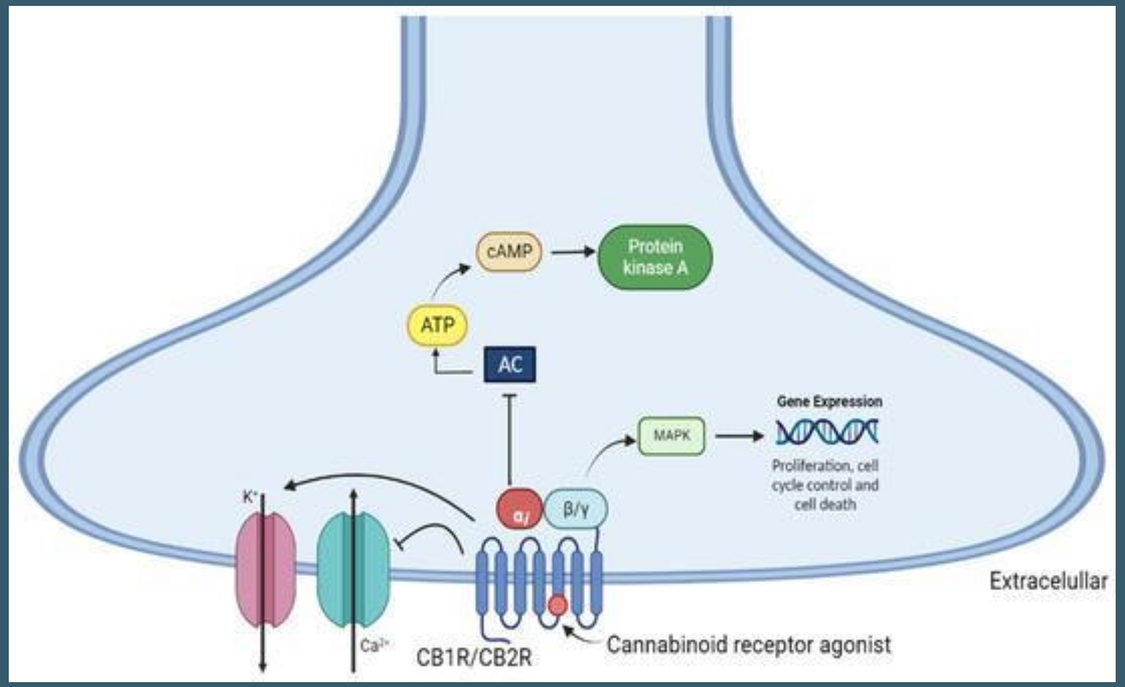
The main endocannabionids

Two main types:

- Anandamide, or AEA
- 2-arachidonoyl glycerol, known as 2-AG.



Chemical structures of the main endocannabinoids



Rezende, B.; Alencar, A.K.N.; de Bem, G.F.; Fontes-Dantas, F.L.; Montes, G.C. Endocannabinoid System: Chemical Characteristics and Biological Activity. Pharmaceuticals 2023, 16, 148. https://doi.org/10.3390/ph16020148

CANNABIS MEDICINES – PATIENT ACCESS

S3

S4

S8

+1600 products available via
TGA Special Access Scheme

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CANNABIS SCHEDULING – THERAPUTIC GOODS

S3: PHARMACIST PRESCRIBED

- CBD (CBD 98% or more of total cannabinoids; THC 1% or less)
- No more than 150mg daily dose; 30-day pack size
- Child-resistant packaging
- 18 years and older
- Registered medicines only

S4: PRESCRIPTION ONLY

- For medicines that contain 98% or more CBD (note – they can contain up to 2mg THC per mL)
- Application via SAS, no NSW health approval needed

S8: PRESCRIPTION ONLY

- For medicines where CBD is less than 98% of total cannabinoid

Schedule 3

CANNABIDIOL in oral, oromucosal and sublingual preparations included in the Australian Register of Therapeutic Goods when:

a) the cannabidiol is either plant derived or, when synthetic, only contains the (-)-CBD enantiomer; and

b) the cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and

c) any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation and of which tetrahydrocannabinol (THC) can only comprise 1 per cent of the total cannabinoid content; and

d) the maximum recommended daily dose is 150 mg or less of cannabidiol; and

e) packed in blister or strip packaging or in a container fitted with a child-resistant closure; and

f) in packs containing not more than 30 days' supply; and

g) for persons aged 18 years and over.

CANNABIDIOL

Schedule 4 – Amend entry

CANNABIDIOL in preparations for therapeutic use or analytical and scientific research where:

a) cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; and

b) any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation;

except when:

i) included in Schedule 3; or

ii) in hemp seed oil at a concentration of 75 mg/kg or less.

Schedule 8 – Amend Entry

CANNABIS (including seeds, extracts, resins and the plant, and any part of the plant) when prepared or packed for human therapeutic use, when:

a) cultivated or produced, or in products manufactured[1], in accordance with the *Narcotic Drugs Act 1967*; and/or

b) for use in products manufactured in accordance with the *Narcotic Drugs Act 1967*; and/or

c) imported as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the *Therapeutic Goods Act 1989*; and/or

d) in therapeutic goods supplied in accordance with the *Therapeutic Goods Act 1989*,

except ~~when~~:

i) when it is in a product to which item 4, 8, 10, 11 or 12 of Schedule 5A to the *Therapeutic Goods Regulations 1990* applies; or

ii) when separately specified in the NABIXIMOLS entry in this Schedule; or

iii) when captured by the CANNABIDIOL entry in Schedule 4 or Schedule 3; or

iv) hemp seed oil containing 75 mg/kg or less of cannabidiol and 10 mg/kg or less of tetrahydrocannabinols.

TGA SPECIAL ACCESS SCHEME – CATEGORIES

Category 1 CBD medicinal cannabis product (CBD ≥98%)

Category 2 CBD dominant medicinal cannabis product (CBD ≥60% and <98%)

Category 3 Balanced medicinal cannabis product (CBD <60% and ≥40%)

Category 4 THC dominant medicinal cannabis product (THC 60-98%)

Category 5 THC medicinal cannabis product (THC >98%)

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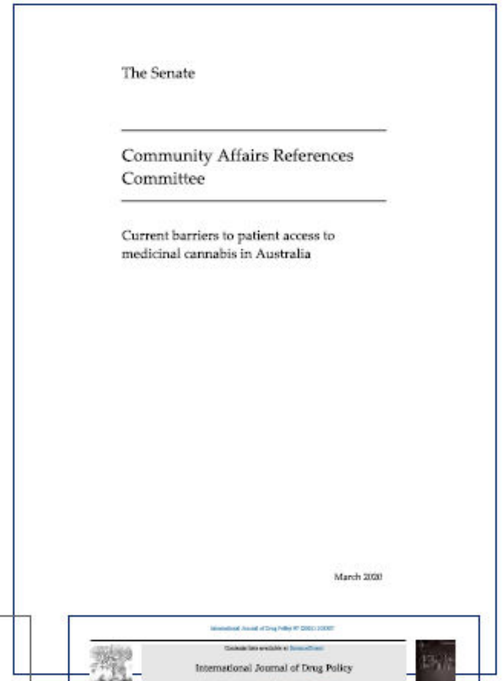
KEY PATIENT ISSUES: COST; ACCESS; DRIVING

Key patient issues with current schemes

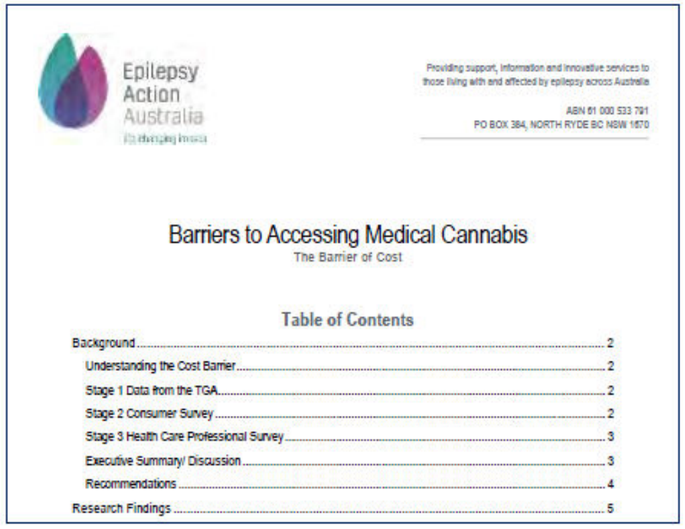
- **Affordability** (~$300 per month).
- **Finding a doctor** willing and able to prescribe.
- **Prescription can't be filled**.
- **Driving restrictions**, with THC products.


The Senate

Community Affairs References Committee

Current barriers to patient access to medicinal cannabis in Australia

March 2020


Epilepsy Action Australia

Providing support, information and innovative services to those living with and affected by epilepsy across Australia

ABN 61 000 533 791
PO BOX 384, NORTH RYDE BC NSW 1670

Barriers to Accessing Medical Cannabis

The Barrier of Cost

Table of Contents


Harm Reduction Journal

RESEARCH Open Access

Medical cannabis use in the Australian community following introduction of legal access: the 2018–2019 Online Cross-Sectional Cannabis as Medicine Survey (CAMS-18)

BMC

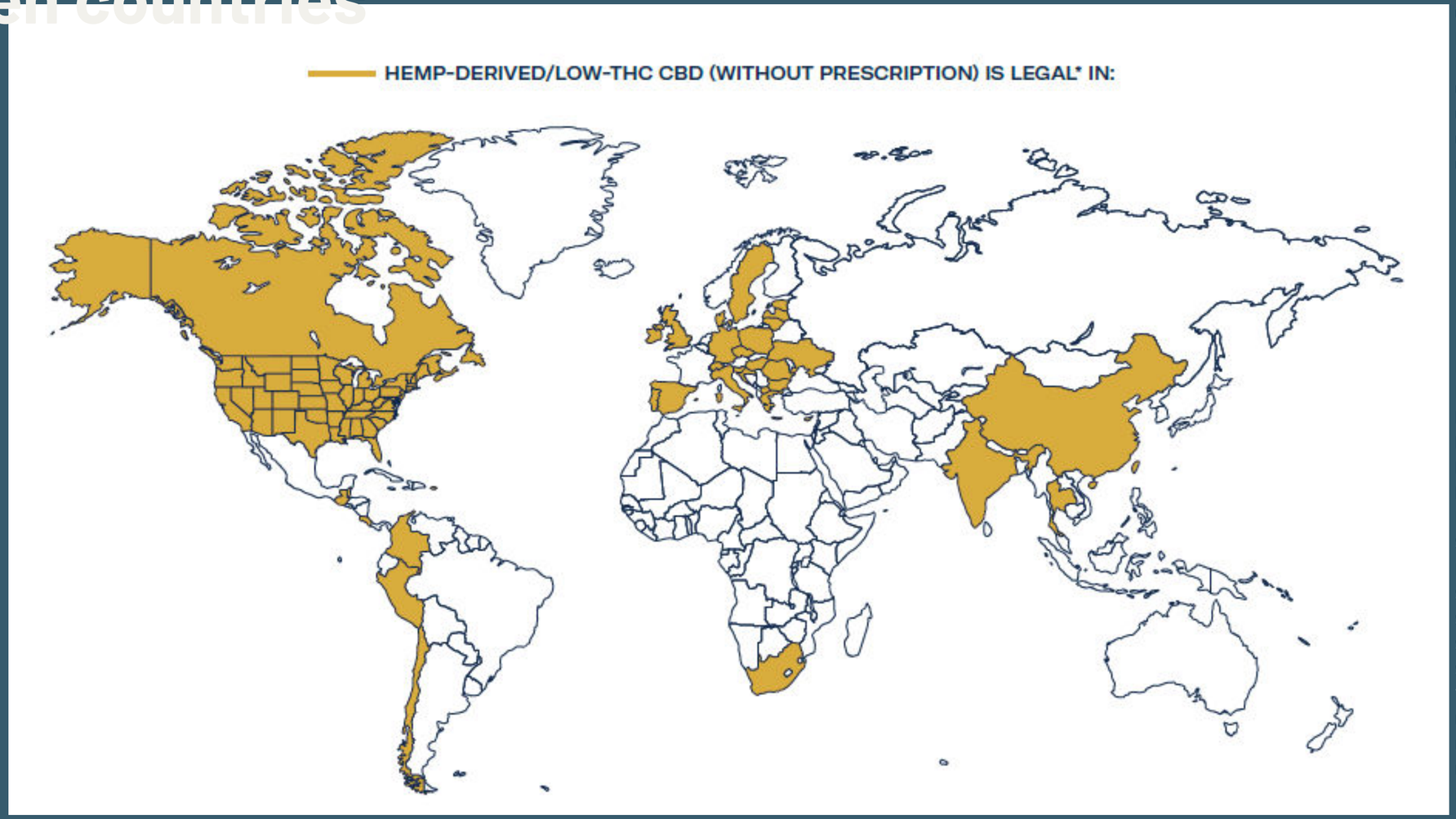

International Journal of Drug Policy

Policy analysis

Medicinal cannabis and driving: the intersection of health and road safety policy

Source: Prof. McGregor, HealthEd 2021 presentation

Although CBD has been legalized in many countries around, legal status and accessibility vary greatly between countries



BELIZE
BULGARIA
CANADA
CHILE
CHINA
COLOMBIA
COSTA RICA
CROATIA
CYPRUS
CZECH REPUBLIC
DENMARK
ESTONIA
GERMANY
GREECE
GUAM
GUATEMALA
HONG KONG
HUNGARY
INDIA
IRELAND
ITALY
LATVIA
LITHUANIA
LUXEMBOURG
MACEDONIA NORTH
PERU
POLAND
PORTUGAL
PUERTO RICO
ROMANIA
SAN MARINO
REPUBLIC OF SLOVENIA
SOUTH AFRICA
SWEDEN
SPAIN
SWITZERLAND
THAILAND
UKRAINE
UNITED KINGDOM
US WITH THE EXCEPTION OF IDAHO AND NEBRASKA.

• Image Source: Prohibition Partners. Reference: The CBD Consumer Report. Prohibition Partners

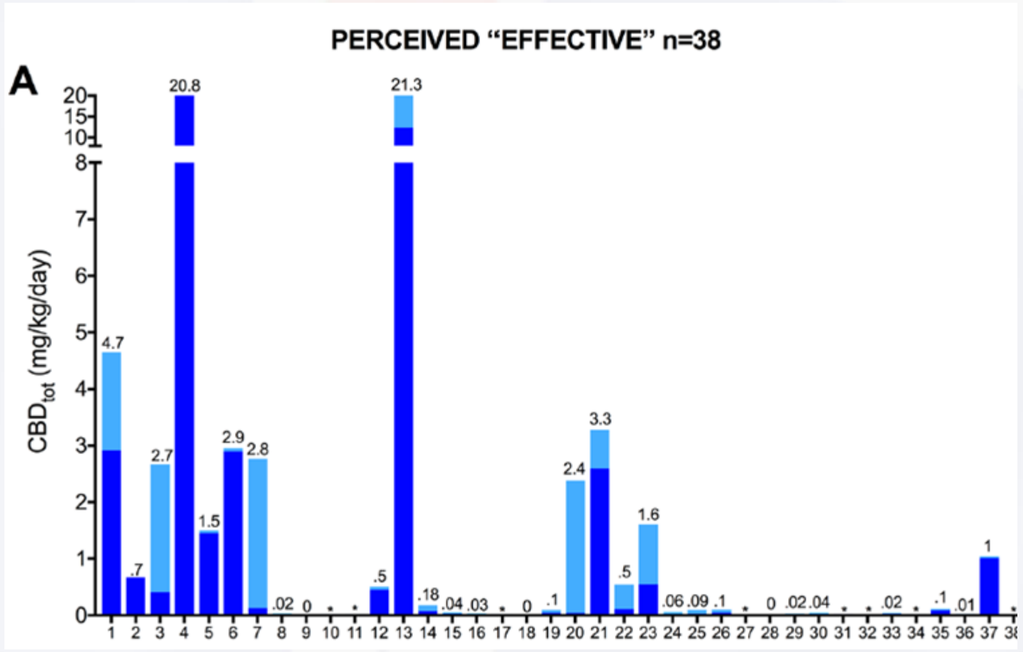
SCIENTIFIC REPORTS

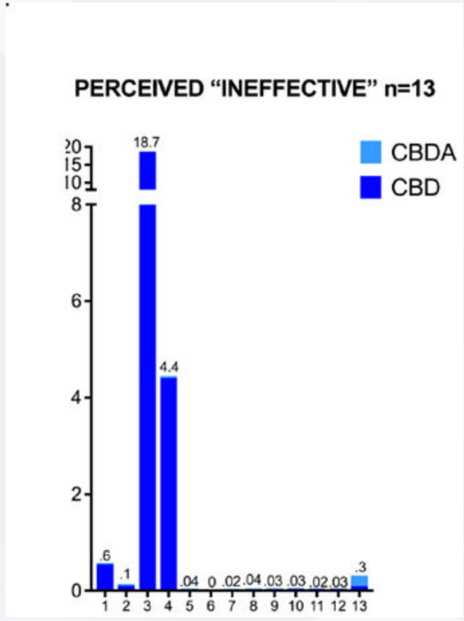
Correction: Author Correction

OPEN

Composition and Use of Cannabis Extracts for Childhood Epilepsy in the Australian Community

Concerningly THC was present in nearly every sample, there was a high variability of CBD with some samples containing no CBD





Dose of cannabinoids found in individual cannabis extract samples that were perceived "effective" or "ineffective" according to the family

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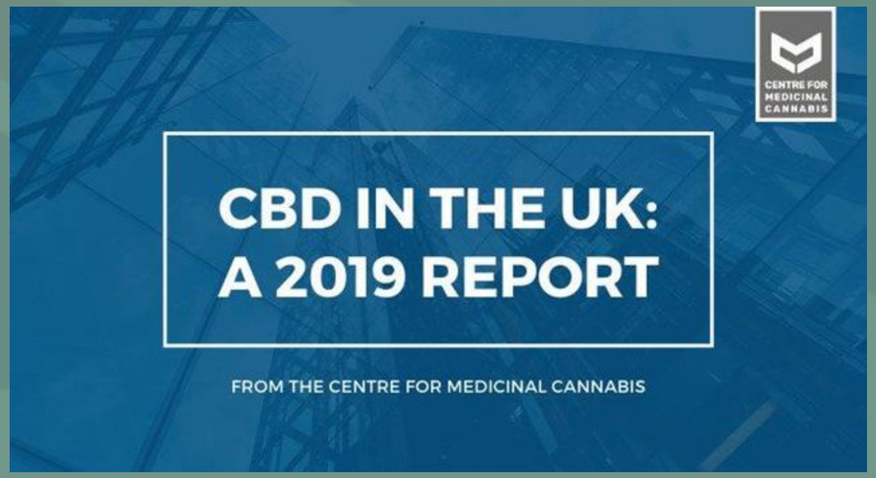

30 oil products tested

38% had less than 50%
of the claimed CBD content

Contamination detectable
in 7 products
(heavy metals and solvent)

One product had 0% CBD

45% technically illegal
For UK OTC due to THC and other cannabinoid content

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Research Letter

November 7, 2017

Labeling Accuracy of Cannabidiol Extracts Sold Online

Marcel O. Bonn-Miller, PhD[1]; Mallory J. E. Loflin, PhD[2]; Brian F. Thomas, PhD[3]; et al

» Author Affiliations | Article Information

JAMA. 2017;318(17):1708-1709. doi:10.1001/jama.2017.11909

US CANNABIS PRODUCTS ANALYSIS

A 2017 analysis of 84 CBD-based products on the market

- 26% of 84 samples accurate concentration as labelled
- 36 % contained less CBD than labelled
- 22% contained more than label
- Other cannabinoids concentration were low
- In some cases, THC were detected over the limit declared

Marcel O. Bonn-Miller et ali. JAMA 2017;318(17):1708-1709

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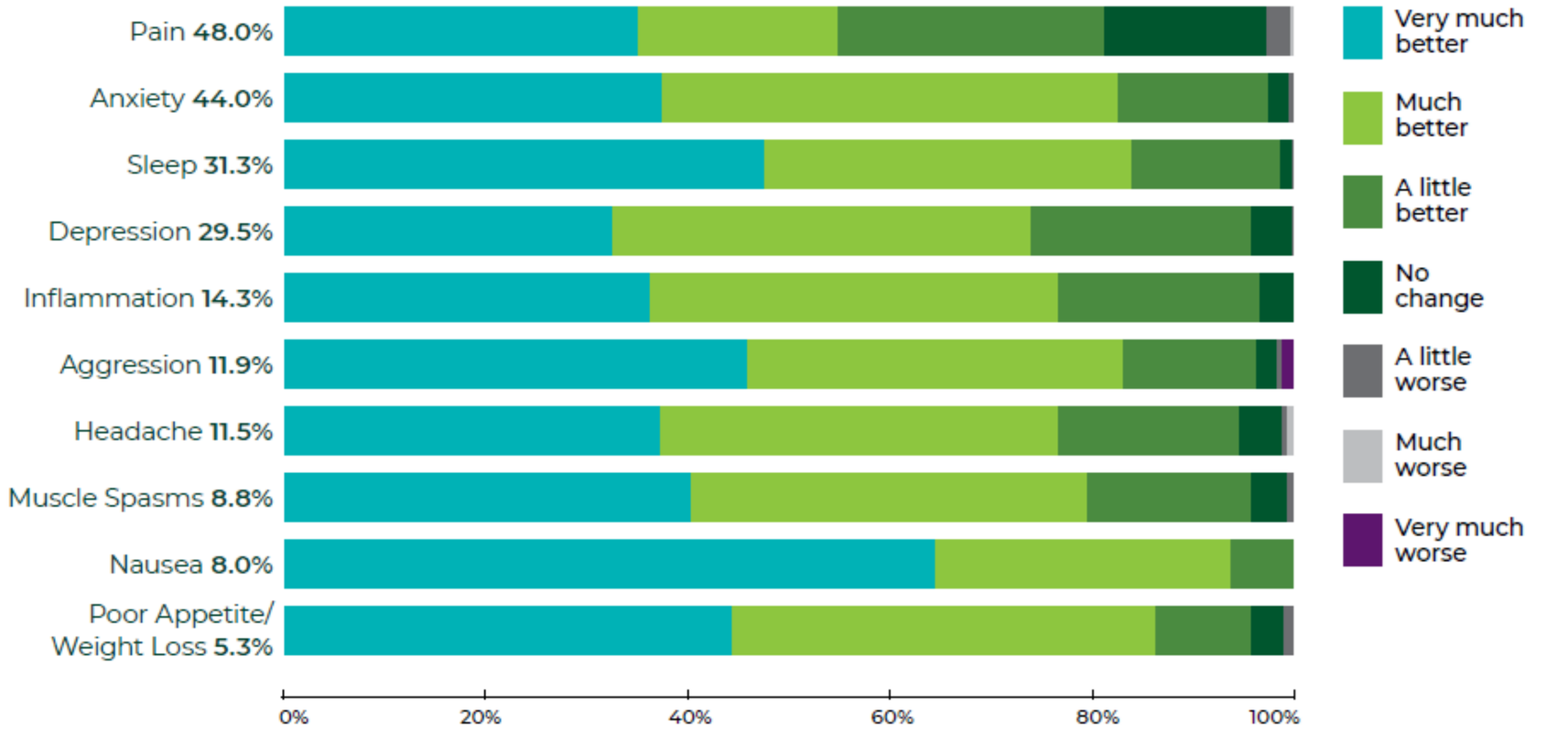
CANNABIS IS USED TO MANAGE A BROAD RANGE OF CONDITIONS



Sourced from: 2020, Lintzeris, N., Mills, L., Suraev, A. et al. Medical cannabis use in the Australian community following introduction of legal access: the 2018–2019 Online Cross-Sectional Cannabis as Medicine Survey (CAMS-18). [4]

80% people using cannabis for medical purposes reported it effectively managed their target symptom[1]

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Plant terpenes have therapeutic effects

PAIN

INFLAMMATION

IMMUNITY

PHYTOTHERAPY RESEARCH
Phytother. Res. **27**: 1–15 (2013)
Published online 12 April 2012 in Wiley Online Library
(wileyonlinelibrary.com) **DOI**: 10.1002/ptr.4686

REVIEW

Monoterpenes with Analgesic Activity—A Systematic Review

Adriana G. Guimarães, Jullyana S. S. Quintans and Lucindo J. Quintans-Júnior*
Departamento de Fisiologia, Universidade Federal de Sergipe (DFS/UFS), São Cristóvão, SE, Brazil

There is still the need for efficacious therapies for pain. In the search for new therapeutic options, plants are a major source of novel biomolecules. Monoterpenes constitute 90% of essential oils, and there is a growing interest in understanding the mechanisms underlying their pharmacological activity. This systematic review reports what is so far known about the analgesic activity of monoterpenes and also provides an overview of their mechanisms of action. The search terms analgesia, anti-inflammatory, anaesthetic and antioxidant were used to retrieve English language articles in SCOPUS, PUBMED and EMBASE published between 1990 and 2012. Forty-five papers were found concerning the potential analgesic activity of 27 monoterpenes. The data reviewed here suggest these compounds are possible candidates for the treatment of painful conditions. Copyright © 2012 John Wiley & Sons, Ltd.

Keywords: monoterpenes; pain; analgesia.

Article

(−)-β-Caryophyllene, a CB2 Receptor-Selective Phytocannabinoid, Suppresses Motor Paralysis and Neuroinflammation in a Murine Model of Multiple Sclerosis

Thaís Barbosa Alberti [1], Wagner Luiz Ramos Barbosa [2], José Luiz Fernandes Vieira [2], Nádia Rezende Barbosa Raposo [3] and Rafael Cypriano Dutra [1,*]

1 Laboratory of Autoimmunity and Immunopharmacology (LAIF), Department of Health Sciences, Center of Araranguá, Federal University of Santa Catarina, Araranguá 88906-072, Brazil; alberti.thais@gmail.com
2 Faculty of Pharmaceutical Sciences, Federal University of Pará, Belém 66075-740, Brazil; zweigw@gmail.com (W.L.R.B.); jvieira@ufpa.br (J.L.F.V.)
3 Research and Innovation in Health Sciences (NUPICS), Federal University of Juiz de Fora, Juiz de Fora 36036-900, Brazil; nadiacritt@gmail.com
* Correspondence: rafaelcdutra@gmail.com or rafael.dutra@ufsc.br; Tel./Fax: +55-48-3721-6448

Academic Editors: Christoph Kleinschnitz and Sven Meuth
Received: 20 February 2017; Accepted: 20 March 2017; Published: 1 April 2017

Abstract: (−)-β-caryophyllene (BCP), a cannabinoid receptor type 2 (CB2)-selective phytocannabinoid, has already been shown in precedent literature to exhibit both anti-inflammatory and analgesic effects in mouse models of inflammatory and neuropathic pain. Herein, we endeavored to investigate

Biochemical and Biophysical Research Communications 404 (2011) 345–348

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

Limonene, a natural cyclic terpene, is an agonistic ligand for adenosine A_{2A} receptors

Hyo Min Park, Ji Hae Lee, Jia Yaoyao, Hee Jin Jun, Sung Joon Lee *

Division of Food Bioscience and Technology, College of Life Sciences and Biotechnology, Korea University, Seoul, 136-713, South Korea

ARTICLE INFO

Article history:
Received 9 November 2010
Available online 4 December 2010

Keywords:
Limonene
Adenosine A_{2A} receptors
Radioligand binding assay
cAMP

ABSTRACT

Limonene is a major aromatic compound in essential oils extracted from citrus rind. The application of limonene, especially in aromatherapy, has expanded significantly, but its potential effects on cellular metabolism have been elusive. We found that limonene directly binds to the adenosine A_{2A} receptor, which may induce sedative effects. Results from an *in vitro* radioligand binding assay showed that limonene exhibits selective affinity to A_{2A} receptors. In addition, limonene increased cytosolic cAMP concentration and induced activation of protein kinase A and phosphorylation of cAMP-response element-binding protein in Chinese hamster ovary cells transfected with the human adenosine A_{2A} receptor gene. Limonene also increased cytosolic calcium concentration, which can be achieved by the activation of adenosine A_{2A} receptors. These findings suggest that limonene can act as a ligand and an agonist for adenosine A_{2A} receptors.

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Cannabis and Hops

Contents lists available at ScienceDirect

European Journal of Medicinal Chemistry

journal homepage: http://www.elsevier.com/locate/ejmech

Review article

Medicinal properties of terpenes found in *Cannabis sativa* and *Humulus lupulus*

Tarmo Nuutinen [a, b, *]

[a] Department of Environmental and Biological Sciences, Univerisity of Eastern Finland (UEF), Finland
[b] Department of Physics and Mathematics, UEF, Finland

ARTICLE INFO

Article history:
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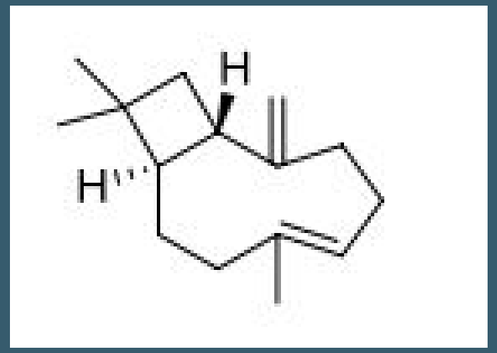
Monoterpene
Sesquiterpene
Cannabis sativa
Humulus lupulus
Medicine

ABSTRACT

Cannabaceae plants *Cannabis sativa* L. and *Humulus lupulus* L. are rich in terpenes – both are typically comprised of terpenes as up to 3–5% of the dry-mass of the female inflorescence. Terpenes of cannabis and hops are typically simple mono- and sesquiterpenes derived from two and three isoprene units, respectively. Some terpenes are relatively well known for their potential in biomedicine and have been used in traditional medicine for centuries, while others are yet to be studied in detail. The current, comprehensive review presents terpenes found in cannabis and hops. Terpenes' medicinal properties are supported by numerous *in vitro*, animal and clinical trials and show anti-inflammatory, antioxidant, analgesic, anticonvulsive, antidepressant, anxiolytic, anticancer, antitumor, neuroprotective, anti-mutagenic, anti-allergic, antibiotic and anti-diabetic attributes, among others. Because of the very low toxicity, these terpenes are already widely used as food additives and in cosmetic products. Thus, they have been proven safe and well-tolerated.

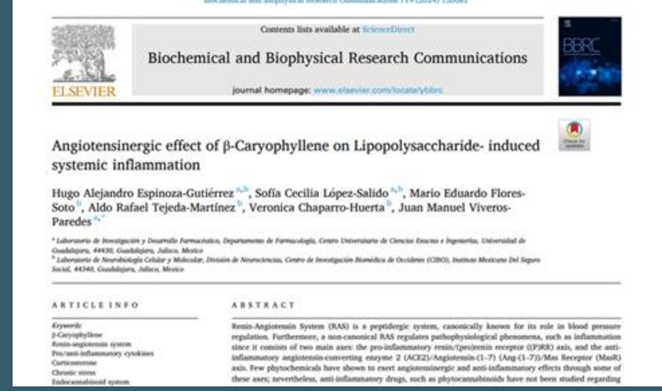
β-Caryophyllene



Syzygium aromaticums	Anti-anxiolytic and depression
Cannabis sativa	Anti-inflammation
Humulus lupulus	Immune modulation
Piper nigrum	Analgesic
Origanum vulgare	Cardioprotective
Cinnamomum ssp	Neuroprotective
Melissa officinalis	Anti-cancer
Rosmarinus officinalis	Anti-arthritis
Lavandula angustifolia	Anti-fibrosis
Valeriana alliariifolia	Lipid metabolism

Wilson, G., Yang, L., Su, X., Ding, S., Li, L., Yang, Y., Wang, X., Wang, W., Sa, Y., Zhang, Y., Chen, J., & Ma, X. (2023). Exploring the therapeutic potential of natural compounds modulating the endocannabinoid system in various diseases and disorders: review. Pharmacological Reports, 75(6), 1410–1444. https://doi.org/10.1007/s43440-023-00544-7

β-Caryophyllene – anti-inflammation



Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

Angiotensinergic effect of β-Caryophyllene on Lipopolysaccharide- induced systemic inflammation

Hugo Alejandro Espinoza-Gutiérrez [a,b], Sofía Cecilia López-Salido [a,b], Mario Eduardo Flores-Soto [b], Aldo Rafael Tejeda-Martínez [b], Veronica Chaparro-Huerta [b], Juan Manuel Viveros-Paredes [a,*]

[a] Laboratorio de Investigación y Desarrollo Farmacéutico, Departamento de Farmacología, Centro Universitario de Ciencias Exactas e Ingenierías, Universidad de Guadalajara, #4430, Guadalajara, Jalisco, Mexico
[b] Laboratorio de Neurobiología Celular y Molecular, División de Neurociencias, Centro de Investigación Biomédica de Occidente (CIBO), Instituto Mexicano Del Seguro Social, #4340, Guadalajara, Jalisco, Mexico

ARTICLE INFO

Keywords:
β-Caryophyllene
Renin-angiotensin system
Pro/anti-inflammatory cytokines
Corticosterone
Chronic stress
Endocannabinoid system

ABSTRACT

Renin-Angiotensin System (RAS) is a peptidergic system, canonically known for its role in blood pressure regulation. Furthermore, a non-canonical RAS regulates pathophysiological phenomena, such as inflammation since it consists of two main axes: the pro-inflammatory renin/(pro)renin receptor ((P)RR) axis, and the anti-inflammatory angiotensin-converting enzyme 2 (ACE2)/Angiotensin-(1–7) (Ang-(1–7))/Mas Receptor (MasR) axis. Few phytochemicals have shown to exert angiotensinergic and anti-inflammatory effects through some of these axes; nevertheless, anti-inflammatory drugs, such as phytocannabinoids have not been studied regarding

"Renin-Angiotensin System (RAS) is……known for its role in blood pressure regulation. Furthermore, a non-canonical RAS regulates pathophysiological phenomena, such as inflammation since it consists of two main axes: the pro-inflammatory renin/(pro)renin receptor ((P)RR) axis, and the antiinflammatory angiotensin-converting enzyme 2 (ACE2)/Angiotensin-(1–7) (Ang-(1–7))/Mas Receptor (MasR) axis.
Few phytochemicals have shown to exert angiotensinergic and anti-inflammatory effects through some of these axes; nevertheless, anti-inflammatory drugs, such as phytocannabinoids have not been studied regarding this subject.
Among phytocannabinoids, β-Caryophyllene stands out as a dietary phytocannabinoid with antiphlogistic activity that possess a unique sesquiterpenoid structure. Although its cannabinergic effect has been studied, its angiotensinergic effect reminds underexplored. This study aims to explore the angiotensinergic effect of β-Caryophyllene on inflammation and stress at a systemic level. After intranasal Lipopolysaccharide (LPS) installation and oral treatment with β-Caryophyllene, the concentration and activity of key RAS elements in the serum, such as Renin, ACE2 and Ang-(1–7), along with the stress hormone corticosterone and pro/antiinflammatory cytokines, were measured in mice serum. The results show that β-Caryophyllene treatment modified RAS levels by increasing Renin and Ang-(1–7), alongside the reduction of pro-inflammatory cytokines and corticosterone levels. These results indicate that β-Caryophyllene exhibits angiotensinergic activity in favor of anti-inflammation. ."

Espinoza-Gutiérrez, H. A., López-Salido, S. C., Flores-Soto, M. E., Tejeda-Martínez, A. R., Chaparro-Huerta, V., & Viveros-Paredes, J. M. (2024). Angiotensinergic effect of β-Caryophyllene on Lipopolysaccharide- induced systemic inflammation. Biochemical and Biophysical Research Communications, 719, 150081-. https://doi.org/10.1016/j.bbrc.2024.150081

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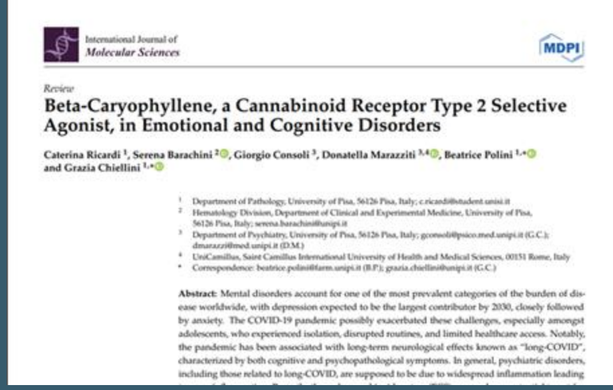
β-Caryophyllene – emotional and cognitive disorders



International Journal of Molecular Sciences

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Review

Beta-Caryophyllene, a Cannabinoid Receptor Type 2 Selective Agonist, in Emotional and Cognitive Disorders

Caterina Ricardi [1], Serena Barachini [2], Giorgio Consoli [3], Donatella Marazziti [3,4], Beatrice Polini [1,*] and Grazia Chiellini [1,*]

[1] Department of Pathology, University of Pisa, 56126 Pisa, Italy; c.ricardi@studenti.unisi.it
[2] Hematology Division, Department of Clinical and Experimental Medicine, University of Pisa, 56126 Pisa, Italy; serena.barachini@unipi.it
[3] Department of Psychiatry, University of Pisa, 56126 Pisa, Italy; gconsoli@psico.med.unipi.it (G.C.); dmarazzi@med.unipi.it (D.M.)
[4] UniCamillus, Saint Camillus International University of Health and Medical Sciences, 00151 Rome, Italy
* Correspondence: beatrice.polini@farm.unipi.it (B.P.); grazia.chiellini@unipi.it (G.C.)

Abstract: Mental disorders account for one of the most prevalent categories of the burden of disease worldwide, with depression expected to be the largest contributor by 2030, closely followed by anxiety. The COVID-19 pandemic possibly exacerbated these challenges, especially amongst adolescents, who experienced isolation, disrupted routines, and limited healthcare access. Notably, the pandemic has been associated with long-term neurological effects known as "long-COVID", characterized by both cognitive and psychopathological symptoms. In general, psychiatric disorders, including those related to long-COVID, are supposed to be due to widespread inflammation leading

"Mental disorders account for one of the most prevalent categories of the burden of disease worldwide, with depression expected to be the largest contributor by 2030, closely followed by anxiety. The COVID-19 pandemic possibly exacerbated these challenges, especially amongst adolescents, who experienced isolation, disrupted routines, and limited healthcare access. Notably, the pandemic has been associated with long-term neurological effects known as "long-COVID", characterized by both cognitive and psychopathological symptoms. In general, psychiatric disorders, including those related to long-COVID, are supposed to be due to widespread inflammation leading to neuroinflammation. Recently, the endocannabinoid system (ECS) emerged as a potential target for addressing depression and anxiety pathophysiology. Specifically, natural or synthetic cannabinoids, able to selectively interact with cannabinoid type-2 receptor (CB2R), recently revealed new therapeutic potential in neuropsychiatric disorders with limited or absent psychotropic activity. Among the most promising natural CB2R ligands, the bicyclic sesquiterpene β-caryophyllene (BCP) has emerged as an excellent anti-inflammatory and antioxidant therapeutic agent. This review underscores BCP's immunomodulatory and anti-inflammatory properties, highlighting its therapeutic potential for the management of depression and anxiety."

Ricardi, C., Barachini, S., Consoli, G., Marazziti, D., Polini, B., & Chiellini, G. (2024). Beta-Caryophyllene, a Cannabinoid Receptor Type 2 Selective Agonist, in Emotional and Cognitive Disorders. International Journal of Molecular Sciences, 25(6), 3203-. https://doi.org/10.3390/ijms25063203

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Kava

Journal of Ethnopharmacology 333 (2024) 118394

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Yangonin, one of the kavalactones isolated from *Piper methysticum* G. Forst, acts through cannabinoid 1 (CB_1) receptors to induce an intrathecal anti-hyperalgesia

Lok-Hi Chow [a,b,c,d], Pin-Chen Lin [d], Ying-Jie Chen [d], Yuan-Hao Chen [e], Eagle Yi-Kung Huang [d,*]

[a] Department of Anesthesiology, Taipei Veterans General Hospital, Taipei, Taiwan
[b] Department of Anesthesiology, School of Medicine and Institute of Clinical Nursing, School of Nursing, National Yang Ming Chiao Tung University, Taipei, Taiwan
[c] Department of Anesthesiology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan
[d] Department of Pharmacology, National Defense Medical Center, Taipei, Taiwan
[e] Department of Neurological Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

ARTICLE INFO

Keywords:
Kavain
Yangonin
Kavalactones
Cannabinoid 1 (CB_1) receptor
Anti-hyperalgesia

ABSTRACT

Ethnopharmacological relevance: Piper methysticum G. Forst (Piperaceae) is traditionally consumed in Polynesian culture. The roots are used to produce an entheogenic drink and traditional medicine with sedative and anxiolytic properties. There is also evidence that it functions as a pain reliever. Kavalactones, its main active ingredients, exhibit psychoactive effects on the central nervous system. However, the active ingredients and pharmacological mechanisms underlying the analgesic effect of kavalactones are unclear.
Aim of the study: This study investigated the effects of kavain and yangonin on nociception, inflammatory

"Results: Intrathecal injection of yangonin demonstrated a rel… potent anti-nociceptive effect and attenuated carrageenan-induced hyperalgesia. These effects were completely reversed by the co-administration of PF 514273, a cannabinoid 1 (CB1) receptor antagonist. However, yangonin did not affect mechanical allodynia at the spinal level. Kavain, another abundant kavalactone, did not affect nociception, hyperalgesia, or mechanical allodynia at the spinal level. Conclusions: Overall, our study demonstrated that yangonin exerts anti-nociception and anti-inflammatory hyperalgesia effects via CB1 receptors at the spinal level. We identified a single kavalactone, yangonin, extracted from kava as a promising treatment for pain."

Lok-Hi Chow, Pin-Chen Lin, Ying-Jie Chen, Yuan-Hao Chen, Eagle Yi-Kung Huang, Yangonin, one of the kavalactones isolated from Piper methysticum G. Forst, acts through cannabinoid 1 (CB1) receptors to induce an intrathecal anti-hyperalgesia, Journal of Ethnopharmacology, Volume 333, 2024, 118394, ISSN 0378-8741, https://doi.org/10.1016/j.jep.2024.118394.

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https://doi.org/10.1007/s43440-023-00544-7

REVIEW

Exploring the therapeutic potential of natural compounds modulating the endocannabinoid system in various diseases and disorders: review

Gidion Wilson[1] · Lingling Yang[1] · Xiaojuan Su[1] · Shuqin Ding[1] · Liuyan Li[1] · Youyue Yang[1] · Xiaoying Wang[1] · Weibiao Wang[1] · Yuping Sa[1] · Yue Zhang[1] · Jianyu Chen[2] · Xueqin Ma[1]

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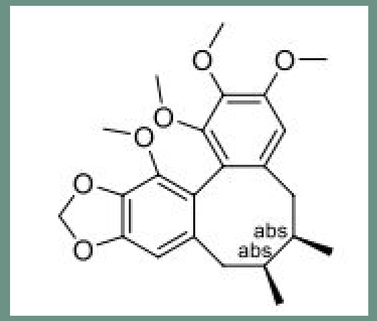
Abstract

Cannabinoid receptors, endogenous cannabinoids (endocannabinoids), and the enzymes involved in the biosynthesis and degradation of the endocannabinoids make up the endocannabinoid system (ECS). The components of the ECS are proven to modulate a vast bulk of various physiological and pathological processes due to their abundance throughout the human body. Such discoveries have attracted the researchers' attention and emerged as a potential therapeutical target for the treatment of various diseases. In the present article, we reviewed the discoveries of natural compounds, herbs, herbs formula, and their therapeutic properties in various diseases and disorders by modulating the ECS. We also summarize the molecular mechanisms through which these compounds elicit their properties by interacting with the ECS based on the existing findings. Our study provides the insight into the use of natural compounds that modulate ECS in various diseases and disorders, which in turn may facilitate future studies exploiting natural lead compounds as novel frameworks for designing more effective and safer therapeutics.

Wilson, G., Yang, L., Su, X., Ding, S., Li, L., Yang, Y., Wang, X., Wang, W., Sa, Y., Zhang, Y., Chen, J., & Ma, X. (2023). Exploring the therapeutic potential of natural compounds modulating the endocannabinoid system in various diseases and disorders: review. Pharmacological Reports, 75(6), 1410–1444. https://doi.org/10.1007/s43440-023-00544-7

Schisandrin B



Schisandra chinensis	Anti-fibrosis Anti-inflammation

Wilson, G., Yang, L., Su, X., Ding, S., Li, L., Yang, Y., Wang, X., Wang, W., Sa, Y., Zhang, Y., Chen, J., & Ma, X. (2023). Exploring the therapeutic potential of natural compounds modulating the endocannabinoid system in various diseases and disorders: review. Pharmacological Reports, 75(6), 1410–1444. https://doi.org/10.1007/s43440-023-00544-7

Schizandra


Phytomedicine 133 (2024) 155929

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Original Article

Schisandra chinensis lignans regulate and cooperate with endogenous cannabinoid systems to ameliorate intestinal barrier injury associated with depression☆

Jinyu Wang[a], Aijuan Zheng[a], Fei Lin[a], Xiaozhuo Zhang[b], Kaifang Shi[b], Tingxu Yan[a,*], Ying Jia[a,*]

[a] Faculty of Functional Food and Wine, Shenyang Pharmaceutical University, Shenyang 110016, PR China
[b] School of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University, Wenhua Road 103, Shenyang 110016, China

ARTICLE INFO

Keywords:
Intestinal barrier injury
Schisandra chinensis lignans
Endogenous cannabinoid systems
Anti-inflammation

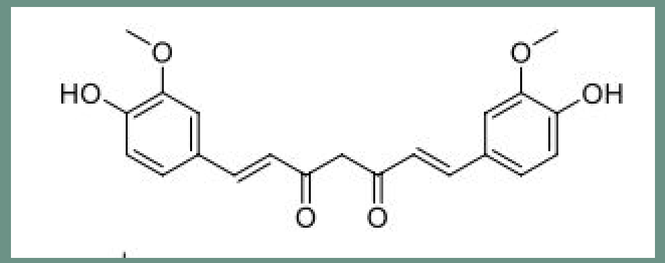
ABSTRACT

Background: Schisandra chinensis lignan (SCL), a major active component of the traditional functional Chinese medicine Schisandra chinensis, has been reported to have antidepressant effects. Its mechanisms include alleviating intestinal barrier injury (IBI) by resolving intestinal microflora, anti-inflammation, and neuroprotection. SCL also regulates endogenous cannabinoid system, and it is closely related to the onset and development of depression.

"Results: The study demonstrated that SCL (Schisandra chinensis lignan) alleviated depressive-like behaviours and ameliorated IBI (intestinal barrier injury). Network pharmacology and Western blotting confirmed that the improvement of IBI was related to the anti-inflammatory and antiapoptotic pathways. Pearson results showed that AEA levels were positively correlated with inflammation and apoptosis, with a greater contribution to apoptosis. .....
Conclusion: Overall, SCL, in collaboration with the endogenous cannabinoid system regulated by SCL, alleviates depression associated IBI. The specific mechanism involves SCL decreasing AEA levels to inhibit colon tissue cell"

Wang, J., Zheng, A., Lin, F., Zhang, X., Shi, K., Yan, T., & Jia, Y. (2024). Schisandra chinensis lignans regulate and cooperate with endogenous cannabinoid systems to ameliorate intestinal barrier injury associated with depression. Phytomedicine (Stuttgart), 133, 155929-. https://doi.org/10.1016/j.phymed.2024.155929

Curcumin



Curcuma longa	Cardioprotective Anti-infammation

Wilson, G., Yang, L., Su, X., Ding, S., Li, L., Yang, Y., Wang, X., Wang, W., Sa, Y., Zhang, Y., Chen, J., & Ma, X. (2023). Exploring the therapeutic potential of natural compounds modulating the endocannabinoid system in various diseases and disorders: review. Pharmacological Reports, 75(6), 1410–1444. https://doi.org/10.1007/s43440-023-00544-7

Palmitoylethanolamide (PEA)

JOURNAL OF DIETARY SUPPLEMENTS
2023, VOL. 20, NO. 3, 505–530
https://doi.org/10.1080/19390211.2021.2005733

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REVIEW

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Palmitoylethanolamide: A Potential Alternative to Cannabidiol

Paul Clayton[a], Silma Subah[b], Ruchitha Venkatesh[c], Mariko Hill[b] and Nathasha Bogoda[b]

[a]Institute of Food, Brain and Behaviour, Oxford, UK; [b]Gencor Pacific Limited, Lantau Island, Hong Kong; [c]School of Medicine, University of Hong Kong, Hong Kong, Hong Kong

ABSTRACT

The endocannabinoid system (ECS) is a widespread cell signaling network that maintains homeostasis in response to endogenous and exogenous stressors. This has made the ECS an attractive therapeutic target for various disease states. The ECS is a well-known target of exogenous phytocannabinoids derived from cannabis plants, the most well characterized being Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD). However, the therapeutic efficacy of cannabis products comes with a risk of toxicity and high abuse potential due to the

KEYWORDS

cannabidiol; efficacy; endocannabinoid; endocannabinoid modulators; endocannabinoid system; palmitoylethanolamide; pharmacology;

"Palmitoylethanolamide(PeA) is an endocannabinoid-like lipid mediator, primarily known for its anti-inflammatory, analgesic and neuroprotective properties. It appears to have a multi-modal mechanism of action, by primarily activating the nuclear receptor PPAR-α while also potentially working through the eCS, thus targeting similar pathways as CBD. With proven efficacy in several therapeutic areas, its safety and tolerability profile and the development of formulations that maximize its bioavailability, PeA is a promising alternative to CBD."

Clayton, P., Subah, S., Venkatesh, R., Hill, M., & Bogoda, N. (2021). Palmitoylethanolamide: A Potential Alternative to Cannabidiol. Journal of Dietary Supplements, 20(3), 505–530. https://doi.org/10.1080/19390211.2021.2005733

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Despina Lord ND, BHSc, MHLM
despina@wellbeingempowered.com.au +61 400329166

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