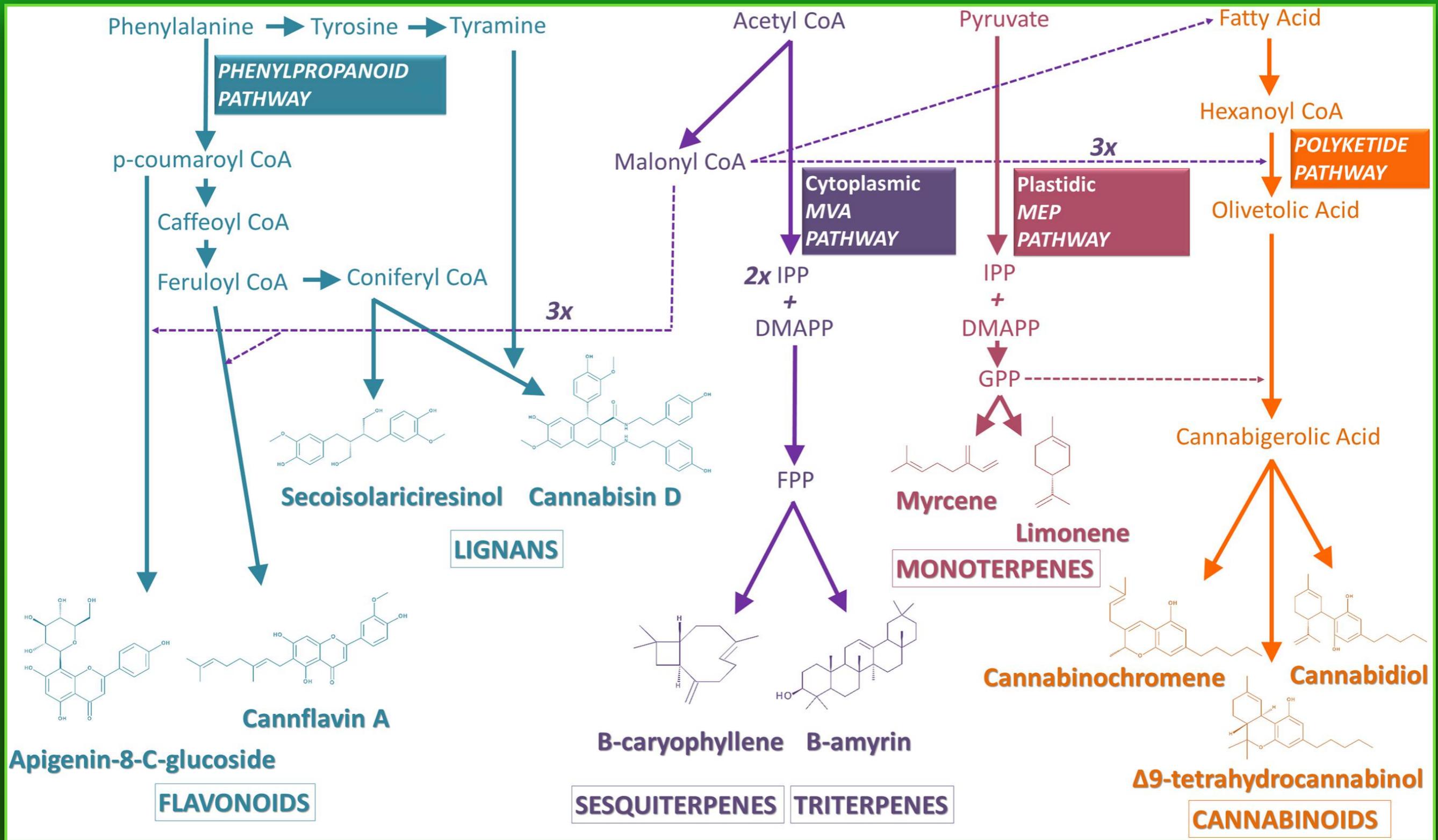


Apport des cannabinoïdes dans la thérapeutique

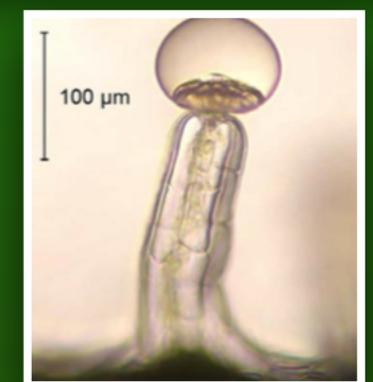
L'EFFET ENTOURAGE

Chemical class	2005	2015
Δ^9 -THC type	9	23
Δ^8 -THC type	2	5
CBG type	8	16
CBC type	6	9
CBD type	7	7
CBND type	2	2
CBE type	5	5
CBL type	3	3
CBN type	7	11
CBT type	9	9
Miscellaneous types	14	30
Total cannabinoids	72	120
Total non-cannabinoids	419	445
Total	491	565

- 11 types de cannabinoïdes
- 120 cannabinoïdes
- 445 composés non-cannabinoïdes
- La proportion de chaque type de composé varie suivant l'organe de la plante, les conditions de culture (environnement) et le chemovar.



Biosynthèse des cannabinoïdes terpènes et flavonoïdes



Ratio CBD/THC: différentes indication thérapeutiques

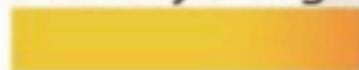
CBD to THC RATIOS

CBD : THC

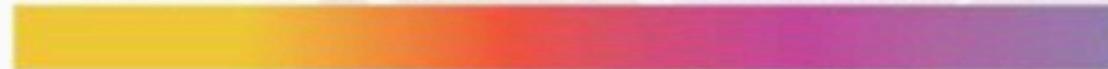
20 : 1 Stress / Anxiety / Migraine / Seizures / Mild Inflammation / Off-Balance / THC Intolerance / Stroke / Trauma / Neurological Disorders / Autism / High Blood Pressure



10 : 1 Anxiety / Migraine / Epilepsy / Menstrual Pain / Autism / Mild Inflammation



3 : 1 PTSD / Cold & Flu / Virus / Immune Deficiencies / Crohn's / IBS / Lupus / Diabetes



1 : 1 High Pain / Fibromyalgia / Insomnia / Low Appetite / Alzheimer's / Cancer / Tumor / Nausea / Chemo / HIV-AIDS / Cachexia / Parkinson's / Neuropathy / Diabetes



THCA Depression / Inflammation / Spasms / Cancer Cells / Parkinson's / Leukemia / MS / Seizures



THC (Sativa) Chronic Pain / Depression / PTSD / IBD / HIV-AIDS / Certain Heart Conditions
(Indica) Insomnia / Chronic Pain / PTSD / IBD / HIV-AIDS / Certain Heart Conditions



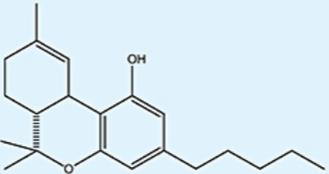
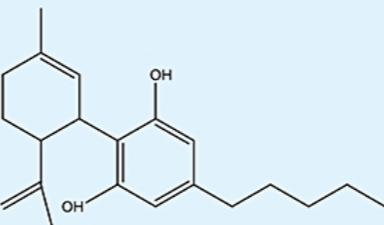
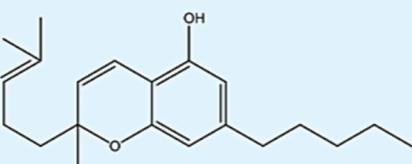
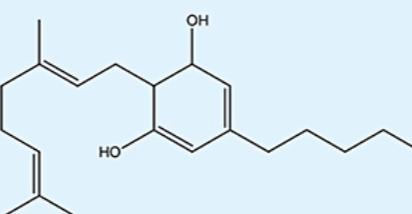
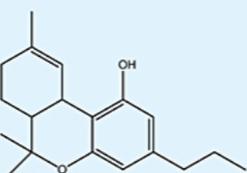
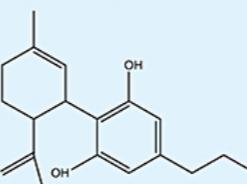
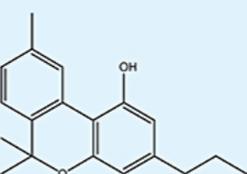
On observe des taux variables de terpènes selon les variétés de cannabis auxquels on attribue différentes vertus thérapeutiques

Cannabis Terpenes

NAME		EFFECTS	STRAINS
MYRCENE		anti-inflammatory sedative muscle relaxant pain relief	Chemdawg Grape Stomper Fire Alien Kush Agent Orange
A-PINENE		boosts energy improves focus bronchodilator improves memory	Vanilla Kush Cookie Cross 9lb Hammer Lavender
CARYOPHYLLENE		pain relief anti-depressant anti-inflammatory anti-anxiety	Gorilla Glue #4 Tangerine Dream Sage N Sour Pineapple Express
LIMONENE		improves mood anti-anxiety anti-depressant relieves nausea	GSC (Cookies) Pre-98 Bubba Kush Tangerine Dream Cush / Green Crack
HUMULENE		anti-inflammatory appetite suppressant pain relief anti-tumor	Liberty Haze Gorilla Glue #4 Cush / Green Crack Sage N Sour
LINALOOL		anti-anxiety sedative pain relief anti-bacterial	Bubble Gum 9lb Hammer Sour Diesel Locomotion

Effets de synergie des terpènes et des cannabinoïdes pour différentes indications

Russo E.B. (2011)

Phytocannabinoid structure	Selected pharmacology (reference)	Synergistic terpenoids
 <p>delta-9-tetrahydrocannabinol (THC)</p>	<p>Analgesic via CB₁ and CB₂ (Rahn and Hohmann, 2009) AI/antioxidant (Hampson <i>et al.</i>, 1998) Bronchodilatory (Williams <i>et al.</i>, 1976) ↓ Sx. Alzheimer disease (Volicer <i>et al.</i>, 1997; Eubanks <i>et al.</i>, 2006) Benefit on duodenal ulcers (Douthwaite, 1947) Muscle relaxant (Kavia <i>et al.</i>, 2010) Antipruritic, cholestatic jaundice (Neff <i>et al.</i>, 2002)</p>	<p>Various Limonene <i>et al.</i> Pinene Limonene, pinene, linalool Caryophyllene, limonene Linalool? Caryophyllene?</p>
 <p>cannabidiol</p>	<p>AI/antioxidant (Hampson <i>et al.</i>, 1998) Anti-anxiety via 5-HT_{1A} (Russo <i>et al.</i>, 2005) Anticonvulsant (Jones <i>et al.</i>, 2010) Cytotoxic versus breast cancer (Ligresti <i>et al.</i>, 2006) ↑ adenosine A_{2A} signalling (Carrier <i>et al.</i>, 2006) Effective versus MRSA (Appendino <i>et al.</i>, 2008) Decreases sebum/sebocytes (Biro <i>et al.</i>, 2009) Treatment of addiction (see text)</p>	<p>Limonene <i>et al.</i> Linalool, limonene Linalool Limonene Linalool Pinene Pinene, limonene, linalool Caryophyllene</p>
 <p>cannabichromene</p>	<p>Anti-inflammatory/analgesic (Davis and Hatoum, 1983)</p>	<p>Various Caryophyllene oxide</p>
 <p>cannabigerol</p>	<p>AEA uptake inhibitor (De Petrocellis <i>et al.</i>, 2011)</p>	<p>–</p>
 <p>tetrahydrocannabivarin</p>	<p>Antidepressant in rodent model (Deyo and Musty, 2003)</p>	<p>Limonene</p>
 <p>cannabidivarin</p>	<p>TRPM8 antagonist prostate cancer (De Petrocellis <i>et al.</i>, 2011) GABA uptake inhibitor (Banerjee <i>et al.</i>, 1975) Anti-fungal (EISOhly <i>et al.</i>, 1982) Antidepressant rodent model (Musty and Deyo, 2006); and via 5-HT_{1A} antagonism (Cascio <i>et al.</i>, 2010) Analgesic, α-2 adrenergic blockade (Cascio <i>et al.</i>, 2010) ↓ keratinocytes in psoriasis (Wilkinson and Williamson, 2007) Effective versus MRSA (Appendino <i>et al.</i>, 2008) AI/anti-hyperalgesic (Bolognini <i>et al.</i>, 2010)</p>	<p>Cannabis terpenoids Phytol, linalool Caryophyllene oxide Limonene</p>
 <p>cannabivarin</p>	<p>Treatment of metabolic syndrome (Cawthorne <i>et al.</i>, 2007)</p>	<p>–</p>
<p>cannabinol (CBN)</p>	<p>Anticonvulsant (Hill <i>et al.</i>, 2010)</p>	<p>Linalool</p>
	<p>Inhibits diacylglycerol lipase (De Petrocellis <i>et al.</i>, 2011)</p>	<p>–</p>
	<p>Anticonvulsant in hippocampus (Hill <i>et al.</i>, 2010)</p>	<p>Linalool</p>
	<p>Sedative (Musty <i>et al.</i>, 1976) Effective versus MRSA (Appendino <i>et al.</i>, 2008) TRPV2 agonist for burns (Qin <i>et al.</i>, 2008) ↓ keratinocytes in psoriasis (Wilkinson and Williamson, 2007) ↓ breast cancer resistance protein (Holland <i>et al.</i>, 2008)</p>	<p>Nerolidol, myrcene Pinene Linalool adjunctive role? Limonene</p>

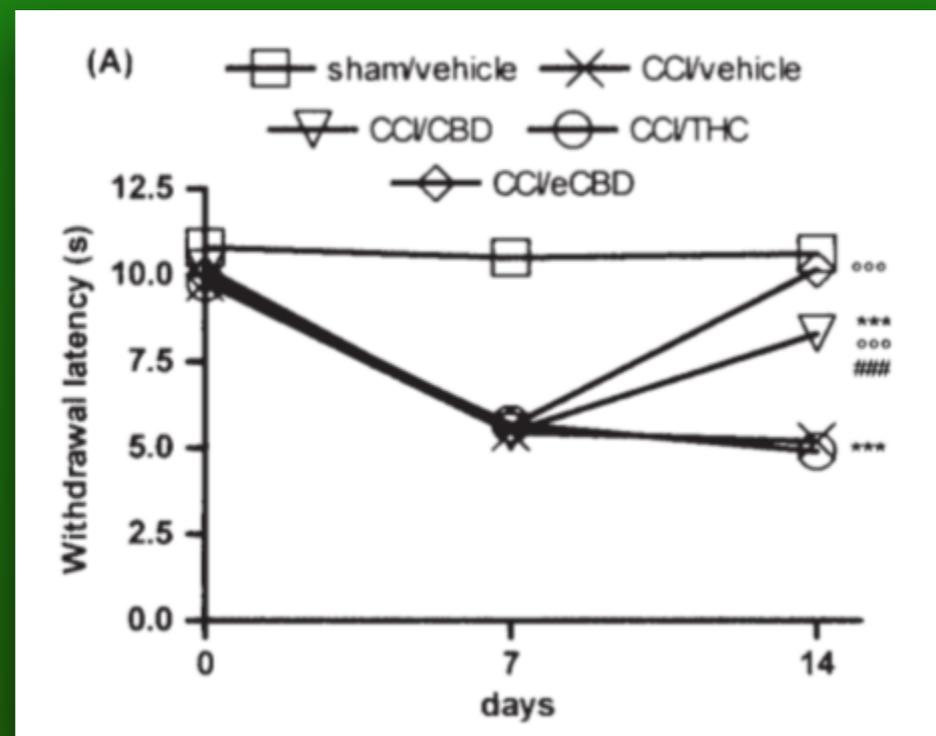
5-HT, 5-hydroxytryptamine (serotonin); AEA, arachidonylethanolamide (anandamide); AI, anti-inflammatory; CB1/CB2, cannabinoid receptor 1 or 2; GABA, gamma aminobutyric acid; TRPV, transient receptor potential vanilloid receptor; MRSA, methicillin-resistant *Staphylococcus aureus*; Sx, symptoms.

Effets de synergie

Quelques exemples d'observations expérimentales de synergies entre différents composés du cannabis

- 1974 (Carlini *et al*) : extraits totaux de cannabis induisent des effets 2 à 4 fois supérieurs qu'une quantité équivalente de Δ^9 - THC pur

- 2008 (Comelli *et al*) : étude sur le rat montre qu'un extrait de cannabis (CBD + THC + Terpènes + Flavonoïdes) est plus efficace contre la douleur que des quantités équivalentes de CBD et THC administrées pures



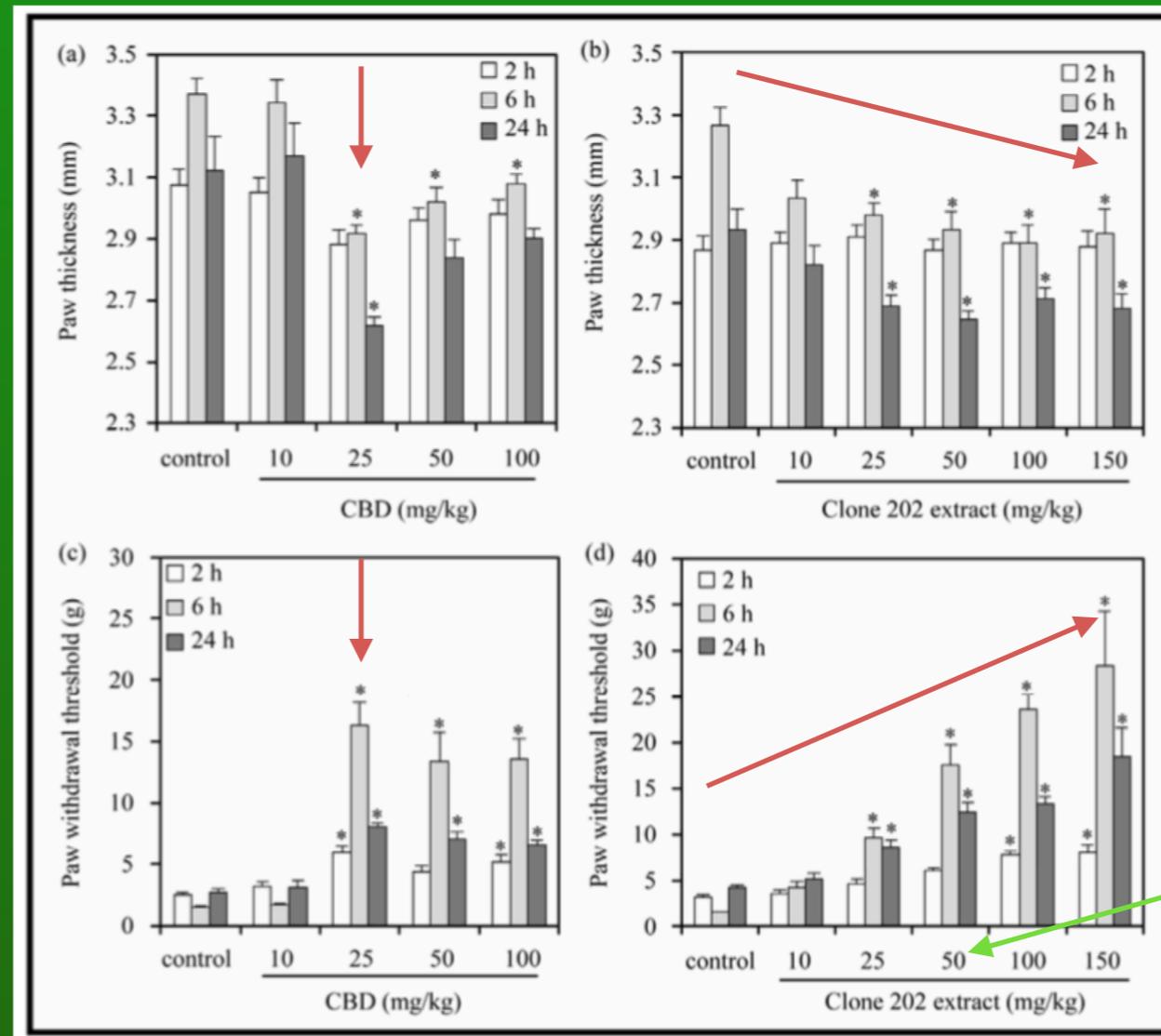
d'autres composés sont en jeu

- 2018 (S Blasco-Benito *et al*): étude sur une action anti-tumorale montre des résultats supérieurs pour un extrait total que pour le THC seul
- Ces résultats ne sont pas dus à la présence des 5 terpènes les plus abondants

2015: (R Gallily *et al*) Comparaison de l'action anti-douleur et anti-inflammatoire du CBD par rapport à un extrait de cannabis

réponse
inflammatoire

résistance
douleur



contient 10 mg/kg CBD

- L'extrait de plante à forte teneur en CBD a une efficacité supérieure au CBD purifié
- Pas de réponse en cloche mais corrélation dose/réponse :
➔ traitement facilité vs. fenêtre étroite de réponse thérapeutique

Traitement de l'épilepsie et CBD (Pamplona et al., 2018)

- Extrait de cannabis avec haute teneur en CBD : efficacité supérieure au CBD purifié
- Extrait = 71% vs. CBD pur = 36% de patients présentant une amélioration
- Dosage CBD:

extrait = 6 mg/kg/j vs. CBD pur = 27 mg/kg/j

 moins d'effets secondaires

- Cannabinoïdes, terpènes, flavonoïdes...
fonctionnent en synergie



Effet entourage

- Nécessité de mieux étudier les propriétés
médicinales de ces composés



Création de **chémovars** adaptés ayant des effets
prédictibles pour différents symptômes

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