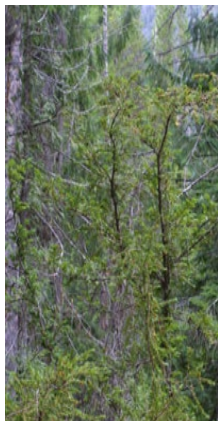


Producing Safe and Compliant Extracts and Isolates of Cannabinoids using Eco-Sustainable Separation Technologies

Gerard Rosse, Ph.D.
President
Arrival Discovery LLC

Natural Products As Medicines

1355 medicines approved (1981-2010), 50% contribution from natural products



Pacific Yew
Tree
TAXOL



Fungus
CYCLOSPORIN



Willow
Bark
ASPIRIN



Opium
Poppy
MORPHINE



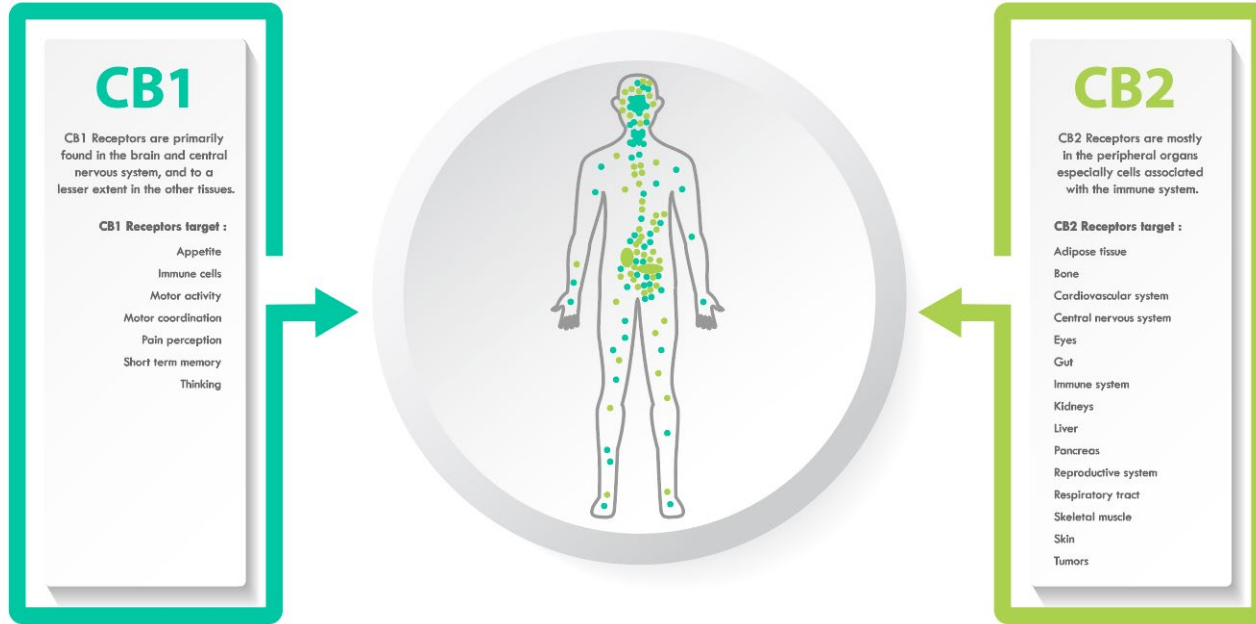
Bugula
Neritina
BRYOSTATIN



Cannabis
Sativa
EPIDIOLEX

Newman, D.J.; Cragg, G.M. J. Nat. Prod. **2012**, 75, 311

Human Endocannabinoid System



Pertwee, R.G.; *Br. J. Pharmacol.*, **2008**, 153, 199

Human Endocannabinoid System

Endocannabinoids (generated inside the body):

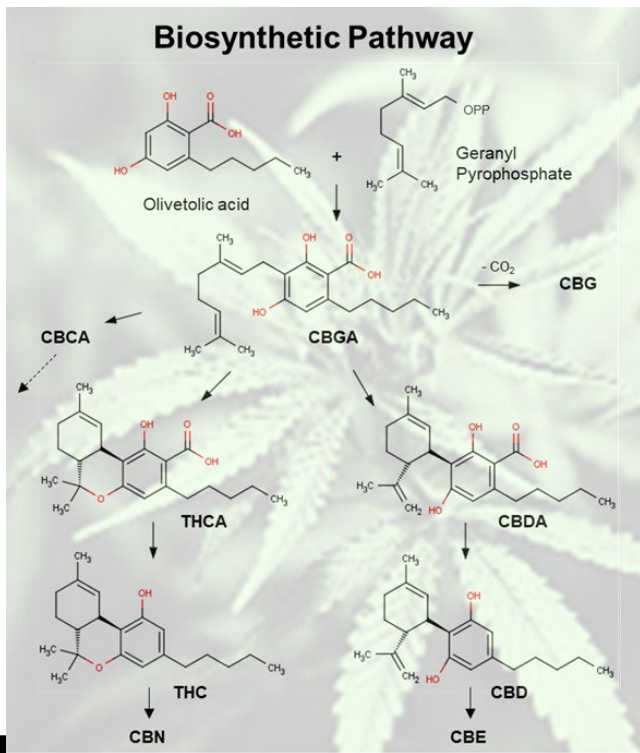
- Anandamine (CB1)
- 2-Arachidonoylglycerol (CB2)

Phytocannabinoids (generated in plant):

- Δ^9 -THC, CBD, CBG, CBN and many more

Pertwee, R.G.; *Br. J. Pharmacol.*, **2008**, 153, 199

Hemp Products – SFE/SFC



Hemp/Cannabis Plants

- Rich source of medicinal compounds
- >150 cannabinoid, 500 compounds
- Full spectrum extracts most desirable
- Compliance: < 0.3% THC (USA)

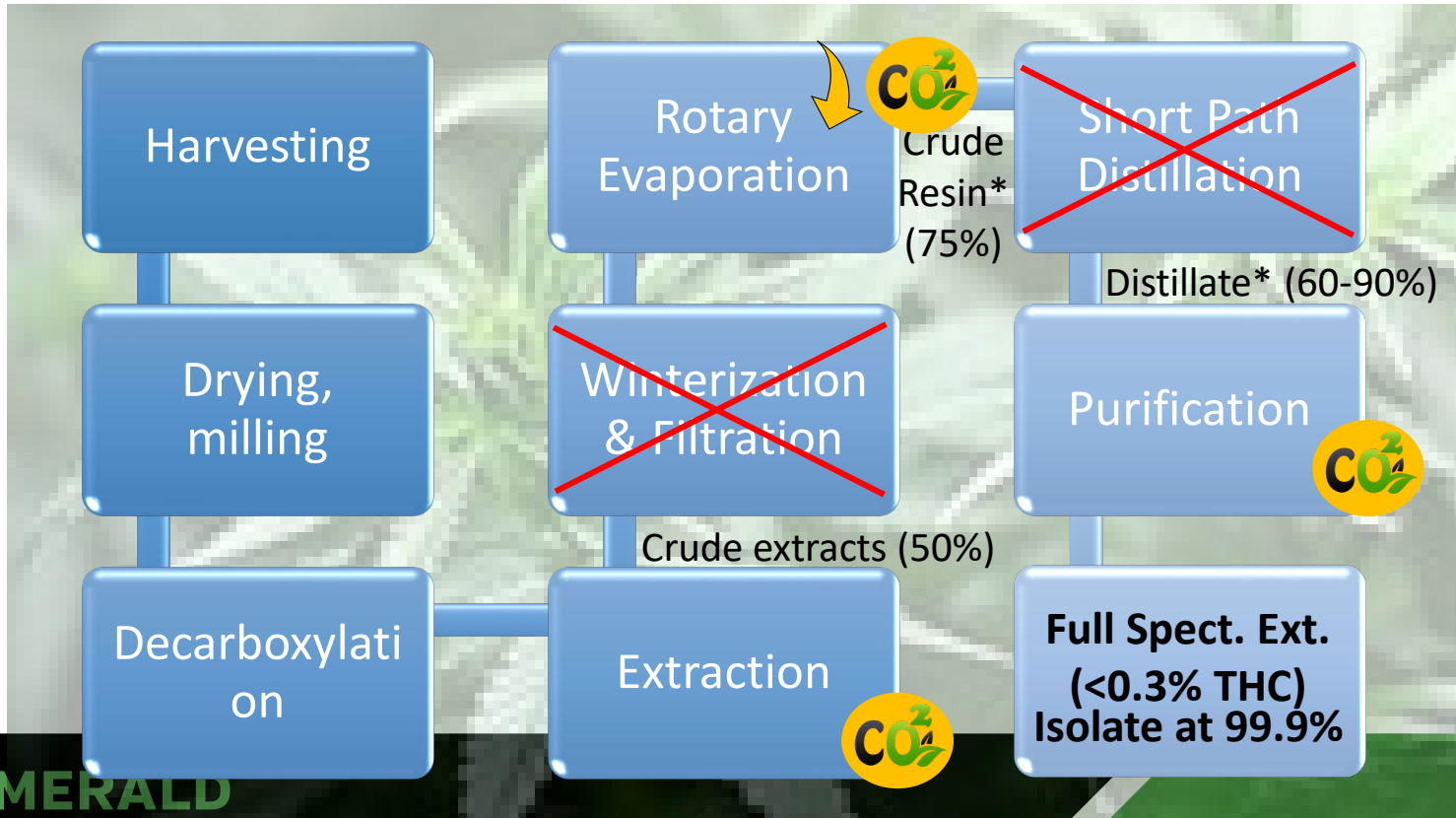
**SFE yields natural, intact extracts
with no toxic solvent**

**SFC excels in separating cannabinoids to
produce safe and compliant ingredients**

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CONFERENCE**

Produced by MJBizScience

Hemp Processing



CO₂ Extraction (SFE)

SFE is a safe, non-flammable and efficient process using carbon dioxide as a solvent

Benefits of SFE

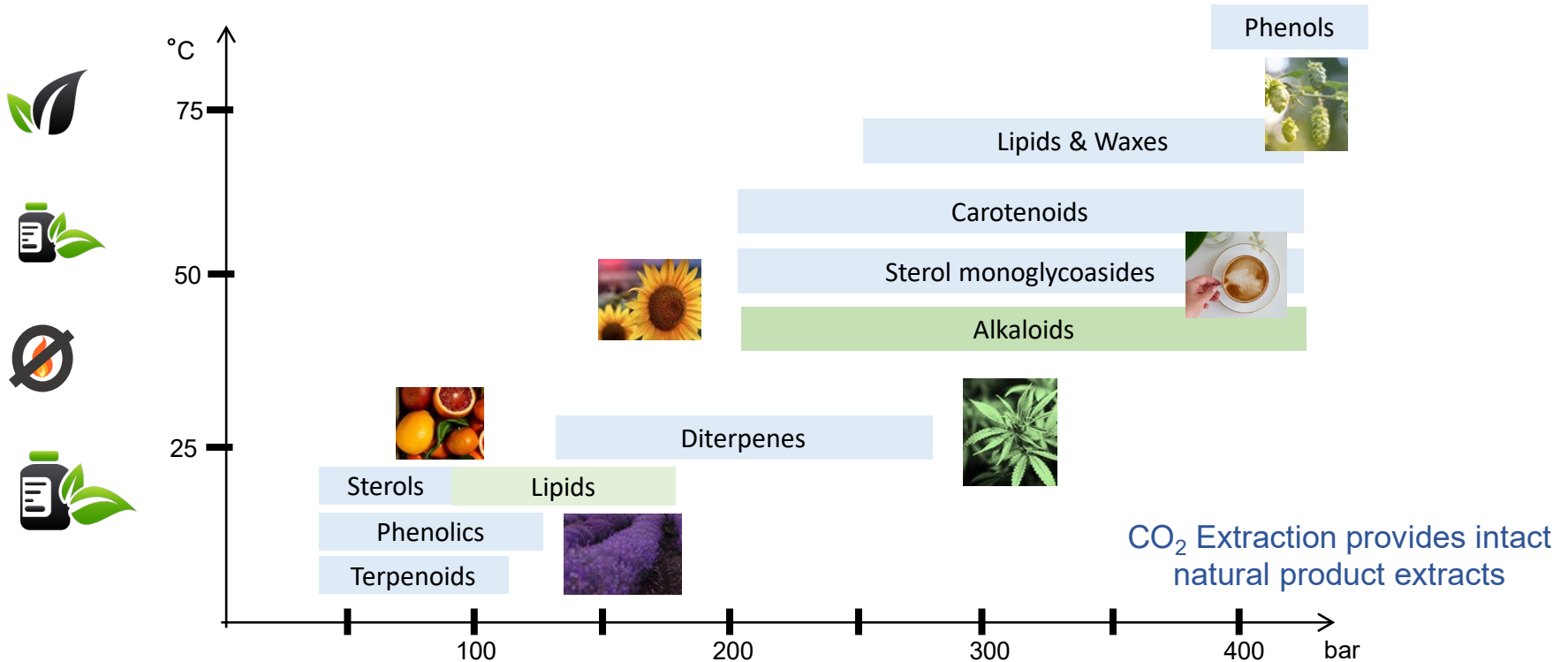
- Intact natural extracts
- Fractional separation
- No use of most toxic organic solvents
- FDA approved Green solvent
- Lower operation costs – High ROI



One-Machine – Many Application



Tunable Properties of CO₂



CO₂ Purification (SFC)

SFC is another form of liquid chromatography that happens to use CO₂ as the mobile phase

Benefits of SFC

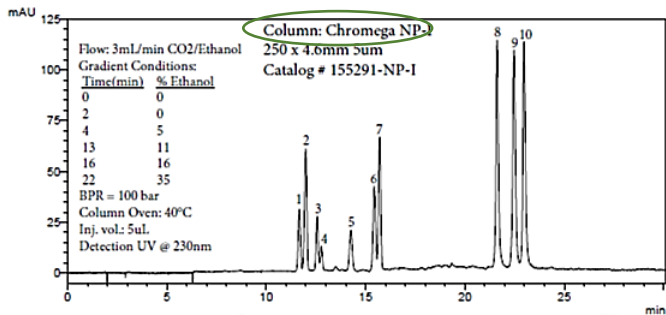
- High Resolution
- Faster than HPLC (3-10 times)
- No use of most toxic organic solvents
- FDA approved Green solvent
- Lower operation costs – High ROI



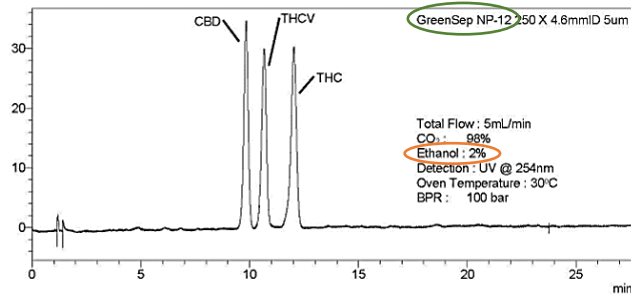
One-Machine – Many Applications



Cannabinoids Separation

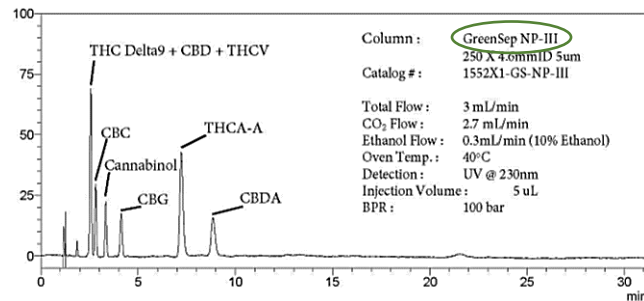


1. CBDV. 2. CBD. 3. Δ^8 -THC. 4. CBC. 5. CBN. 6. Δ^9 -THC.
7. CBG. 8. Δ^9 -THCA. 9. CBDA. 10. CBGA.



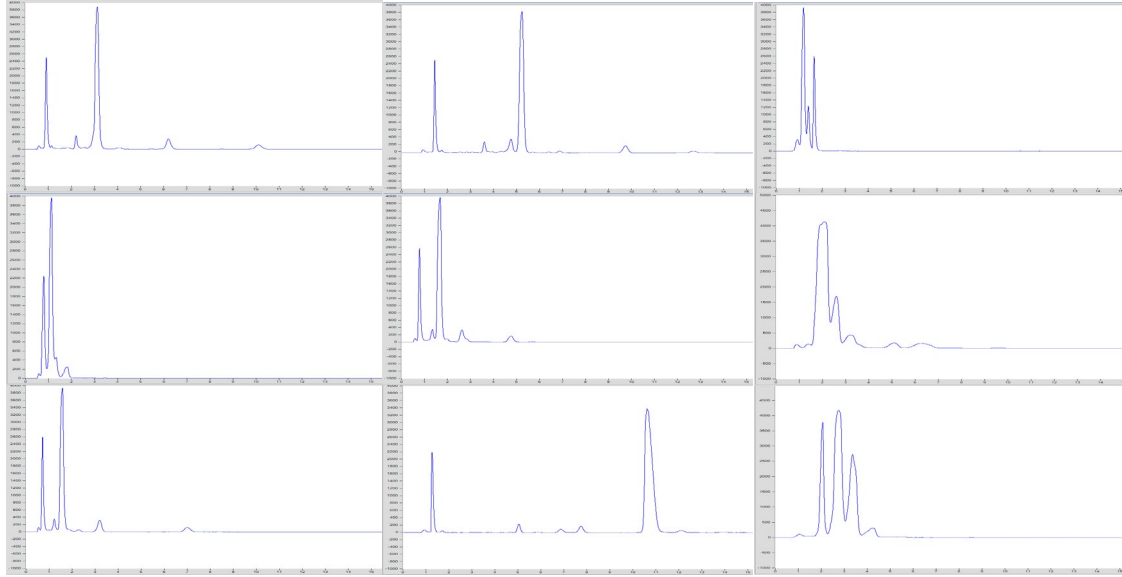
Challenges with stationary phase:

- Good separation, robustness
- High loading, low usage of co-solvent
- Not expensive



Data provided by ES Industries

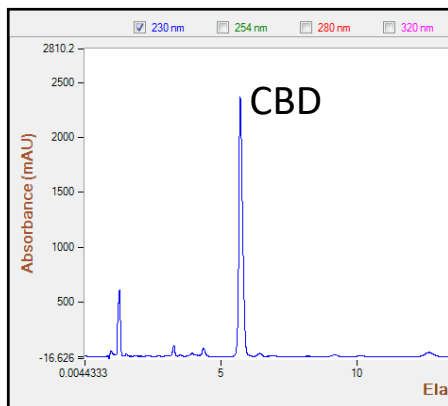
CO₂ Separation Case Studies: CBD Sample



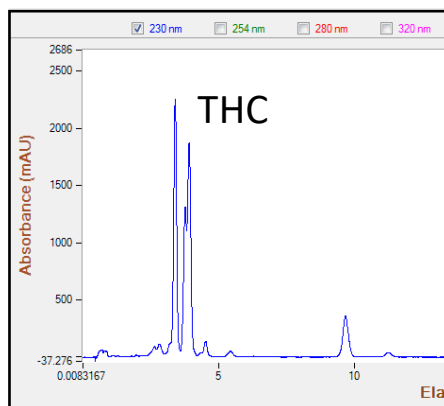
Fast and intelligent method development to find good separation conditions;
optimal T, P, flow, solvent and stationary phases

CO₂ Separation Case Studies: CBD Sample

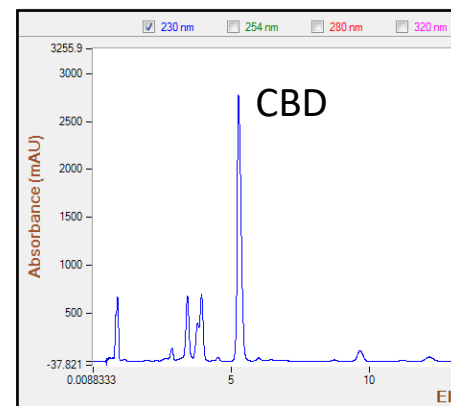
Distillate Sample



Reference Sample

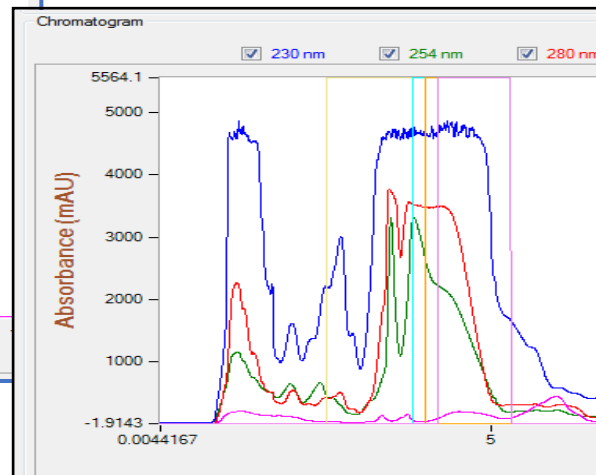
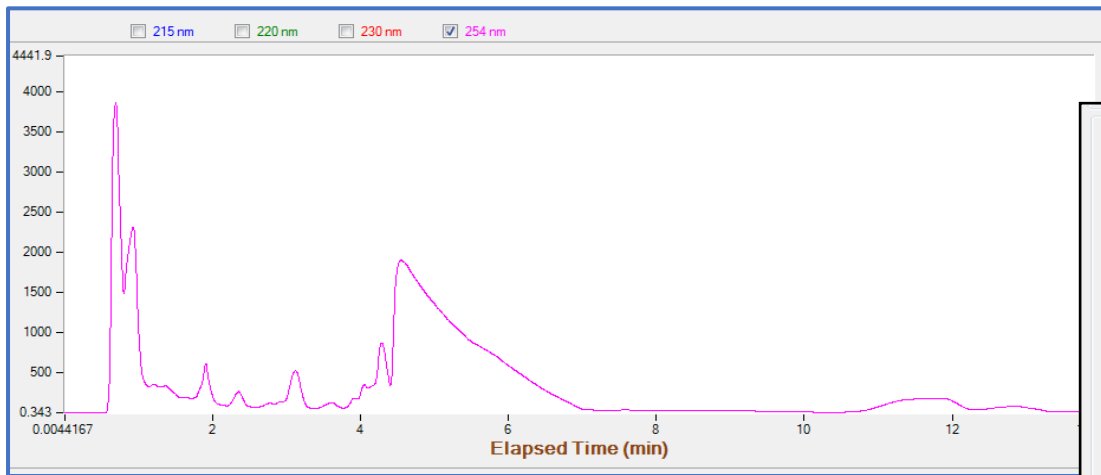


Distillate + Reference

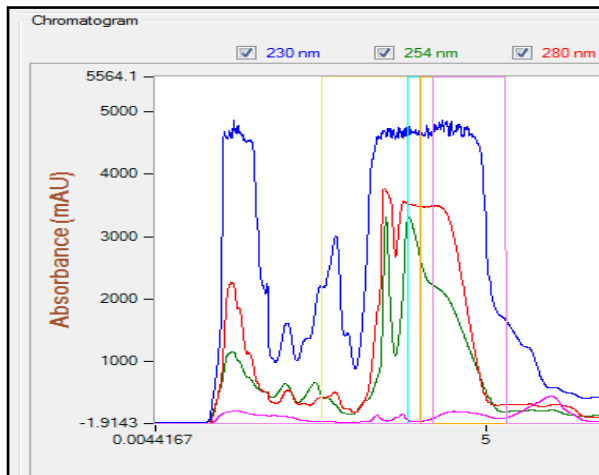


- Many unknown peaks (compounds) in distillate sample
- Reference sample contains many other peaks
- Acid form of cannabinoid(s) still present; inefficient decarboxylation

SFC Scale-up Studies: CBD Sample



SFC Scale-up Studies: CBD Sample

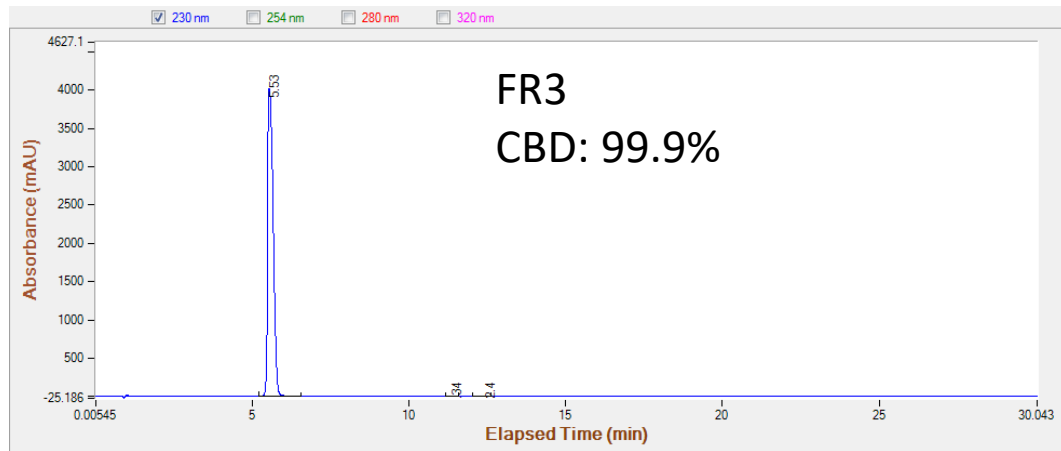


5% Ethanol

Productivity: 2.0 Kg/kg SP.Day

Four fractions collected (CBD purity)

- Fraction 1: 49%
- Fraction 2: 99.9%
- Fraction 3: 99.9%
- Fraction 4: 99.9%



SFC – Cost of Owning

Remediation of Hemp Oil at a Productivity of 3-4 kg per 24h

	SFC	HPLC
Total Flow Rate / Column	120 L/H ; 10 cm ID	60 L/H ; 15 cm ID
Solvents	CO ₂ :EtOH (95:5)	EtOH:H ₂ O (85:15)
Solvent Consumption per 24 hours	144 L *	1440 L
Cost of Solvents per 24 hours	\$1,030	\$10,200
Cost of Solvents per month (5 days)	\$25,750	\$204,000

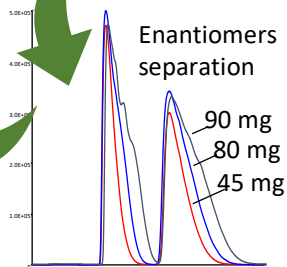
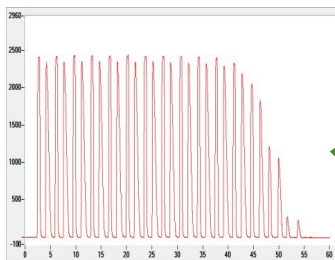
SFx CO₂ Technologies

In-line Extraction-Purification

A. Biomass in extractor



B. Attach extractor



Extraction or Purification



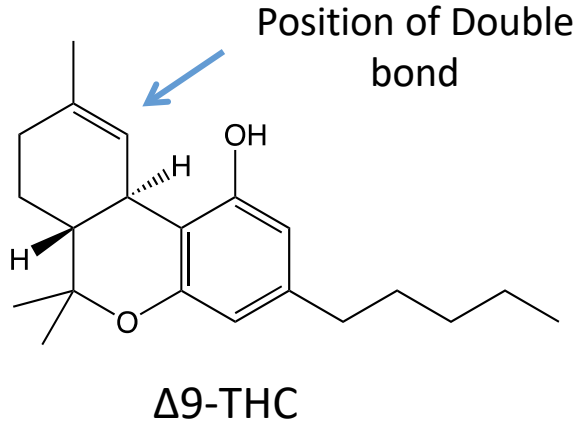
One instrument operating
in 2 modes

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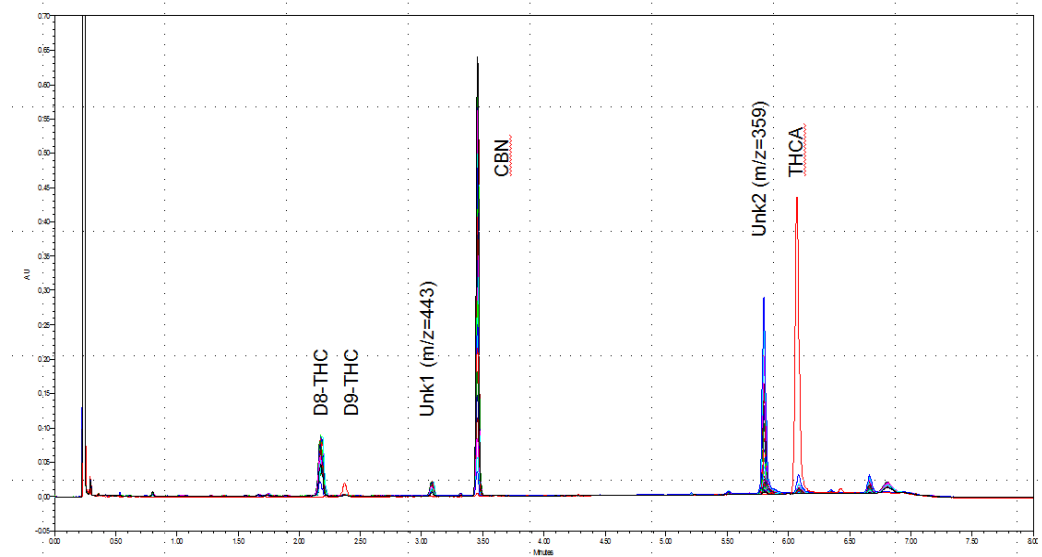
Produced by MJBizScience

Cannabinoids Isomers

Δ^9 -THC, Δ^8 -THC, Δ^{10} -THC, Δ^7 -THC



Monitoring conversion of THCA to D8-THC



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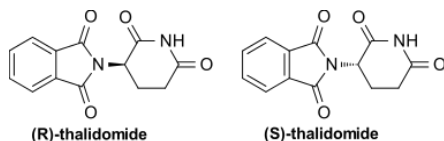
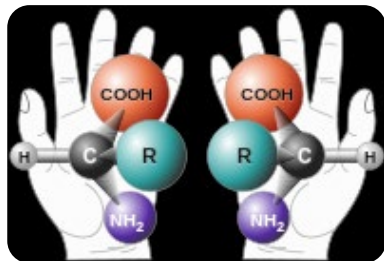
(could irritate nose) (could cause fetal damage)

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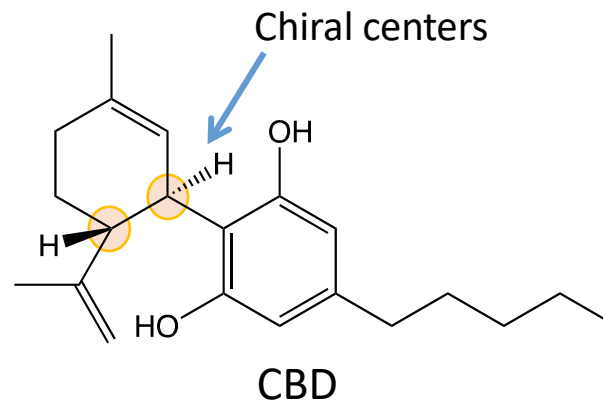
Cannabinoids Chirality

What is Chirality?

- The configuration of an asymmetric, optically active chemical compound.
- Chiral compounds have the same number of atoms arranged differently in space



(R)-thalidomide (S)-thalidomide
(used to treat nausea) (could cause fetal damage)



For terpenes chirality see Micalizzi et. Al.,
Molecules **2021**, 26, 1588.

Benefits of CO₂ Technologies



Cost Effective



Fast
Automated



Efficient and
High Productivity



Non-toxic
non-flammable



Minimize
waste



Reclaimed CO₂
Recycling



“One machine –
Multiple Use”



Sustainable
Minimize energy used

Summary and Future Directions

- Compliant and consistent extracts and individual cannabinoids formulation needed to ensure consumer safety
- **CO₂ Extraction (SFE)** yield intact, natural extracts with no toxic solvent
- **CO₂ Separation (SFC)** excels in analyzing and separating cannabinoids and other natural products. No toxic solvent left
- More detailed analysis of isomers ($\Delta 8$, $\Delta 9$, $\Delta 10$ -THC) including stereoisomers (chirality) possible by SFC



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