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medical cannabis technology

# Production Tools

## from Plant to Extract

Tobias Schappeler
Managing Director

# About us

- Established in 1989, family owned
- Extensive experience in relevant chemistry & pharma
- 21 Team Members, growing quickly
  - Chemists with pharma experience
  - Analytical Chemists
  - Engineers (Mechanical, Electronics, Mechatronics)
  - Cannabis Processing Specialists*
- Covering Australia and New Zealand with offices in Sydney, Brisbane and Melbourne
- Services include equipment consulting, application and technology support, equipment sales, installation, training and after sales & calibration service

*currently recruiting

# Typical Production Workflow

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| | |
|---|---|
| Terpene Extraction | Microwave, Steam, $CO_2$ |
| Drying | Hang Drying, Oven Drying, Vacuum Drying, Freeze Drying |
| Grinding / Milling<br>optional Size Verification | Cutting Mills<br>Sieve Shakers |
| Primary Extraction | $CO_2$, Hydrocarbon, Ethanol |
| Winterisation / Dewax | “Bucket&Freezer”, Chemical (Filter) Reactors |
| Filtration | Filter Press, Nutsche Filter, Filter Reactor |
| Ethanol Evaporation | Rotary Evaporators, Distillation Plants |
| Decarboxylation | Chemical Reactors, Decarb Ovens |
| Concentration | Wiped Film Evaporators |
| Isolate Production | FCPC Chromatography, Chemical Reactors |

# Terpene Extraction

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## Why?

- Recovery after primary extraction may be difficult or even near impossible (solvent dependent)
- Compromised yield if done during primary extraction
- Damage or loss in downstream processing
- Collect & re-introduce during formulation for
  - Entourage effect
  - Dose consistency
  - Consumer experience (more recreational)
- Sell as separate product (very desirable, good prices)
- Use in clinical trials to camouflage placebo

Primary Extraction Solvent Compatibility for Terpene Extraction

☺ Hydrocabon

☺ $CO_2$ (but winterisation typically done with ethanol)

☹ Ethanol

# Terpene Extraction

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- Microwave

☺ Solvent Free
☺ Fast
☺ Easy-to-use
☺ No detected impact on cannabinoids (scientific data)
☹ Extra production step
☹ Limited capacity without good scale up path (currently)

- Steam

☺ Water as solvent
☺ Easy-to-use
☹ Extra production step
☹ Limited good options for small scale production

- $CO_2$

☺ Can be done on primary extraction tool
☺ No additional machine investment
☹ Terpene pull done sub critical, extra process step
☹ Limited separation efficiency
☹ Limited extraction yield

# Terpene Extraction

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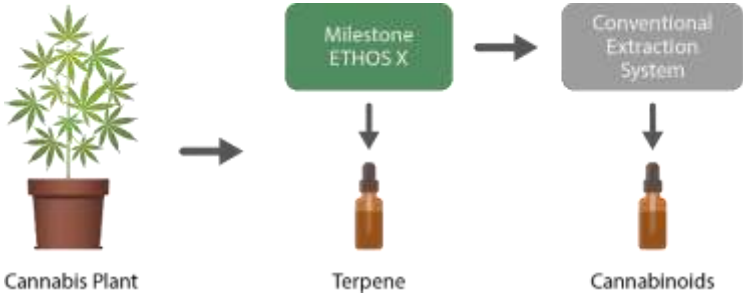
## Patented Microwave Extraction




- Wet or frozen biomass
- Uses water content of biomass
- Directly after harvest, prior to drying
- GMP, CFR 21 P11

Simple Workflow

1) Load glass extraction container with flower
2) Place container into microwave and connect
3) Start run via PLC
4) Collect terpenes (with minor residual water)
5) Winterise

Use 2nd vessel for condenser wash runs
Use 3rd product vessel to speed up turnaround times

# Terpene Extraction

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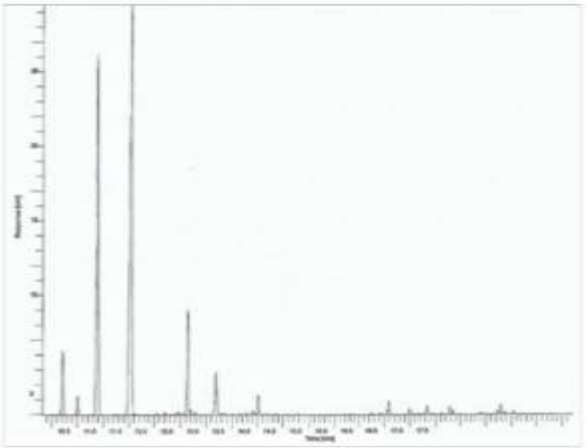
- Patented Microwave Extraction

- 1kg starting material
- Analysis via GC-MS
- Results in % of dry weight

Hydrocarbon Extraction Result

| | Plant Raw Material[b] | ETHOS X extract | ETHOS X processed plant material[b] |
|---|---|---|---|
| Terpenes[a] | 1.4 | 1.6 | 0.1 |
| Total Cannabinoids[a] | 78 | –[c] | 77 |



- 0.1% Terpene post Ethos
- 1% variance between raw and post Ethos

➔ Statistical testing errors

- No cannabinoids detected in Ethos terpenes

# Terpene Extraction

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- Patented Microwave Extraction

Limited Batch Capacity – Suitable for Production?

Single Batch (no cleaning between runs) = 6t per year
3 kg per vessel
1h run time
8 runs per 8h, 24 kg per shift, 250 working days

Multi Batch = 4.5t per year
3 kg per vessel
1h run time, 20 min changeover (vessel change, solvent run)
6 runs per 8h, 18 kg per shift, 250 working days

- Ethos works well in < 10t per year range (running 2 machines seems reasonable)
- Not suitable for large productions if all biomass terpene is targeted
- Terpene collection may not be required for every of your products, so microwave extraction may still make sense

# Terpene Extraction

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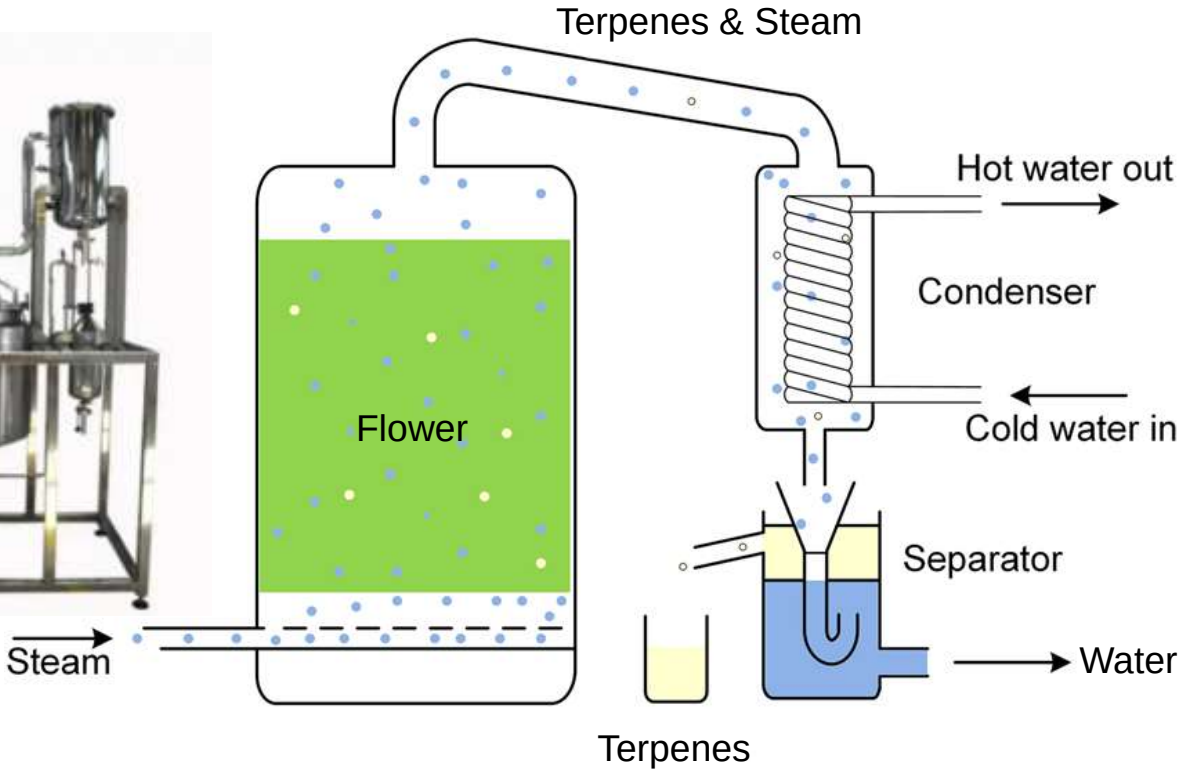
## Steam Extraction




- Winterisation will be needed for residual water removal
- Well established in essential oils and pharma botanical extraction
- High throughput and GMP options available

# Terpene Extraction

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## $CO_2$ Extraction

- Sub critical $CO_2$
- Typically 60-70 bar, 5-10 C

- Production steps
  1) Load biomass
  2) Terpene pull
  3) Cannabinoid Extraction
  4) Clean (CIP)

- Saves double handling of biomass

- Discharge of terpenes mixed with (residual) biomass water content
- Post processing needed for terpene purification

# Drying Methods

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## Hang Drying

”Near ambient” temperature & low humidity

- ☺ Potentially positive effects, if buds are sold for smoking
- ☹ Hanging and collecting is labour intensive
- ☹ Slow – takes 4 - 7 days
- ☹ Drying room – expensive & large infrastructure

## Oven Drying

Elevated temperature with/without vacuum applied

- ☺ Scalable processing with batch separation
- ☺ Scalable investment in line with batch size
- ☺ Vacuum enables low product temperature drying
- ☺ Fast – takes <1 day
- ☹ Terpene loss if temperatures are too high

## Freeze Drying

In frozen state under ultra-low vacuum

- ☺ Scalable processing with batch separation
- ☺ Scalable investment in line with batch size
- ☺ Ultra-low vacuum enables sublimation / lyophilisation
- ☺ Best possible plant integrity and volatile retention
- ☹ High investment for capacity

# Drying Room

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☺ High capacity
☺ Reasonable terpene retention (low temp)
☹ Slow
☹ High operating cost (power, dehumidifier...)

# Oven Drying

- ☺ Vacuum Drying Oven = heat > 60C
- ☺ In-process decarb possible
- ☺ Simple install and operation
- ☹ Terpene loss

# Vacuum & Freeze Drying

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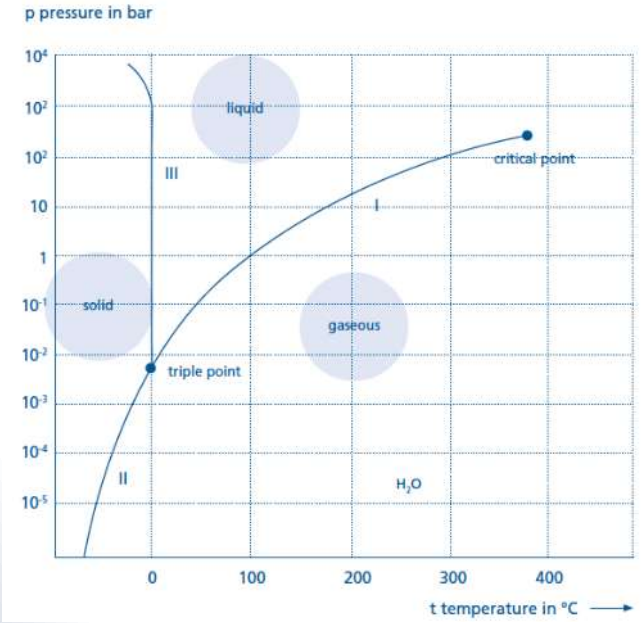
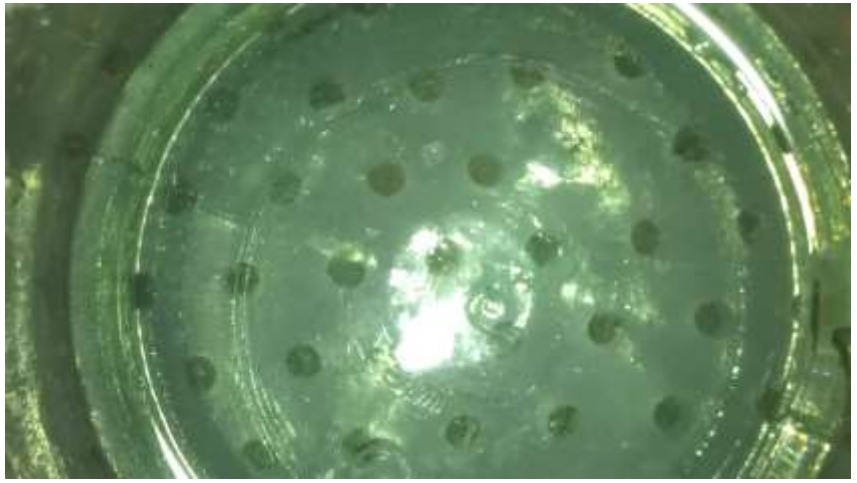
- Basics

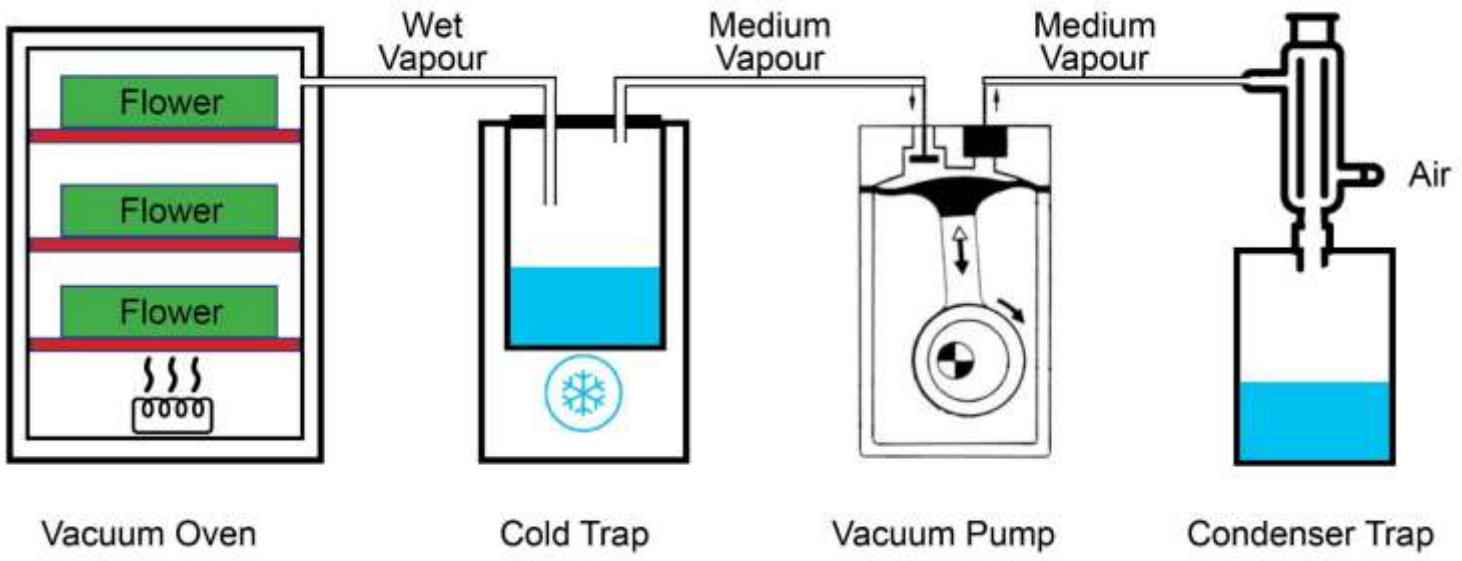


Freeze water by applying vacuum, no cooling!

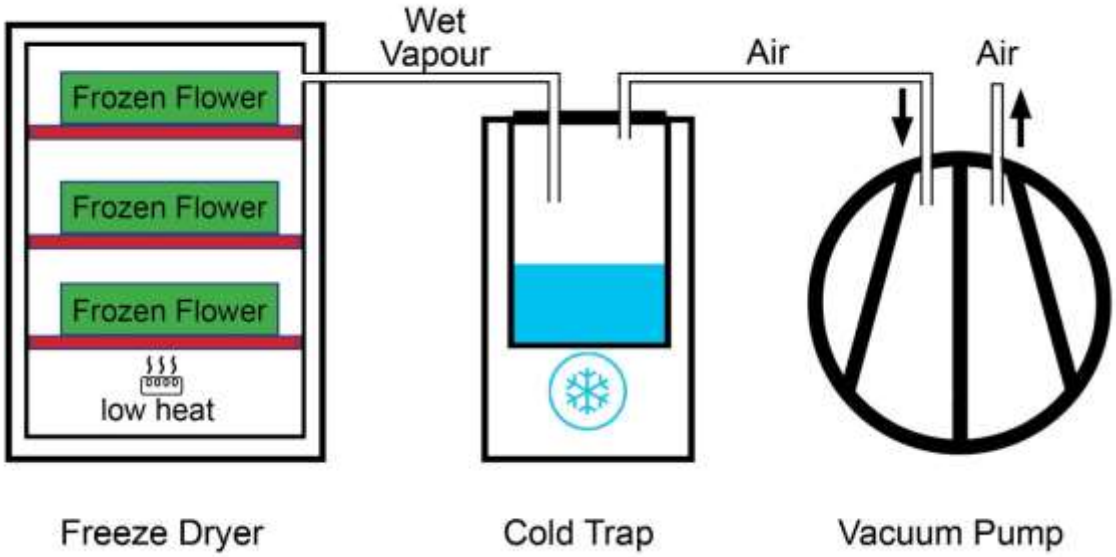
- Vacuum Drying or Distillation = above freezing point
  - Liquid Phase ➔ Gas Phase
- Freeze Drying = below freezing point
  - Solid (Frozen) Phase ➔ Gas Phase
- Product Temperature = Function of Pressure
  - Product can remain cold / frozen even with heat (energy) applied
- Freeze Drying = most gentle method with best volatile retention
  - Freeze dried flowers, herbs, fruit, instant coffee…

# Vacuum Drying




Vacuum Drying Oven = heat < 60C
Cold Trap = - 60C to -105C (colder is better for terpene collection)
typical recovery rate 60 – 80%
Vacuum Pump = < 10 mbar operating pressure
Condenser = < 5C (secondary terpene and water collection)
typical recover rate >96%
Process time < 12h

# Freeze Drying




Freeze Dryer = shelves –60C to +20C
Cold Trap = -60C to -85C (colder is better)
typical recovery rate 80 – 95%
Vacuum Pump = < $10^{-2}$ mbar operating pressure
Process Time = 16 - 48h

# Milling

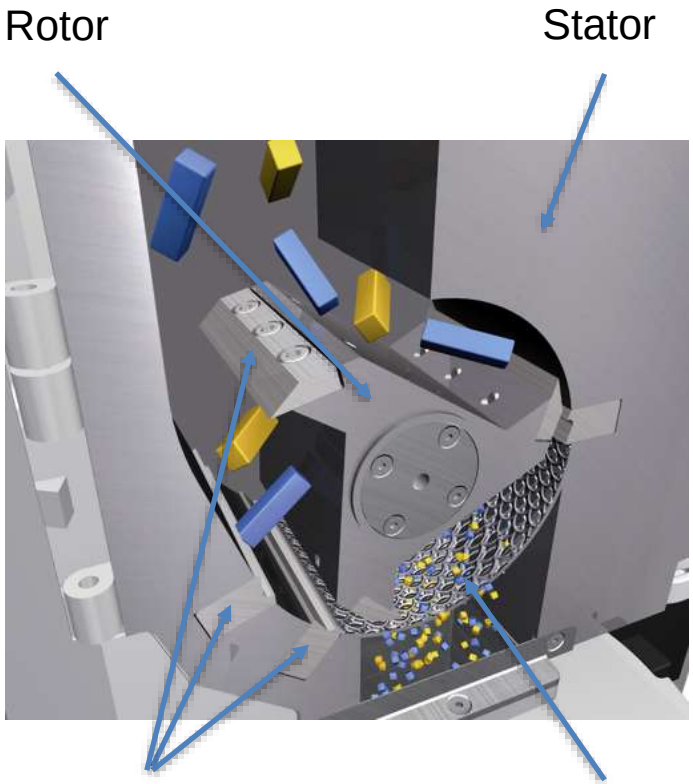
## Cutting Mills


Industry standard

- ☺ Designed for cutting of fibrous (=plant) material
- ☺ Target particle size via in-built sieve
- ☺ Active cooling possible with dry ice (or $lN_2$)
- ☺ Rotors can be pre-cooled
- ☺ Relatively easy to clean
- ☺ Cyclone options for fast throughput, extraction, operator protection & to keep ambient clean
- ☺ GMP options available
- ☹ Labour intensive
- ☹ Mill can block (if used incorrectly)
- ☹ May warm product (if used incorrectly)
- ☹ Limited throughput for non-industrial size

# Milling

- Cutting Mills

# Particle Size Verification

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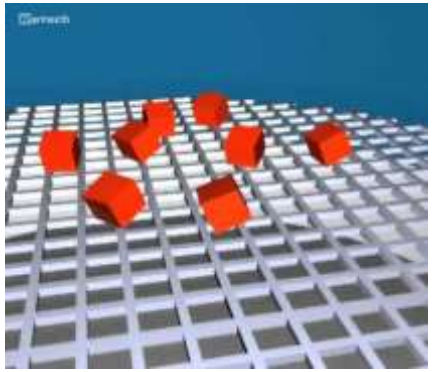
## Sieve Shakers

Industry standard

- ☺ Straightforward technology
- ☺ Improves extraction consistency
- ☺ Good GMP tool
- ☺ Inexpensive
- ☹ Labour intensive for loading & cleaning
- ☹ Not practical for high throughput production

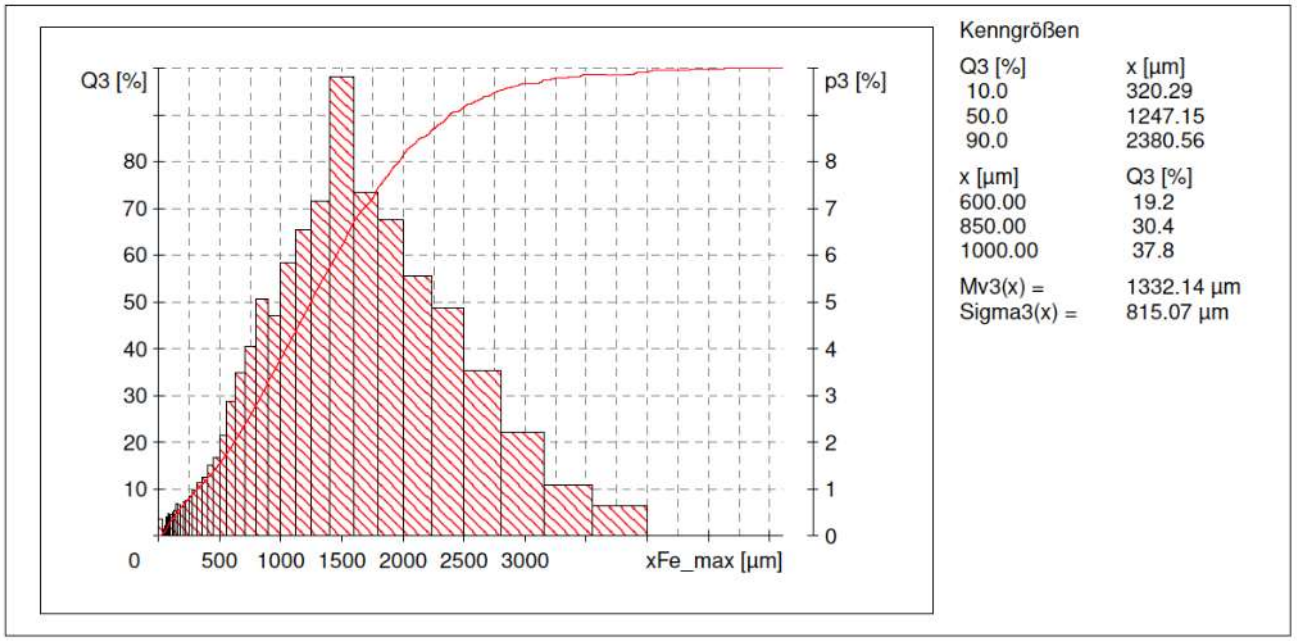


Large

Fine

# Particle Size Verification

- Sieve Shakers




- Particle too large = poor extraction times & yield
  - ➔ reprocess
- Particle too small = block extractor filters or pass into extract
  - ➔ discard or pelletise for extraction

# Primary Extraction Solvents

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## Supercritical $CO_2$

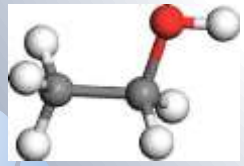
- ☺ Considered safe (but can kill!)
- ☺ Full spectrum extraction
- ☹ Poor extraction performance
  - Very Slow – commonly >3h to 8h per batch
  - 10+ times slower than ethanol
- ☹ Extract requires extensive clean up (winterisation)
  - adding significant production cost and time
  - causing terpene loss (if not collected prior)

## Hydrocarbon

Butane
Propane
Pentane

- ☺ Fast – extraction times under 1h possible
- ☺ Extraction selectivity (via different hydrocarbons)
- ☺ Approved (but must be purged)
- ☹ Solvent re-use challenging but cheap (<$1 per liter)
- ☹ High explosion risk

## Ethanol



- ☺ Considered safe
- ☺ Super fast – extraction times under 30 min possible
- ☺ Best overall extraction yields
- ☹ Loss of terpenes
- ☹ Solvent re-use challenging but cheap (<$2 per liter)
- ☹ Medium explosion risk

# Extraction Technology

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## Supercritical $CO_2$

- ☺ Process can be automated – user skill independence
- ☺ Equipment can be “GMP compliant”
- ☹ Equipment needs to be pressure vessel certified
- ☹ Extract requires clean up (winterisation)
- ☹ High capital investment, significant maintenance cost
- ☹ Longest return on investment (by far)
- ☹ Limited scalability for high throughput production

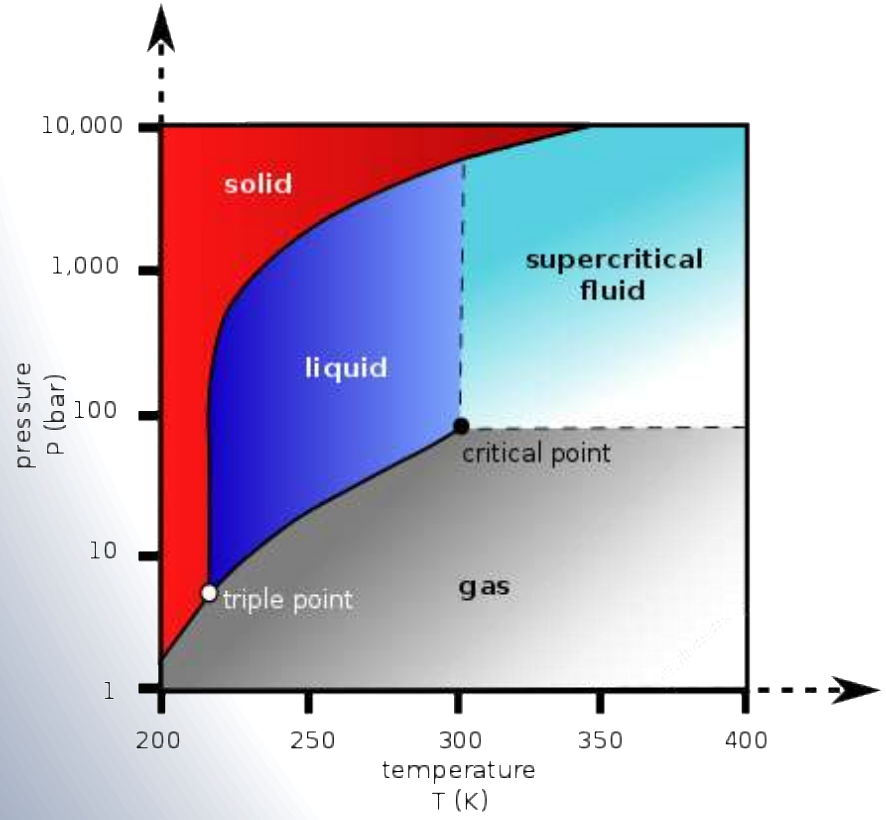
## Hydrocarbon

- ☺ Manual and automated options available
- ☺ Equipment can be “GMP compliant”
- ☺ Scalable with production throughput
- ☺ In column dewax
- ☹ High explosion risk

## Ethanol

- ☺ Currently preferred for highest throughput
- ☺ Manual small scale, fully automated large scale
- ☺ Best extraction yields
- ☺ Lowest investment
- ☺ Cold extraction may not require winterization
- ☺ Equipment can be “GMP compliant”
- ☹ Moderate explosion risk

# $CO_2$ Extraction




Supercritical Critical Point:

31.10 °C (304.25 K)
73.9 bar (1,071 psi)

Sub Critical:
Typical < 55 bar (800 psi)
Typical 5-10 °C (approx. 280 K)

Impact of Pressure:

Higher pressure = faster extraction
Higher pressure = more by-product
(chlorophyll, fats, waxes, lipids…)

Lower pressure = cleaner extract
Lower pressure = slower extraction

- Key yield parameters = $CO_2$ pressure & flow rate
  Time

# $CO_2$ Extraction

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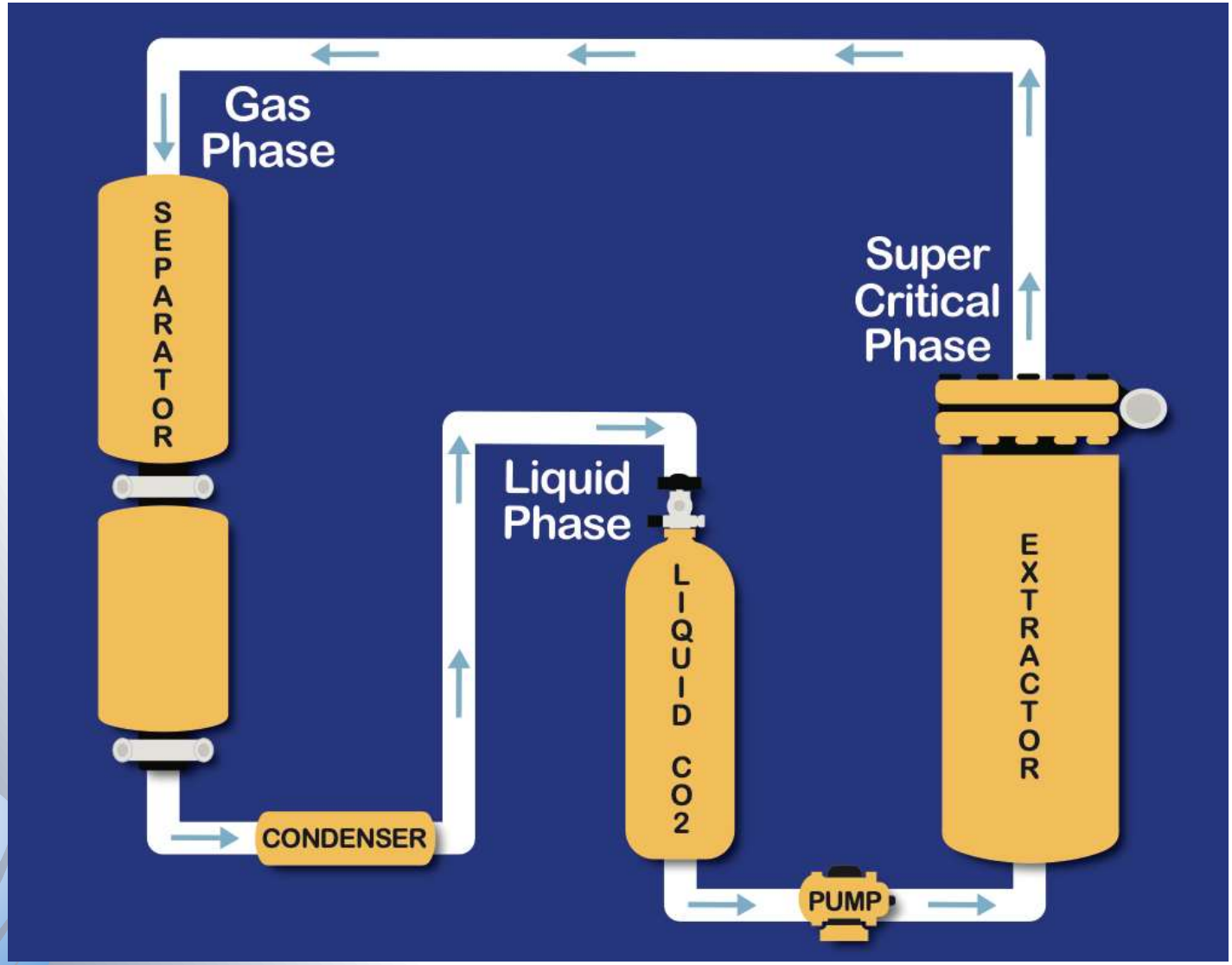

# Ethanol Extraction

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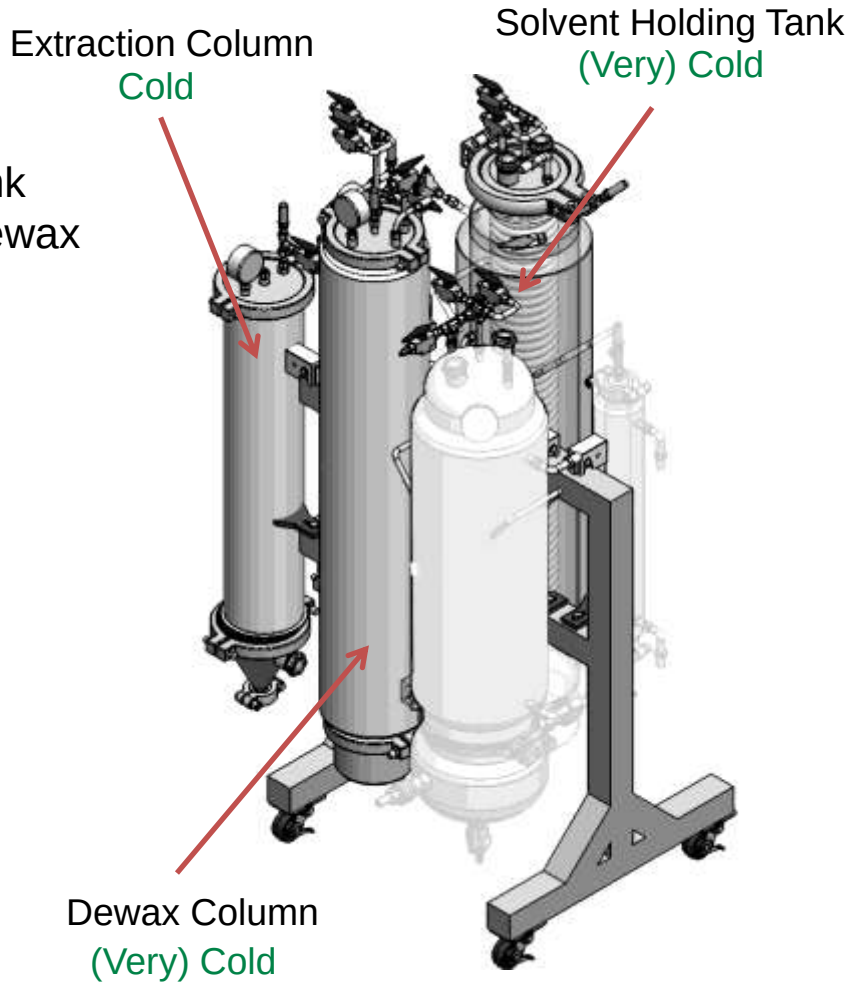
- Low to Medium Throughput

Key System Components:

- Extractor
- Low Temperature Chiller for Solvent Tank
- (Optional) low temperature chiller for Dewax
- Vacuum pump
- Nitrogen supply




Simplified Workflow:

1) Evacuate
2) Purge with N2
3) Add & Cool Solvent in Holding Tank
4) Soak Material
5) Filtration in filtration cone
6) Optional dewax
7) Transfer crude to ethanol reclaim

# Ethanol Extraction

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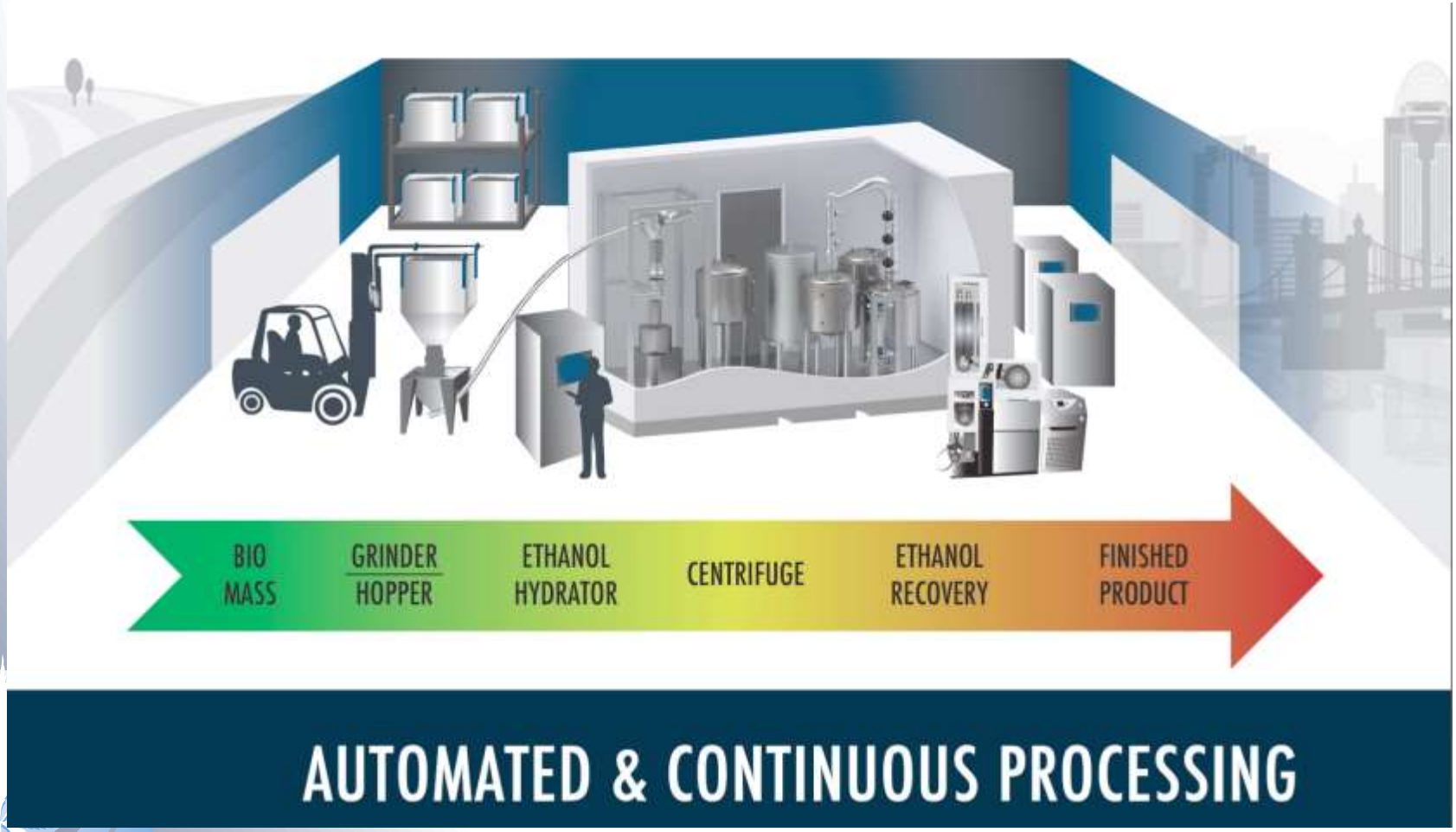
- High Throughput



# Hydrocarbon Extraction

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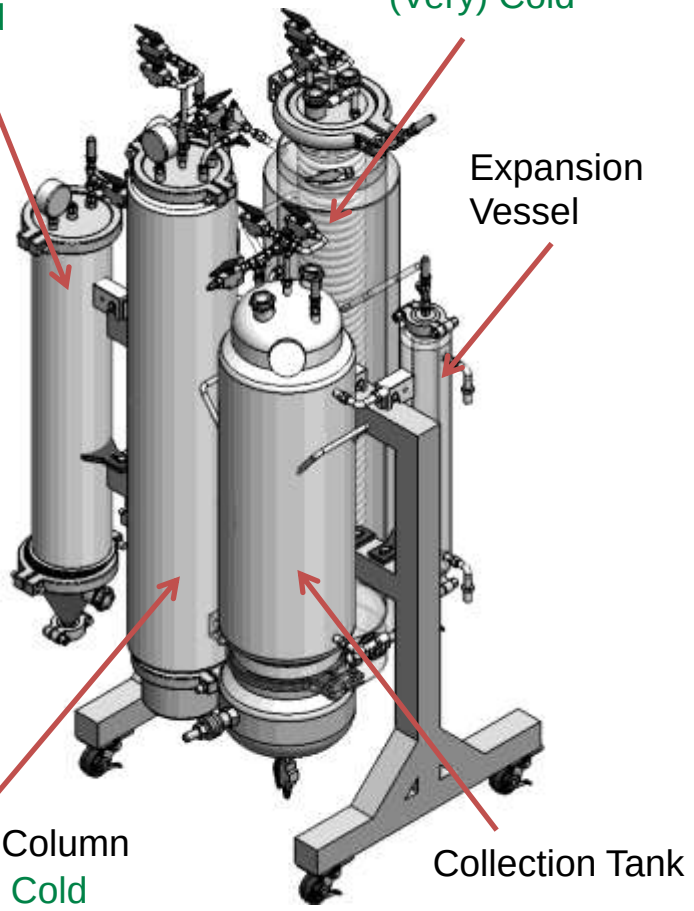
## Low to Medium Throughput

Key System Components:

- Extractor
- Low Temperature Chiller for Solvent Tank
- (Optional) low temperature chiller for Dewax
- Vacuum pump
- Nitrogen supply
- Heater for Collection Tank (not shown)
- Compressor and Condenser Coil (not shown)
- Chiller for Condenser Coil (not shown)

Simplified Workflow:

1) Evacuate
2) Purge with N2
3) Add & Cool Solvent in Holding Tank
4) Soak Material in Extraction Column
5) Filtration in filtration cone
6) Dewax
7) Solvent reclaim (distillation) in Collection Tank
8) Solvent collection in Expansion Vessel and external Condenser (not shown)



# Hydrocarbon Extraction

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- High Throughput

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# from Plant to Extract

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# Production Tools

## from Extract to API

Tobias Schappeler
Managing Director

# Typical Production Workflow

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| | |
|---|---|
| Terpene Extraction | Microwave, Steam, $CO_2$ |
| Drying | Hang Drying, Oven Drying, Vacuum Drying, Freeze Drying |
| Grinding / Milling<br>optional Size Verification | Cutting Mills<br>Sieve Shakers |
| Primary Extraction | $CO_2$, Hydrocarbon, Ethanol |
| Winterisation / Dewax | “Bucket&Freezer”, Chemical (Filter) Reactors |
| Filtration | Filter Press, Nutsche Filter, Filter Reactor |
| Ethanol Evaporation | Rotary Evaporators, Distillation Plants |
| Decarboxylation | Chemical Reactors, Decarb Ovens |
| Concentration | Wiped Film Evaporators |
| Isolate Production | FCPC Chromatography, Chemical Reactors |

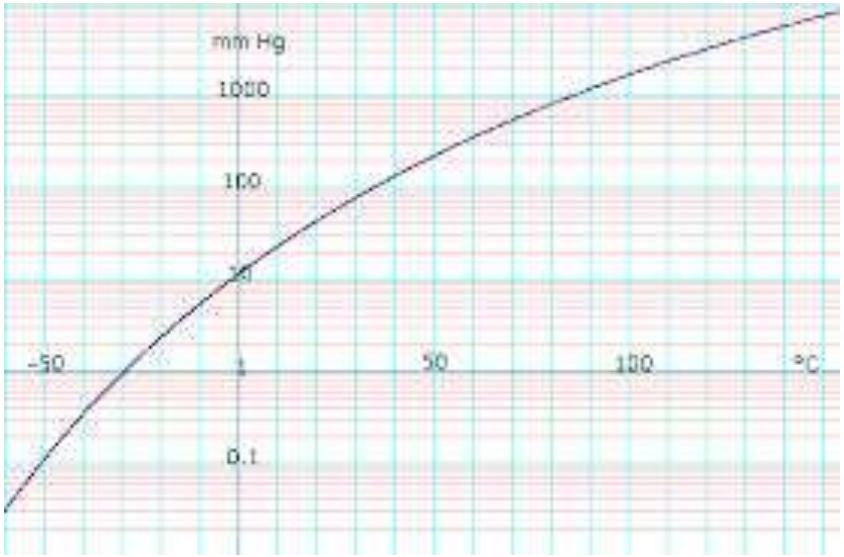
# Winterisation / Dewax

- What is it? Cold Precipitation / Liquid Liquid Chromatography

Dewax ➔ use of extraction solvent (mostly hydrocarbons)
Winterisation ➔ use of specific winterisation solvent (ethanol)

Simplified Ethanol Workflow:

1) Add ethanol into crude (10:1)
2) Stir (optional gentle heat to assist)
3) Cool to < -40C (industry standard)
4) Hold till separation happens
5) Syphon winterised oil
6) Filter as required

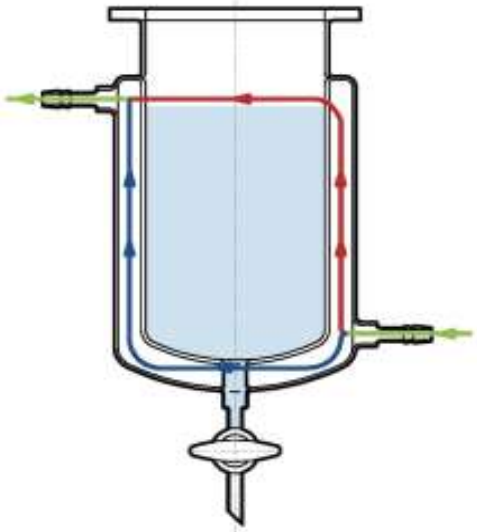



Most waxes start to solidify < +30C

# Winterisation

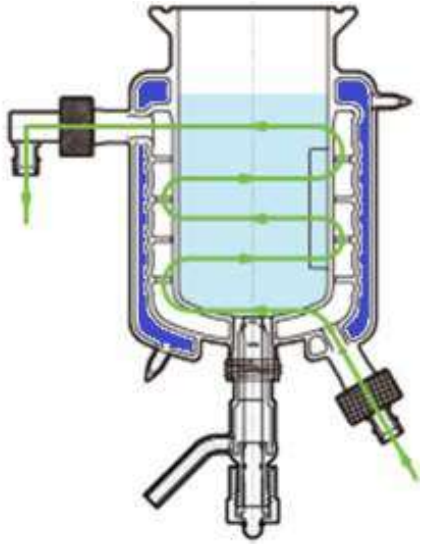
- “Bucket&Freezer”
  - ☺ Cheap
  - ☹ Slow
  - ☹ Manual
  - ☹ GMP?
- Chemical Reactor
  - ☺ Established technology in pharma
  - ☺ Typically 2x faster
  - ☺ Accurate process control
  - ☺ GMP
  - ☺ Scalable
  - ☺ Integrated Filtration saves time & labour
  - ☹ High Investment Cost

# Chemical Reactors



## Double Wall

- No insulation – will ice up or get hot
- Limited process visibility if insulated
- Requires stronger heaters and chillers
- Limited temperature range



## Tripple Wall

- Vacuum insulation protects staff
- Far superior performance
- Perfect process visibility
- Wider temperature range
- Save on thermoregulator cost

# Filtration


- Manual Small Batch / Lab Filtration shown (non GMP)

# Filtration

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- Nutsche Filter
  - ☺ Basic technology
  - ☺ Cheap (if not temperature controlled)
  - ☺ Scalable
  - ☹ Manual
  - ☹ Potential crystalisation (if not temp controlled)

- Filter Press
  - ☺ Very common in pharma and food
  - ☺ Separates solids & fats, waxes
  - ☺ Scalable
  - ☺ Good price point
  - ☹ Not viable for low throughput

- (Filter) Reactor
  - ☺ Versatile (winterization, filtration, decarb, isolate production)
  - ☺ Well established in pharma
  - ☺ Accurate process temperature control
  - ☺ Scalable
  - ☹ High investment

# Ethanol Reclaim

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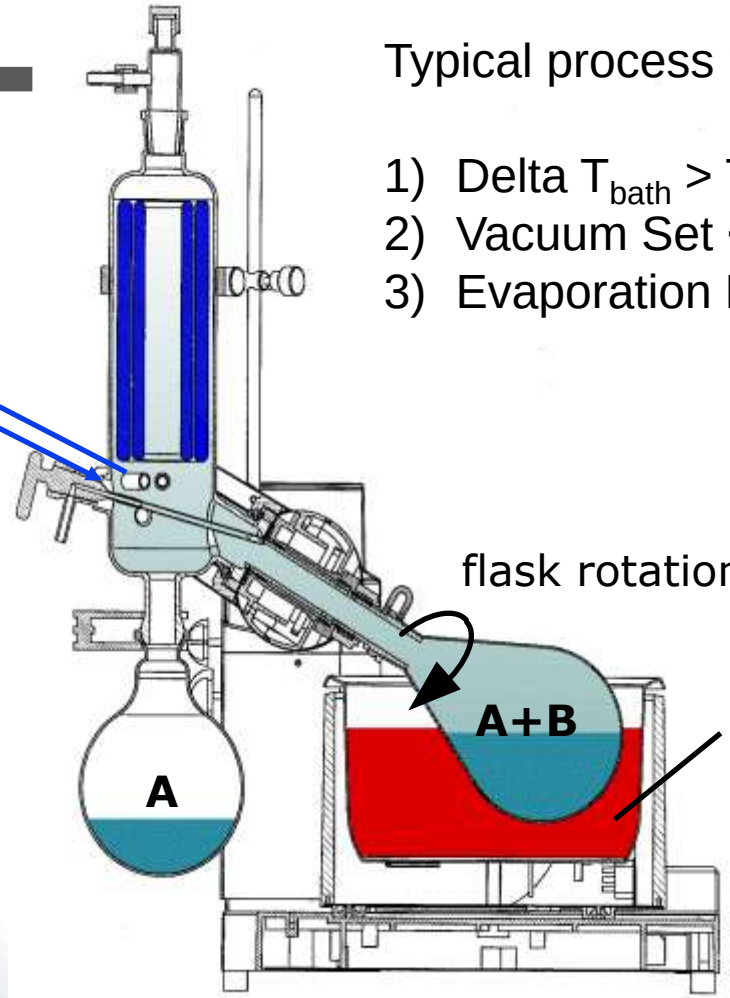
## Rotary Evaporation

- ☺ Industry Standard
- ☺ GMP
- ☺ Relatively fast - up to 25l/h for 100l
- ☺ Automated process controls
- ☺ 24/7 continuous evaporation solutions
- ☺ Extremely reliable (if top brand)
- ☺ Small footprint, easy on facility
- ☺ Low capital investment

## Falling Film, Short Path

- ☺ Scalable for highest throughput
- ☺ GMP
- ☺ Very fast - commonly > 100 l/h
- ☺ Less operators needed (compared to multi evaps)
- ☹ Generally requires explosion protection
- ☹ Significant investment (> 4 rotary evaporators)

# Rotary Evaporation




Typical process parameters:

1) Delta $T_{bath}$ > $T_{chill}$ = >40C
2) Vacuum Set < 450 mbar
3) Evaporation Flask Speed 50-100 rpm

# Rotary Evaporation

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Simplified Crude Oil Mix Workflow:

1) Start chiller and heating bath
2) Load winterised oil mix into evaporation flask
3) Start process program
4) Complete batch or add more product
   (manually or automatically)
5) Harvest cannabis oil
6) Drain waste receivers
7) Cleaning protocol
   1) Clean flask
   2) Cleaning solvent run (ethanol)
   3) Potential purified water run as required

# Rotary Evaporation


- Capacity & Cost Considerations:

  20l rotary evaporator = 14l per hour throughput
  50l RE = 20l per hour
  100l RE = 25l per hour

  2 x 20l RE cost similar to 1 x 100l but gain production uptime protection
  Continuous feed options to save operator cost and enable 24/7 runs

- Tech Considerations:

  Chiller spec (at coolant temperature!) must equal or better RE heater spec
  Chiller pump speed matters – faster is better

  Only use corrosion resistant chemistry diaphragm vacuum pumps
  ➔ ethanol attacks many elastomers (seals) used in other pumps

  Consider amount of Ethanol processed for potential EX protection

# Falling Film Evaporation

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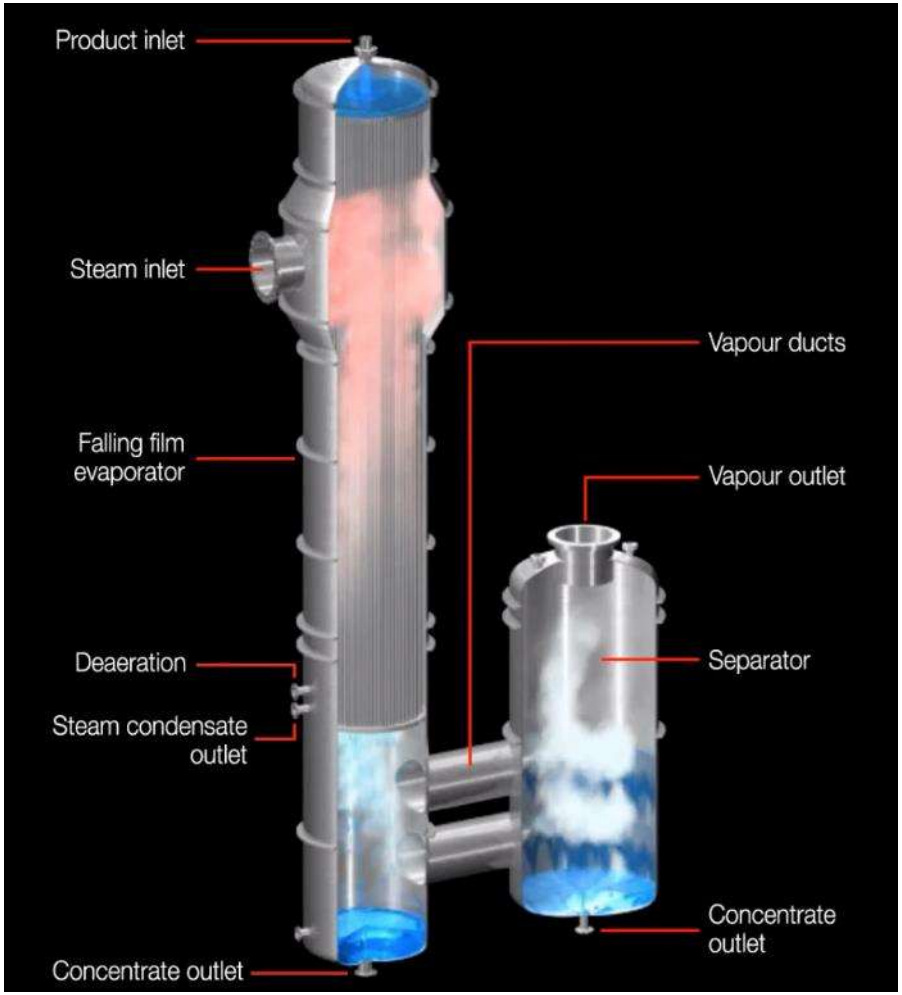


Heating & Cooling:

Small Production Scale
= Thermoregulators

Industrial Scale
= Steam and plant cooling water

- Process Parameters similar to Rotary Evaporator

# Decarb Technologies

- Question: When to best decarb in production?
- Decarb Oven (buds)

  - ☺ Straightforward Technology
  - ☺ Inexpensive
  - ☹ Labour intensive (loading&unloading, bagging)
  - ☹ Slow
- Vacuum Oven (buds) — Dry & Decarb in one combined process
  - ☺ Save space and money
  - ☺ Dual use of equipment
- Chemical Reactor (crude or distillate) — Decarb crude or distillate

  - ☺ Typically 2-3x faster than oven based decarb
  - ☺ Process much smaller volumes (post extraction)
  - ☺ Far superior process temperature uniformity
  - ☺ Save labour on bag / dish filling & transfers, cleaning…
  - ☺ Established pharma technology, so easy to validate
  - ☺ Connect directly to rotary evaporator or process flow
  - ☹ Investment

# Decarb Technologies

- Decarb & Vacuum Oven (buds)

Simplified Workflow:

1) Fill flower into drying bags
2) Place bags into oven
3) Start drying process
4) Allow cool down (naturally)
5) Remove bags & empty
6) Clean

- Chemical Reactor (crude or distillate)

Simplified Workflow:

1) Fill reactor
2) Start process (2-3 times faster)
3) Force cool down (thermoregulator)
4) Drain oil
5) Clean

# Distillation / Concentration

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- Thin Film vs Short Path Evaporation vs Molecular Distillation
  WARNING INDUSTRY CONFUSION!

Wiped Film Evaporation
often called Thin Film
GMP - yes

Short Path Evaporation
often confused with
Wiped Film
GMP - yes

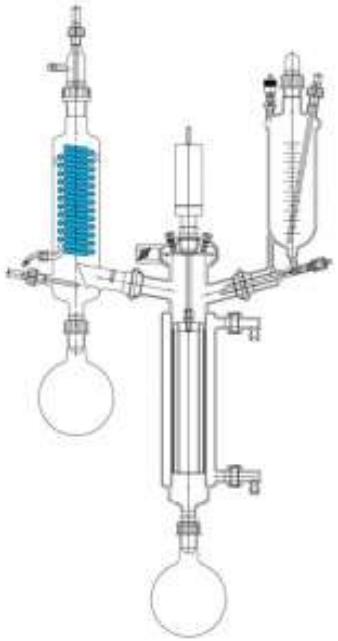
Molecular Distillation
often confused with
Short Path
GMP ??

# Concentration

- Wiped Film Evaporation vs Short Path Evaporation

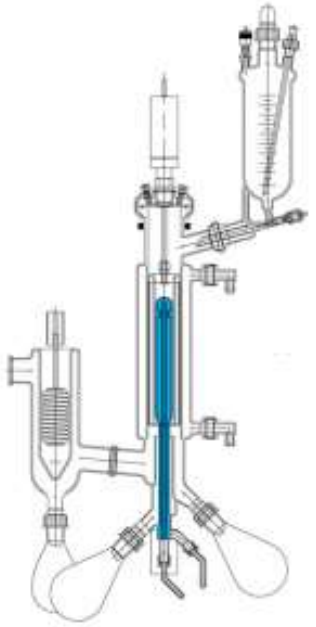
Common:

- Internal wiper to increase product surface area
- Very short product dwell times protect product integrity
- High temperatures
- Low vacuum



Wiped Film
External Condenser

- Lower price
- Less throughput



Short Path
Internal Condenser

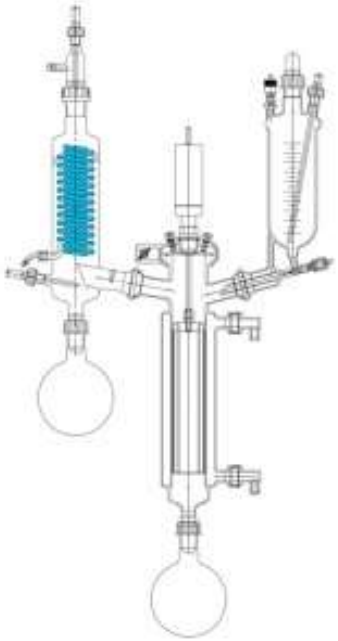
- Higher price
- Better throughput
- Better vacuum

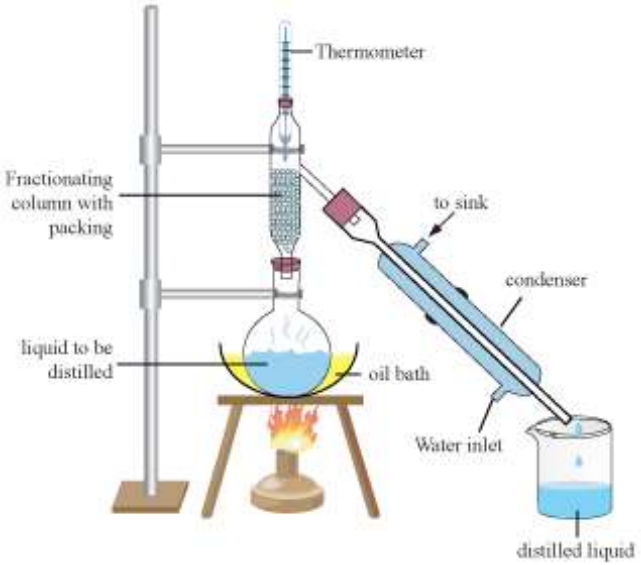
# Concentration

- Wiped Film Evaporation vs Molecular Distillation

Common:

- High temperatures
- Low vacuum






## Wiped Film & Short Path

- Far superior throughput
- Short dwell time protects product
- Automation available
- GMP

## Molecular Distillation

- Slow
- Manual
- Extended product high temperature exposure (can cause product breakdown)

# Concentration

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- Wiped Film Evaporator


☺ Best performing concentration tech for the job
☺ Standard technology in cannabis (and pharma)
☺ GMP
☺ Scalable to highest throughput
☺ Protects cannabinoid integrity

☹ All product exposed surfaces require heating to avoid condensation / crystalisation
☹ Relatively high maintenance (to vacuum system)
☹ If built without CIP, regular cleaning is labour intensive
☹ High investment (especially for GMP)

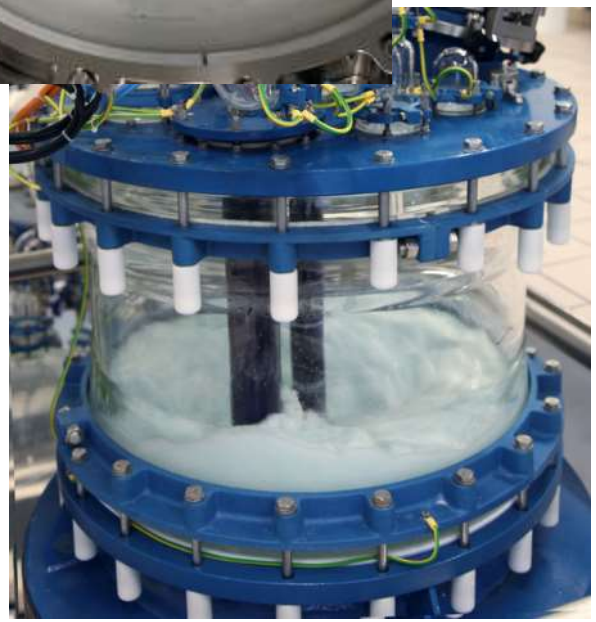
- Note US Recreational Market Prices
  CBD Crude (Winterised) = US $ 1,500 - $ 2,000 per kg
  CBD Distillate = US $ 4,000 – $ 6,000 per kg

US $750K for full GMP machine @ 2K extra income per kg = 375 kg
(calculation simplified)

# Isolate Production

- Crystalisation in Chemical Reactors

☺ Purity >95%
☺ Precipitation in chemical reactor
☺ GMP
☺ Relatively cheap and simple process
☹ High solvent consumption
☹ Crystals need to be purged to remove residual

Simplified Workflow:

1) Add distillate
2) Add solvent matrix (often proprietary)
3) Gently heat and stir till homogenious
4) Gently stir and cool
5) Stop stirring and hold cold temperature
6) Hold to await crystalisation
7) Filter crystals from solvent matrix
8) Purge crystals in vacuum ovens

# Isolate Production

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## Chromatography (Column, Solid Phase)

- ☺ Well established and understood
- ☺ Scalable from lab to production
- ☺ Purity >95 – 99.9%
- ☹ Solid column packing material which is expensive to buy, replace, re-process and dispose
- ☹ Risk of poor separation results due to inconsistent column packing
- ☹ Cartridge changeover (if pre-packed columns are used)

## Fast Centrifugal Partition Chromatography


- ☺ 3-5 times faster than column chromatography
- ☺ 10-20% typical lower solvent consumption
- ☺ Near zero product loss in the solid phase
- ☺ No denaturation risk for fragile molecules due to interaction with solid phase
- ☺ No solid column packing material, which is expensive to buy, replace, re-process and dispose
- ☺ Consistent separation results due to elimination of inconsistent column packing

# FCPC Basics

- Preparative (meaning large volume) chromatography technique
- Bi-phase solvent system (2 non miscible phases)
- Separation and elution of compounds based on partition between the two liquid phases
- Stationary phase is maintained inside the column through centrifugal force
- Mobile phase travels through stationary phase
- Countless parameters to work with – FCPC is extremely versatile

Cell

Disc

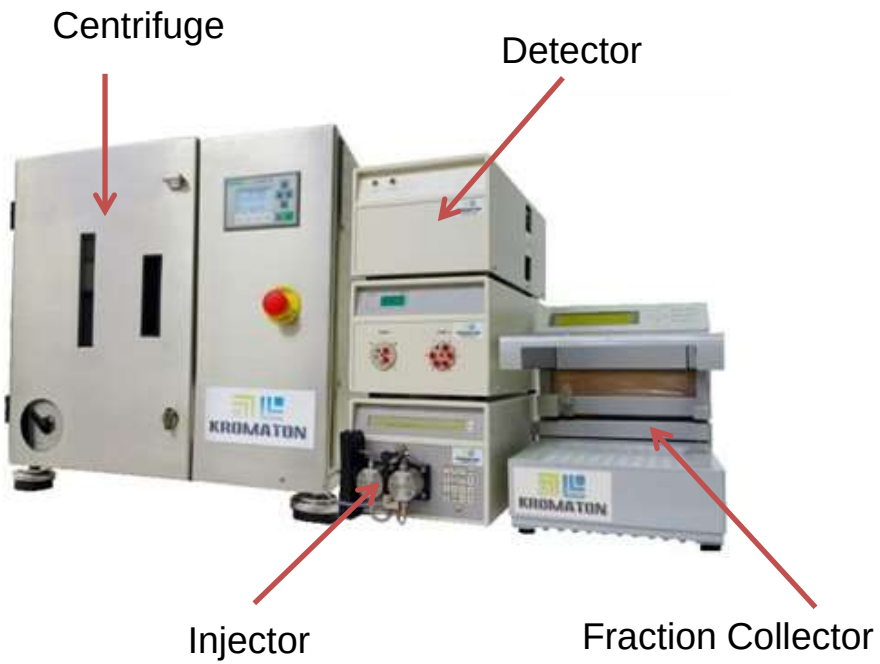
Column

- No1 Application – THC knockout from full spectrum

# FCPC Basics

Simplified Workflow:

1) Prepare stationary phase matrix
2) Take winterised crude or distillate
3) Dissolve in mobile phase solvent matrix
4) Inject
5) Separate in centrifuge
6) Detect fractions
7) Divide fractions
8) Collect



# Final Words

- When making equipment / tool decisions
  - Consider best tools for your specific product – there are many options
  - Start from your final product and work backwards
  - Ensure key local (ANZ) standards are met (for example)
    - AS/NZ 3000 Wiring Rules
    - AS1210 Pressure Vessel
    - ASNZEx / IECEx Explosion Protection
  - Important pharma industry standards / regulatory requirements (e.g)
    - GMP
    - PIC/S
    - CFR 21 P 11/ PICS Annex 11
  - Protect your revenue through partnering with a local supplier who
    - Has experience with equipment import, installation and ongoing training
    - Assists with local certifications and registrations as required
    - Provides local engineering support
    - Consider lifetime cost, not only buy price
    - Consider downtime cost and service response times from overseas suppliers

# Thank you!

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