

THE EMERALD CONFERENCE

Produced by MJBizScience

Purification of Cannabis Extracts using Polysaccharide-Based 'Nanosponge' Adsorbents

Dr. Christopher J. Cordier, PhD

Head of Chemistry Research, Grow Biotech LTD

Grow Group PLC

chris.cordier@growbiotech.com

Cannabis Extract Purification



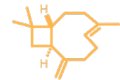
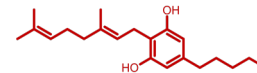
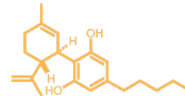
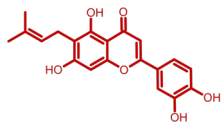
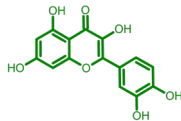
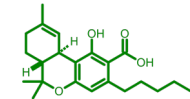
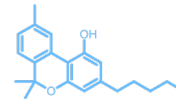
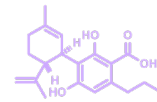
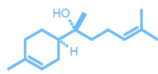
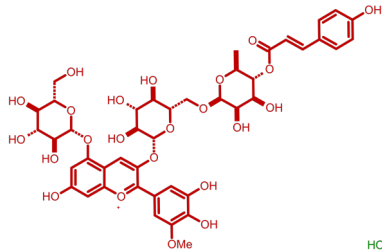
crude extract



refined oil



active ingredient



Cannabis Extract Purification



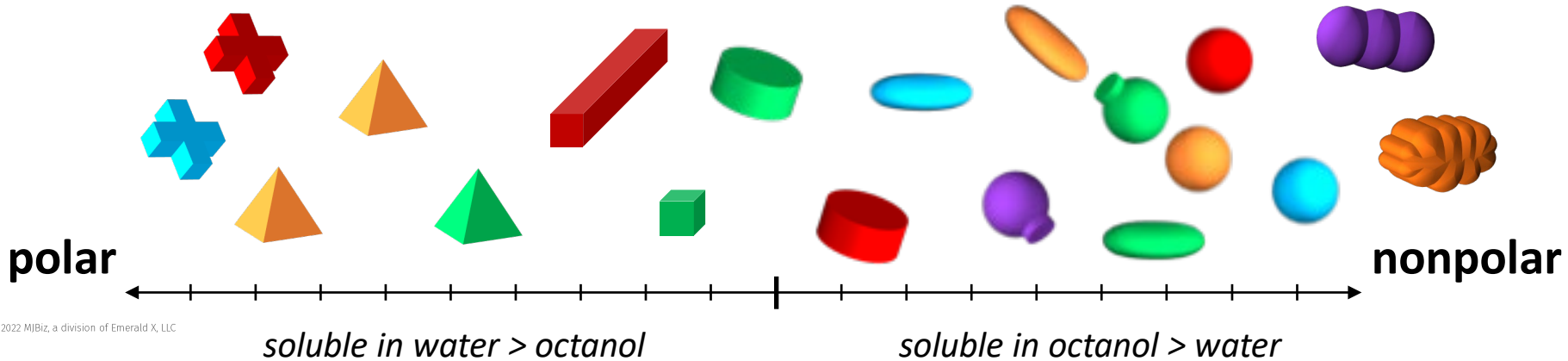
crude extract



refined oil



active ingredient



Cannabis Extract Purification



Advanced Machinery



Energy Intensive



Multi-Stage



Time Considerations



Expensive



Special Understanding



Highly Trained Staff



Cannabis Extract Purification



Advanced Machinery



Energy Intensive



Multi-Stage



Time Constraints



Expensive



Special Understanding



Highly Trained Staff



Cost



Reversible



Operationally Simple



Reusable



Tuneable



Targeted



Low Tech Kit



Complementary

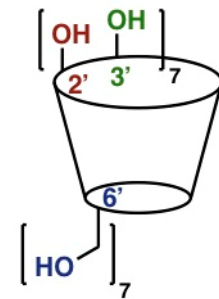
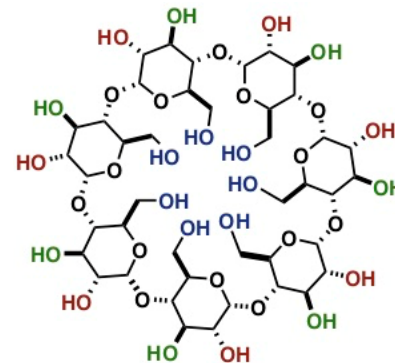
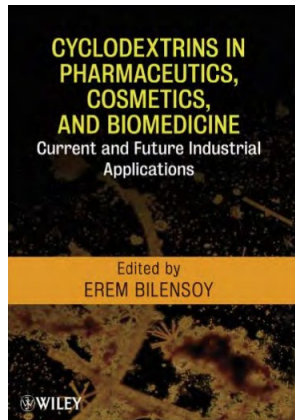
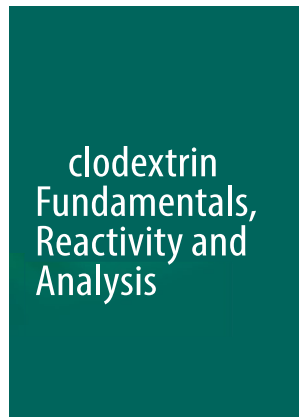
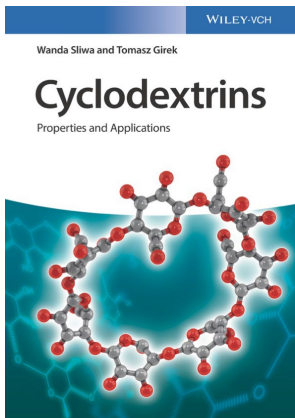


Scalable



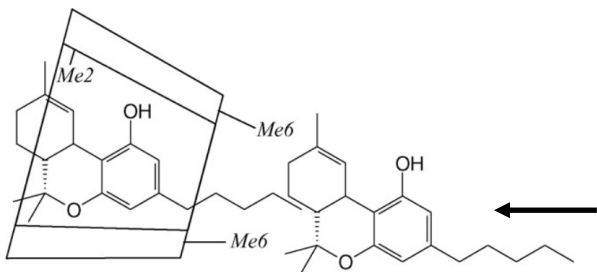
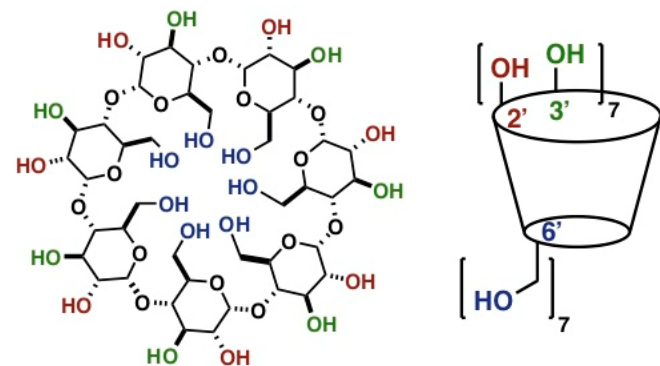
Cyclodextrins: Guest–Host Platform

- Hydrophobic core, H-bonding periphery
- Encapsulation of lipophilic drugs
- β -Cyclodextrin is cheap & ready available



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- Encapsulation of lipophilic drugs
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- **CD-Cannabinoid complexes known**
 - **Δ^9 -THC, Δ^8 -THC, CBD: Enhanced stability**

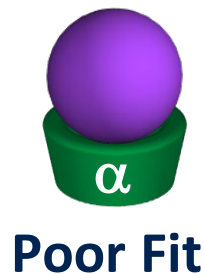
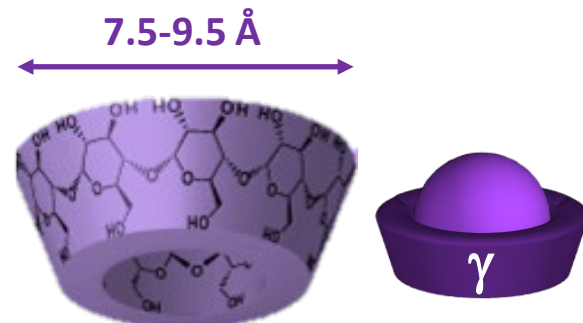
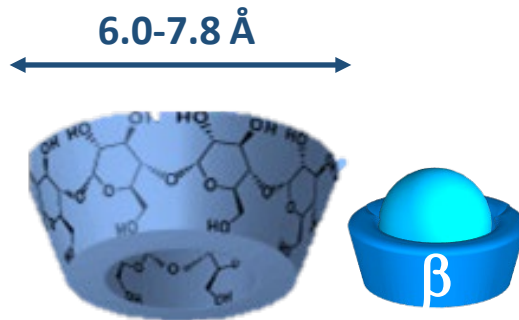
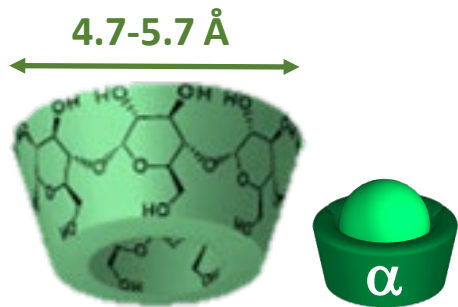


Seminal: Preparation and Stability of Δ^9 -THC- β -Cyclodextrin Complex
Shoyama et al.
J. Nat. Prod. **1983**, 633

Detailed Study: Structural elucidation of Δ^9 -THC-RAMEB Complex
Hazekamp et al.
Eur. J. Pharm. Sci. **2005**, 340

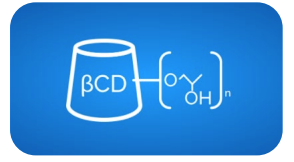
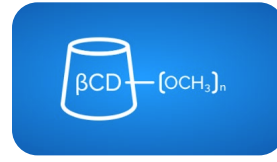
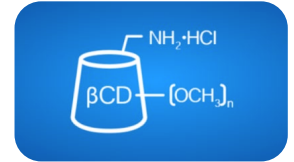
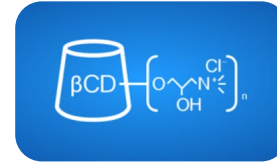
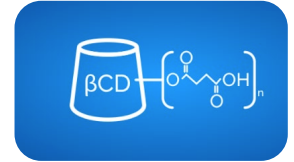
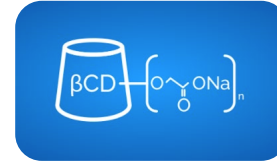
Cyclodextrins: Guest–Host Platform

- Hydrophobic core, H-bonding periphery
- Encapsulation of lipophilic drugs
- β -Cyclodextrin is cheap & ready available
- CD–Cannabinoid complexes known
- **Ring diameter is tuneable**



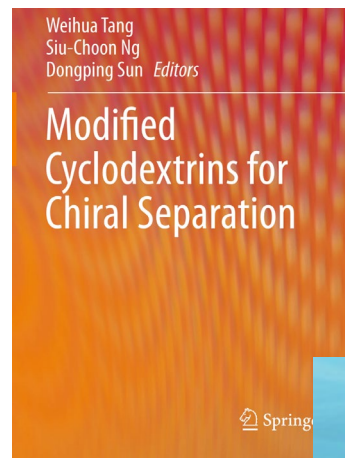
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- Ring diameter is tuneable
- **Derivatization is well-established**
 - **Alkylated**
 - **Acylated**
 - **Anionic / Acidic**
 - **Cationic / Basic**



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- Derivatization is well-established
- **Polymeric & matrix-supported forms are known**
 - **Silica-supported (HPLC)**
 - **Cross-linked forms (Water Treatment)**



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- Derivatization is well-established
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Cost 

Reversible 

Operationally Simple 

Reusable 

Tuneable 

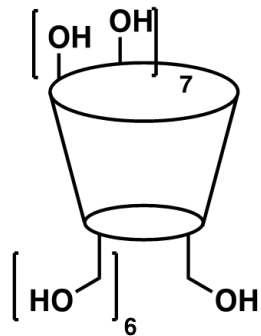
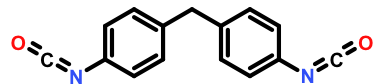
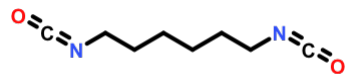
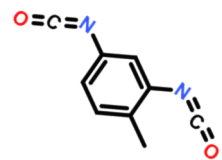
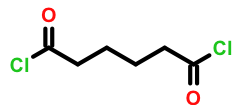
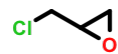
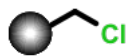
Targeted 

Low Tech Kit 

Complementary 

Scalable 

Cyclodextrin Polymer Synthesis

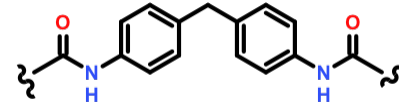
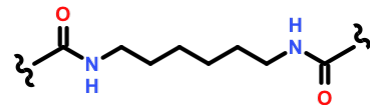
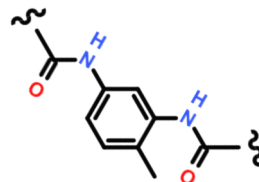
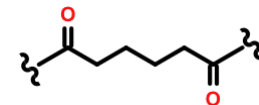
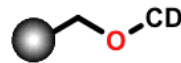
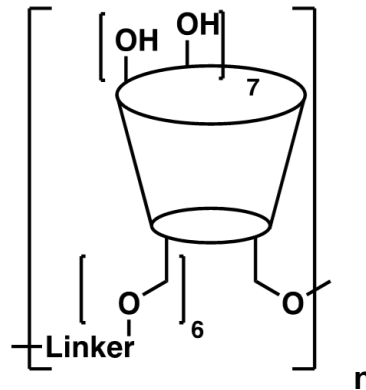


1. Cross-link / Immobilize



2. Filter, Wash, Dry

3. Form powder or bead



<75 μm



<400 μm

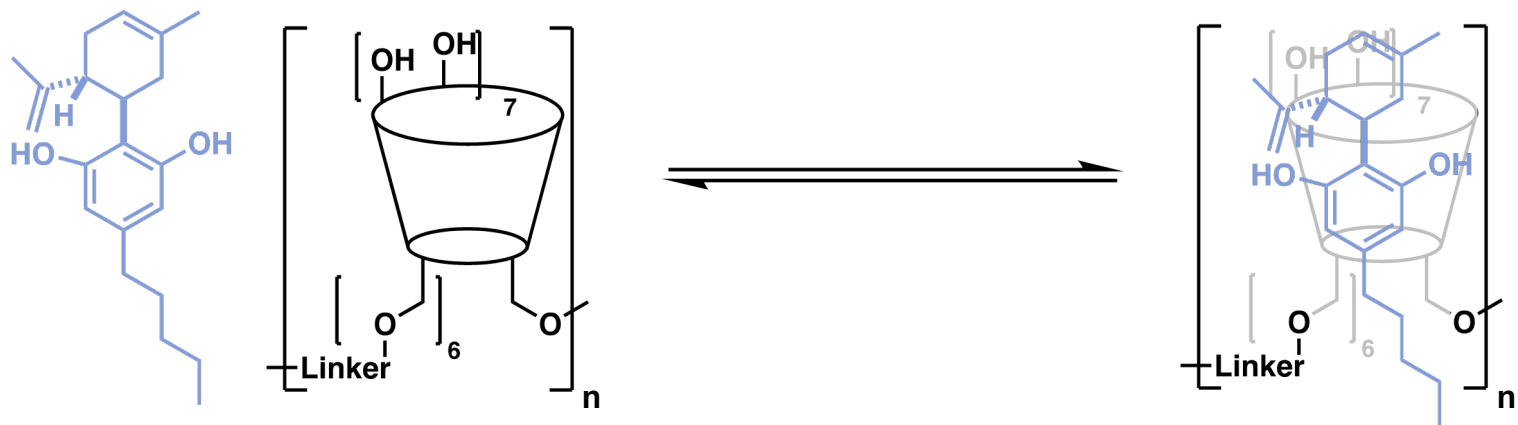


<1 mm

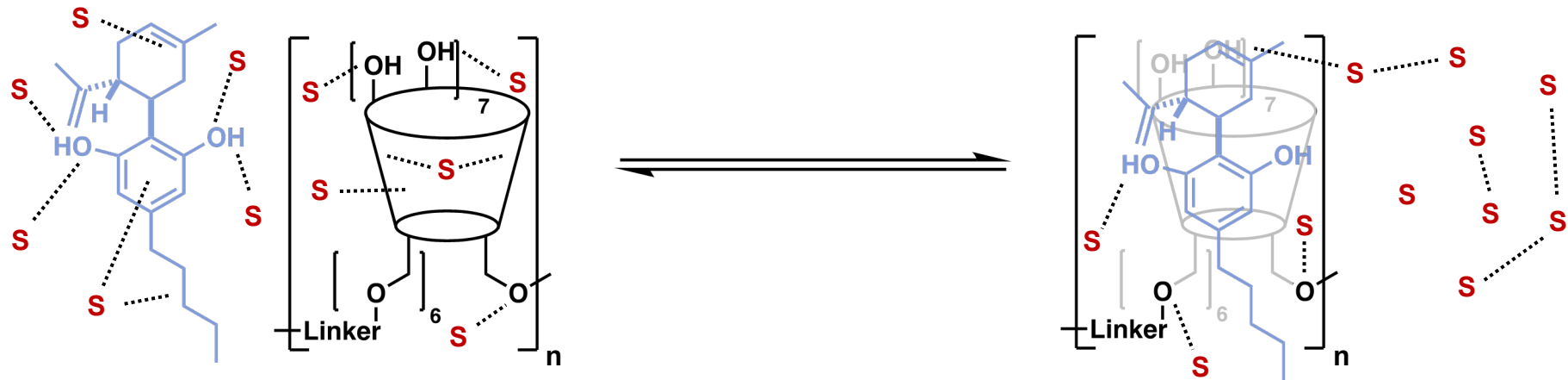


<5 mm

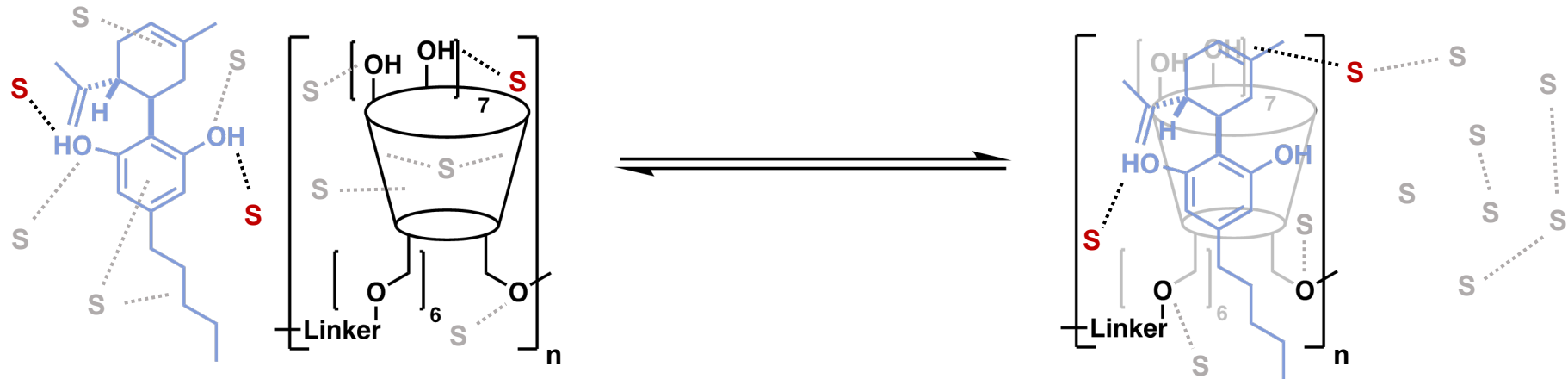
Cyclodextrin Guest–Host Equilibria



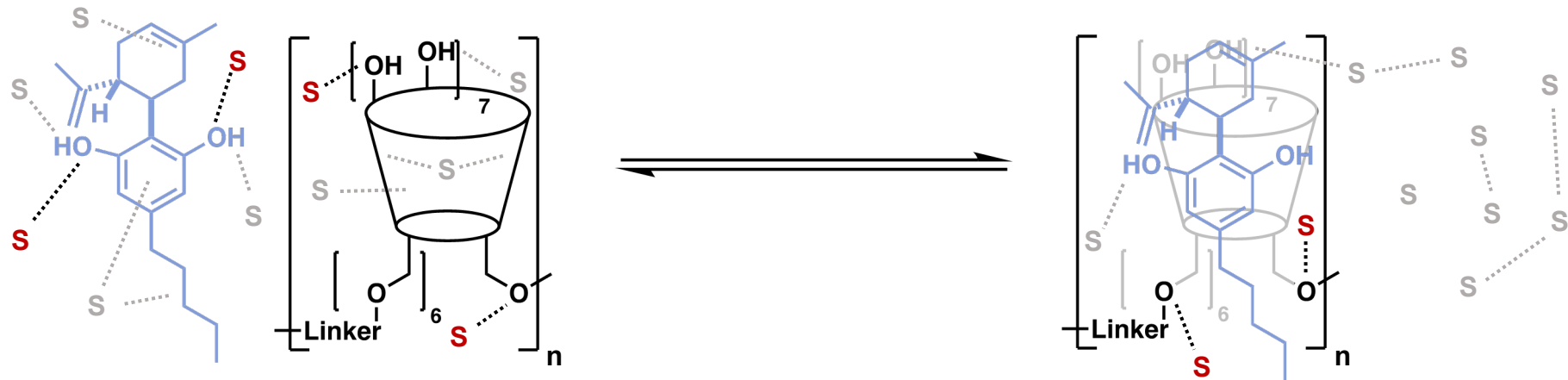
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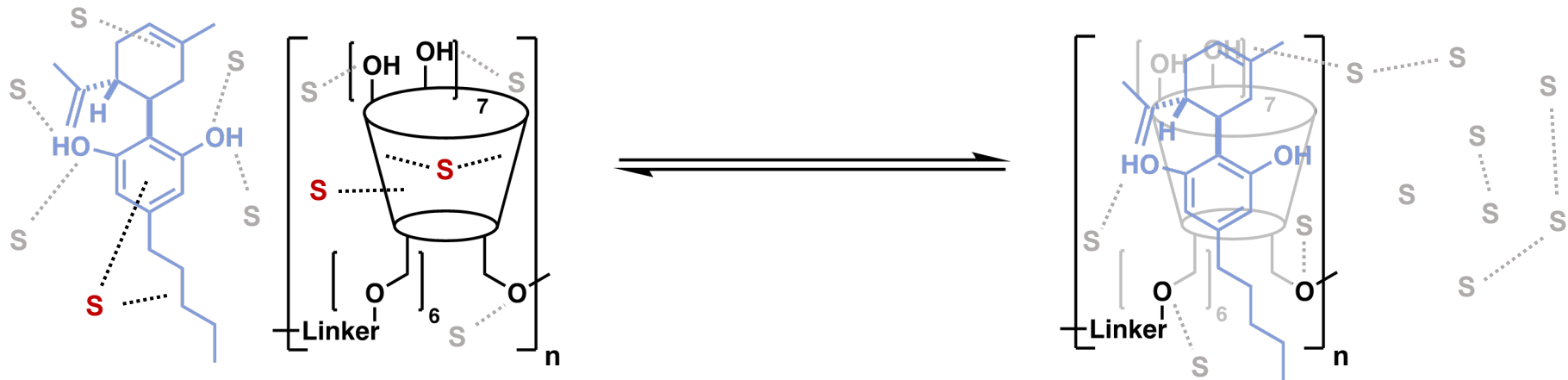
Cyclodextrin Guest–Host Equilibria



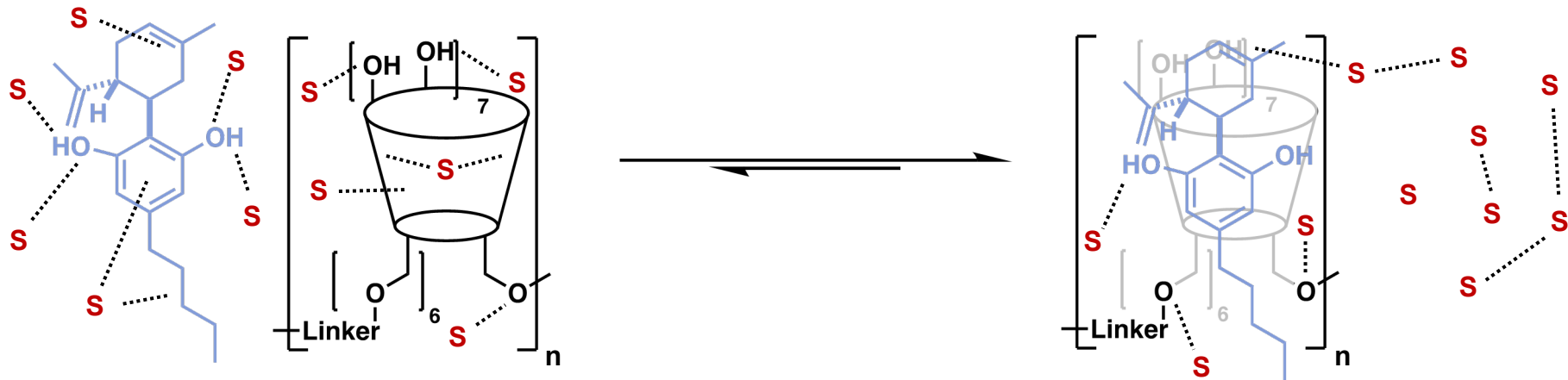
Cyclodextrin Guest–Host Equilibria



Cyclodextrin Guest–Host Equilibria



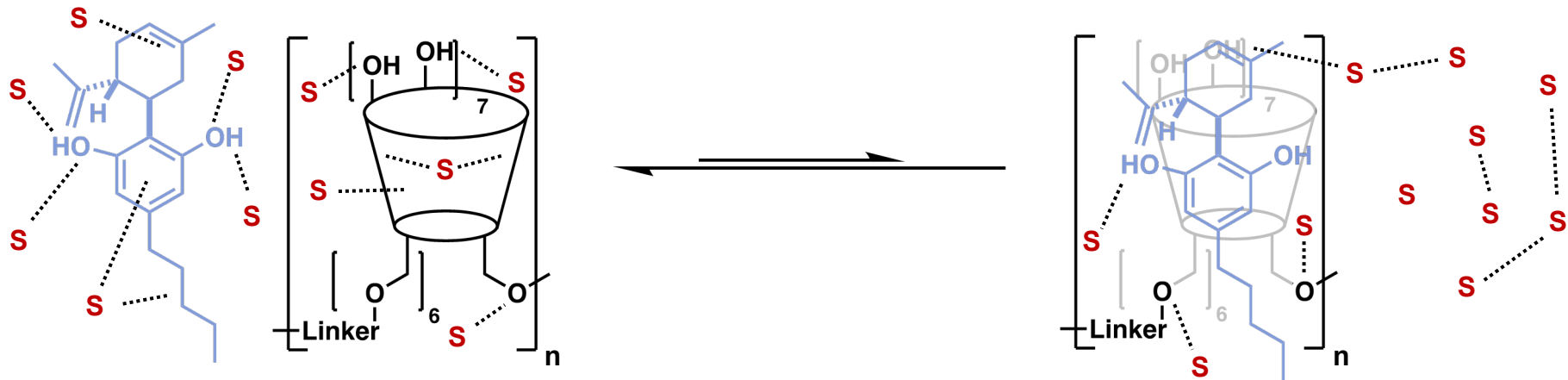
Cyclodextrin Guest–Host Equilibria



Solvent Considerations:

- Solvent choice will affect position of equilibrium
- “Poor” solvent will promote binding

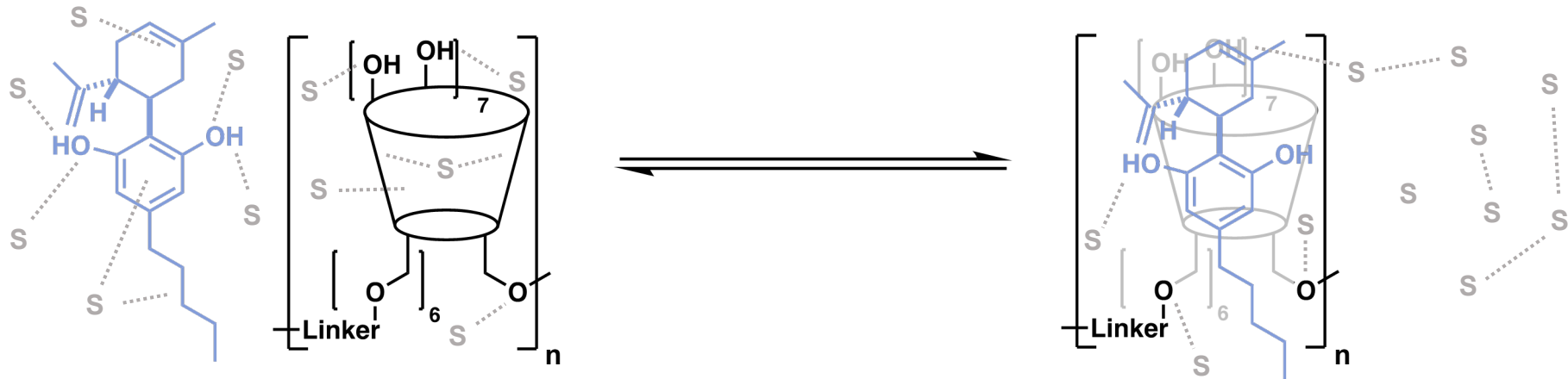
Cyclodextrin Guest–Host Equilibria



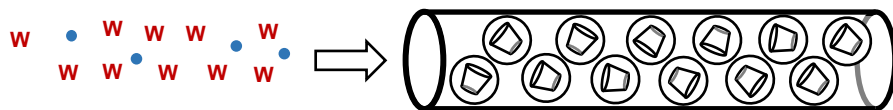
Solvent Considerations:

- Solvent choice will affect position of equilibrium
 - “Poor” solvent will promote binding
 - “Good” solvent will dissociate CBD

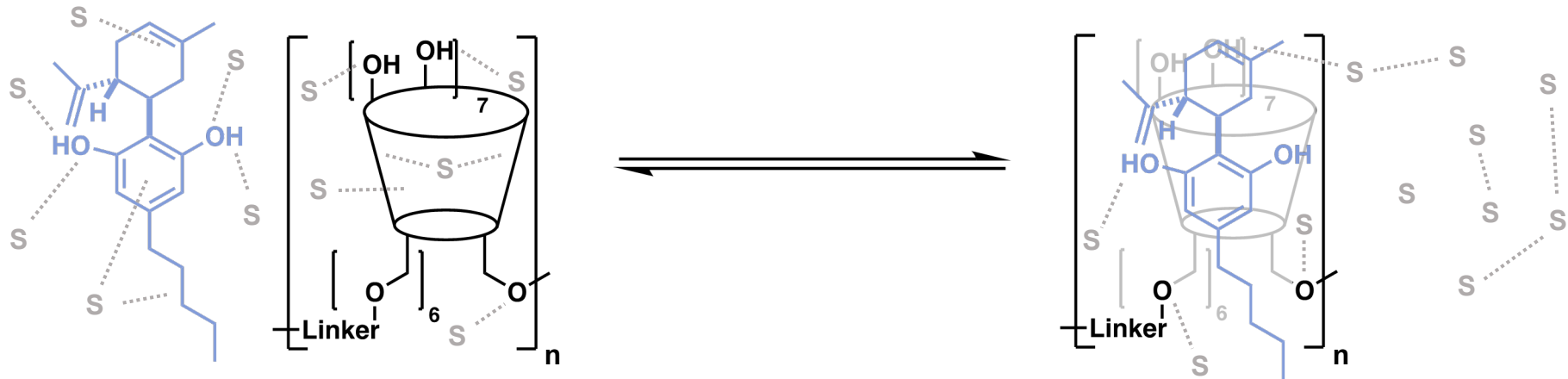
Protocol Design & Proof-of-Concept



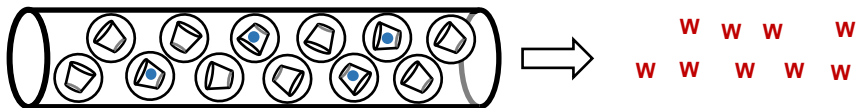
Water Purification Protocol



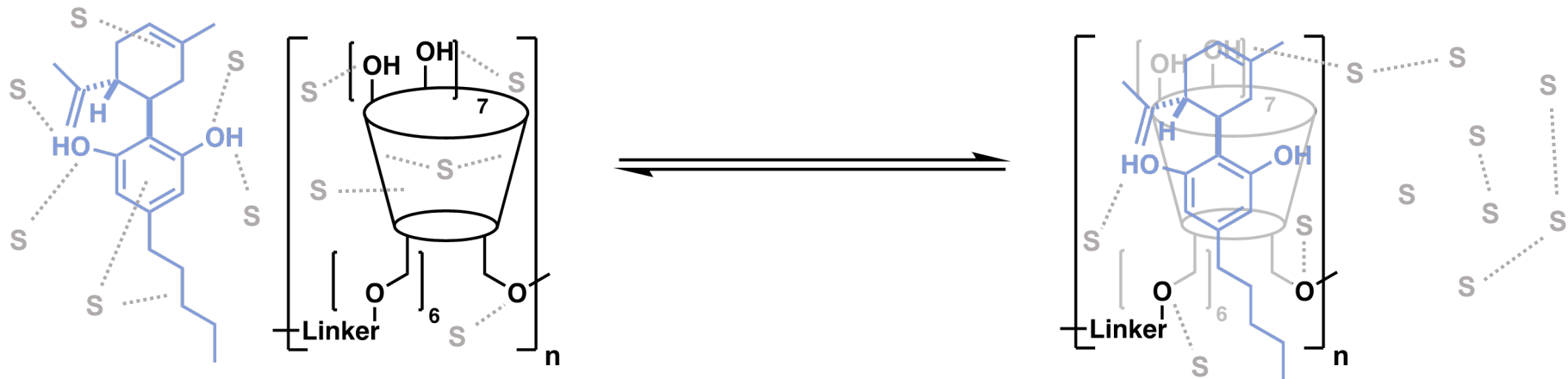
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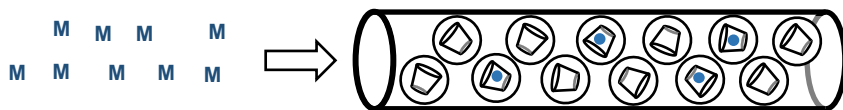
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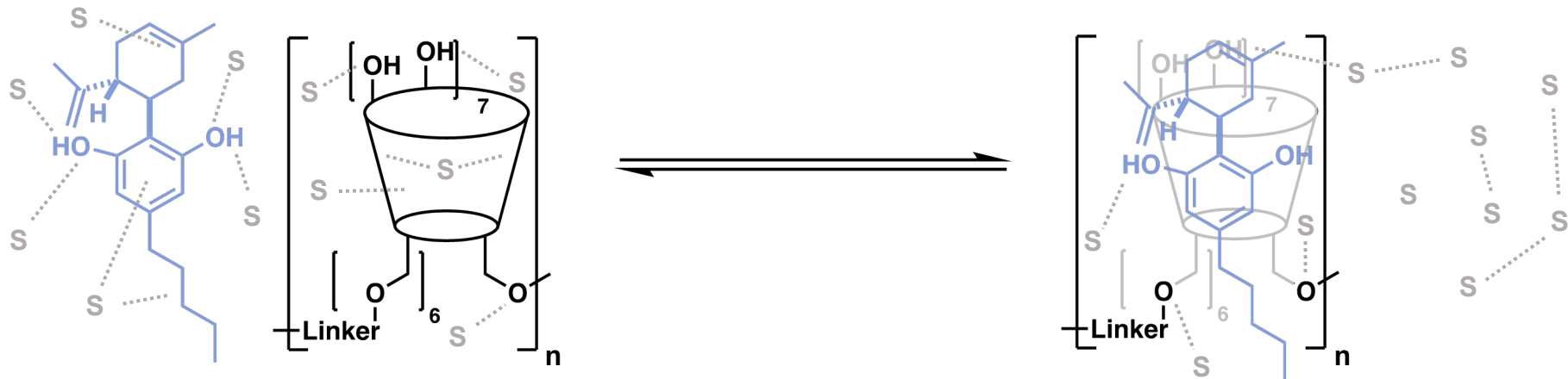
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Water Purification Protocol



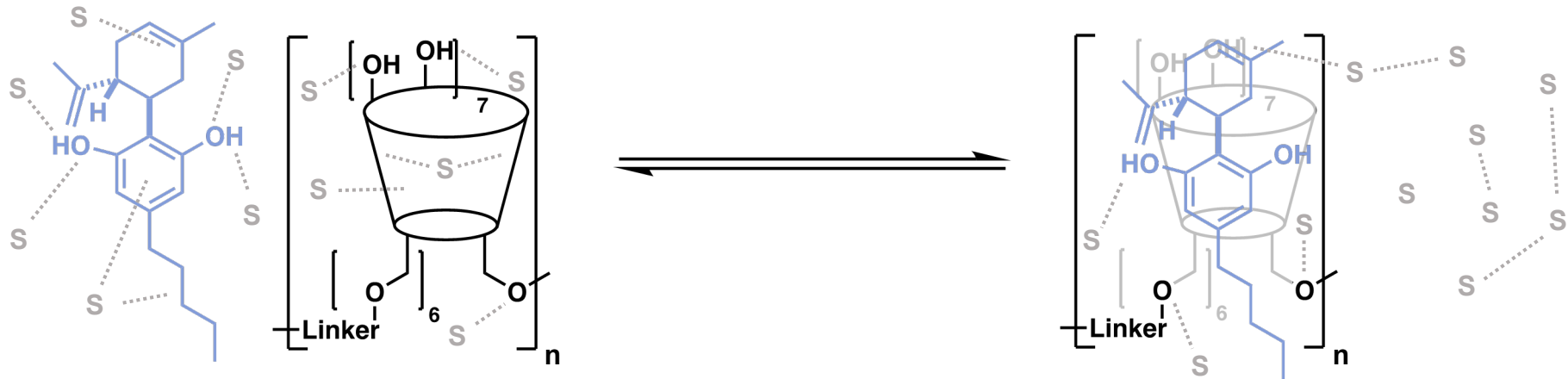
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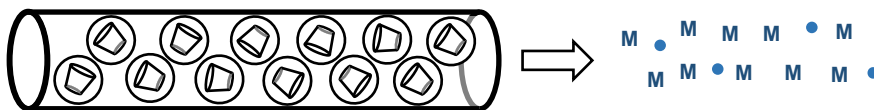
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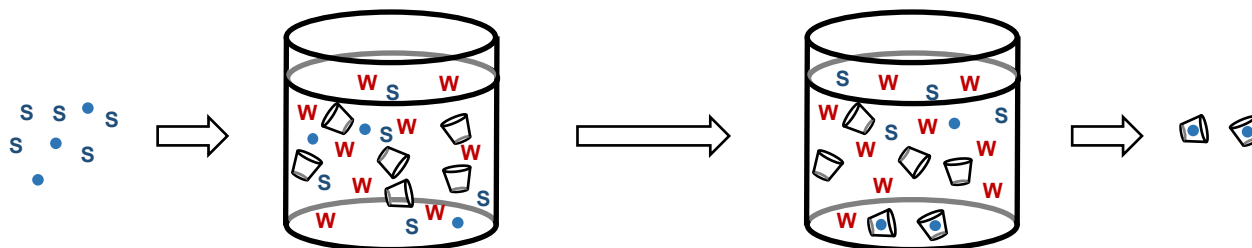
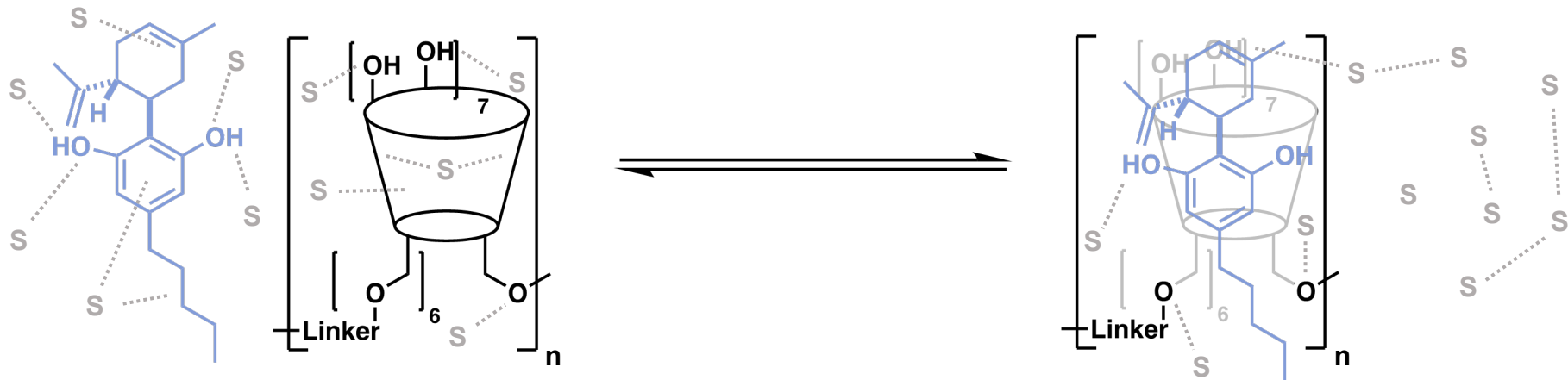
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Water Purification Protocol

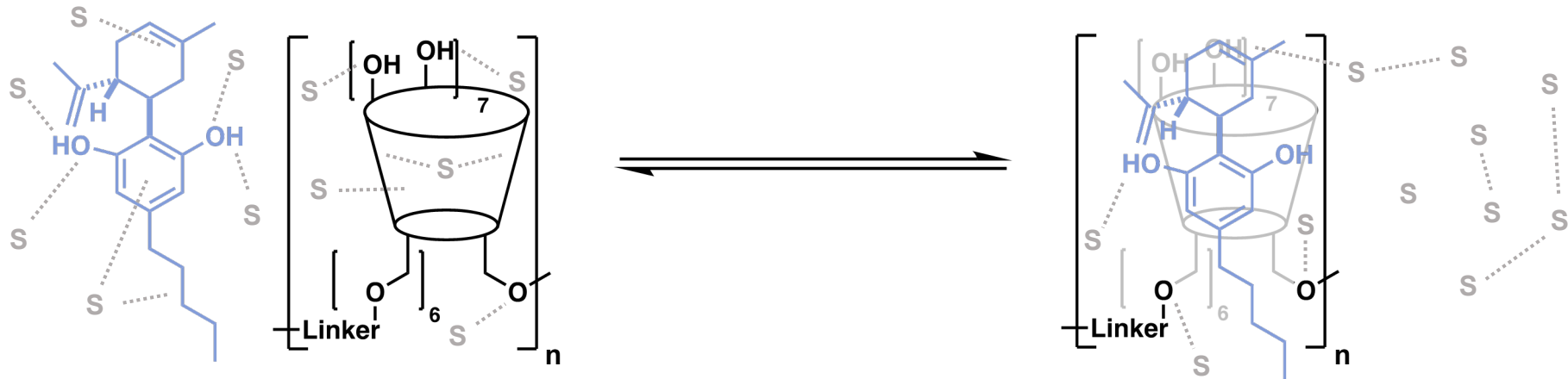


Protocol Design & Proof-of-Concept



Complex Precipitation Protocol

Protocol Design & Proof-of-Concept

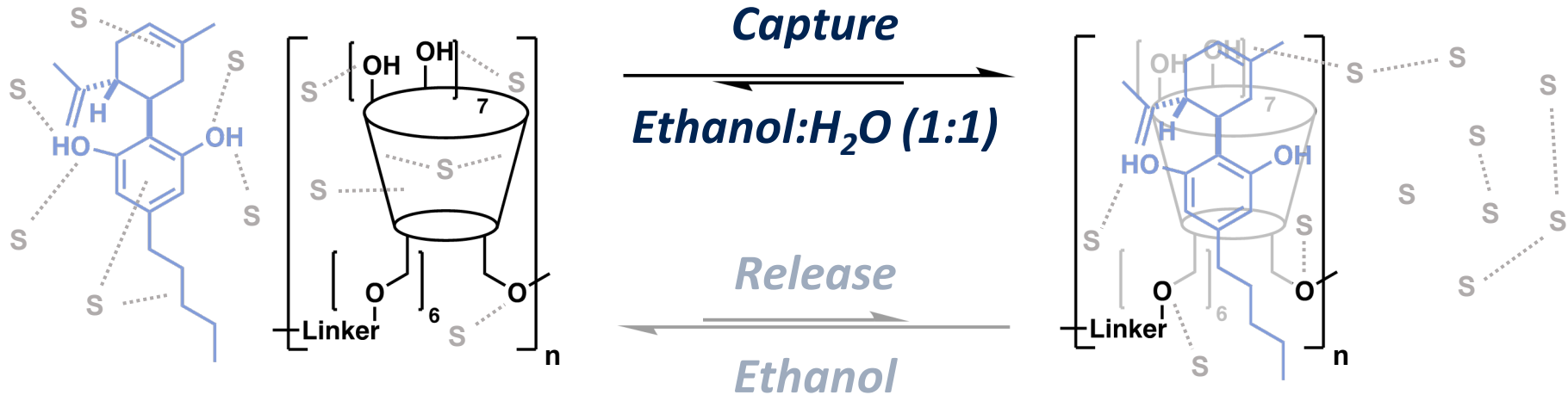


>95
85

Ethanol
Ethanol:H₂O (1:1)

<5
15

Protocol Design & Proof-of-Concept

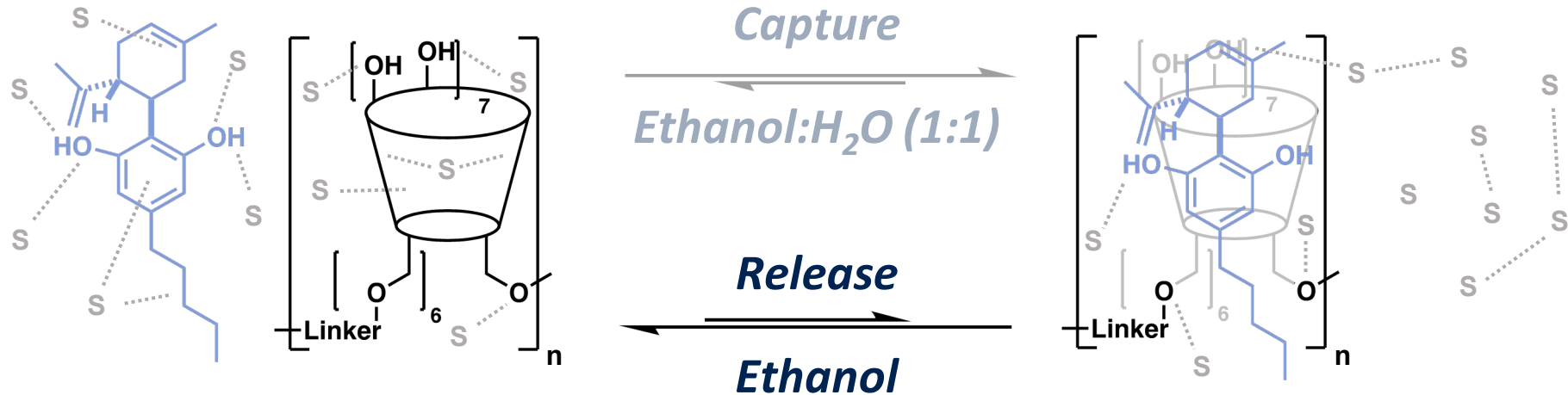


**>95
85**

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Protocol Design & Proof-of-Concept

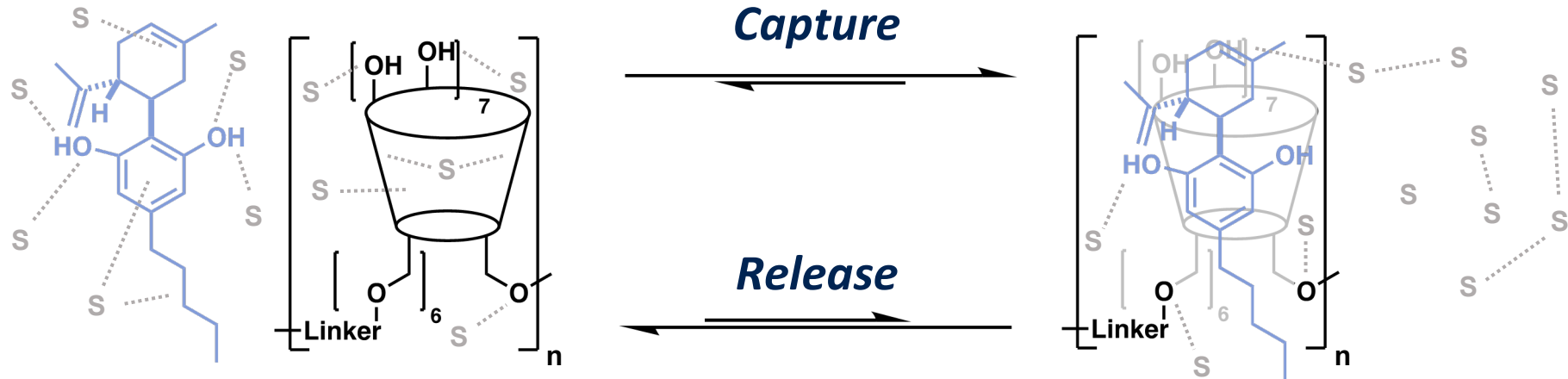


>95
85

Ethanol
Ethanol:H₂O (1:1)

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Protocol Design & Proof-of-Concept



Early Studies

Fast (5-15 min)

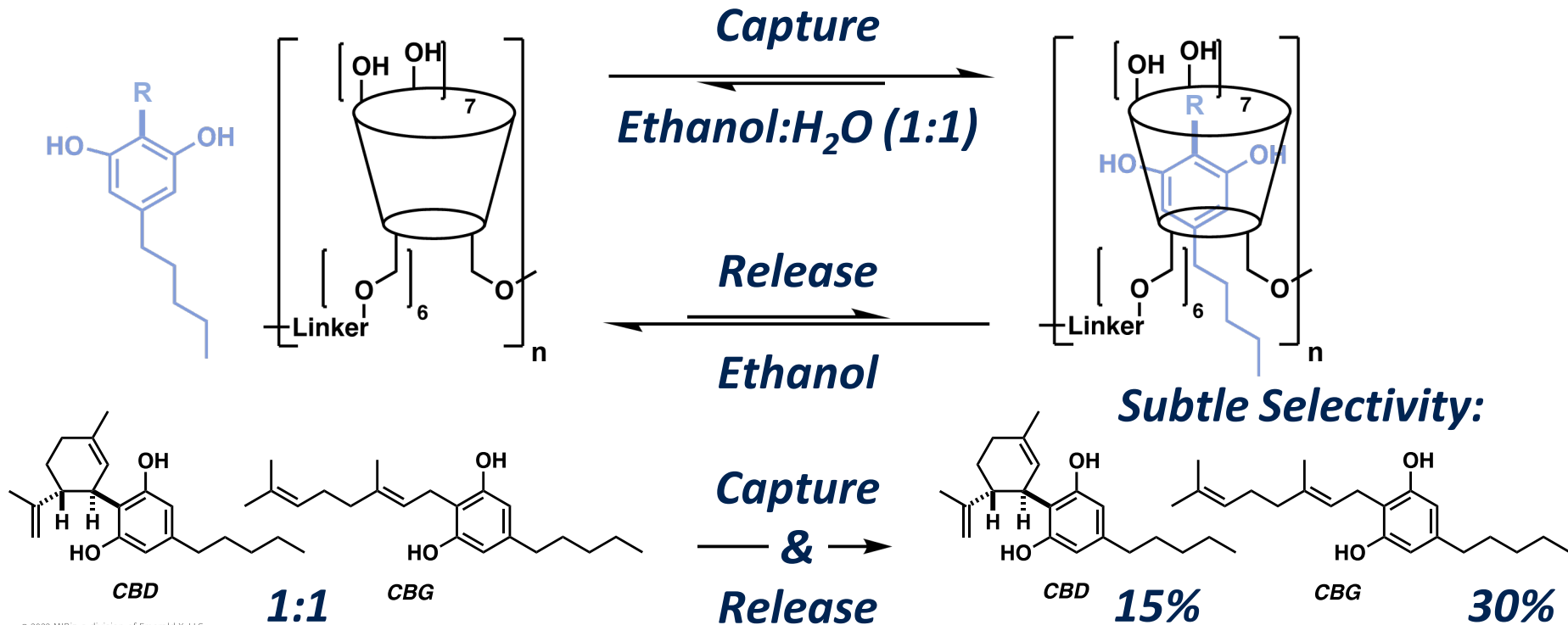
Binding Capacity of 10-20%

Reusable

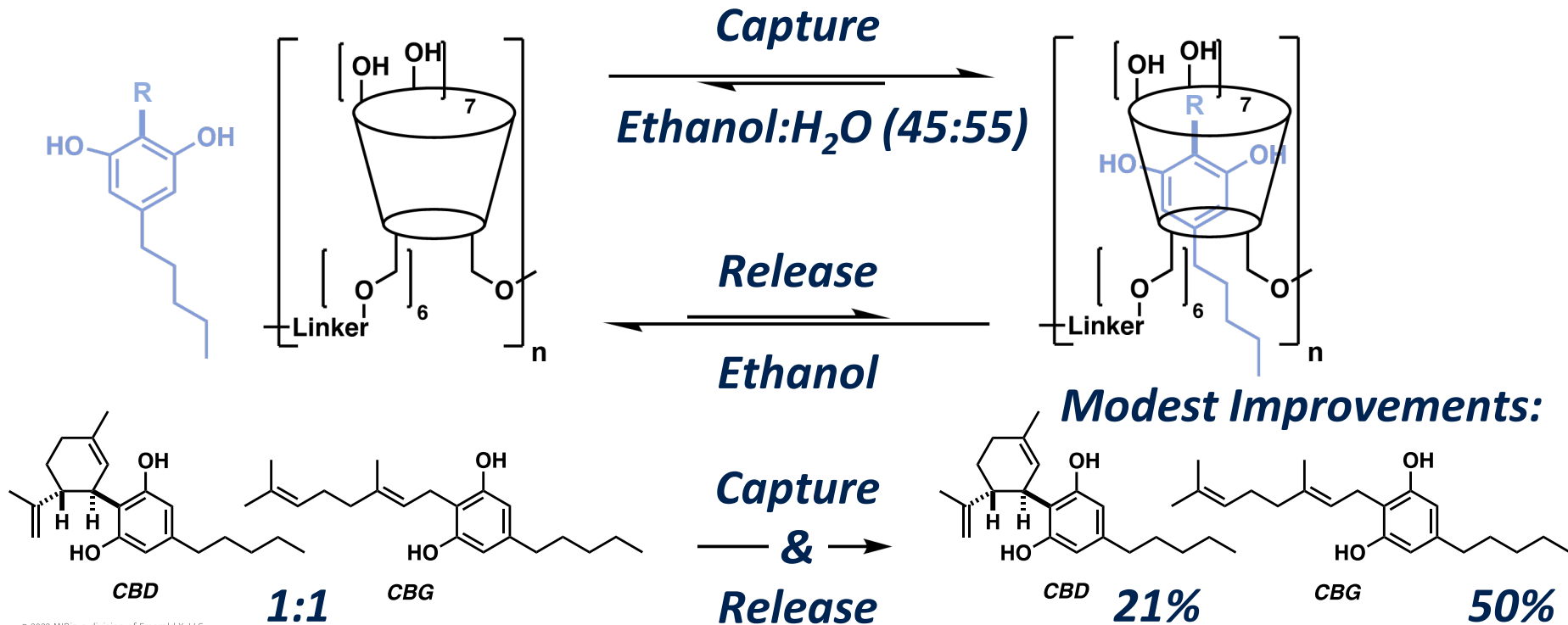
Non-Specific at >20%

Temp, Mixing Rate, Salts Range of Solvents Trialled

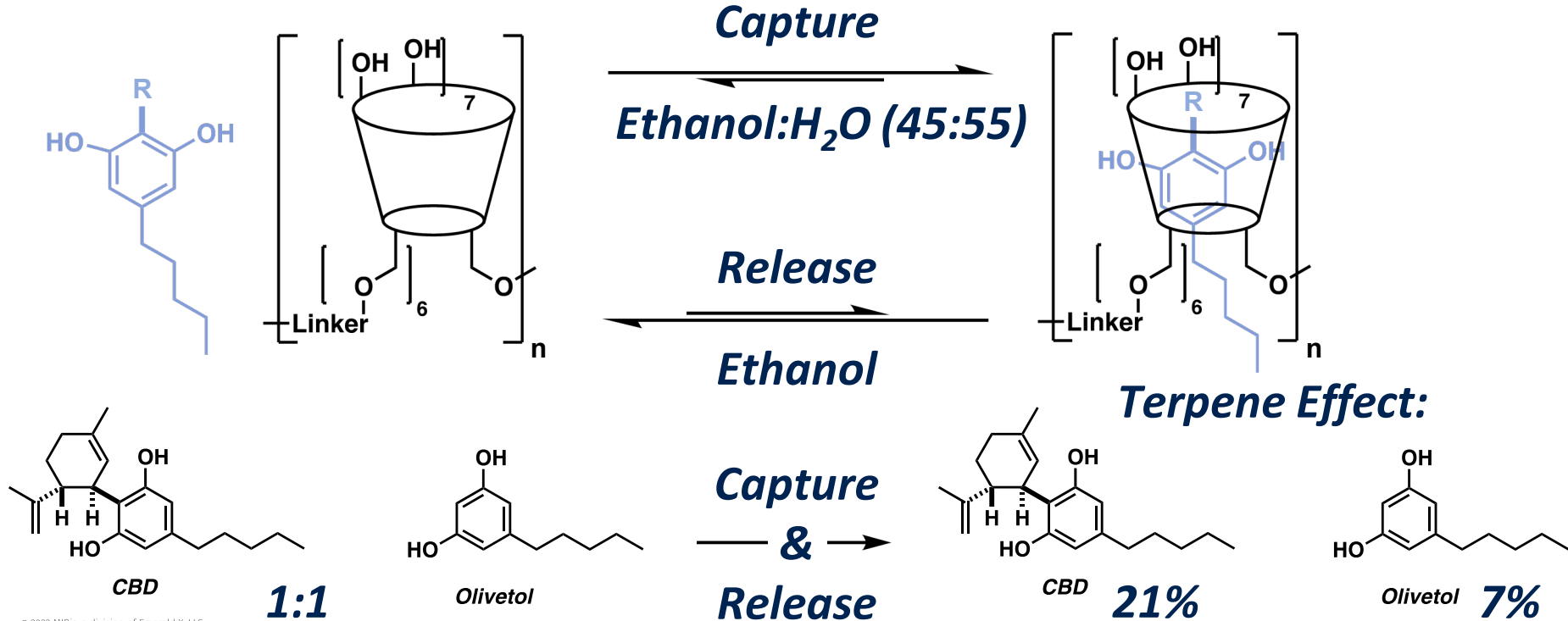
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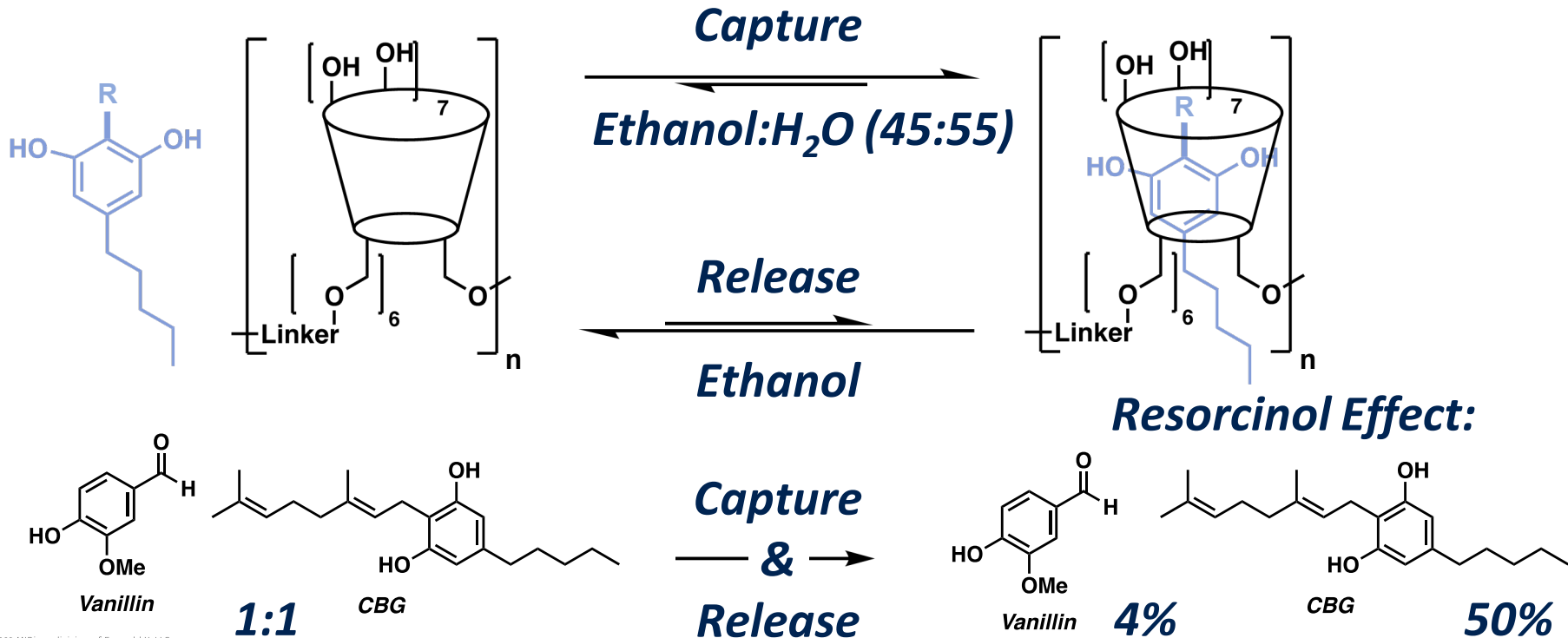
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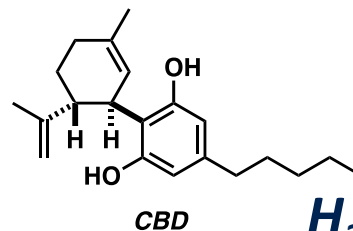
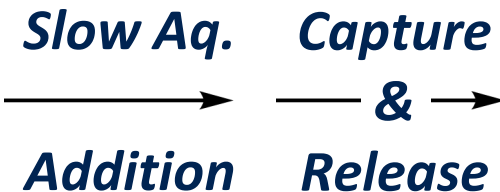
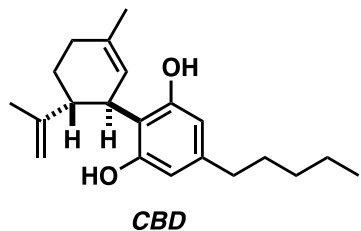
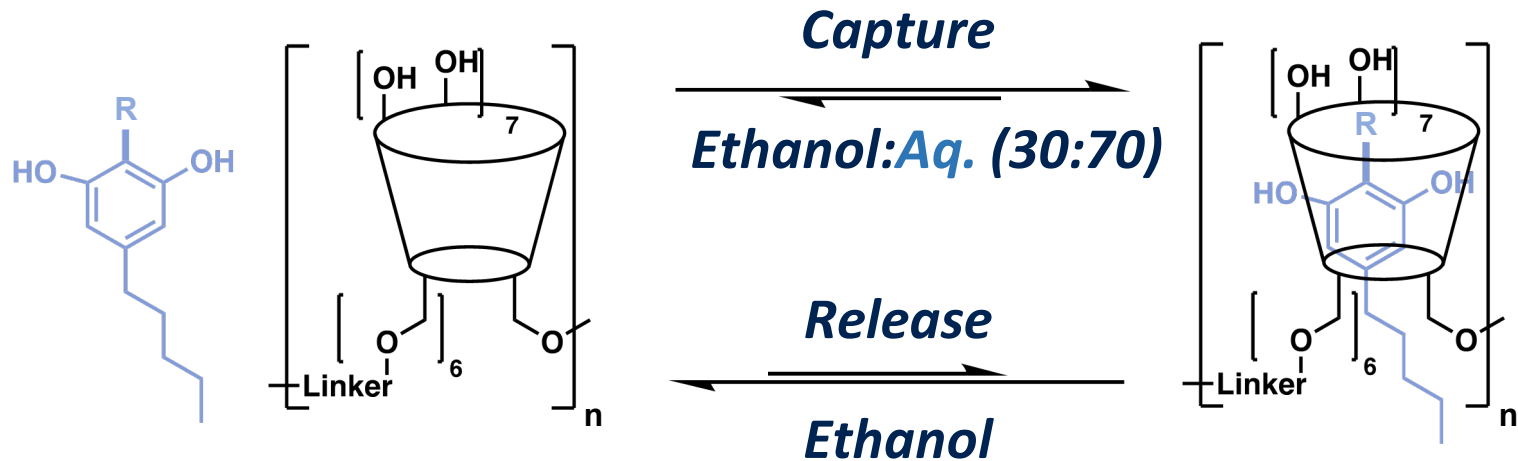
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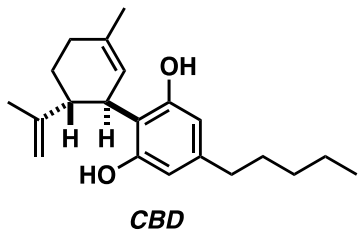
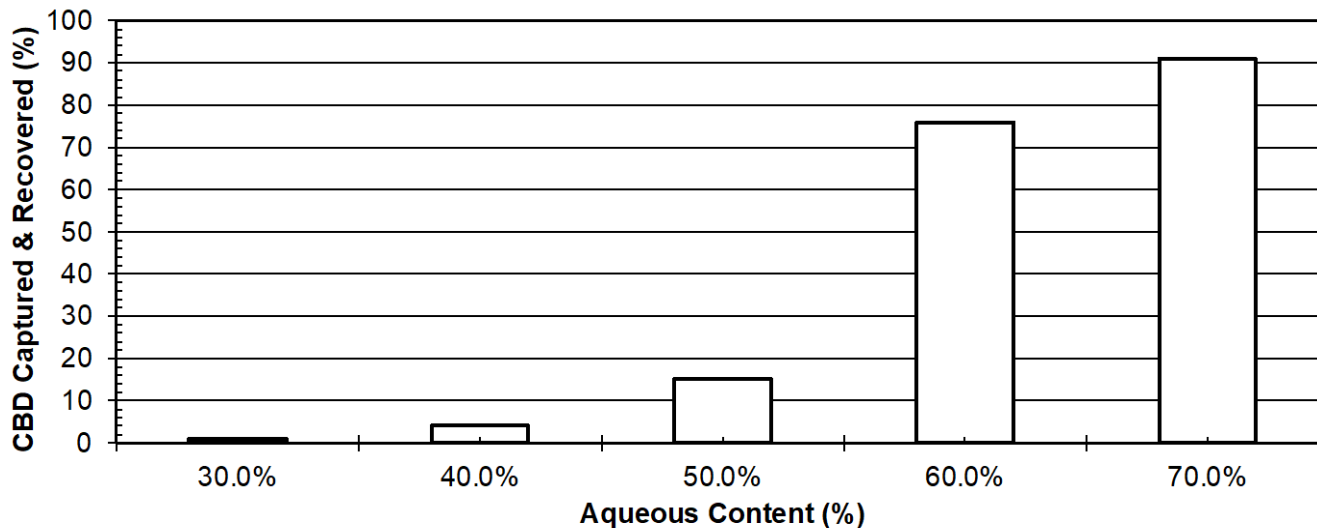


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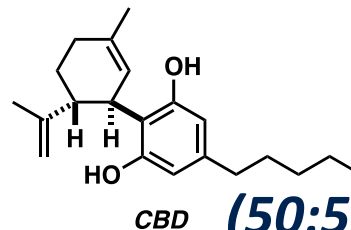


H₂O: 91%
Brine: 97%

Exploring Tuneability & Selectivity

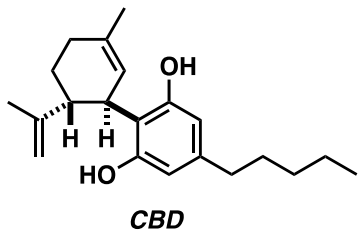
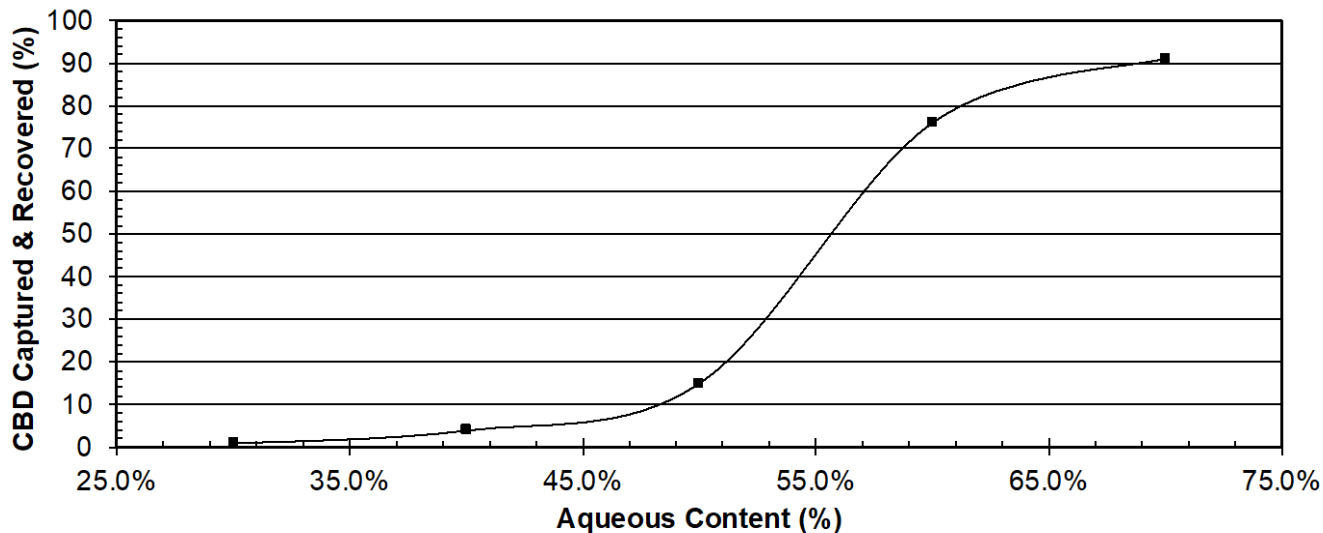


Slow Aq. Addition → *Capture & Release*

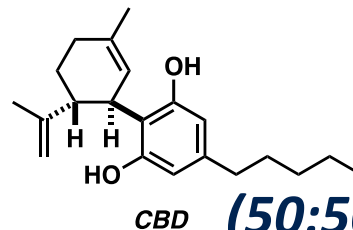


(50:50 H₂O): 15%
(30:70 H₂O): 91%

Exploring Tuneability & Selectivity

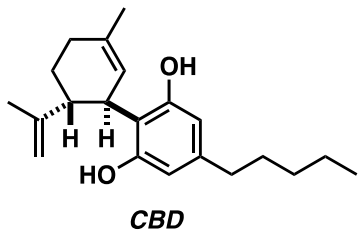
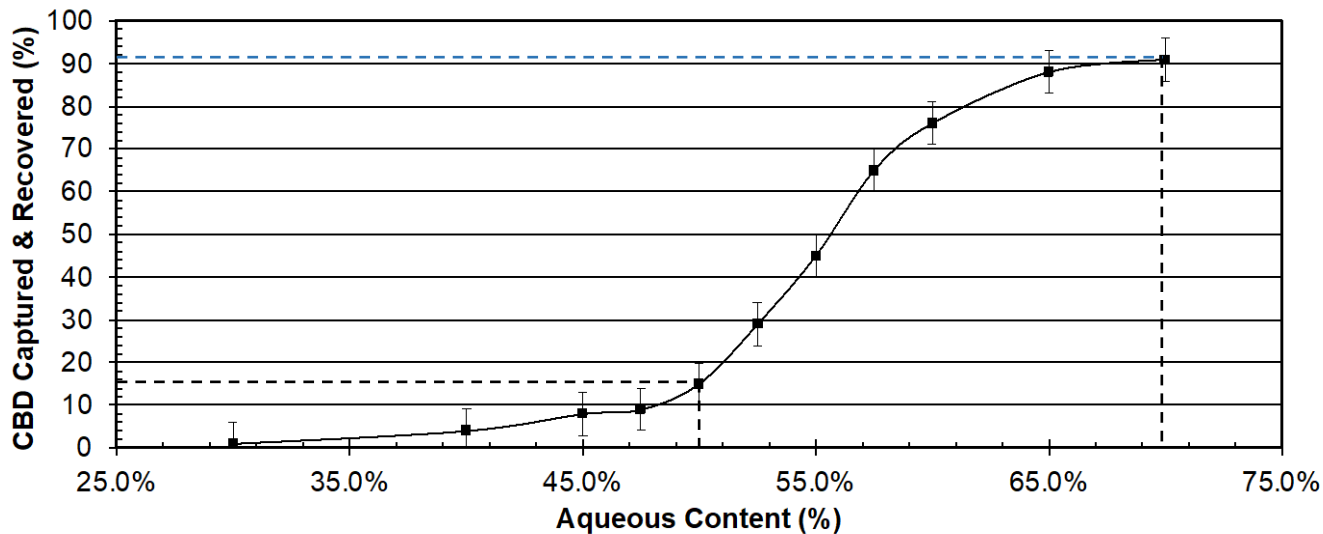


Slow Aq. Addition → *Capture & Release*

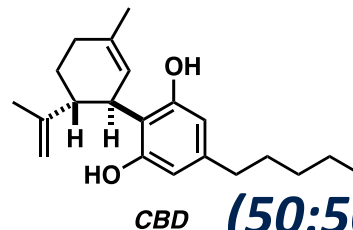


(50:50 H₂O): 15%
(30:70 H₂O): 91%

Exploring Tuneability & Selectivity

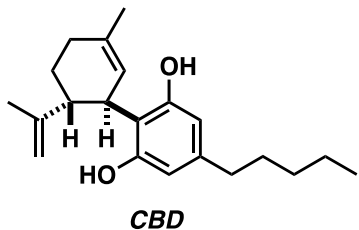
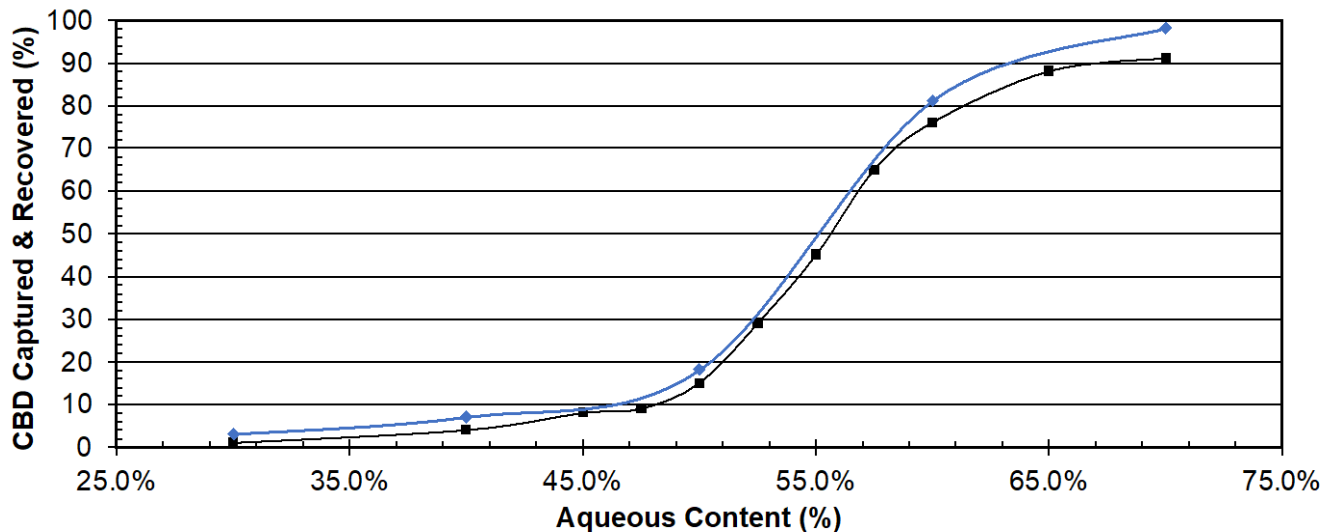


Slow Aq. Addition → *Capture & Release*

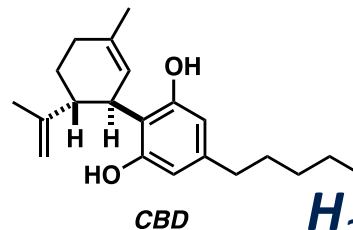


(50:50 H₂O): 15%
(30:70 H₂O): 91%

Exploring Tuneability & Selectivity

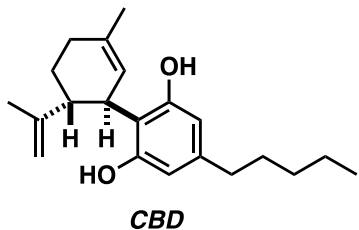
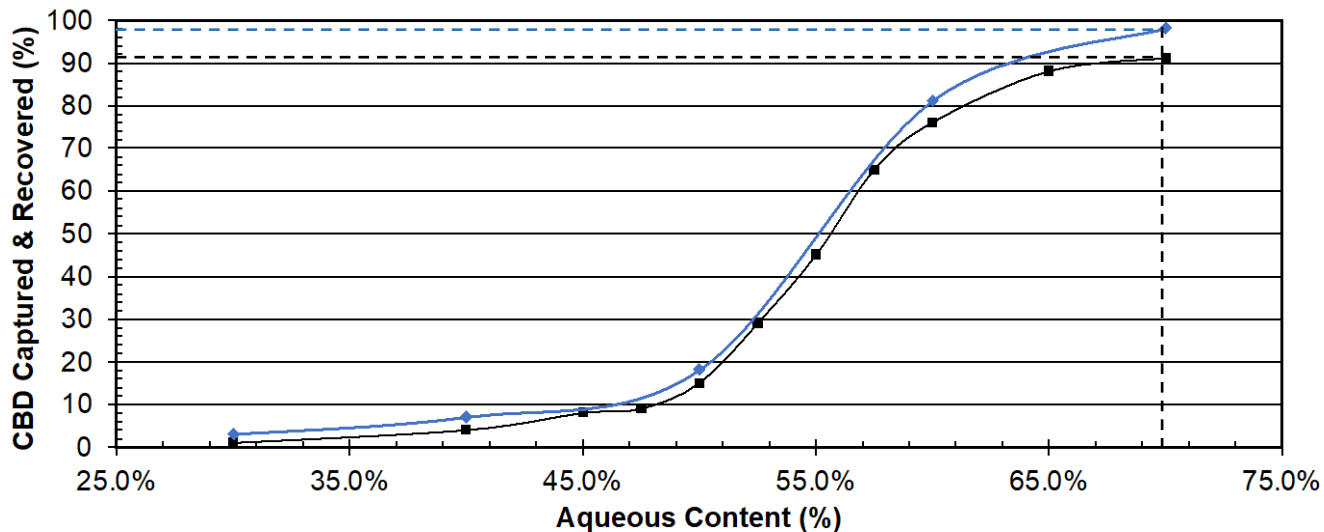


Slow Aq. Addition → *Capture & Release*

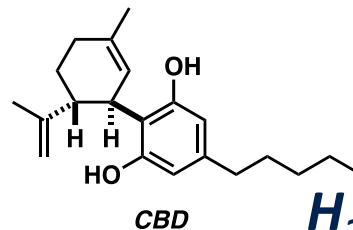


H₂O: 91%
Brine: 97%

Exploring Tuneability & Selectivity

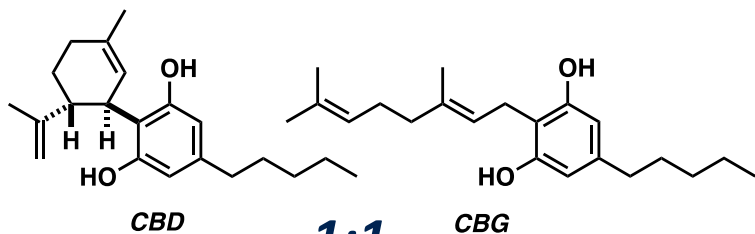
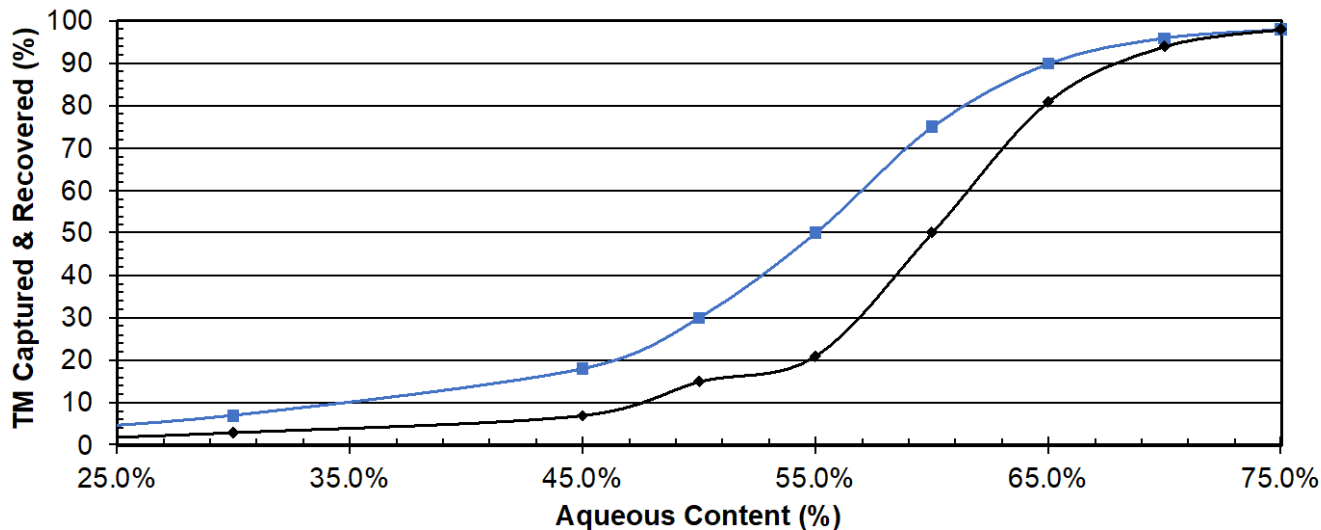


Slow Aq. Addition → *Capture & Release*

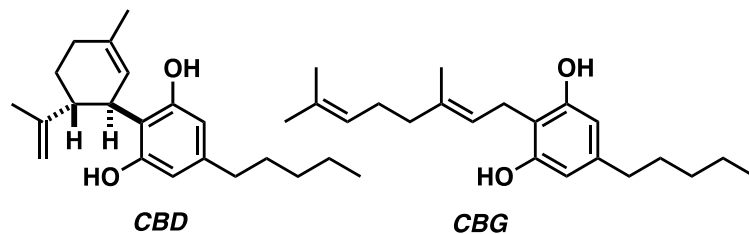


H₂O: 91%
Brine: 97%

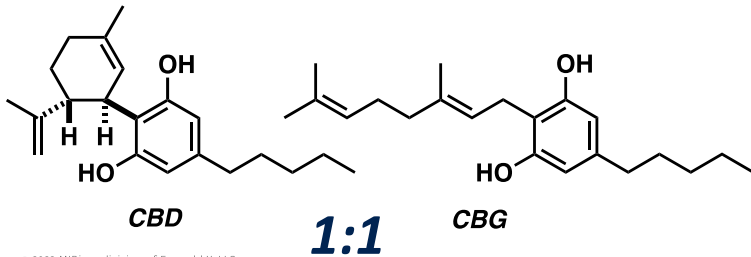
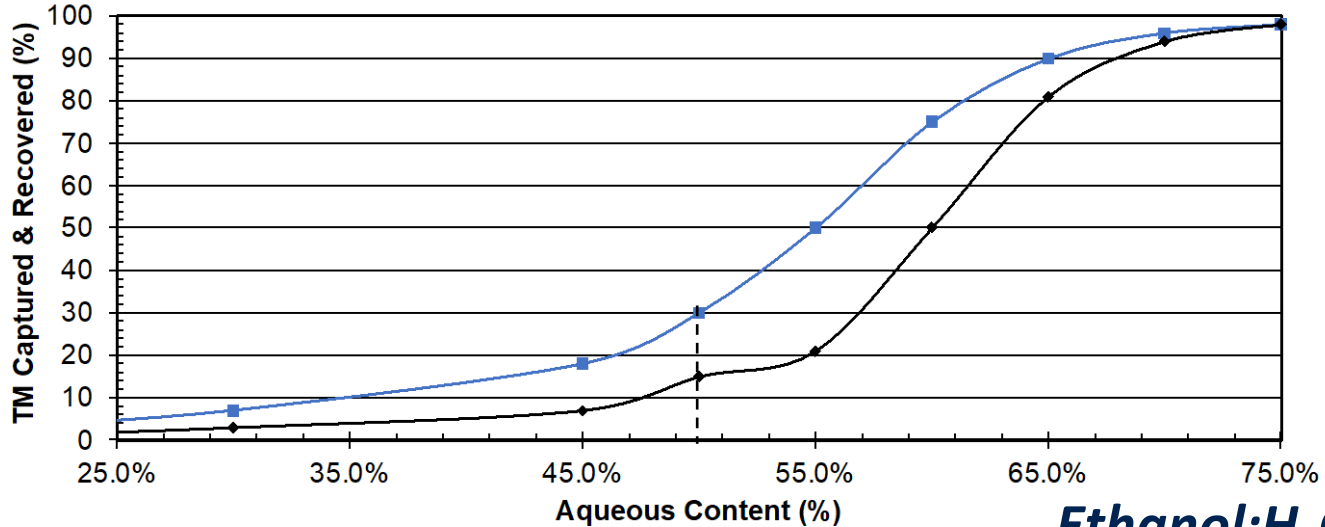
Exploring Tuneability & Selectivity



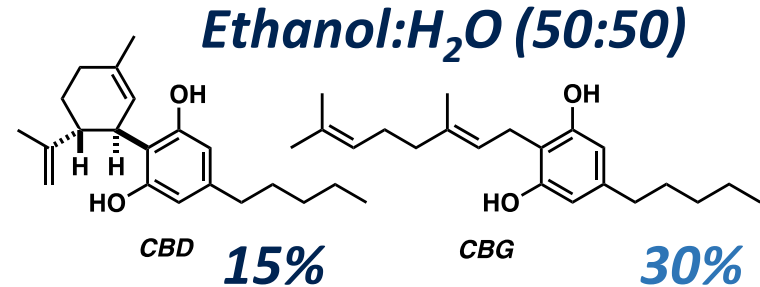
Capture
→
&
→
Release



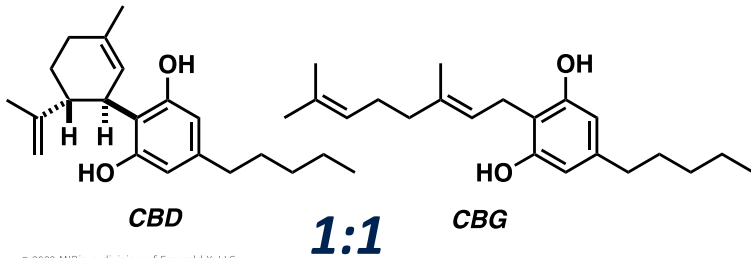
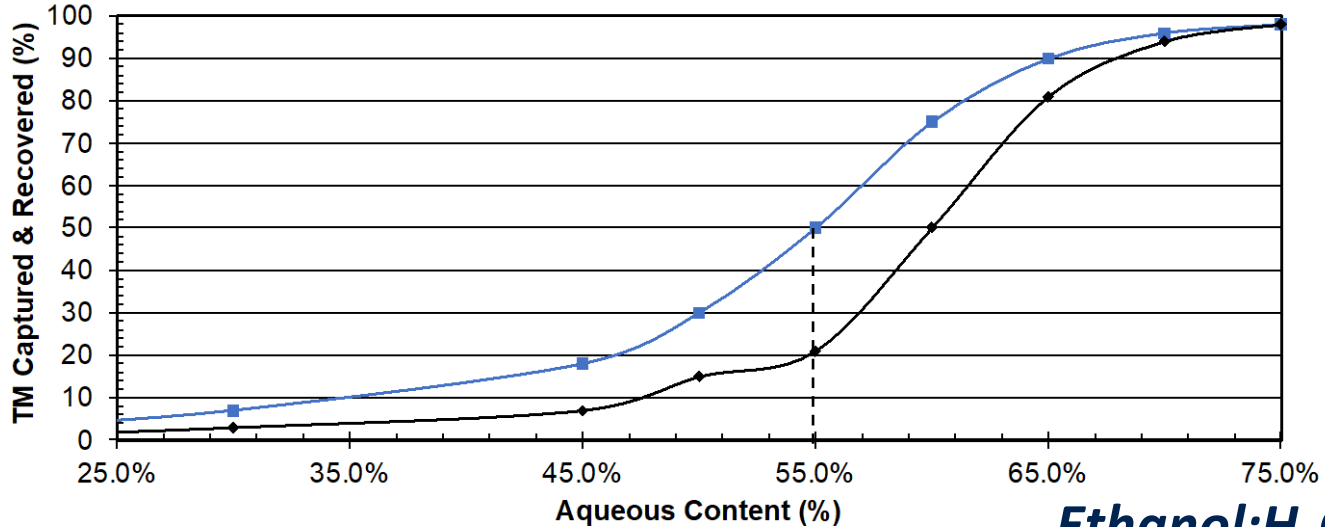
Exploring Tuneability & Selectivity



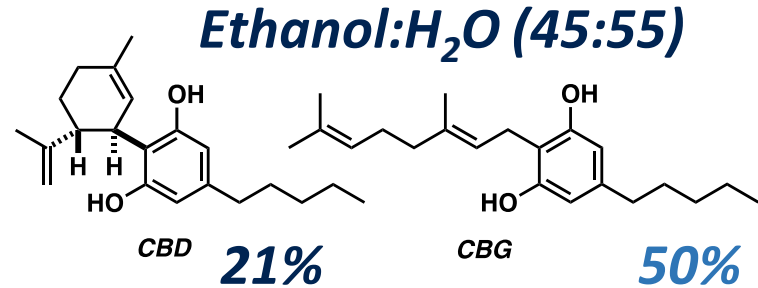
**Capture
&
Release**



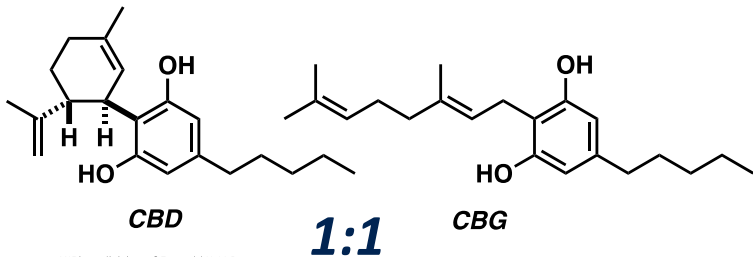
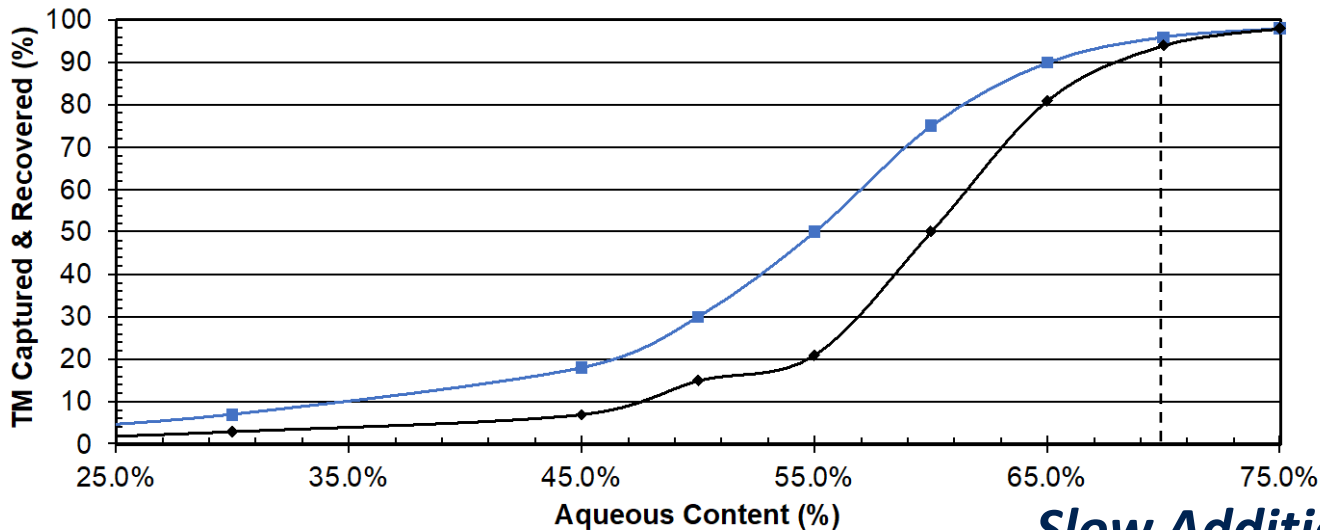
Exploring Tuneability & Selectivity



**Capture
&
Release**

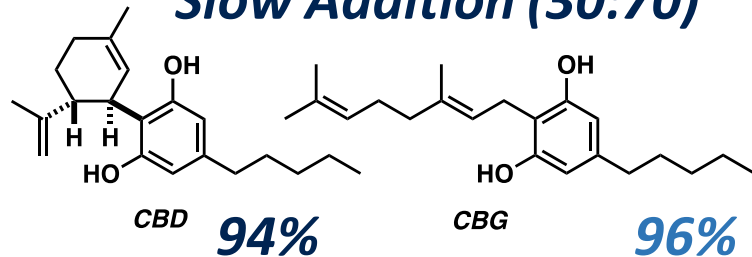


Exploring Tuneability & Selectivity



**Capture
&
Release**

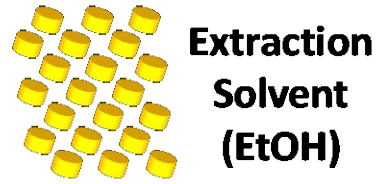
Slow Addition (30:70)



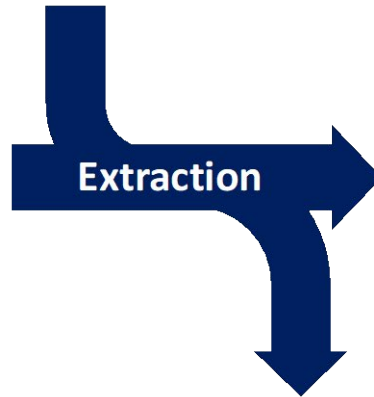
Current Workflow



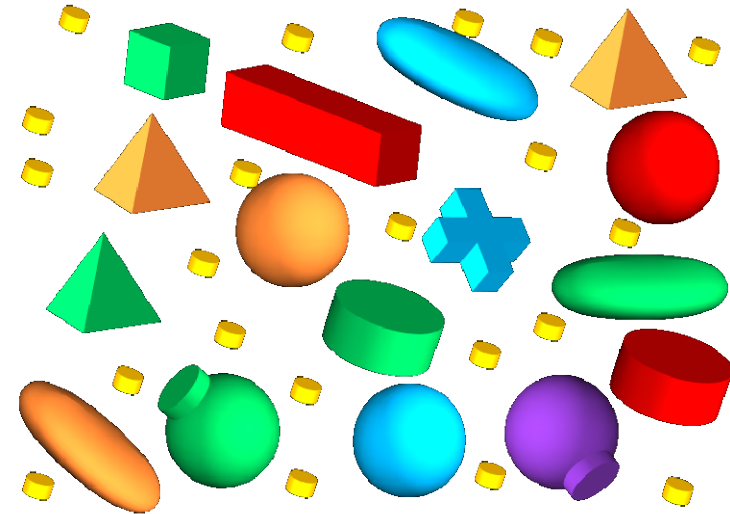
Target Compounds in Biomass



**Extraction
Solvent
(EtOH)**

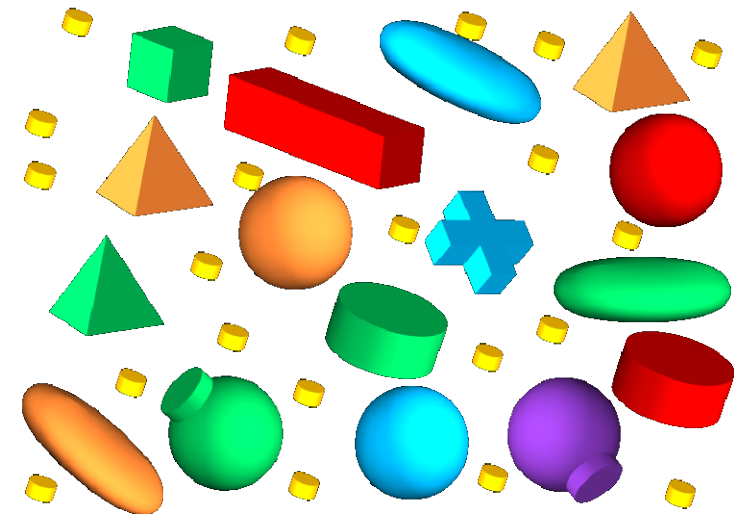


**Exhausted
Biomass**

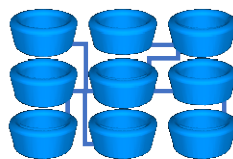


Target Molecules in Solution

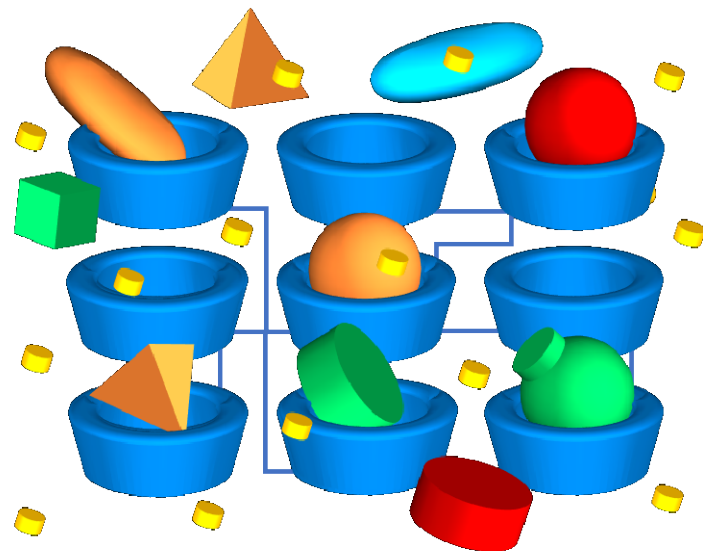
Current Workflow



Target Molecules in Solution

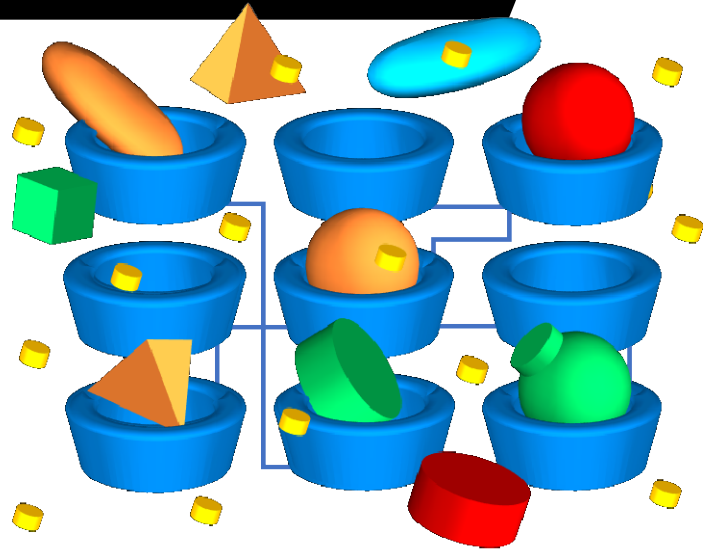


**Nano
Sponge**

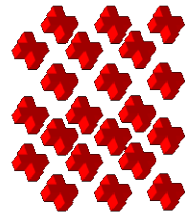
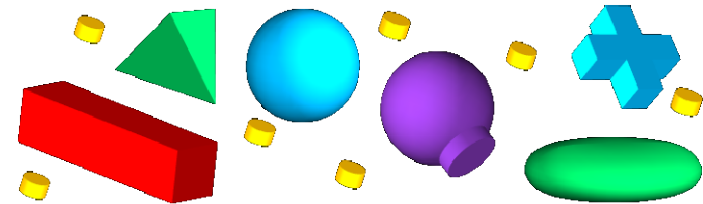


Partial Binding to Polymer

Current Workflow



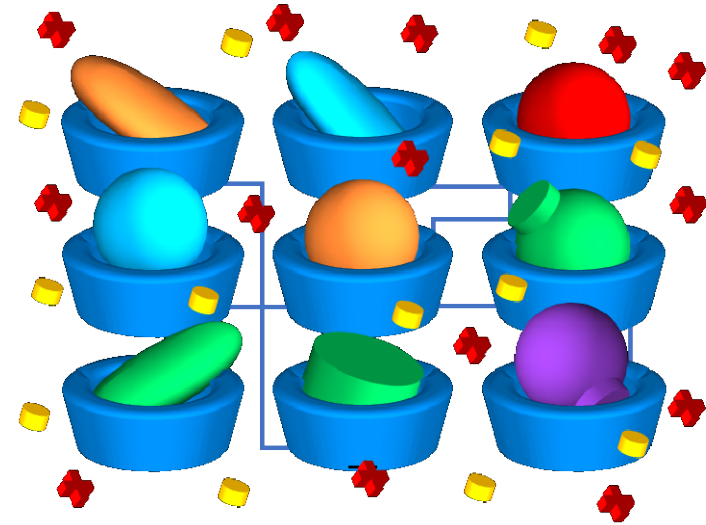
Partial Binding to Polymer



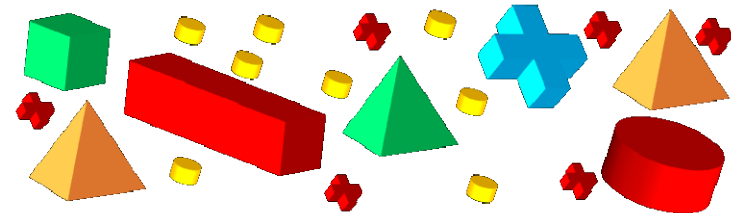
**Aqueous
Solution**



Driving Force

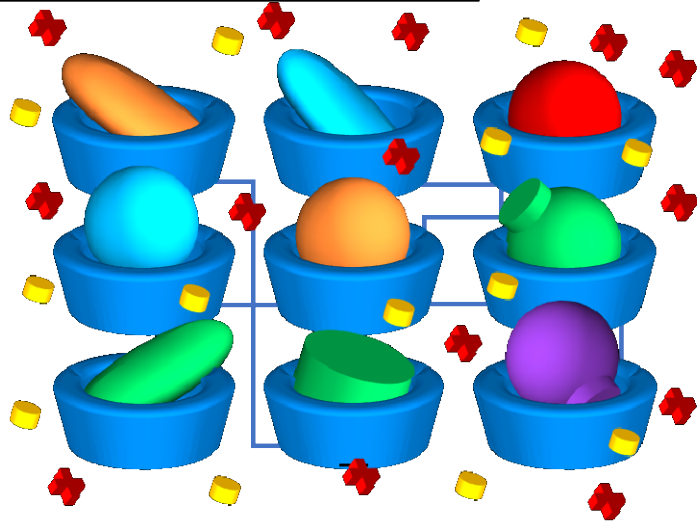


Targets Bound to Solid Phase



Impurities in Solution Phase

Current Workflow

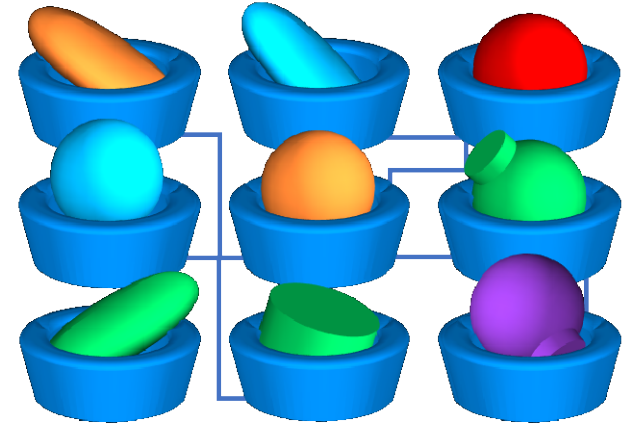


Targets Bound to Solid Phase

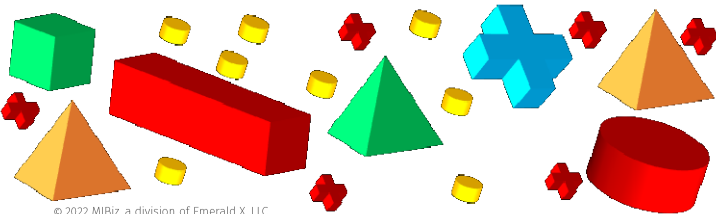


Common
Filtration
Kit

Filter-Wash-Dry

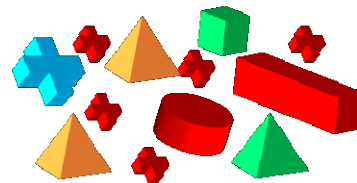


Free-Flowing Powder



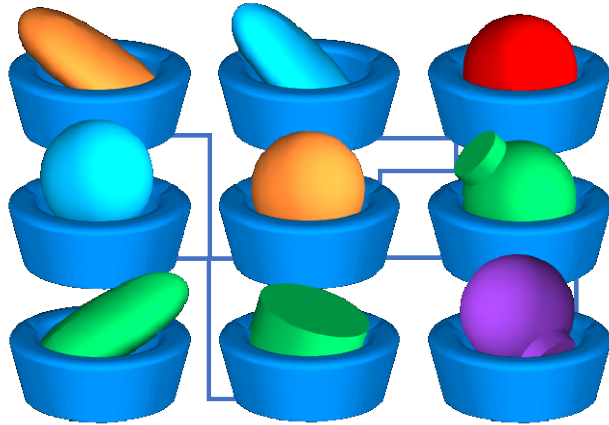
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Impurities in Solution Phase

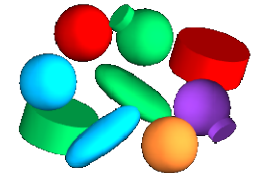


Non-Targets Removed

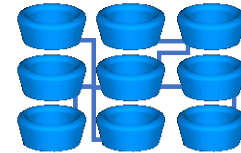
Current Workflow



Free-Flowing Powder

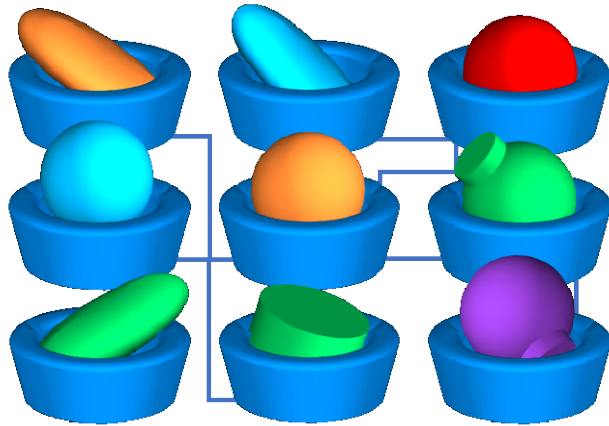


**Full Spectrum
Extract**



Reusable Polymer (>10x cycles)

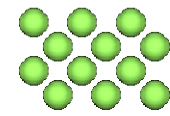
Current Workflow



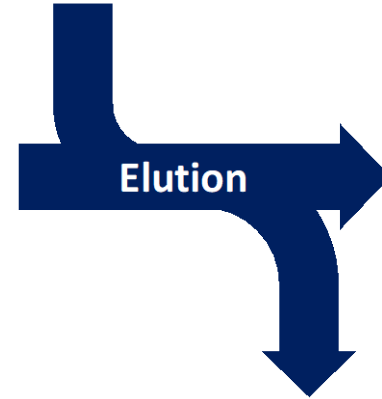
Free-Flowing Powder



**Shelf-Stable
>12 Months**

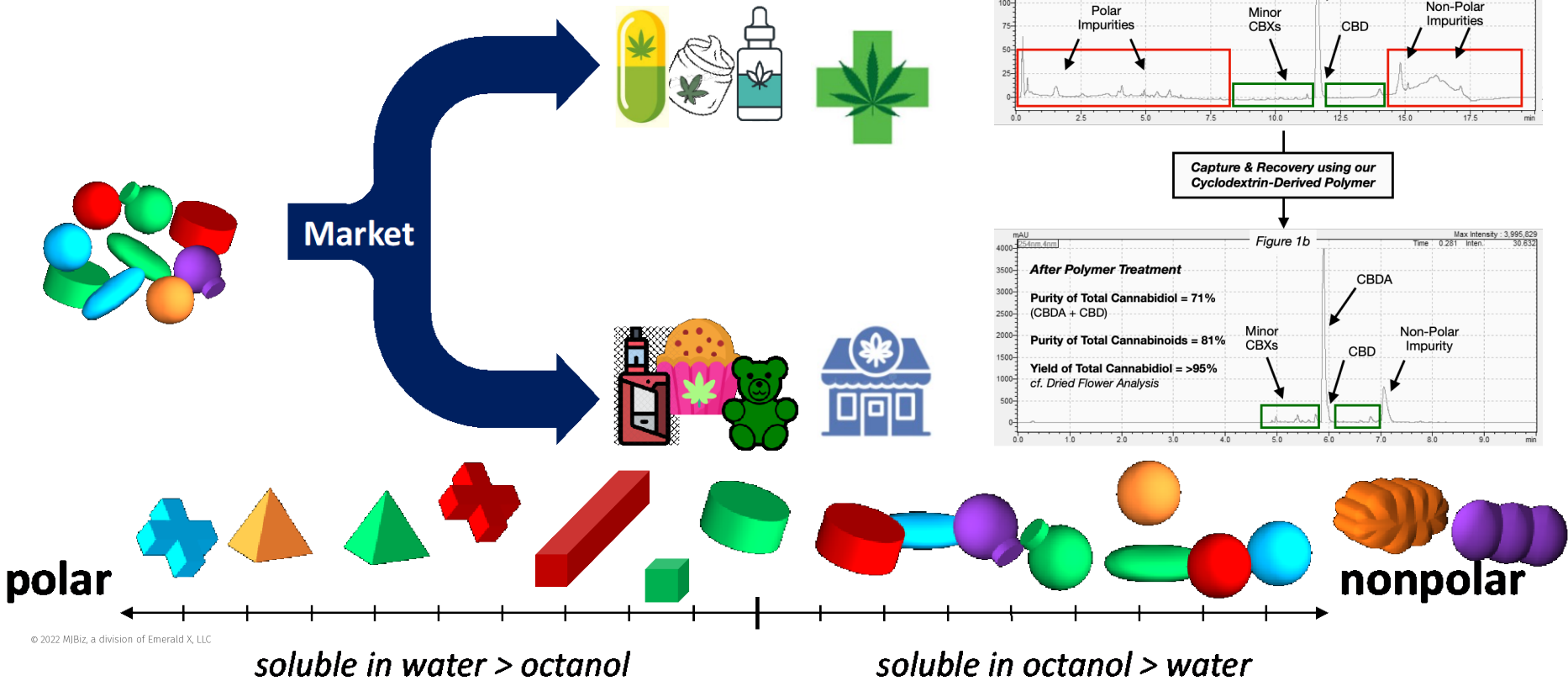


**Release
Solvent
(sc CO₂)**



**Extract
on Demand**

Current Direction



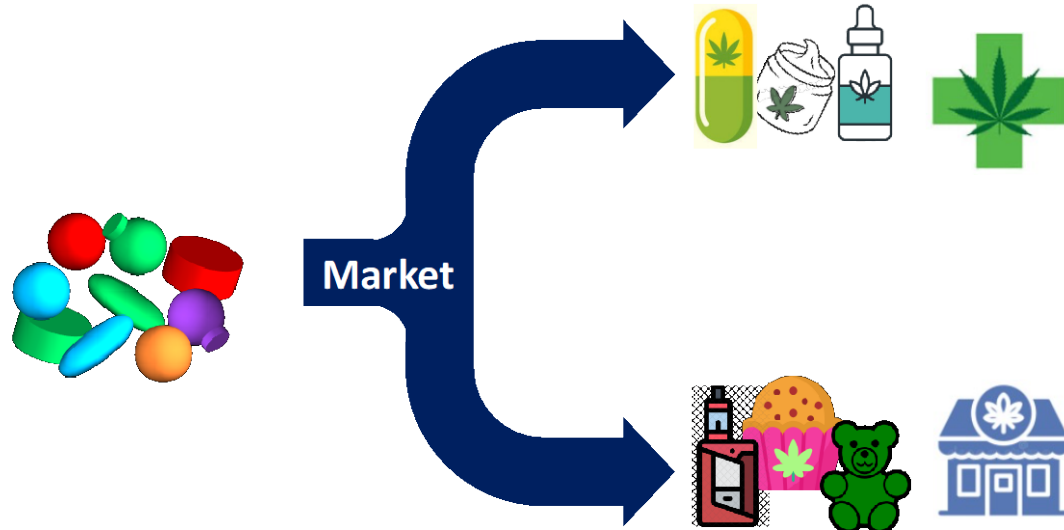
Current Direction



Broad Spectrum Protocol:

- High CBX recovery (>95%)
- Acids & Decarboxylated
- Binds to CBG/A, CBD/A, THC/A, CBN/A, CBC/A
- Captures terpenes
- Polar impurities removed
- Waxes & lipids are avoided
- Initial pigment removal

Current Direction



Broad-Spectrum Protocol:
1-10+ kg scale with partner processors in EU & NA
Detailed chemical analysis

- Cost** 
- Reversible** 
- Operationally Simple** 
- Reusable** 
- Tuneable** 
- Targeted** 
- Low Tech Kit** 
- Complementary** 
- Scalable** 

Alternative Workflows

Continuous Extractions:

Built-in solvent recycling

Uses EtOH-H₂O Mixture

Azeotrope: 95% EtOH

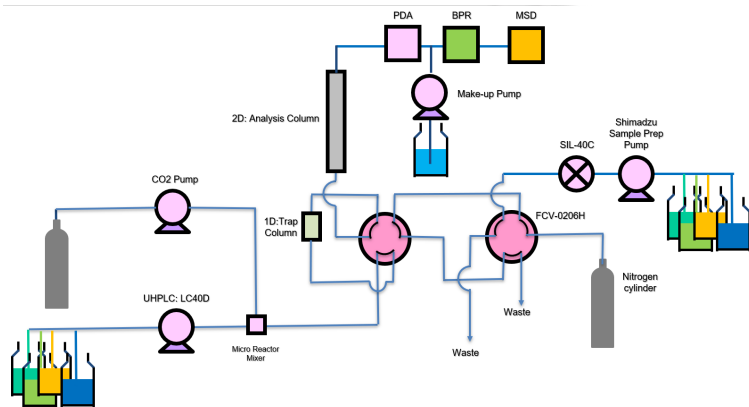
Capture occurs in lower flask

Performed under vacuum

Close to ambient temperature



Chromatographic Applications:



Automated Dual LC-SFC Systems

Loading in EtOH-H₂O

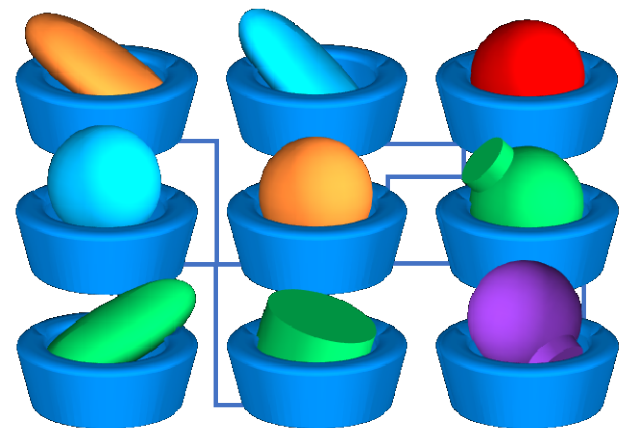
N₂ Purge -> scCO₂ Elution



Raymond Wong

Senior Product Manager at Shimadzu UK Limited

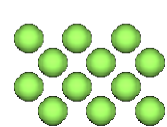
Current Workflow



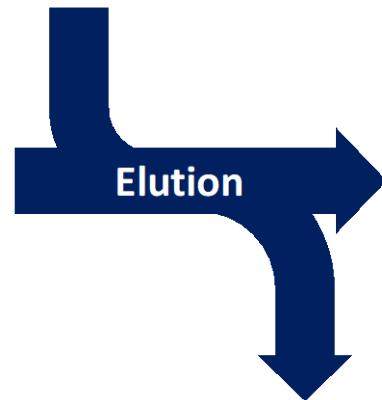
Free-Flowing Powder



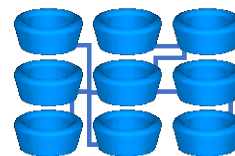
**Shelf-Stable
>12 Months**



**Release
Solvent
(sc CO₂)**

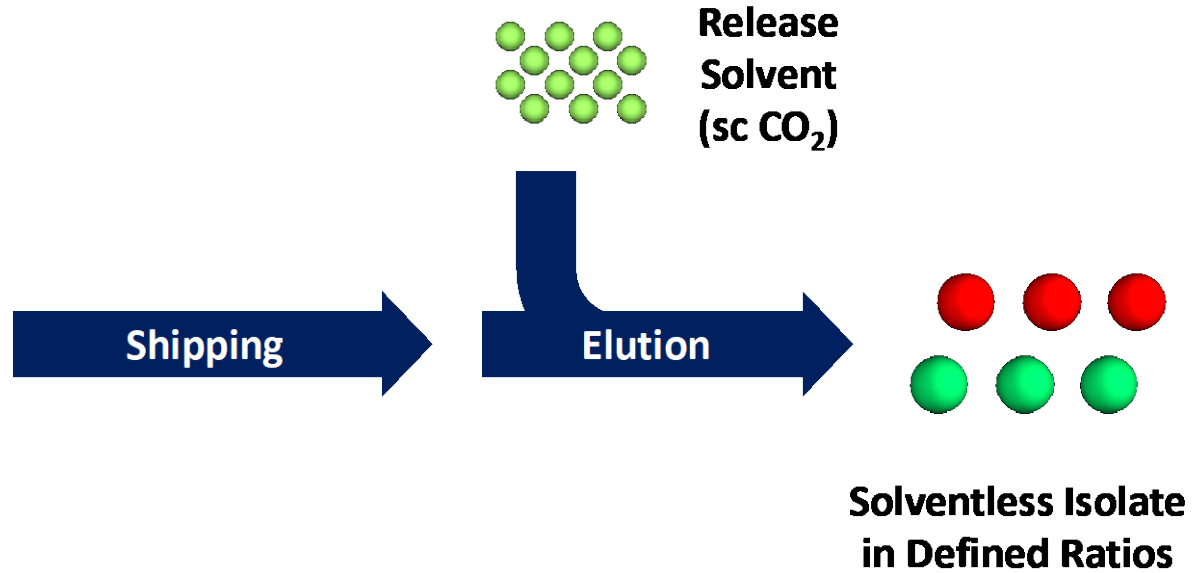
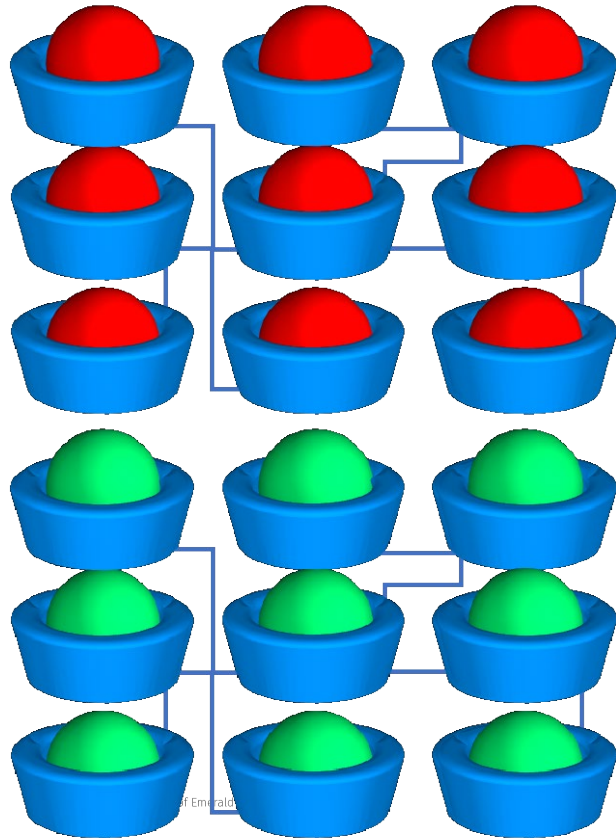


**Extract
on Demand**

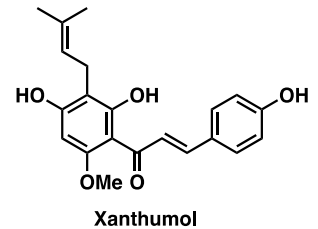
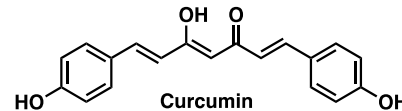
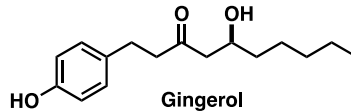


Reusable Polymer (>10x cycles)

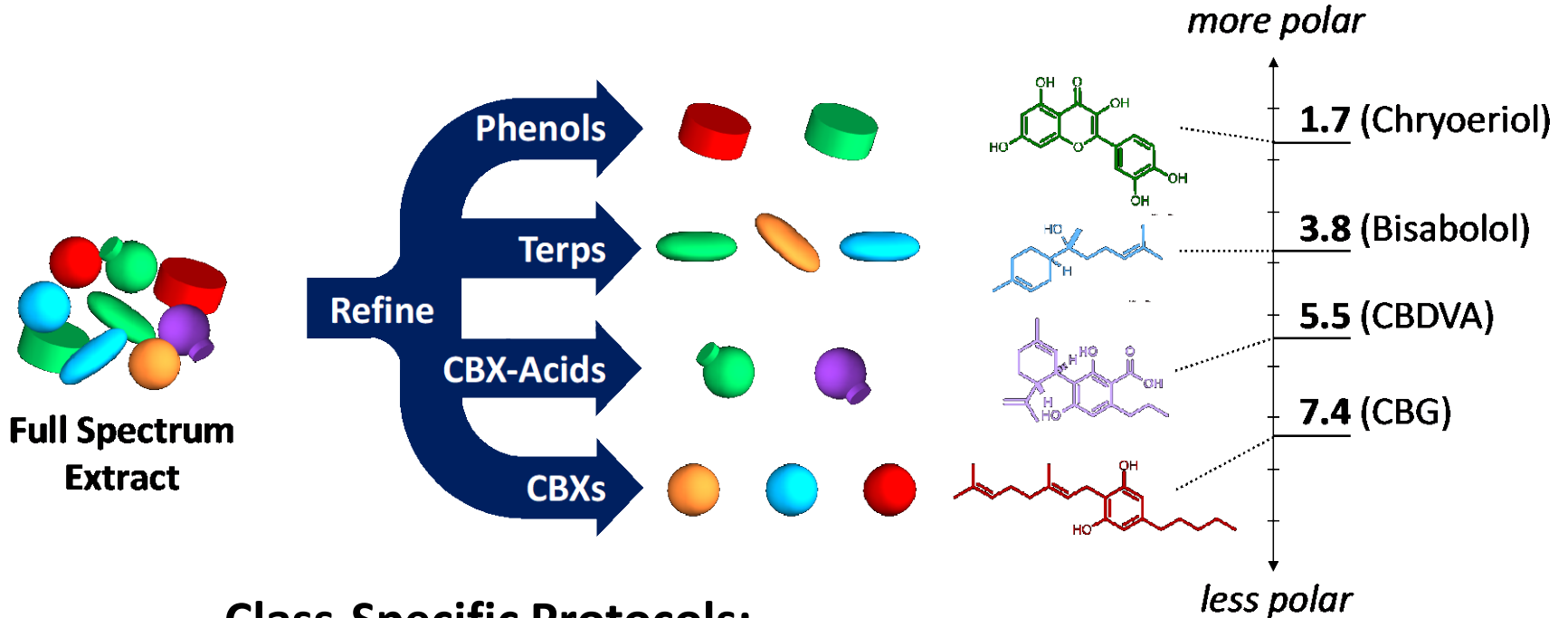
Alternative Applications



Beyond Cannabis Extracts:



Current Direction

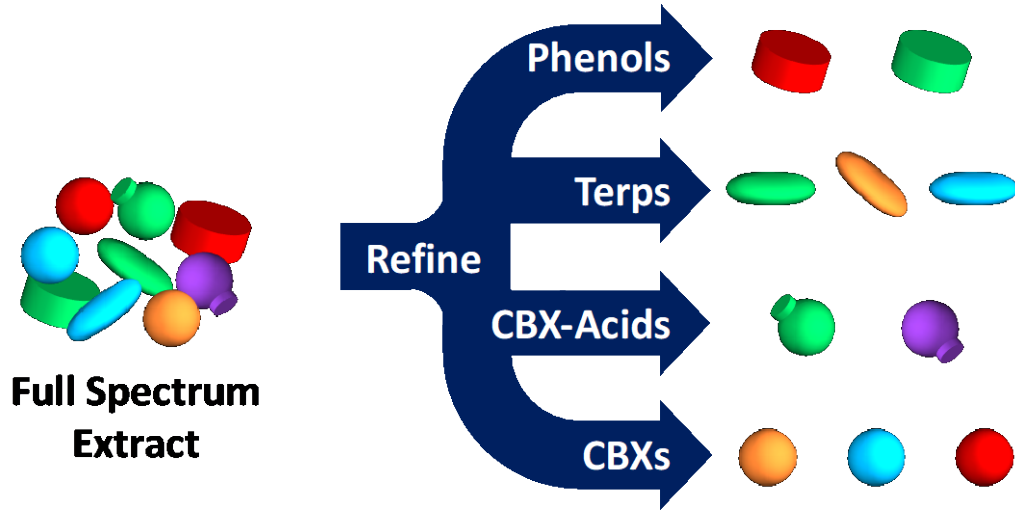


Class-Specific Protocols:

Exploit Unique Polarity Distinctions

Log P & Log D Analyses

Current Direction



Full Spectrum
Extract

Refine

Phenols

Terps

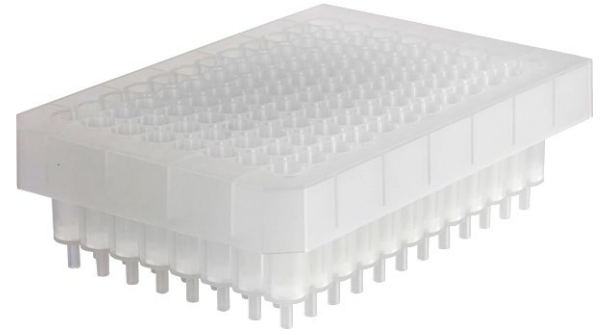
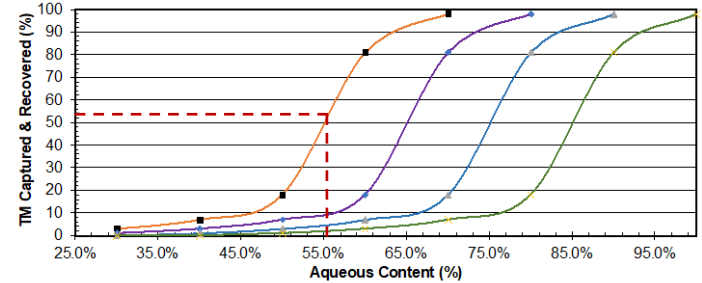
CBX-Acids

CBXs

Class-Specific Protocols:

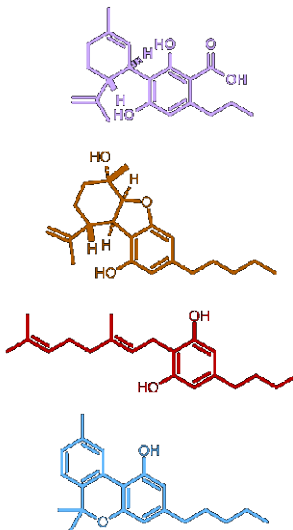
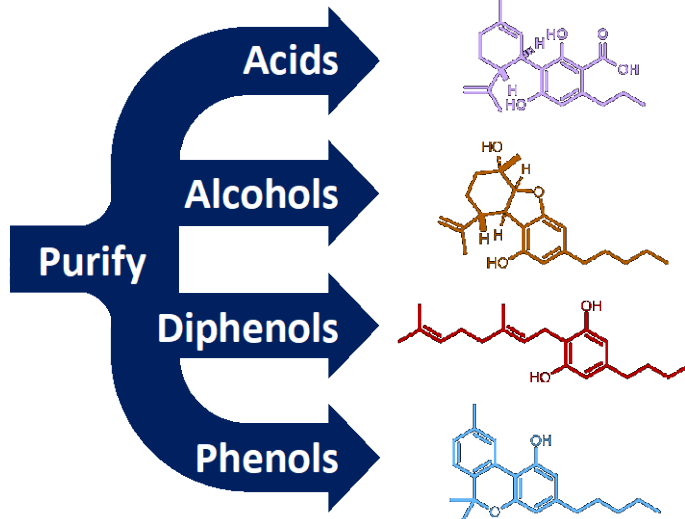
Exploit Unique Polarity Distinctions

Log P & Log D Analyses





**Full Spectrum
Extract**



Target-Selective Protocols:

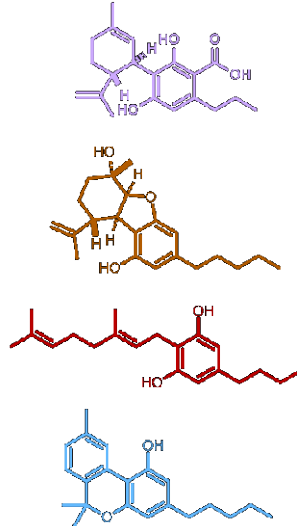
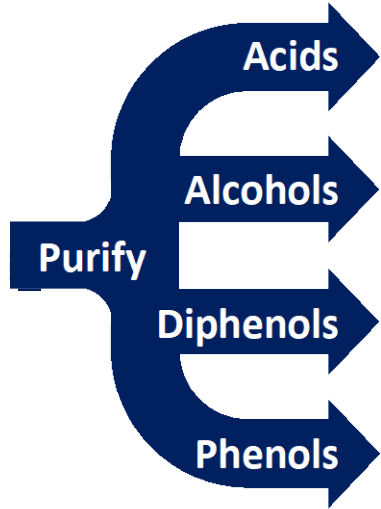
Exploit Unique Polymer Binding

Computational Modelling

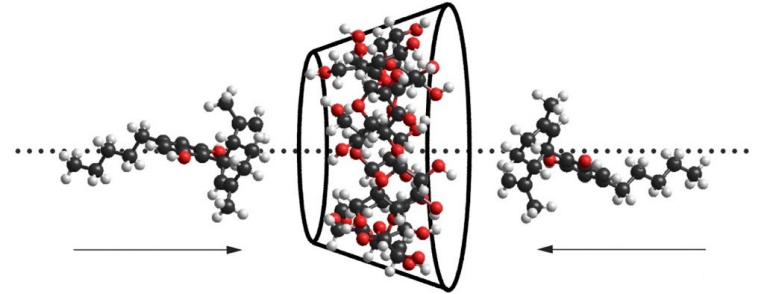
Current Direction



Full Spectrum Extract



+24-33 kcal/mol

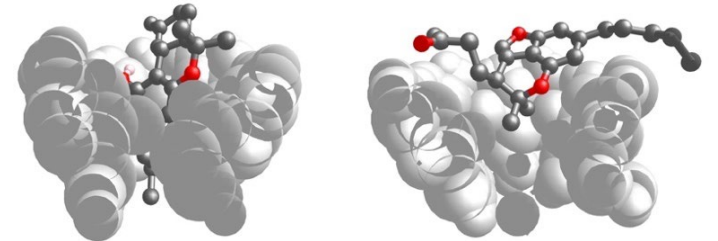


Aryl First

Terpene First

β -CD: CBN vs CBD (+1.5 kcal/mol)

α -CD: THCV vs CBG (+3.7 kcal/mol)



Target-Selective Protocols:

Exploit Unique Polymer Binding

Computational Modelling

Summary & Acknowledgements

Summary

- Procedurally simple, fast, low-tech
- Applicable to many plant extracts
- Dry biomass not needed
- Collaborations:
 - Contract Manufacturers
 - Licensed Processors
 - Analytical Teams
 - Computational Groups

Thanks to

- Rothamsted Agricultural Research Institute, UK
- University College London, UK
- Shimadzu, M-Tek Glass, ITA Labs, UK
- Intertek, Switzerland
- Grow Group: Grow Pharma, Grow Trading, Grow Germany, Grow Biotech

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the presentation.**

