Extraction and Isolation of Artemisinin with HFC-134a

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Outline of Presentation

• Why HFC-134a is a good extraction solvent?
• Design features of HFC-134a equipment
• Development/optimisation of methods for extraction and isolation of artemisinin from *A. annua*
• Progress towards evaluating scale-up and commercial viability HFC-134a system
HFC-134a

Other names:
- 1,1,1,2-tetrafluoroethane
- R-134a

Replacement for HCFC-R12
- NOT ozone-depleting
- IS a greenhouse gas
- Restrictions on use
- available for foreseeable future
HFC-134a

Properties:

- Clear liquid/gas
- Bpt. -26.3°C
- Vp. @ 20°C is 5.7 bars
HFC-134a - vs - CO$_2$

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Vapor pressure in bars (at 20 $^\circ$C)</th>
<th>B.pt $^\circ$C (at 1 bar)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFC-134a</td>
<td>4.7</td>
<td>-26.2</td>
</tr>
<tr>
<td>scCO$_2$</td>
<td>57.3</td>
<td>-78.5</td>
</tr>
</tbody>
</table>

- HFC-134a systems operate under moderate pressures
- significantly less expensive than CO2 system
- BUT solvent cost higher
Uses of HFC-134a
Exploiting Fridge principles
HFC-143a Extraction Principle

Simple and robust technology
HFC-134a Technology for Extraction and Isolation of Artemisinin
Levels of waxes and pigments are dependent on nature of extraction solvent.
Composition of primary extracts

Pigments + Waxes → ART rich → Polar impurities → Pigments

R134a and CO2 ← Hexane ← Toluene ← Ethanol
Silica gel column fractions of HFC-134a extract

- Non-polar fraction
- Art rich fraction
- Polar fraction
Silica gel column fractions from HFC-134a extract

Hexane extract

Non-polar fraction  Art rich fraction  Polar fraction
Isolation of ART from primary extracts

• In a typical hexane extraction system only ca70% ART in primary extract is isolated.
• Overall costs are high. Typically for 1 ton ART crystals:
  – 300 kg of charcoal
  – 40,000 L of ethanol
  – Silica gel?
  – Several days
HFC-134a purification process

- Coat crude extract onto an inert solid material e.g. mix with Celite or even spent *A. annua* leaves [can use oils instead of inert solid materials]
- Extract with R134a
- Evaporate solvent
- Either crystallise directly or after filtration
Purification of extracts with HFC-134a

- HFC-134a efficiently removes pigments and waxes
- >90% ART recovery
- ca 30-40% ART content

Primary hexane, toluene or HFC-134a extract
Purification of extracts with HFC-134a

HFC-134a extract

Filter

Crude ART crystals
(>85% purity)
[1 part]

Pale yellow oil
(<<10%ART)
[2 parts]
Isolation of Artemisinin

33+% (Art purity) → Filter under vacuum and wash → 90+% → Re-crystallise → 96+%
Summary – HFC-134a as a solvent

• More selective than hexane and scCO$_2$ for wax and pigment rejection
• Modular system design allows multipurpose applications
• Approved for food and pharmaceutical applications
• Robust and reproducible technology
• Medium pressures – low capital costs
HFC-134a for ART isolation

<table>
<thead>
<tr>
<th>Extraction system</th>
<th>% ART isolated from primary extract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional solvents</td>
<td>70</td>
</tr>
<tr>
<td>R134a</td>
<td>&gt;90</td>
</tr>
</tbody>
</table>

Advantages of R134a system:
- more efficient
- more economical
- shorter processing time
Future/ongoing Plans funded by MMV/FSC

• Identify viable designs for commercial scale HFC-134a systems especially for purification of primary extracts
• Estimate costs for commercial-scale extraction and purification plants
• Carry out economic analysis and commercial viability of HFC-134a processes
HFC-134a system should be more economical and efficient than conventional systems
Acknowledgments

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