Role of impurities in purification of artemisinin from Artemisia annua extracts

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Published in:
Planta Medica

DOI:
10.1055/s-0036-1596818

Publication date:
2016

Document version
Other version

Citation for published version (APA):
Artemisinin is used in combination with other drugs against *Plasmodium falciparum* induced malaria. Artemisinin is obtained mainly from dried leaves of *Artemisia annua* L. (sweet wormwood). Existing processes include extraction of leaves of *A. annua* by using organic solvents, ionic liquids, or supercritical fluids and subsequent purification of artemisinin from crude extract [1]. Most of the processes used for manufacturing of artemisinin report poor yield during crystallization and attribute it to the interference of impurities on the crystallization of artemisinin [2]. Understanding the role of impurities is therefore essential for the design of an optimal process for recovery of artemisinin. The aim of this study was to investigate the effect of impurities in extracts on the overall recovery of artemisinin.

**EXTRACTION AND PROCESS FOR RECOVERY OF ARTEMISININ**

- Dried leaves of *A. annua*
  - Organic solvent
  - Extraction
  - Crude extract
  - Mobile phase: 
    - n-hexane—ethyl acetate
  - Flash CC
  - Fractions with artemisinin
  - Crystallization
  - Artemisinin

**PURIFICATION OF ARTEMISININ FROM DICHLOROMETHANE EXTRACT**

- Dichloromethane extract of *A. annua* leaves partially purified with flash CC.
- Fractions containing artemisinin combined and analyzed by LC-MS.
- Solubility of artemisinin was measured in the mobile phase *n*-hexane—ethyl acetate (77.7:22.3 v/v) together with impurities (Table 1, Fig. 2).
- Crystallization of artemisinin from combined flash CC fraction was performed (Fig. 3).

**Table 1. Composition of combined fraction containing artemisinin**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artemisinin</td>
<td>1.82</td>
</tr>
<tr>
<td>Artemisetene</td>
<td>0.015</td>
</tr>
<tr>
<td>Dihydroartemisinic acid</td>
<td>0.0745</td>
</tr>
<tr>
<td>Artemisinic acid</td>
<td>0.01</td>
</tr>
<tr>
<td>Arteannuin B</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Coumarin</td>
<td>0.0051</td>
</tr>
</tbody>
</table>

**CONCLUSIONS**

- Impurities in the dichloromethane extract increased solubility of artemisinin, i.e., showed co-solvency effect.
- Impurities in the dichloromethane extract did not affect the yield of artemisinin in the crystallization step.
- Maximum yield of artemisinin in the overall process was obtained with acetone (0.29 wt %), followed by ethyl acetate (0.26 wt %), methanol (0.18 wt %), n-hexane (0.15 wt %) and dichloromethane (0.11 wt %).
- The composition of extracts, i.e., impurities may in some cases have a significant effect on the purification of artemisinin.

**REFERENCES**