Spray Drying of Cubosomes for Oral Vaccine Delivery

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**Title:** Spray Drying of Cubosomes for Oral Vaccine Delivery

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**Purpose**

To prepare cubosomes carrying the model antigen ovalbumin and its adjuvant Quil A using spray drying as a method, as well as to in vitro characterize these particles.

**Method**

A spray dried powder of cubosomes was heated to 90°C for 24h. This reduced electrostatic charges in the powder, allowed easy reconstitution to a colloidally stable suspension, and induced weight loss of 8%. The powder was rich in cubosomes after reconstitution (Fig. 2).

**Results**

**Particle Morphology**

The spray dried powder was heated to 90°C for 24h. This reduced electrostatic charges in the powder, allowed easy reconstitution to a colloidally stable suspension, and induced weight loss of 8%.

**Particle Characterization**

Table 1: Size and zeta-potential of cubosomes with and without adjuvant as measured by dynamic light scattering in Milli-Q water. Mass median aerodynamic diameter (MMAD) measured by time-of-flight mass spectroscopy.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Size (nm)</th>
<th>PDI</th>
<th>Zeta potential (mV)</th>
<th>MMAD (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cubosomes with OVA</td>
<td>256±10</td>
<td>0.42</td>
<td>-31.7±1.4</td>
<td>4.1±0.4</td>
</tr>
<tr>
<td>Cubosomes with OVA and Quil A</td>
<td>233±13</td>
<td>0.24</td>
<td>-38.3±1.7</td>
<td>4.1±0.02</td>
</tr>
</tbody>
</table>

**Ovalbumin release from cubosomes**

![Ovalbumin release from cubosomes](chart)

**Ovalbumin content in formulation**

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>OVA content in powder</td>
<td>20.3±0.5 µg/mg</td>
</tr>
<tr>
<td>OVA load in particles</td>
<td>5.1±0.1% wt</td>
</tr>
</tbody>
</table>

**Loading into microcontainers**

Microcontainers were fully and homogenously filled with cubosome powder by an embossing method. The microcontainers offer the possibility to protect the formulation during passage through the stomach and provide release of the cubosomes in the intestine.

**Conclusion**

The developed cubosomes show properties suitable to be used for oral vaccine delivery in microcontainers.

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