Hyperforin stabilization by solid lipid nanoparticles processed in microsystems

Thomas Kellner¹,², Christel C. Müller-Goymann¹,²

¹Institut für Pharmazeutische Technologie, Technische Universität Braunschweig, Mendelssohnstraße 1, 38106 Braunschweig, Germany
²Center of Pharmaceutical Engineering (PVZ), Technische Universität Braunschweig, Franz-Liszt-Straße 35a, 38106 Braunschweig, Germany

Introduction

- Nanosuspense formulations such as solid lipid nanoparticles (SLN) are widely examined as carriers for poorly water soluble drugs
- SLN were manufactured using a novel microchannel high pressure hot melt homogenization device [1, 2]
- Previous studies have shown, that albumin stabilizes the hyperforin diclohexylammonium salt (HYP-DCHA) [3]
- This study evaluates the influence of albumin addition into the outer phase of a SLN dispersion

Experimental Methods

Preparation of SLN
- Lipid matrix 5 %
  - 30 % phosphatidylcholine (Phospholipon® 900G, Lipoid)
  - 70 % hydrogenated palm oil (Solutan® 154, Condens)
- Aqueous phase 95 %
  - 1 % macrool 15-hydroxystearate (Solutol® H8515, BASF)
  - 99 % double distilled water (all w/w) [4]
- Microchannel high pressure hot melt homogenization device
  - Pneumatic pressure intensifier
  - Microchannel
  - Full temperature control (70 °C)
- Pressure booster: 1:59

Results and Discussion

Process understanding and storage of unloaded SLN
- Central Composite Design of Experiment (DoE) examines the influencing factors of the particle size
- Narrow particle size distribution
- Pressure of homogenization 1240 bar
- Number of cycles 4
- Stable over three months

HYP-DCHA stability in lipid matrix
- HYP-DCHA concentration decreases upon storage
- No antioxidants or stabilizers such as BSA
- Location of HYP-DCHA at the surface of the solid lipid matrix without protection against environmental influence

Sample Preparation for HPLC
- The amount of HYP-DCHA in the outer phase was determined after ultracentrifugation with a centrifuge
- The amount of HYP-DCHA in the lipid matrix or the SLN dispersion was determined from the supernatant after the following sample preparation

HYP-DCHA stabilities in SLN formulations
- Three different aqueous phases (AP)

Parameters (in %)

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<th>AP1</th>
<th>AP2</th>
<th>AP3</th>
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<tr>
<td>DMEM</td>
<td>50</td>
<td>100</td>
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</tr>
<tr>
<td>FBS</td>
<td>5</td>
<td>15</td>
<td>80</td>
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<tr>
<td>1 % BSA</td>
<td>100</td>
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HYP-DCHA concentration in the SLN formulations of three different aqueous phases

The different aqueous phases (AP) for the SLN dispersions
- No HYP-DCHA recovery within the outer aqueous phases
- AP2 and AP3 had the highest HYP-DCHA recovery

Conclusion

- A setup with homogeneous pressure of 1240 bar and 4 cycles (bar) and a narrow particle size distribution of a D50 value of 64 nm, a D90 value of 148 nm and a mean of 101 nm
- HYP-DCHA concentration decreases upon storage in lipid matrix
- Slower decrease in SLN dispersion with DMEM and FBS (which contains BSA as major component)
- An addition of BSA into the aqueous phase could protect part of HYP-DCHA

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References