Introduction

Self-emulsifying drug delivery systems (SEDDS) are lipid based formulations which spontaneously form stable emulsions under mild agitation in gastro intestinal (GI) fluids (Czajkowska et al., 2013). Although liquid SEDDS and SMEDDS are beneficial to enhance drug bioavailability, low stability, leaching, drug precipitation, shelf- stability and compatibility with capsule shells as well as potential GI irritation have led to the development of solidification techniques, which transform SEDDS to solid SEDDS (Kallaiappan et al., 2012).

Batch manufacture is often associated with difficulties of scale-up, high cost, high resource needs and difficulties in consistent production. In contrast, a continuous process can increase yields, reduce development times, production times, failures of scale-up, resource uses and costs (Lee et al., 2015).

Here, a continuous manufacturing process (two screw extruder) was developed for adsorbing liquid SEDDS onto mesoporous silica carriers in order to produce solid free flowing SEDDS powders. Key process parameters were identified and produced solid SEDDS characterised.

Materials

SEDDS: Labrasol M1944CS, Labrasol and Capryol 90 were provided by Gattefosse (SAS, France).

Solid carriers: Syloid XDP3050 and Syloid XDP3150 were provided by Grace GmbH & Co KG (Worms, Germany).

Butters: All other ingredients were purchased from Sigma Aldrich and were of analytical grade.

Lipid Loading - Loss on Ignition

Solid SEDDS were heated to 600°C for 1 hour in a furnace and the loss in weight determined. Solid SEDDS were heated to 600°C for 1 hour in a furnace and the loss in weight determined.

Methods

Preparation of liquid SEDDS

A suitable SEDDS formulation was developed employing Labrafilm M1944CS (5-55%), Labrasol (60-90%) and Capryol 90 (4-15%). Manufacture of solid SEDDS

Solid carriers were fed into zone 3 of a Thermo Scientific® Process 11 twin screw extruder. Liquid SEDDS were added in zone 4. Liquid loading of 1:1, 2:1 and 3:1 (liquid/carrier) was targeted. Two screw configurations were tested a) 29 conveying elements (C) only and b) two kneading zones (each with 7 mixing elements assembled at a 60° angle). (Figure 1).

Figure 1: Screw configuration with two kneading zones.

Results and Discussion

SEDDS: The optimised formulation (F3) was composed of 15 % Labrasol M1944CS, 30 % Labrasol and 5 % Capryol 90 (%w/v). F3 spontaneously formed a homogenous emulsion with a droplet size of less than 200 nm (in water) and possessed pH robustness at pH 1.2 and pH 6.8.

Solid SEDDS manufacture — conveying elements only

Poor mixing efficiency, resulting in inhomogeneous distribution of liquid SEDDS on Syloid XDP 3050 (small and large particles) was observed (Figure 2a-b). Due to poor mixing, Syloid XDP 3150 was not tested.

Concluding remarks

In a previous study, we investigated the continuous processing of adsorbing liquid SEDDS onto solid carriers produced solid SEDDS with good flow properties. Syloid XDP 3150 seemed more robust to the process than Syloid XDP 3050. Changes in droplet size distributions were observed after solidification of SEDDS.

Future Work

Future studies will look at excipient desorption studies, as well as silica particle size distribution and pore structure characterisation.

Acknowledgements

The authors would like to thank Fraser Mahbott for the help with SEM images.

References:


Table 1: SEDDS specifications

<table>
<thead>
<tr>
<th>Trade name</th>
<th>Syloid® XDP 3050</th>
<th>Syloid® XDP 3150</th>
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</thead>
<tbody>
<tr>
<td>Physical form</td>
<td>White powder</td>
<td>White powder</td>
</tr>
<tr>
<td>Oil Absorbing Capacity (mg/100 ml)</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Mean particle size (µm)</td>
<td>45.66</td>
<td>120-170</td>
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<tr>
<td>Specific surface area (m2/g)</td>
<td>320</td>
<td></td>
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<tr>
<td>Tapped Bulk density (g/ml)</td>
<td>0.275</td>
<td>4.0-8.0</td>
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Table 2: Dynamic test results for Syloid XDP powders and solid SEDDS.

<table>
<thead>
<tr>
<th>Ratio by weight of solid carriers to liquid SEDDS</th>
<th>BFE (mJ)</th>
<th>SI</th>
<th>FRI</th>
<th>SE (mJ/g)</th>
<th>CBD (g/ml)</th>
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<tbody>
<tr>
<td>Syloid XDP3050</td>
<td>42.32</td>
<td>0.89</td>
<td>1.54</td>
<td>4.12</td>
<td>0.2484</td>
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<td>Syloid XDP3150</td>
<td>118.11</td>
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<td>Syloid XDP3150</td>
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<td>Syloid XDP3150</td>
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<td>1.10</td>
<td>0.96</td>
<td>9.62</td>
<td>0.3787</td>
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</tbody>
</table>

Figure 5: Droplet size - solid SEDDS Syloid XDP3050

Figure 6: Droplet size - solid SEDDS Syloid XDP3150

Figure 7: SEM images of Syloid XDP powders and solid SEDDS

Figure 8: SEM images of Syloid XDP powders and solid SEDDS

Figure 9: SEM images of Syloid XDP powders and solid SEDDS