Production and Characterization of Alginat-based Microcapsules Produced by a Vibrational Encapsulation Device for Cell Immobilization

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INTRODUCTION

Immobilization of living cells in alginate beads is a technology in an increasing range of different applications. Besides alginate modified hydrogel biomaterials, made from PEG or Pluronic® F127, can be used for 3-D cell cultivations of mammalian cells, stem cells and for tissue engineering. Especially stem cells have a significant interest as a renewable source of therapeutically useful cells. Clinical applications will require cultivation and bioprocessing efficiency that cannot be provided by conventional adherent cell culture technologies. Therefore the development of scalable methodologies for 3-D suspension cultures that are readily adaptable to large-scale bioreactors are necessary.

MICROBEAD FORMATION

Monodisperse alginate beads were produced using an Encapsulator B-395 Pro (Büchi GmbH). It is based on the principle that a laminar flowing liquid jet breaks up into equal sized droplets by a superimposed vibration. Generated droplets were collected in a hardening solution via ionotropic gelation under continuous stirring (Fig. 1).

CORE-SHELL-MICROBEAD FORMATION

With a concentric nozzle system core-shell-microbeads can be produced in an one-step procedure (Fig. 2). Capsules with an alginate shell and core, consisting of modified hydrogel biomaterials, can be generated. Therefore two advantages can be combined: The simple gelation process with a high production rate and the cell proliferating support through the hydrogel which makes 3-D cell cultivations possible.

RESULTS

Monodisperse Ca-alginate-beads in the size range of 180 – 600 µm were produced using 1.5 % Na-alginate different nozzle diameter, vibration frequencies and pump rates (Fig. 3). The standard deviation (SD) for all samples was < 5 %.

<table>
<thead>
<tr>
<th>Figure</th>
<th>Nozzle [µm]</th>
<th>Vibration frequency [Hz]</th>
<th>Electrode tension [V]</th>
<th>Pump rate [mL/min]</th>
<th>Bead-Ø [µm]</th>
<th>SD [%]</th>
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</thead>
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<tr>
<td>3.A</td>
<td>80</td>
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<td>700</td>
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<td>1500</td>
<td>700</td>
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<td>261</td>
<td>1.7</td>
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<tr>
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<td>150</td>
<td>1500</td>
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<td>3.00</td>
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<td>1500</td>
<td>2000</td>
<td>6.00</td>
<td>378</td>
<td>2.7</td>
</tr>
</tbody>
</table>

Fig. 3: Co alginate-microbeads produced with different nozzle sizes and constant vibration frequency.

A PEG fibrinogen-based hydrogel with particles for contrast was used to generate core-shell-microbeads. The core diameter can be varied by increasing the pump rate (Fig. 4).

OUTLOOK

The production process of the core-shell-microbead formation will be improved and other modified hydrogel biomaterials will be tested. Adherent cells will be encapsulated and cultivated in different suspension bioreactors. Furthermore an image analysis algorithm capable of computing bead diameter, roundness and cell number will be developed and validated.