Application Note No. 136
Producing cellulose sulphate microcapsules

Encapsulator B-390 / B-395 Pro: Production of Cellulose Sulphate-PolyDADMAC microcapsules for application within medical, biotech and pharmaceuticals fields
1. Introduction

Cellulose sulphate is a biocompatible ester and microcapsules are obtained by dripping solutions of the polymer into a precipitation bath containing the synthetic polycation polydiallyldimethylammonium chloride (polyDADMAC). This results in a rapid electrostatic interaction at the interface between the two oppositely charged polymers, cumulating in the formation of a mechanically stable hydrogel membrane in a single step process. These microcapsules have excellent mechanical properties due to strongly interacting sulphate groups and do not initiate immune response. In addition membranes have a homogenous structure and a narrow pore size, and the latter can be pre-determined.

The method is mainly used for the encapsulation of animal and stem cells for medical and biotechnological applications, and has being used in clinical trials for transplantation of cells within humans to treat many diseases. It can also be used for encapsulating API's.

Aim: To produce cellulose sulphate-polyDADMAC microcapsules using a single step process compared to other cell encapsulation process (alginate-poly-L-lysine) which require multiply steps.

2. Equipment

- Product: Encapsulator B-390/B-395 Pro
- Set up: Single-flow nozzle system – 300 µm nozzle
- Pumping: Syringe pump/air pressure system
- Blender

3. Chemicals and Materials

Chemicals:
- Polymer: 2% (w/v) Cellulose sulphate (Biorefinary, Germany)
- Gelling sol: 4% PolyDADMAC (Mw 35 kDa) (Biorefinary, Germany)
- Deion. water

Picture 1: Polymer preparation

4. Procedure and Parameters

Remove pre-filter from bead producing unit.

Dissolve 2 g of cellulose-sulphate in 100 mL of water. Use the blender to dissolve the cellulose sulphate completely (picture 1). Let the solution sit until it is clear and has released all the air within it. The air bubbles can be removed quicker by placing in a sonication bath or placing under vacuum.

Add 8 g of PolyDADMAC (Mw 35 kDa) into 200 mL of water and stir until it is completely dissolved.

Materials which are to be encapsulated are added to the cellulose sulphate after it has been mixed. During capsule production these materials become entrapped (encapsulated) within the cellulose sulphate core, which is completely enveloped with the polyDADMAC membrane.
Use 20 mL of the Cellulose-sulphate solution. Begin production (hardening) after obtaining a stable droplet chain of droplets. Use electrostatic charge to disperse droplets and prevent collision. After cellulose sulphate droplets have landed in polyDADMAC bath, allow to harden for at least 30 min (T=0, when last drop lands in gelling bath). Wash capsules with copious amount of water to remove any unreacted polyDADMAC, which may be present around the particles.

4.1 Process parameters

- Flow rate 8 mL/min
- Frequency 400 - 600 Hz
- Pressure 0.5 bar
- Amplitude 5
- Charge > 1000 V

5. Result

- Amount Extruded 20 mL
- Yield > 99%
- Morphology spherical
- Size 745 µm
- Std. Dev. ± 2.3%

6. Conclusion

The Encapsulator B-390 and B-395 Pro are able to produce spherical cellulose sulphate-polyDADMAC microcapsules in a single step process with the produced particles having an extremely narrow size distribution. These capsules can also be produced under sterile conditions by using the reaction vessel of the B-395 Pro for encapsulation of animal and stem cells for biomedical applications.

Many studies have shown that these types of capsules function more optimally compared to alginate-poly-L-lysine capsules system as they do not initiate immune response and form a more stable structure.

With the different nozzle sizes available for the Encapsulator the cellulose sulphate capsule size can be chosen in the range of 400 - 2500 µm and capsule size can also be varied by using different molecular weight polyDADMAC.
7. References