Production of uniform poly-lactic acid beads

Encapsulator B-390 / B-395 Pro: Production of uniform poly-lactic acid (PLA) microbeads using a three-step process with solvent evaporation and the concentric nozzle system

Poly-lactic acid (PLA) microbeads with spherical shape having a diameter around 550 µm were produced using a three-step process. Firstly, uniform PLA droplets (dissolved in DCM) were stabilized in a calcium-alginate shell. Then the organic solvent was evaporated and finally, the PLA microspheres were recovered by dissolution of the alginate shell in tri-sodium citrate solution.

Active pharmaceutical ingredients (APIs) could be embedded in the PLA matrix to extend the shelf live, increase the bioavailability as well as retarding its release.

1. Introduction

Over the last years, PLA has received great attention from the biomedical field and the pharmaceutical industry, as biocompatible, non tissue-reactive and biodegradable material. PLA microbeads can be used to encapsulate a wide variety of active materials. The described method enables the encapsulated substance (termed encapsulant) to be protected from many different environmental conditions such as oxygen, water, pH etc., and can help prolong its shelf life. In addition, encapsulation also enables the controlled release of the encapsulant. The size of the PLA beads produced depends on the concentric nozzle set in place and on the ratio between core and shell feeds. The possible range in diameter lies between 50 and 700 µm.

2. Experimental

Equipment: Encapsulator B-390 / B-395 Pro, concentric nozzle set, hand blender, external syringe pump (optional for Encapsulator B-395 Pro)

Chemicals and Materials: 0.75 g PLA (Resomer® RG 755 S) was dissolved in 7.5 mL methylene chloride (DCM). A 2 % (w/v) sodium alginate solution, a 16 g/L $CaCl_2$ solution in H_2O (saturated with DCM over night) and a 200 mM tri-sodium citrate solution were prepared. Sodium alginate was dissolved using a hand blender.

PLA microspheres were produced using a three-step procedure:

1) PLA solution droplets were stabilized within core-shell alginate capsule using Encapsulator with concentric nozzle set (Table 1).

Table 1: Encapsulator process settings for first step.

Nozzle set	Concentric nozzle set: 150 µm inner, 300 µm outer opening
Feeding	Shell: alginate solution / pressure bottle Core: PLA solution / syringe pump
Feed rate core	2.0 mL/min
Vibration frequency	600 Hz
Electrode tension	2300 V
Pressure	500 mbar
Hardening bath	$CaCl_2$ solution, gently strirred

Both feed lines were connected and the shell feed was shut by the liquid flow regulating valve. Stirrer, vibration, electrode tension and pressure parameters were set and activated. The core feed flow rate was adjusted to 2.0 mL/min. Then, the shell feed rate was adjusted to form homogenous droplets under stable conditions. Finally, the core-shell capsules (Figure 1) were dripped in the stirred hardening bath. The capsules were hardened during 10 min.

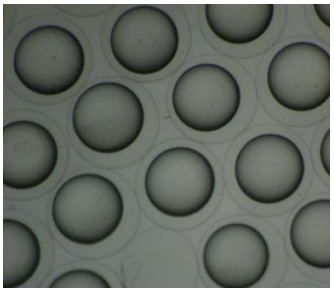

Figure 1: Mono-dispersed, homogenous and spherically shaped liquid-core microcapsules with a DCM-PLA core.

2) The capsules were washed four times with distilled water to remove excessive $CaCl_2$ and DCM. Do not stir at a high speed as this can result in the loss of DCM from the core.
3) Then, the PLA microspheres were released by dissolution of the alginate shell in tri-sodium citrate solution. Add the citrate solution very slowly and gently to the liquid-core microcapsules, and do not mix or stir, as this can cause the formation of bigger or smaller sized micro-beads. Leave this mixture for 2-3 h, to enable all the DCM to evaporate off and alginate shell dissolving, resulting in the formation of stable PLA microbeads with the required characteristics (Figure 2).

3. Results

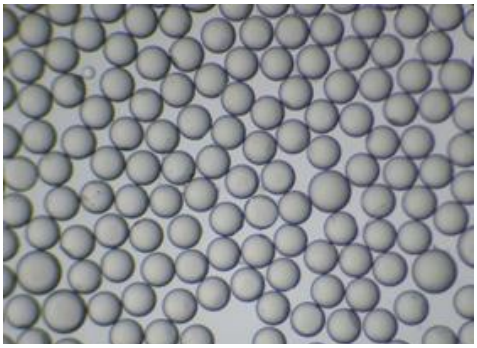

Figure 2: Mono-dispersed and spherical PLA micro-beads of equal shape and size.

4. Conclusion

The BUCHI Encapsulator B-390 / B-395 Pro is able to produce spherical and mono-dispersed PLA micro-beads in the size range of 550 µm. Variation of feed rates and nozzle sizes enables to adjust the PLA bead size.