Development of Biodegradable Oil Encapsulated Microbeads

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Introduction

Encapsulation from the verb encapsulate can be defined as "*enclose in or as if in a capsule*". Encapsulation is a method to enclose an internal material, either solid or liquid, with an outer containment shell.

In this study, a ternary phase poloxamer mixture using a dual nozzle to create a shell and core type microbead will encapsulate oil. Bead requirements are:

- 500-1500 micrometers in diameter
- Water soluble at all temperatures
- Shiny & aesthetic properties
- Biodegradable

Various encapsulation techniques are available ranging from chemical techniques like coacervation (Bachtsi, 1996) to physical techniques like ultrasonic vibrating nozzles (Brandenberger 1998 & 1999). The encapsulation technique that is used in this paper is the extrusion method. The extrusion method can be further divided into sub-groups such as extrusion-spheronization (Soh, 2006), electrostatic-extrusion (Goosen, 2002) along with many others. For this article, a simple dual nozzle was used for the investigation. The research was broken up into four stages:

1. Mathematical modeling of droplet & bead formation
2. Investigation of ternary gel formation mixing poloxamer, water & solvent
3. Film coating investigation
4. Investigation into using a fluidized bed to further coat beads

For this paper, the first stage of mathematical modeling & bead formation will be discussed. Eight types of poloxamer have been chosen which differ in the number of - (POE -) and - (POP-) units. These units provide different characteristics to the molecules, which define their molecular weights, physical form and HLB values.

Materials and Methods

Pluronic (poloxamer) F68 (M_w 8400) and F127 (M_w 12600) were purchased from BASF ChemTrade GmbH, UK & Ireland. The remaining samples L35 (M_w 1900), 17R4 (M_w 2650), P65 (M_w 3400), F38 (M_w 4700), F98 (M_w 13000), F108 (M_w 14600) were obtained as a gift from BASF Corporation, NJ, USA. All eight poloxamer samples shall be used in the initial characterization experiments. For the mathematical modeling F68 shall solely be used. The glass dual nozzle was produced within the university.

Viscosity
The viscosity of the eight poloxamer samples were performed using Carri-Med Rheometer CSL[2] 100, made by TA instruments.

XRD

All eight samples crystallinities were investigated using a PANalytical X-Pert Pro Diffraction System using a beam power of 35 kV / 30 mA. The sample spinner PW3064 was used at a speed of 1 rps. The scans had a range from 3[°2Θ] to 40 [°2Θ].

DSC

The DSC used in this research was a Perkin-Elmer model DSC 4. The samples were heated from 20°C to 150°C at a rate of 5°C/min.

Surface Tension & Interfacial Tension

The item of equipment used in relation for determination of surface tension and interfacial surface tension of liquids was the Model 'OS' Balance/Tensiometer. All experiments were performed at 25°C.

Mathematical Modelling

COMSOL Multiphysics® has been used for modeling of the velocity profiles of the dual nozzle equipment.

Results and Discussion

Viscosity

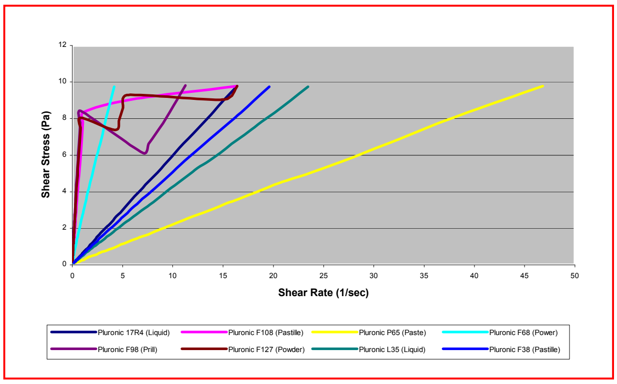

Figure 1: Viscosity of Poloxamers

From the rheogram (figure 1), it is evident that the majority of the poloxamer's exhibit Newtonian characteristics. For Pluronics F98 and F127, both plots at a region of 8 Pa on the stress axis develop a turning point and the gradients change from being positive to negative. At points further on the plots, further turning points shows how the gradient changes back to positive. This seems very irregular; a possible explanation that may cause this would be due to the presence of solid particles or lumps when the procedure was carried.

XRD

From the diffraction graph (figure 2) it is now possible to tell whether the respective pluronics are crystalline or amorphous. Where there are no peaks in the graph, the materials tested are amorphous. So the poloxamers that are amorphous are Pluronics 17R4 and L35, they produce no peaks and only a halo is reflected in the graph. P65 partly amorphous and partly crystalline will produce a graph that consists of the amorphous halo with peaks superimposed. The remaining samples are all crystalline producing sharp peaks.

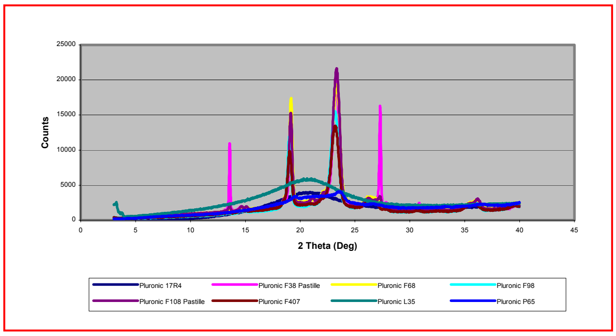

Figure 2: XRD of Poloxamers

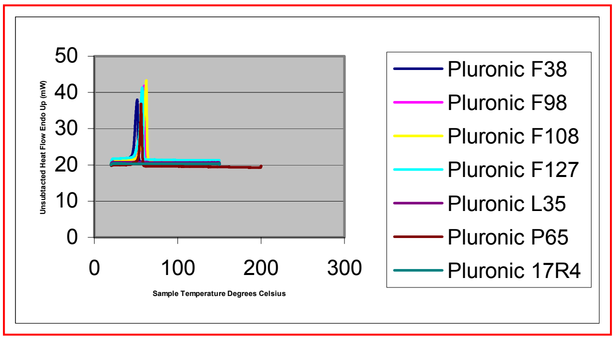

Figure 3: DSC of Poloxamers

DSC

In this DSC (figure 3), a clear pattern can be distinguished between the crystalline & amorphous materials. The crystalline materials can be shown to have peaks, which show their change from a crystalline state to an amorphous state. This is in contrast to the liquid amorphous poloxamers, which produces a relatively straight line. Hence not much heat is required to break the disordered bonds within these amorphous structures.

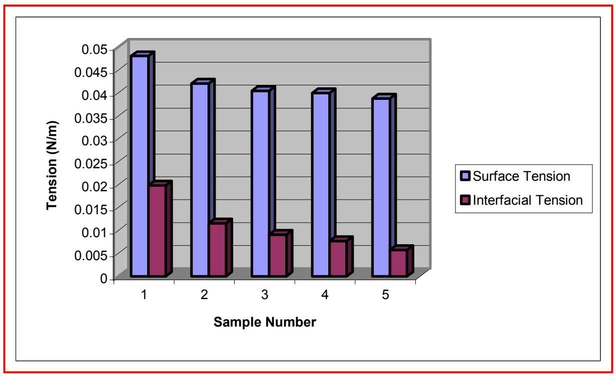

Figure 4: Interfacial Tension & Surface Tension of F68

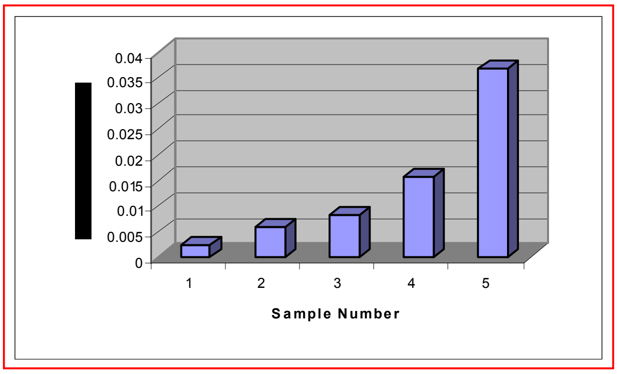

Figure 5: Viscosity of Various Concentrations of F68

Surface Tension & Interfacial Tension

Samples 1-5 are 1, 5, 10, 20, 40 %w/v F68 respectively. Figure 4, shows that increasing the concentration reduces the surface tension & interfacial tension. This is understandable as poloxamer is an amphiphilic molecule. The viscosity of the samples also increases with increase in concentration (figure 5).

COMSOL Multiphysics®

Figure 6 illustrates , the velocity of both the inner and outer stream increase tremulously from top to bottom of the dual nozzle, it is quite relevant to remember that the overall length of the equipment is just 0.16m therefore it is a considerably change over just a short distance. Figure 6, shows that for the outer annulus the velocity increases by a factor of 13, roughly from 0.027 m/s to 0.35 m/s. As for the inner tube, its velocity increases by a factor of 31.5 roughly, 0.105m/s to 3.3m/s. From the graphs it is clearly visible that stream velocities become more parabolic further down the dual nozzle suggested by the gradient of the curves, which would be expected as velocity increases downwards. The plot gives us very good visual representation of the velocity profile difference between the inner pipe and the outer annulus. Ideally at the bottom of the nozzle these profiles should be closely similar so that droplet formation and encapsulation process is successful. The other model (figure 7) provides a clear picture how there is a pressure drop across the dual nozzle.

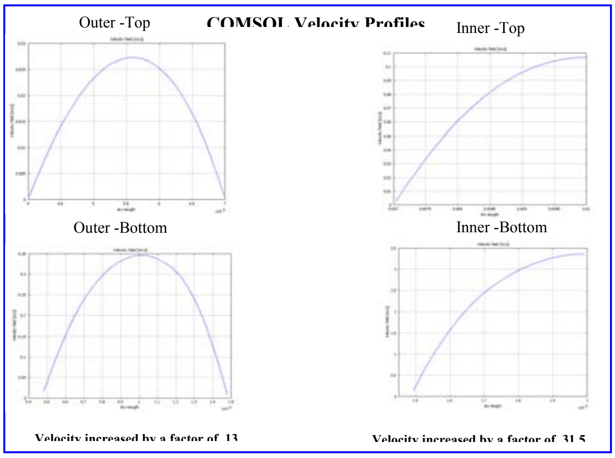

Figure 6: Velocity Profiles produced by COMSOL

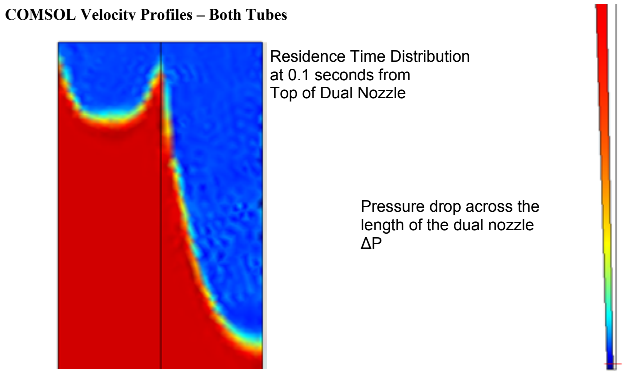

Figure 7: Visual Velocity Profiles produced by COMSOL and Pressure Drop

The blue colour represents atmospheric pressure at the end of the nozzle, as the colour changes from green to yellow to eventually red, this represents the gradual increase in pressure upwards in the dual nozzle.

Conclusion

First of all, with respect to achieving a suitable material to satisfy the design criteria, Poloxamers (Pluronics) show real potential in this process. Many materials investigated could not achieve the entire factors required. The main problems within the design criteria was encapsulating the oil core and producing beads of a clear clarity, poloxamer managed these with ease. In relation to the design of the dual nozzle extrusion equipment it was the first step in achieving micro-capsules; it formed beads of the required size which was a success. On the other hand, there are some difficulties connected with flow through the equipment, since the nozzle is so fine blockage can occur frequently. This means that achieving the right viscosity and makeup of the extrusion material is vital. Using equations such as Navier Stokes and Bernoulli's the fluid flow characteristics within the piece of equipment were investigated, and the velocity profiles were established. To gain a more accurate model and a better visual representation of results, the use of COMSOL Multiphysics was found very beneficial.

References

- Bachtsi, *A.R. et al.* (1996) *"Synthesis and release studies of oil-containing poly(vinyl alcohol) microcapsules prepared by coacervation"* Journal of Controlled Release 38, 49-58
- Brandenberger, H et al. (1999) *"Monodisperse particle production: A method to prevent drop coalescence using electrostatic forces"* Journal of Electrostatics 45, 227-238.
- Brandenberger, H et al. (1998*) "A new multinozzle encapsulation/immobilization system to produce uniform beads of alginate"* Journal of Biotechnology 63, 73-80.
- Goosen, M.F.A. (2002) *"Experimental and modeling studies of mass transfer in microencapsulated cell systems"* Tropical Journal of Pharmaceutical Research (Vol. 1) 1, 3-14
- Soh, J.L.P. et al. (2006) *"Torque rheological parameters to predict pellet quality in extrusion-spheronization"* International Journal of Pharmaceutics 315, 99-109