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Case Study



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Case Study - Process Engineering

Microencapsulation by Coacervation: Innovating Drug Delivery in the Pharmaceutical Industry

Microencapsulation through coacervation represents a cutting-edge technique at the forefront of drug delivery innovation within the pharmaceutical industry. This method, rooted in colloid chemistry, involves the phase separation of a solution into two distinct liquid phases: a dense coacervate phase enriched with polymers and a dilute phase primarily composed of solvent. This process enables the encapsulation of active pharmaceutical ingredients (APIs) within protective polymer shells at a microscale level.

In pharmaceutical applications, coacervation serves as a versatile tool for microencapsulation, offering precise control over the release kinetics and stability of encapsulated substances. By forming coacervate droplets around APIs, pharmaceutical engineers can tailor the release profiles of drugs, ensuring sustained and controlled delivery over extended periods. This capability enhances therapeutic efficacy, reduces dosing frequency, and minimizes potential side effects, thereby improving patient compliance and treatment outcomes.

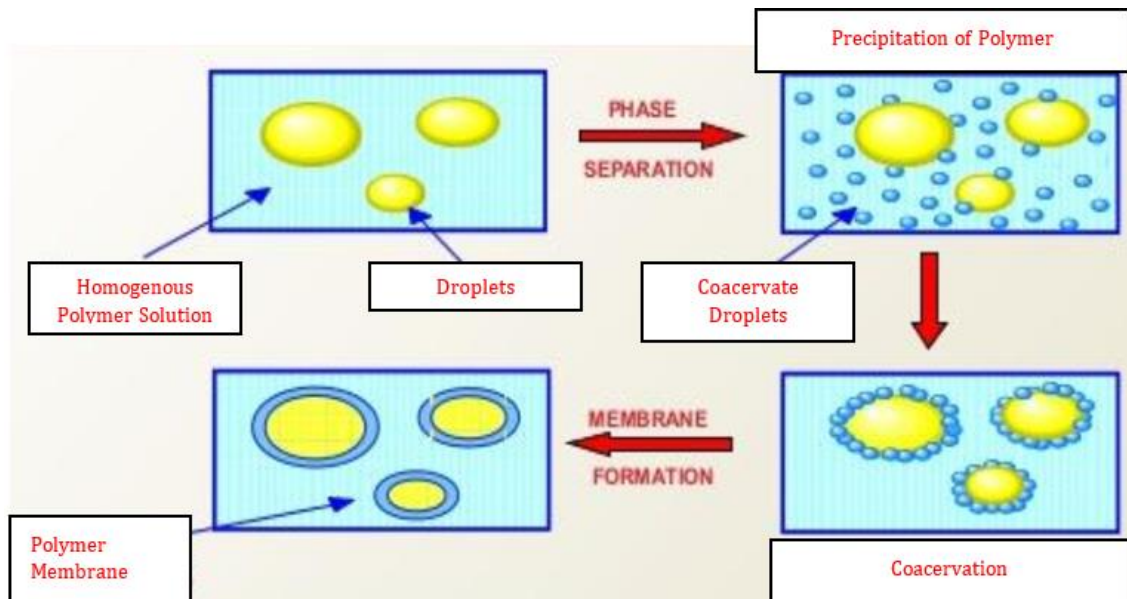
Chemical engineers play a crucial role in optimizing and scaling up coacervation-based microencapsulation processes for pharmaceutical applications. They leverage their expertise in colloid chemistry, polymer science, and process engineering to fine-tune formulation parameters such as polymer composition, solvent selection, and operating conditions. This interdisciplinary approach ensures the reproducibility, efficiency, and safety of microencapsulated drug formulations, meeting stringent regulatory standards and clinical requirements.

In conclusion, microencapsulation by coacervation exemplifies the convergence of theoretical principles and applied engineering within the pharmaceutical sector. This innovative approach not only enhances the stability and bioavailability of drugs but also opens avenues for targeted and personalized medicine. As research and development continue to progress, coacervation-based microencapsulation holds immense promise for addressing complex healthcare challenges and improving patient care worldwide.

Through ongoing collaboration and technological advancements, chemical engineers remain at the forefront of advancing coacervation-based microencapsulation technologies, paving the way for safer, more effective drug delivery solutions that meet the diverse needs of modern healthcare.



Coacervation Process



Questionnaire

A scientist is developing microsphere formulations for sustained release of an Active Pharmaceutical Ingredient (API) over a 30-day period. The goal is to estimate the diameter of the microspheres required to achieve specific daily release targets of API, considering a known diffusivity of the API from the polymer matrix. Assume that in 30 days, the entire API is released from the polymer matrix.

Objective:

i. Assuming the Diffusivity of API in the polymer matrix: $D_{API} = 1 \times 10^{-7} \text{ g/m}^2/\text{hr}$ (Constant), estimate the diameter of the microspheres needed to achieve the following daily release targets of API over 30 days:

- Day 1: 2.0 grams
- Day 2: 2.5 grams
- Day 3: 3.0 grams
- Day 4: 3.5 grams
- Day 5: 4.0 grams
- Day 6: 4.5 grams
- Day 7: 5.0 grams
- Day 8: 5.5 grams
- Day 9: 6.0 grams
- Day 10: 6.5 grams

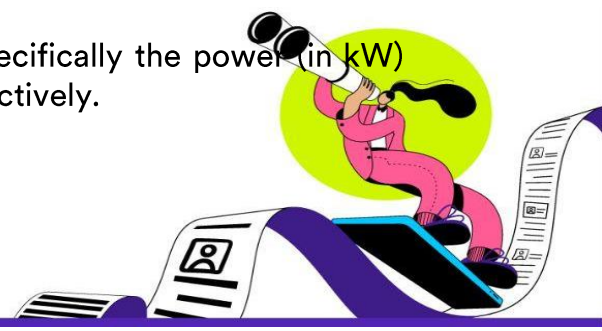


- Day 11: 7.0 grams
- Day 12: 7.5 grams
- Day 13: 8.0 grams
- Day 14: 8.5 grams
- Day 15: 9.0 grams
- Day 16: 9.5 grams
- Day 17: 10.0 grams
- Day 18: 10.5 grams
- Day 19: 11.0 grams
- Day 20: 11.5 grams
- Day 21: 12.0 grams
- Day 22: 12.5 grams
- Day 23: 13.0 grams
- Day 24: 13.5 grams
- Day 25: 14.0 grams
- Day 26: 14.5 grams
- Day 27: 15.0 grams
- Day 28: 15.5 grams
- Day 29: 16.0 grams
- Day 30: 16.5 grams

- ii. If the diffusivity is $\frac{1}{4}$ of the above value, how much time would it take to release the entire API (Active Pharmaceutical Ingredient).
- iii. Discuss the influence of microsphere shape (e.g., spherical vs. non-spherical) on the release kinetics of the API. How does shape affect diffusion rates, surface area-to-volume ratio, and overall release profile? Provide recommendations for optimizing shape to achieve desired release kinetics.

Assumptions:

- The drug release follows the Higuchi model, indicating a diffusion-controlled release from the polymer matrix of the microspheres.
 - The diffusivity of API in the polymer matrix is known and constant.
 - Ideal behaviour of microspheres in drug release.
 - Neglect any external factors beyond specified conditions.
1. In a manufacturing plant, a top-mounted Pitch Blade Turbine (PBT) agitator is required for mixing a batch of viscous fluid with a total volume of 5000 litres. The agitator is mounted on a **cylindrical vessel** with a diameter of 2 meters and then. The vessel is equipped with a **cylindrical body and dished ends with 10% torispherical heads**. The fluid has a viscosity of 1000 cP (centipoise) and a density of 1000 kg/m³. The agitator blade diameter is 1 meter.
 - i. Estimate the motor requirement, specifically the power (in kW) needed to drive the PBT agitator effectively.



- ii. If 4 rectangular baffles are installed and mixing efficiency i.e. shear, Reynold's no. etc. is not compromised, will the above motor suffice the requirement?

Assumptions and Requirements:

- The Pitch Blade Turbine (PBT) agitator provides adequate mixing for the viscous fluid.
- The vessel geometry (cylindrical with dished ends and 10% torispherical heads) is suitable for the PBT agitator and the process requirements.
- Assume standard efficiency for the motor and pump system (typically around 85%).
- Neglect losses in the transmission system (shaft losses, gearbox losses).
- The agitator operates in a constant viscosity fluid with uniform density.
- The PBT agitator operates effectively without cavitation at the specified rotational speed.

Given:

- Vessel type: Cylindrical with dished ends (10% torispherical heads)
 - Vessel diameter: 2 meters
 - Batch volume: 5000 liters (5 m^3)
 - Agitator type: Pitch Blade Turbine (PBT)
 - Agitator rotational speed: 100 rpm
 - Fluid viscosity: 1000 cP (centipoise)
 - Fluid density: 1000 kg/m^3
 - Agitator blade diameter: 1 meter
 - Agitator tip speed: 1.5 m/s
3. Coacervation is known to be influenced by pH changes. Design an experiment to investigate how varying pH affects the coacervation process and the stability of the coacervate phase. Discuss potential implications for drug delivery applications.
4. A pharmaceutical process involves the coacervation of a polymer solution using dichloromethane (DCM). Into a polymer solution of 150 kg, an API solution is added. The API solution is prepared by mixing 600 g of API (Active Pharmaceutical Ingredient which is soluble in methanol) in 3.6 kg of methanol. A silicone oil is used Coacervating agent to extract the Dichloromethane which will initiate the encapsulation process i.e. API getting encapsulated inside polymer.

The details are as follows:

- Polymer concentration in the solution: 6% (w/w) of polymer in DCM.



- Silicone oil is used as the extracting solvent.
- DCM dissolves in silicone oil at a rate of 15 grams per litre of oil at the operating temperature.
- Extraction efficiency of silicone oil: 80%
- Molecular weight of API: Assume 200 g/mol
- Polymer molecular weight (Mw): Assume 100,000 g/mol
- Viscosity of silicone oil: Assume 100 centistokes (cSt), density of silicone oil: 950 kg/m³

Questions:

- i. Determine the mass of DCM that needs to be extracted to increase the concentration of Polymer to 65% (w/w) in the polymer solution (Consider conc. independent of silicone oil). Additionally, Calculate the volume of silicone oil required to achieve the calculated mass of extracted DCM.
- ii. Discuss the potential impact of temperature variation (+/- 5°C) on the efficiency of the extraction process. Include considerations for both DCM solubility's in silicone oil and API solubility in ethanol. Also, consider the volatilities of DCM and ethanol.
- iii. Explain the potential risks associated with the use of DCM and silicone oil in pharmaceutical manufacturing. Propose risk mitigation strategies for each solvent. Additionally, propose alternative solvent systems that could potentially replace DCM and evaluate their suitability based on solubility, efficiency, and safety considerations.
- iv. Discuss the role of Addition rate of silicone oil's in the effectiveness of coacervation process. Additionally, discuss how might viscosity impact the extraction process, and what adjustments could be made to optimize performance?
- v. The Particle size is the critical quality parameter for encapsulated drug which all determines the release of the drug. Considering the process is the done in an agitated vessel, elaborate on the role of agitation and agitator selection for the coacervation process.

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