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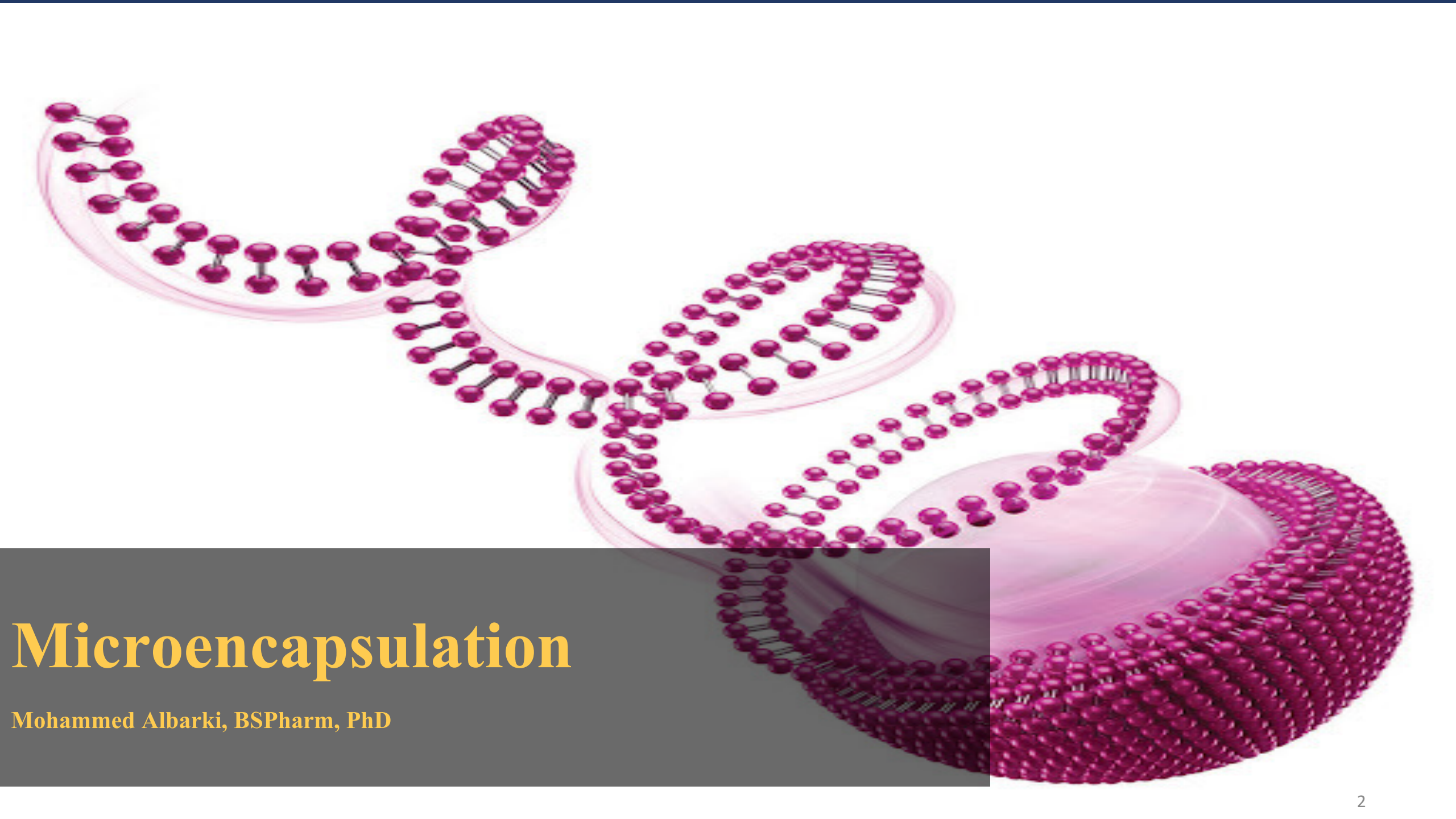
جامعة المستقبل



Microencapsulation

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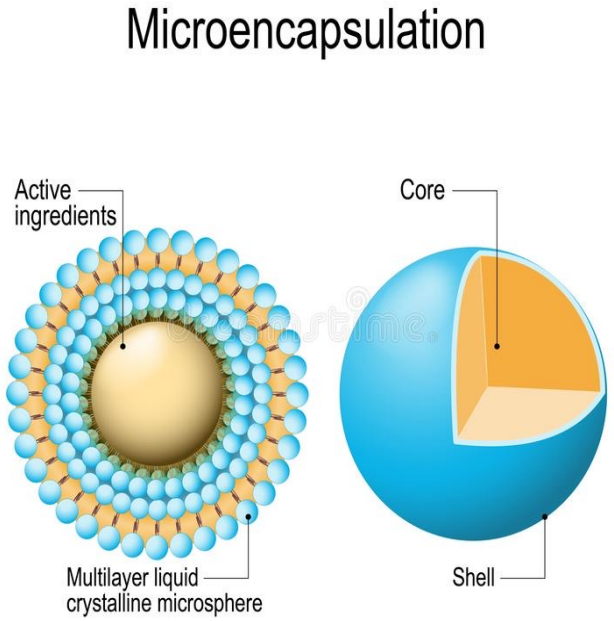
Microencapsulation

- It is a means of applying a relatively thin coating to small particles of solids or droplets of liquids.
- **Advantages of microencapsulation:**
  1. The smallness of the particles, so, the active ingredient can be widely distributed throughout the GIT, thus **improving drug absorption**.
  2. taste-masking
  3. Formulation of tablets or capsules containing incompatible ingredients.
- **Disadvantages or challenges:**
  1. No single microencapsulation process is useful for all materials.
  2. Difficulties, such as incomplete or discontinuous coating, and inadequate stability of sensitive drugs.



Core and Coating materials

- The **core** material (the drug particles) can be liquid or solid in nature.
- The solid core material can be an active ingredient alone or as a mixture with diluents and other excipients.

- The **coating material** should be:

1. Capable of **forming a film** that is cohesive with the core material.
2. Be chemically **compatible** and noncreative with the core material.

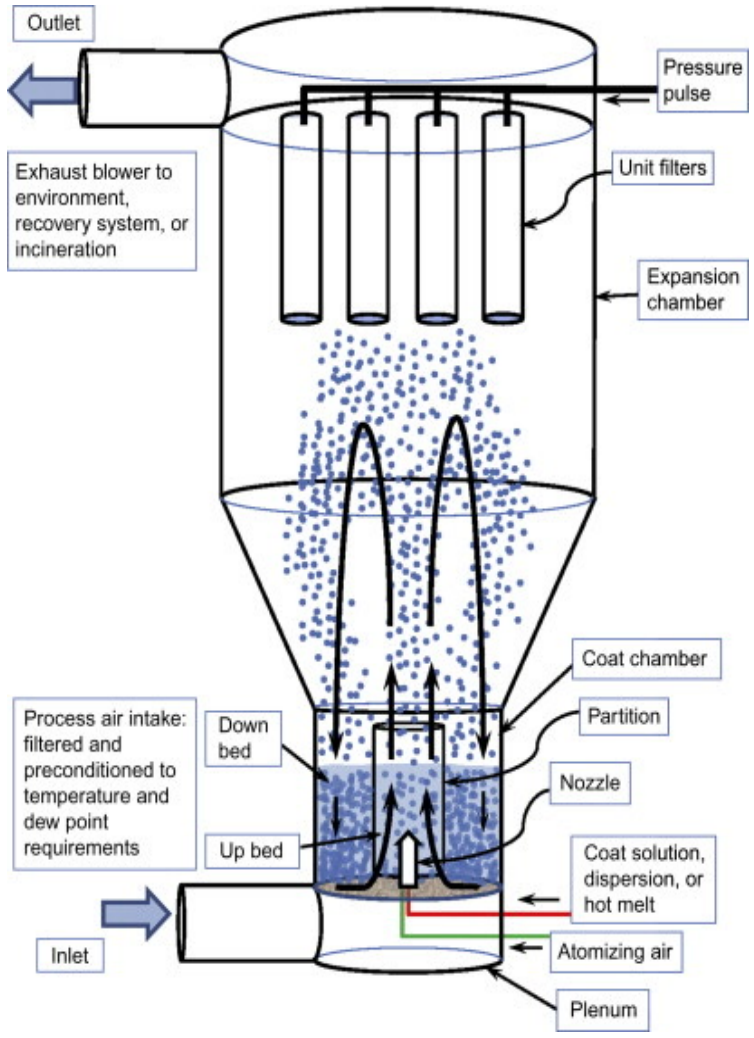
Examples of Core Material	Characteristic Property	Purpose of Encapsulation	Final Dosage Form
Acetaminophen	Slightly water soluble solid	**Taste masking**	**Tablet**
Aspirin	Slightly water soluble solid	Taste masking, sustained release, reduced gastric irritation.	Dry powder
Islet of Langerhans	**Viable cells**	Replacement therapy for diabetic patients	Injection
Isosorbide dinitrate	Water soluble solid	**Sustained release**	**Capsule**
Menthol, methyl Salicylate, camphor mixture	Volatile **solution**	**Reduction of volatility**; sustained release	**Lotion**
Vitamin A palmitate	Nonvolatile liquid	Stabilization to prevent oxidation	**Dry powder**

(NOT FOR SAVE).

Method of Microencapsulation

1. **Air suspension**: (for **solid core only**)

- This method consists of suspending the solid material in the air and spraying the coating material with the air.



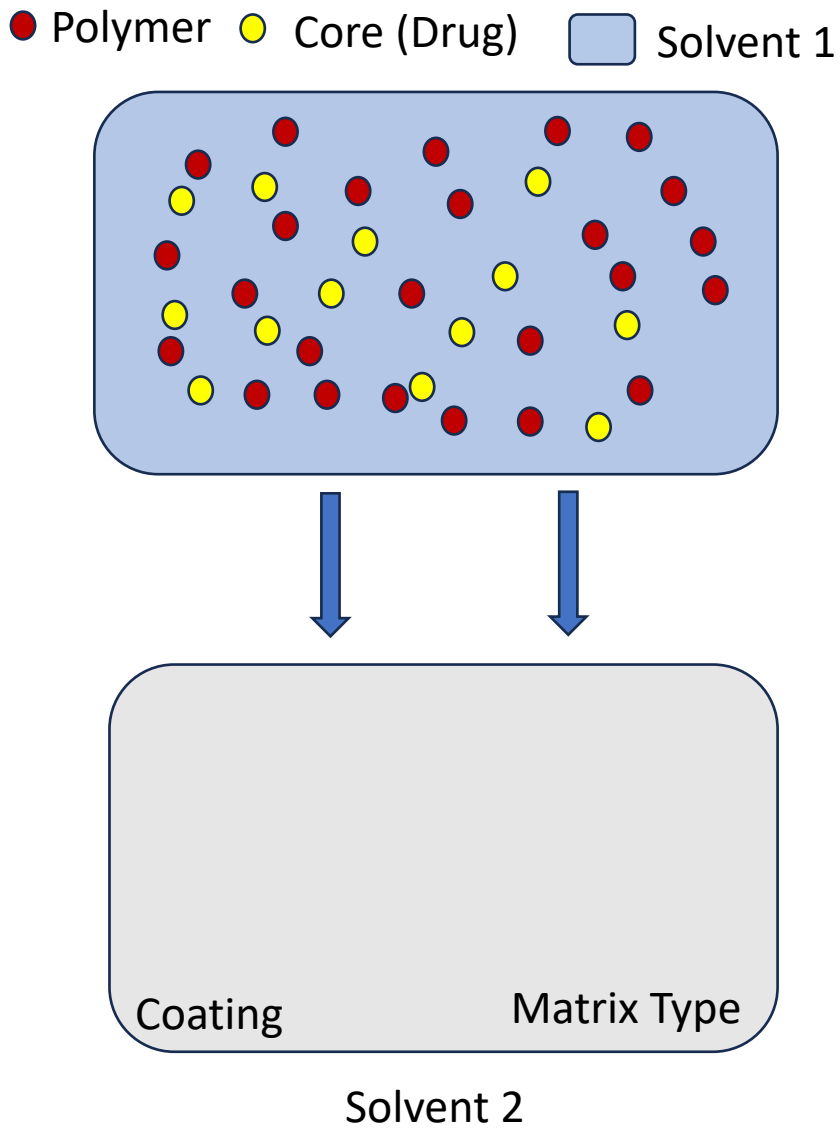
- However, this process generally is considered to be suitable only for the encapsulation of **solid core** materials.

Method of Microencapsulation

2. **Pan Coating**: (only for solids)
   - In this method, the coating is applied as an atomized spray to the desired ***solid*** core material in the coating pan. To remove the coating solvent, warm air is used in a process similar to that of tablet coating.

3- Solvent Evaporation

- The core material is dissolved **or** dispersed in a coating polymer solution (contains a volatile solvent for polymer ((solution 1)= core material (drug) + polymer + solvent)).
- Solution 1 is added **with agitation** to solution 2 which is a **solvent** that is immiscible with solution 1 (and coating polymer is insoluble in this solvent).
- The polymer will shrink on itself and **coat** the core material.
- Note: if the core material (drug) was soluble in **solution 1** it will form a matrix-type microcapsule (mixture) with polymer (not coating)
- Then solvent 1 is removed by evaporation with or without the aid of heat.
- **Note**: The resulting microcapsules can be used in suspension form or isolated as a powder



Method of Microencapsulation

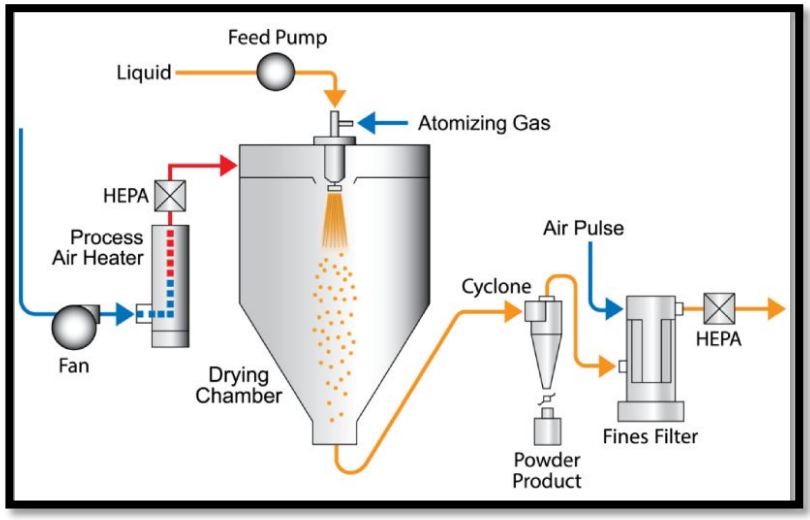
- **Spray drying and spray congealing:**
- These methods can be used for both **liquid and solid** drugs. Because of the similarity of these two processes, they are discussed together.
- Both involve:

1. **Dispersing the core material in a liquid coating material.**
2. Spraying the core-coating mixture (drug + polymer) into certain environmental conditions, whereby rapid solidification of the coating is achieved.

- The principal **difference** between the two methods is the means by which the solidification is achieved.
- Coating solidification in the case of **spray drying** is achieved by rapid evaporation (**heating**) of a solvent in which the coating material is dissolved.
- Coating solidification in **spray congealing** methods is accomplished by thermally congealing (**cooling**) of a molten coating material.

Method of Microencapsulation

- In practice, microencapsulation by spray drying is done by dispersing a core material in a coating solution, **in which the core material is insoluble,** and then atomizing the mixture into an air stream.
- The air (**hot air**) supplies the heat of vaporization required to remove the solvent from the coating material, thus forming the microencapsulated product.
- The equipment used for this purpose is the usual spray dryer.

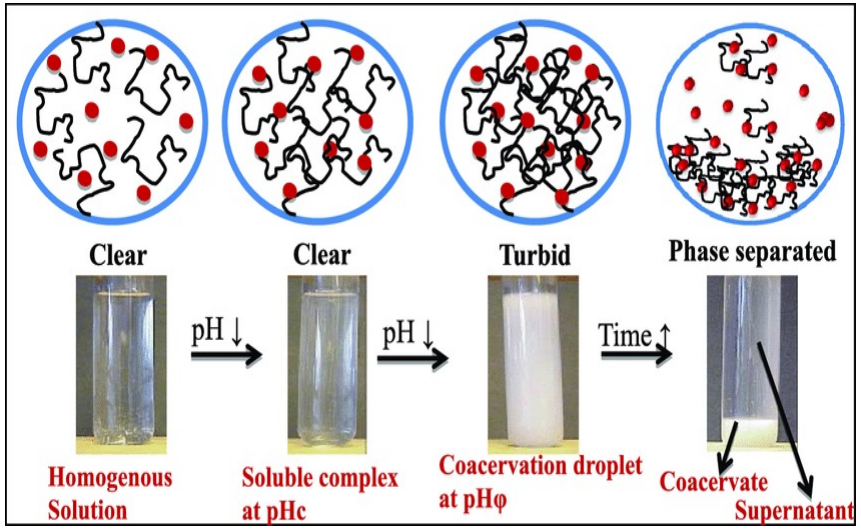


Method of Microencapsulation

- Microencapsulation by spray **congealing** can be accomplished with a **spray drying device**.
- Coating solidification (and microencapsulation) is accomplished by spraying the hot mixture into **cool** air.
- Waxes, fatty acids, and certain polymers which are **solids at room temperature** but meltable at high temperatures, are applicable to the spray congealing technique.

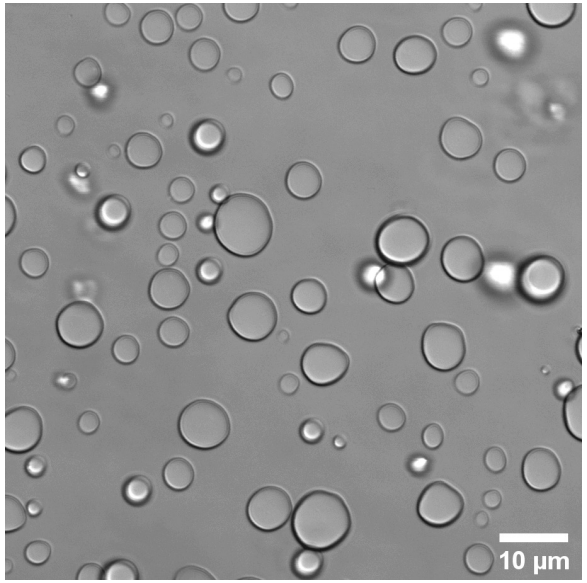
Coacervation-Phase separation:

- It can be used for **both liquid and solid** drugs. It consists of three steps.
- **Step 1: Formation of three immiscible phases:**
- Which are the
  - Liquid manufacturing vehicle phase.
  - Coating material phase (polymer).
  - Core material phase
- To form the three phases, polymer is **dissolved** in liquid manufacturing phase (**phase 1+ phase 2**), then the core material is **dispersed** into that liquid (**phase 3**).
  - Until this point we have **two phases** (polymer + vehicle) and dispersed core material.



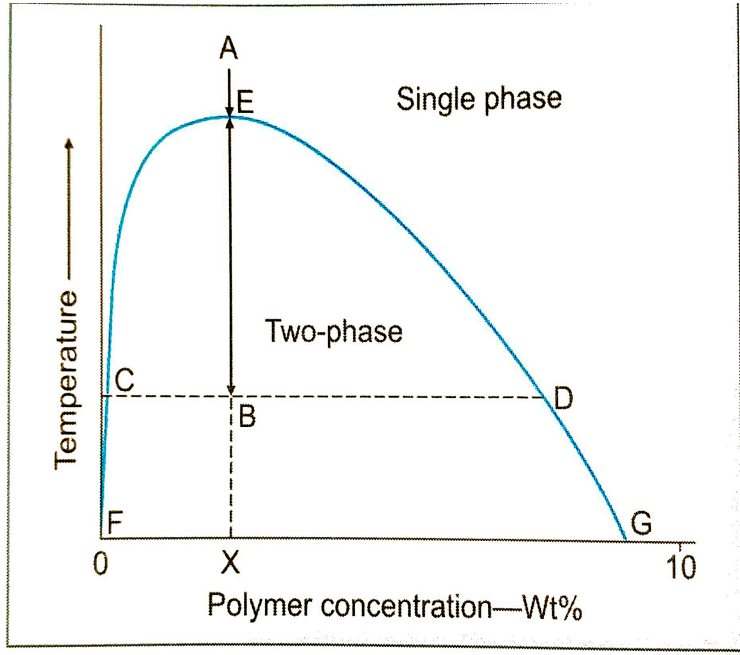
Step 1 (continue)

- To form three immiscible phases: the solubility of the polymer (the coating material) in the solvent is altered to form a third immiscible phase.
- This polymer-rich phase will contain **most** of the polymer in the solution and it is called as a **coacervate**.
- The process of coacervation-phase separation (phasing out the polymer) is formed by utilizing one of the methods:
- by changing the **temperature** of the polymer solution.
- or by adding **salt**.
- or a **nonsolvent**.
- or adding another polymer.



Method of Microencapsulation

- **Step 2: Deposition of the coating.**
- It consists of depositing the liquid coating material on the core material under controlled agitation by: for example further change in temperature.
- Deposition of the liquid polymer coating around the core material occurs if the coating polymer is adsorbed at the **interface between the core material and the immiscible solvent phase,** and this adsorption phenomenon is a **prerequisite** to effective coating.
- **Step 3: Rigidizing the coating.**
- It involves rigidizing the coating, usually by thermal techniques, to form the microcapsules.



ig. 15.10: General phase diagram-coacervatio
nduced thermally

Method of Microencapsulation

- The following example illustrates this technique.
- Ethyl cellulose (a water-insoluble **coating** polymer) is applied to N-acetyl-p-aminophenol (paracetamol) powder (**core material**) by utilizing the temperature characteristics of the polymer in the cyclohexane (**solvent**).
- Ethyl cellulose is insoluble in cyclohexane at **room temperature**, but it is soluble at elevated temperatures. The ethyl cellulose and cyclohexane mixture is **heated** to form a homogeneous (one-phase) solution.
- The aminophenol is **dispersed** (as insoluble powder) in the solution with stirring.
- Allowing the mixture to cool with continuous stirring results in coacervation-phase separation of the ethyl cellulose from cyclohexane and microencapsulate the core material.
- Allowing the mixture to cool further to room temperature causes gelation and solidification of the coating.
- The microencapsulated product can then be collected from the cyclohexane by filtration or centrifugation.