MICROENCAPSULATION

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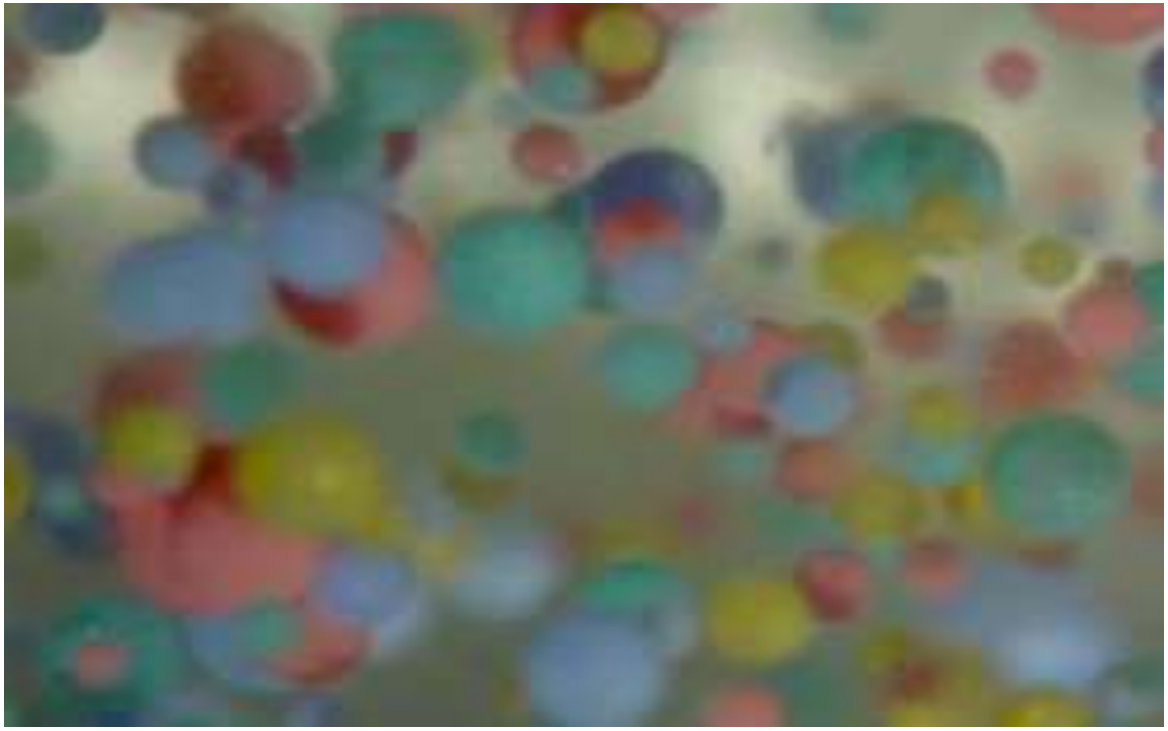


INTRODUCTION

- ✓ Microencapsulation is a process by which very tiny droplets or particles of liquid or solid material are surrounded or coated with a continuous film of polymeric material.

- ✓ The product obtained by this process is called as micro particles, microcapsules.

- ✓ Particles having diameter between 3 - 800µm are known as micro particles or microcapsules or microspheres.

- ✓ Particles larger than 1000µm are known as Macroparticles .

Fundamental Considerations

The realization of the potential that microencapsulation offers involves a basic understanding of the general properties of microcapsules, such as the nature of the core and coating materials, the stability and release characteristics of the coated materials, and the microencapsulation methods. One should note, however, that the method employed in the manufacture of microcapsules may well result in products of varied composition, quality, and utility.

Core Material

The composition of the core material can be varied, as the liquid core can include dispersed and/or dissolved material. The solid core can be a mixture of active constituents, stabilizers, diluents, excipients, and release-rate retardants or accelerators. The ability to vary the core material composition provides definite flexibility and utilization of this characteristic often allows effectual design and development of the desired microcapsule properties.

Coating Materials

The selection of a specific coating material from a lengthy list of candidate materials presents the following questions to be considered by the research pharmacist.

1. What are the specific dosage or product requirements—stabilization, reduced volatility, release characteristics, environmental conditions, etc?
2. What coating material will satisfy the product objectives and requirements?
3. What microencapsulation method is best suited to accomplish the coated product objectives?

Coat thickness

depending on the coating-to-core ratio and the particle size (surface area) of the core material.

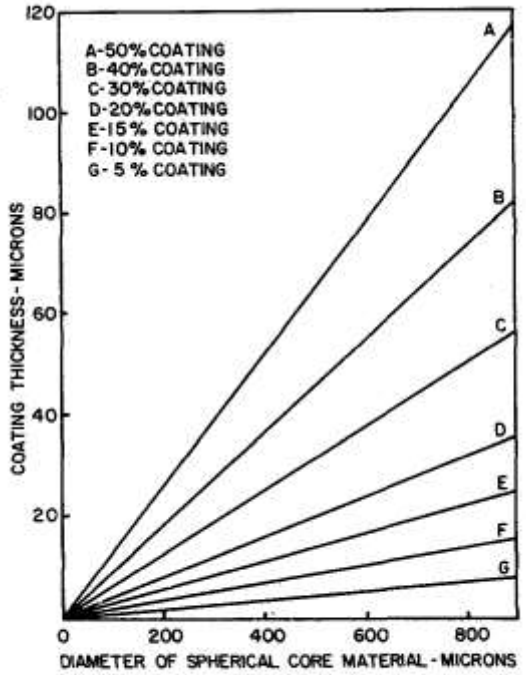


FIG. 13-31. *Theoretic coating thickness for spherical core material having various amounts of coating. (From Herbig.[2] Courtesy John Wiley and Sons.)*

TABLE 13-7. *Representative Coating Materials and Applicable Microencapsulation Process*

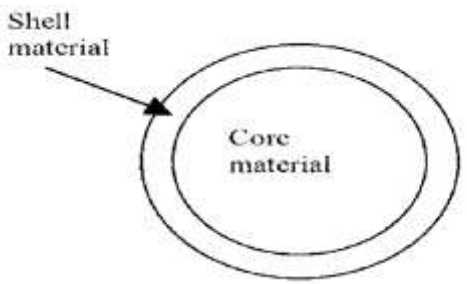
Coating Materials	*Processes*					
	Multiorifice—Centrifugal	*Phase Separation—Coacervation*	*Pan Coating*	*Spray Drying and Congealing*	*Air Suspension*	*Solvent Evaporation*
Water-soluble resins						
Gelatin	X	X	X	X	X	X
Gum arabic		X	X	X	X	X
Starch		X	X	X	X	
Polyvinylpyrrolidone	X	X	X	X	X	
Carboxymethylcellulose		X	X	X	X	
Hydroxyethylcellulose		X	X	X	X	X
Methylcellulose		X	X	X	X	
Arabinogalactan		X	X	X	X	
Polyvinyl alcohol	X	X	X	X	X	X
Polyacrylic acid		X	X	X	X	X
Water-insoluble resins						
Ethylcellulose		X	X	X	X	X
Polyethylene	X				X	X
Polymethacrylate		X	X	X	X	X
Polyamide (Nylon)					X	X
Poly [Ethylene-Vinyl acetate]	X	X	X	X		X
Cellulose nitrate	X	X	X	X		X
Silicones			X	X		
Poly (lactide-co-glycolide)		X	X			X
Waxes and lipids						
Paraffin	X	X	X	X	X	
Carnauba			X	X	X	
Spermaceti		X	X	X	X	
Beeswax			X	X	X	
Stearic acid			X	X		
Stearyl alcohol			X	X	X	
Glyceryl stearates			X	X	X	
Enteric resins						
Shellac		X	X	X	X	
Cellulose acetate phthalate		X	X	X	X	X
Zein		X			X	

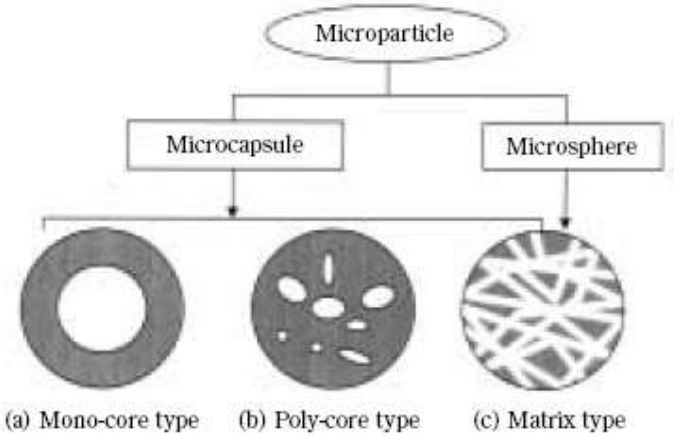
CLASSIFICATION OF MICROPARTICLE

Generally Micro particles consist of two components

a) Core material

b) Coat or wall or shell material.





1.Microcapsules: The active agent forms a core surrounded by an inert diffusion barrier.

2.Microspheres: The active agent is dispersed or dissolved in an inert polymer.

ADVANTAGES:

To Increase of bioavailability ✓

To alter the drug release ✓

To improve the patient's compliance ✓

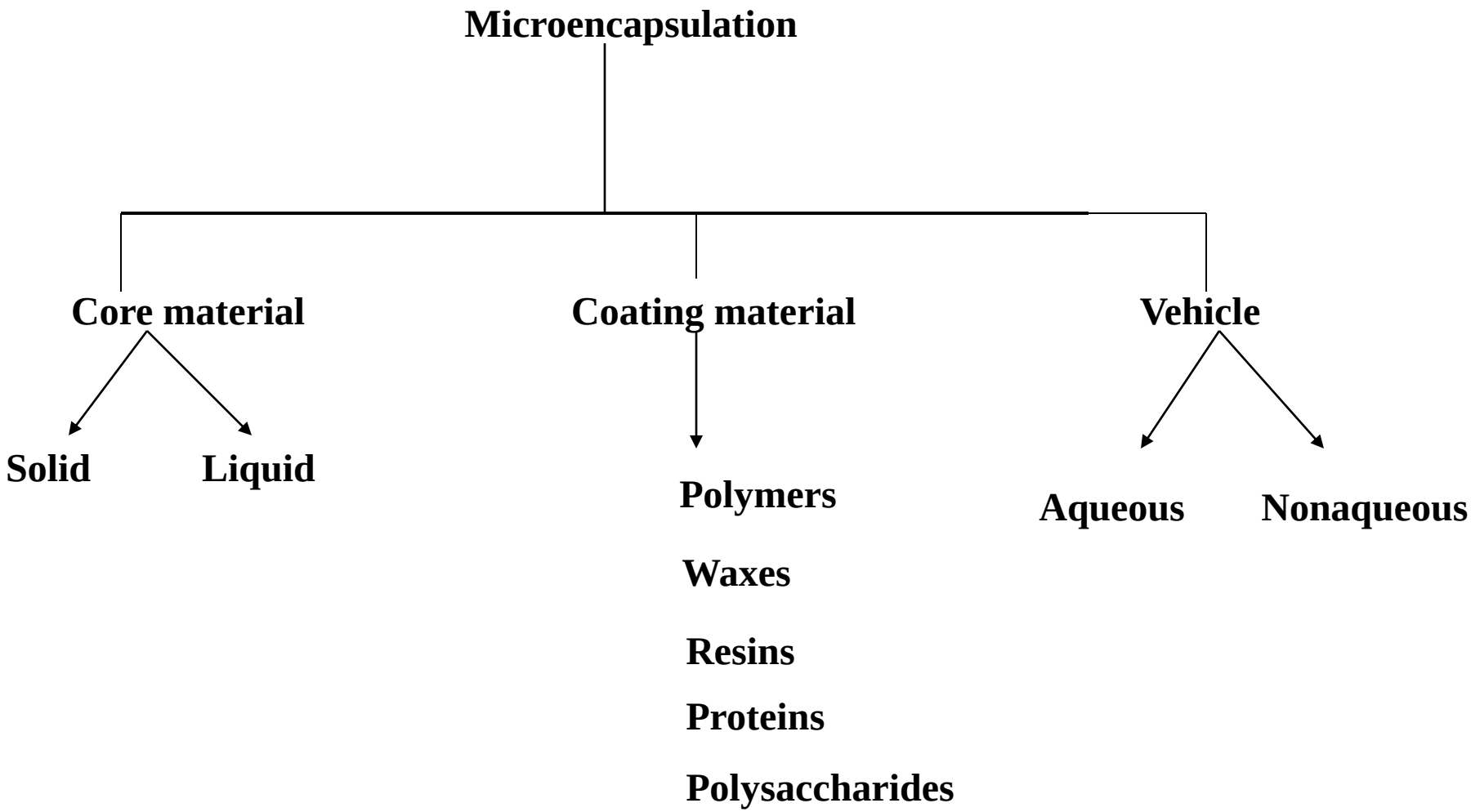
To produce a targeted drug delivery ✓

To reduce the reactivity of the core in relation to the outside environment ✓

To decrease evaporation rate of the core material. ✓

To convert liquid to solid form & To mask the core taste. ✓

FUNDAMENTAL CONSIDERATION:



ROLE OF POLYMERS :

- ✓ **Polymers are substances of high molecular weight made up by repeating monomer units.**

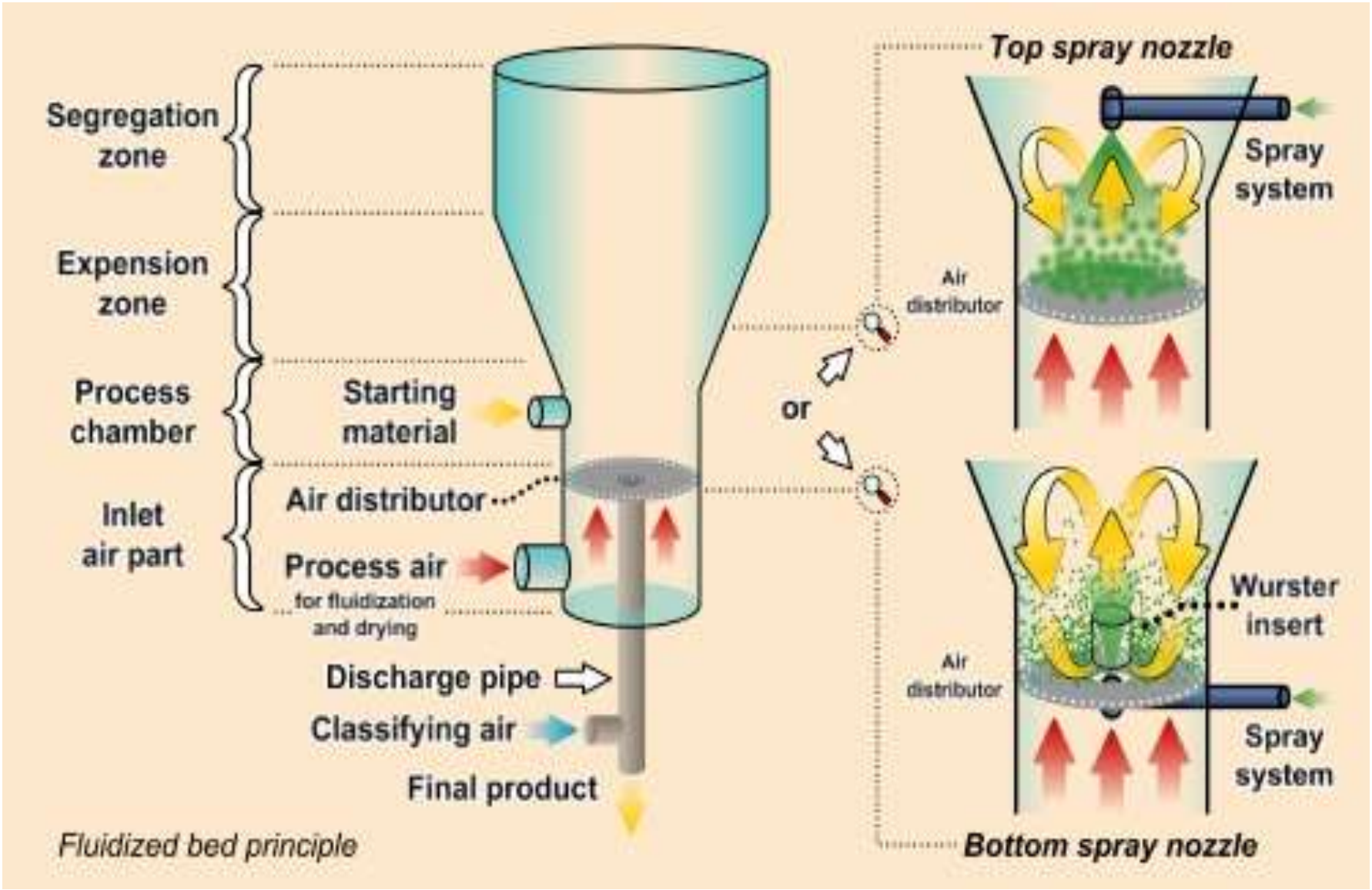
- ✓ **Polymer molecules may be linear or branched, and separate linear or branched chains may be joined by crosslinks.**

- ✓ **Polymers are used widely in pharmaceutical systems as adjuvants, coating materials and, a components of controlled and site- specific drug delivery systems**

MICROENCAPSULATION TECHNIQUES:

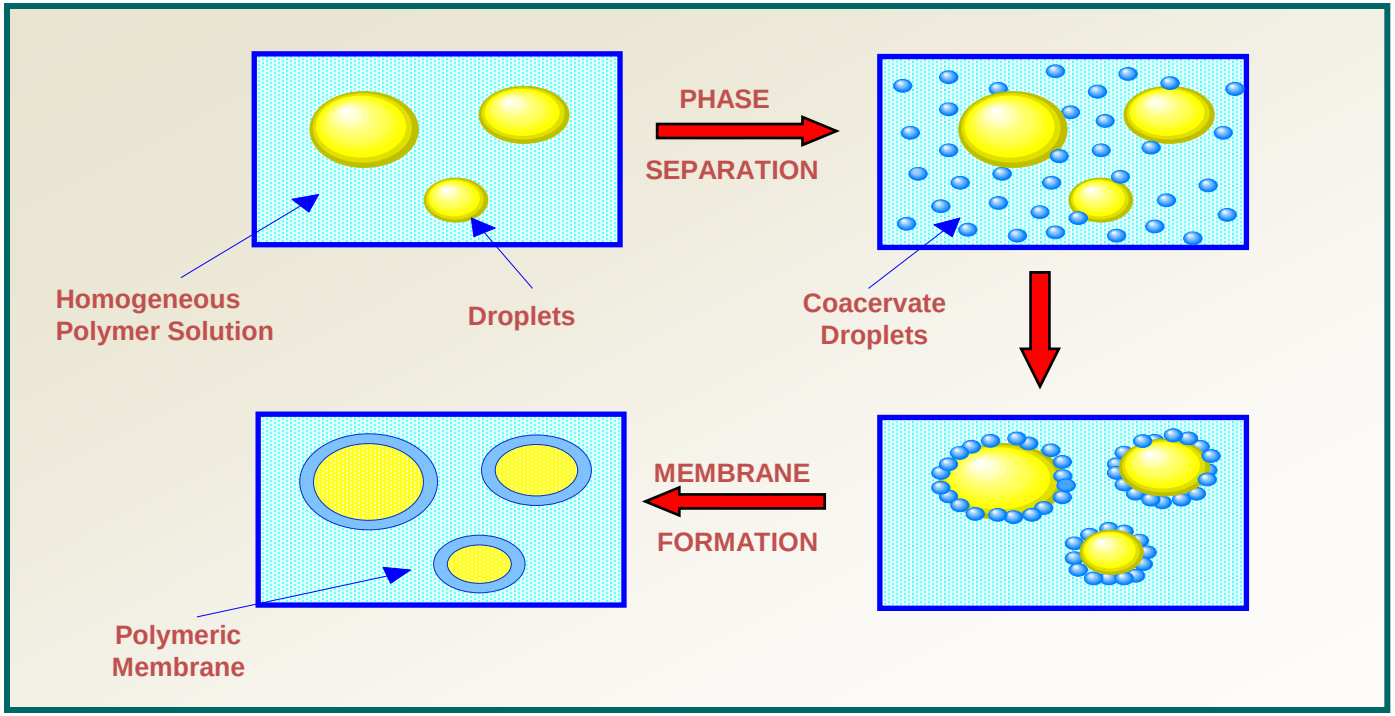
- ✓Air suspension techniques
- ✓ Coacervation process
- ✓ Spraydrying & congealing
- ✓ Pan coating
- ✓ Solvent evaporation
- ✓ Polymerization

Air suspension tech.:



Wurster process consists of the dispersing of solid, particulate core materials in a supporting air stream and the spray-coating of the air-suspended particles.

COACERVATION / PHASE SEPARATION

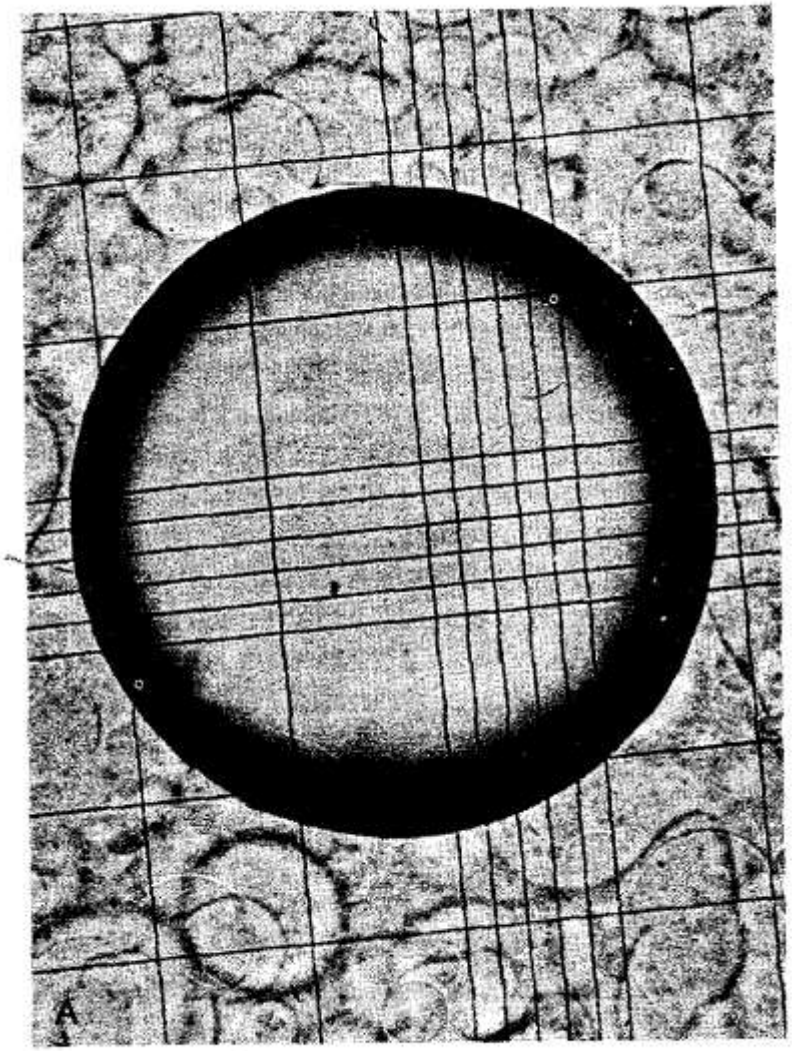


1. Formation of three immiscible phase
2. Deposition of coating
3. Rigidization of coating.

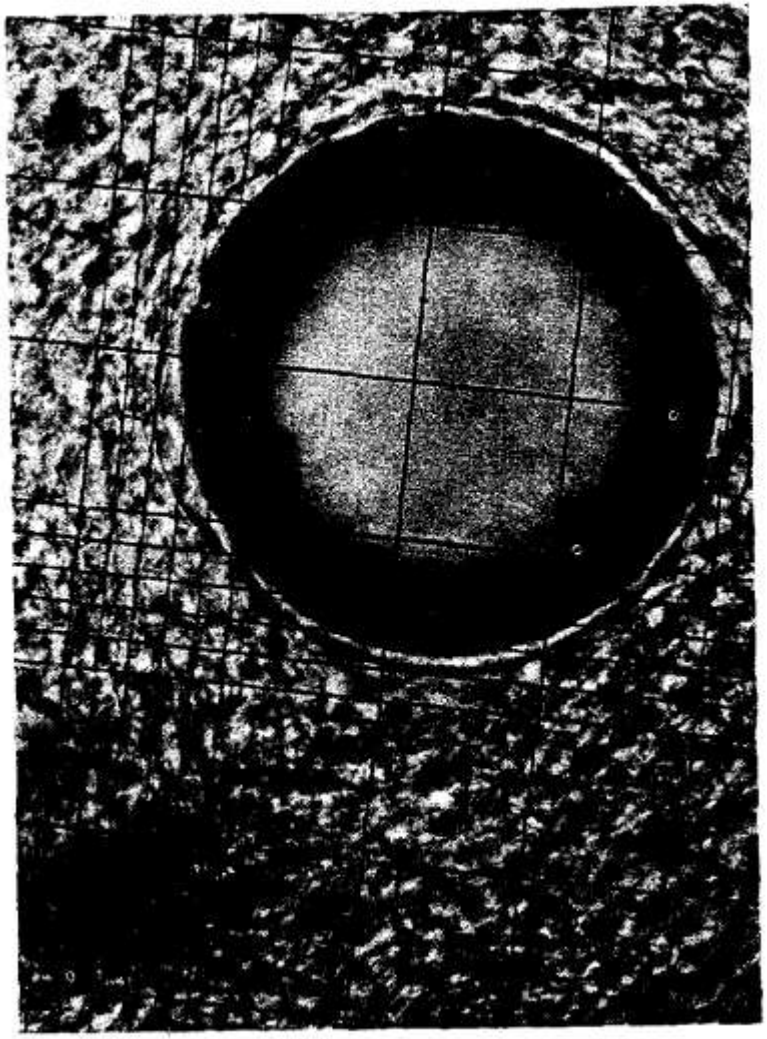
Step 1 of the process is the formation of three immiscible chemical phases: a liquid manufacturing vehicle phase, a core material phase, and a coating material phase. To form the three phases, the core material is dispersed in a solution of the coating polymer, the solvent for the polymer being the liquid manufacturing vehicle phase. The coating material phase, an immiscible polymer in a liquid state, is formed by utilizing one of the methods of phase separation-coacervation, that is, by changing the temperature of the polymer solution; or by adding a salt, nonsolvent, or incompatible polymer to the polymer solution; or by inducing a polymer-polymer interaction.

Step 2 of the process consists of depositing the liquid polymer coating upon the core material. This is accomplished by controlled, physical mixing of the coating material (while liquid) and the core material in the manufacturing vehicle. Deposition of the liquid polymer coating around the core material occurs if the polymer is adsorbed at the interface formed between the core material and the liquid vehicle phase, and this adsorption phenomenon is a prerequisite to effective coating. The continued deposition of the coating material is promoted by a reduction in the total free interfacial energy of the system, brought about by the decrease of the coating material surface area during coalescence of the liquid polymer droplets.

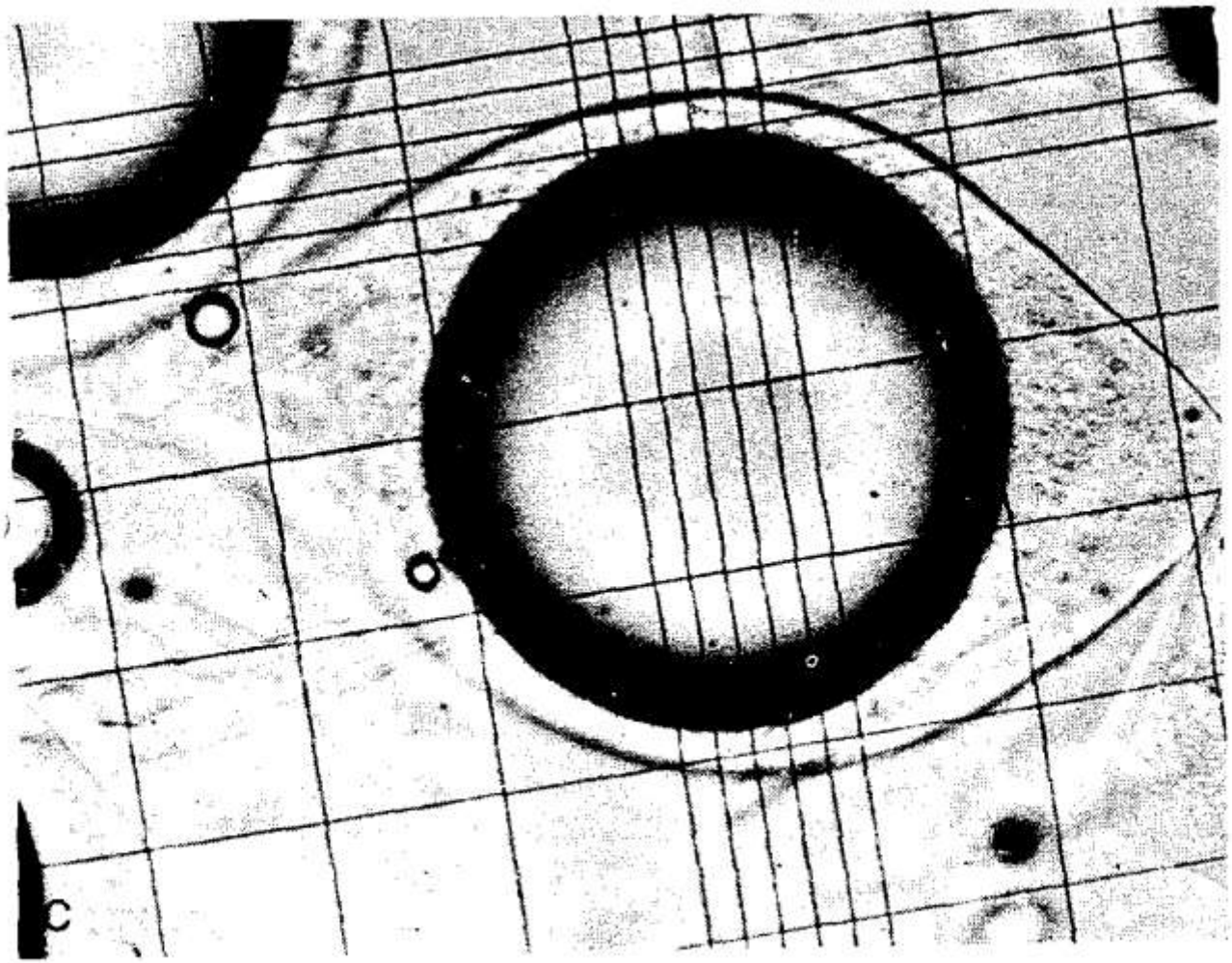
Step 3 of the process involves rigidizing the coating, usually by thermal, cross-linking, or desolvation techniques, to form a self-sustaining microcapsule.



Step 1. Core and Liquid Coating in Manufacturing Vehicle



Step 2. Deposition of Liquid Coating Material



Step 3. Completed Capsules in Manufacturing Vehicle

Rigidizing of coating was done by:

Temp. changes temp., ex. Ethylcellulose to N-acetylp-aminophenol in solvent cyclohexane.

Incompatible polymer addition

Non solvent addition

Salt addition

Polymer-polymer interaction

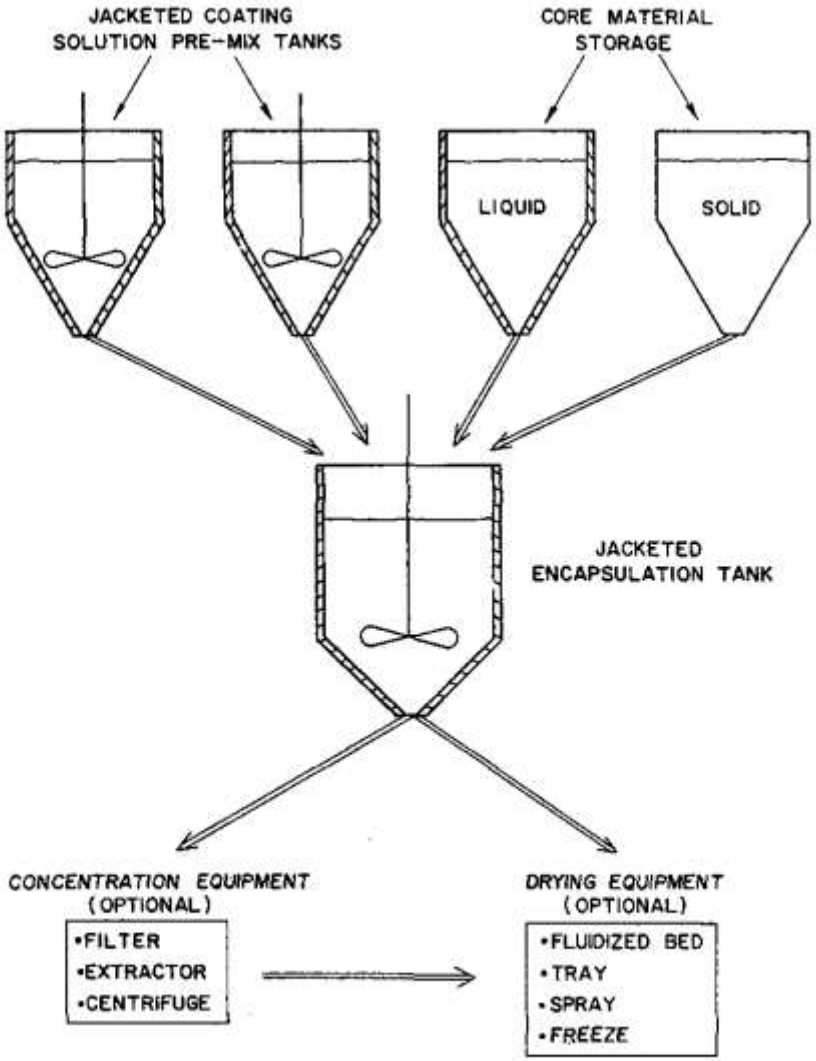


FIG. 13-44. *Flow diagram of a typical phase-separation/coacervation process. (From Bakan.*[28]*)*

Multiorifice-Centrifugal Process

a mechanical process for producing microcapsules that utilizes centrifugal forces to hurl a core material particle through an enveloping microencapsulation membrane, thereby effecting mechanical microencapsulation.[29] The

Pan Coating

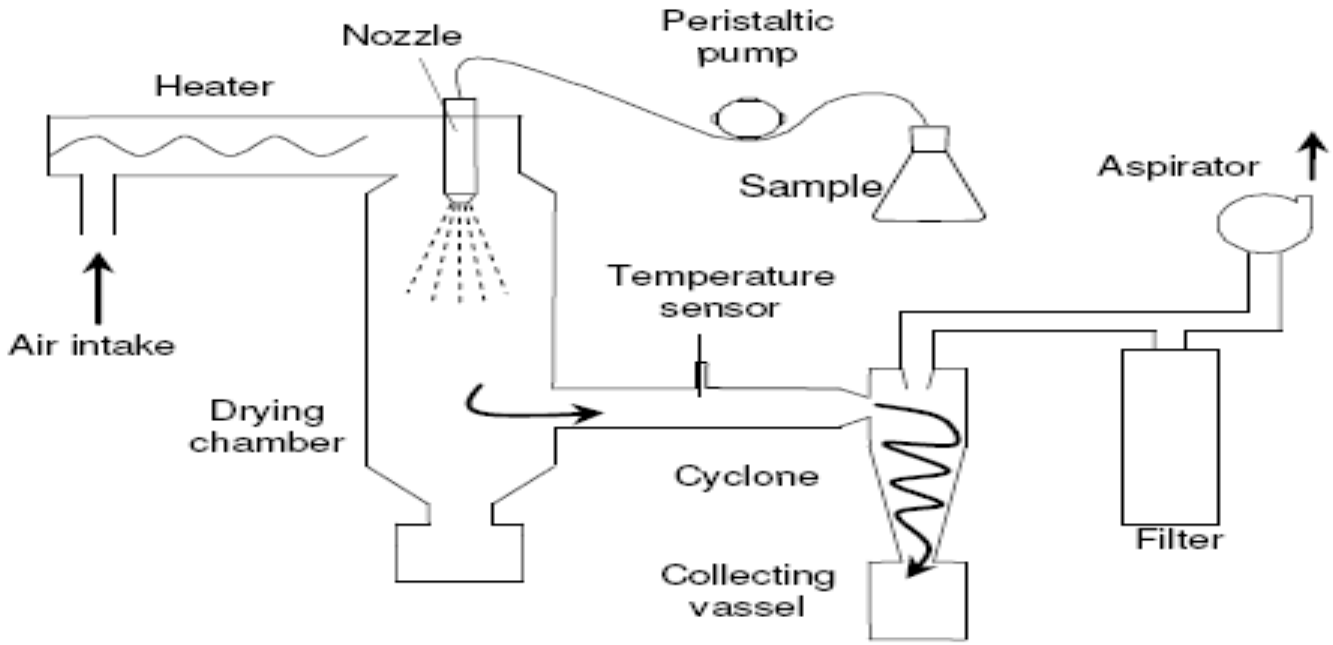
The macroencapsulation of relatively large particles by pan methods has become widespread in the pharmaceutical industry.

In practice, the coating is applied as a solution, or as an atomized spray, to the desired solid core material in the coating pan. Usually, to remove the coating solvent, warm air is passed over the coated materials as the coatings are being applied in the coating pans. In some cases, final solvent removal is accomplished in a drying oven.

Spray Drying and Spray Congealing

Spray-drying and spray-congealing processes are similar in that both involve dispersing the core material in a liquefied coating substance and spraying or introducing the core-coating mixture into some environmental condition, whereby relatively rapid solidification (and formation) of the coating is effected. The principal difference between the two methods, for the purpose of this discussion, is the means by which coating solidification is accomplished. Coating solidification in the case of spray drying is effected by rapid evaporation of a solvent in which the coating material is dissolved. Coating solidification in spray congealing methods, however, is accomplished by thermally congealing a molten coating material or by solidifying a dissolved coating by introducing the coating-core material mixture into a nonsolvent. Removal of the nonsolvent or solvent from the coated product is then accomplished by sorption, extraction, or evaporation techniques.

SPRAY DRYING & CONGEALING (COOLING)



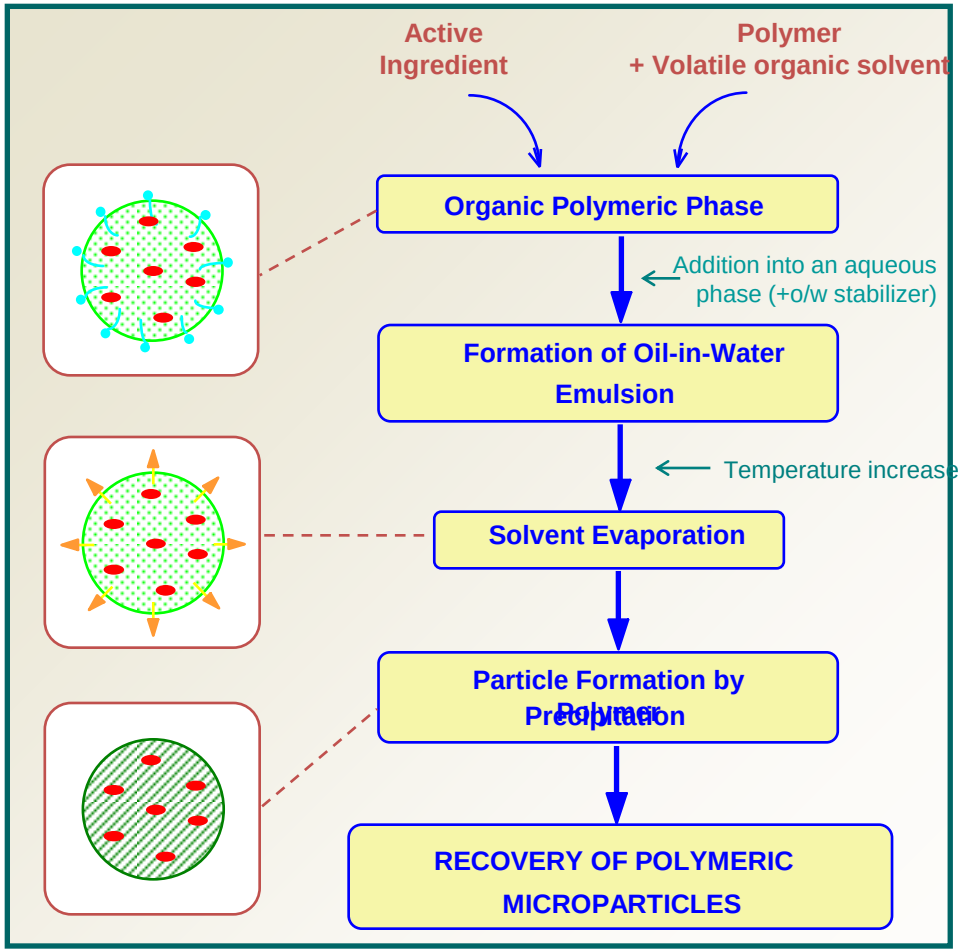
Spray drying : spray = aqueous solution / Hot air

Spray congealing : spray = hot melt/cold air

Solvent Evaporation

The microcapsule coating is dissolved in a volatile solvent, which is immiscible with the liquid manufacturing vehicle phase. A core material to be microencapsulated is dissolved or dispersed in the coating polymer solution. With agitation, the core coating material mixture is dispersed in the liquid manufacturing vehicle phase to obtain the appropriate size microcapsule. The mixture is then heated (if necessary) to evaporate the solvent for the polymer. In the case in which the core material is dispersed in the polymer solution, polymer shrinks around the core. In the case in which the core material is dissolved in the coating polymer solution, a matrix-type microcapsule is formed. Once all the solvent for the polymer is evaporated, the liquid vehicle temperature is reduced to ambient temperature (if required) with continued agitation. At this stage, the microcapsules can be used in suspension form, coated on to substrates or isolated as powders.

SOLVENT EVAPORATIONS



Step 1:

Formation of a solution/dispersion of the drug into an organic polymer phase.

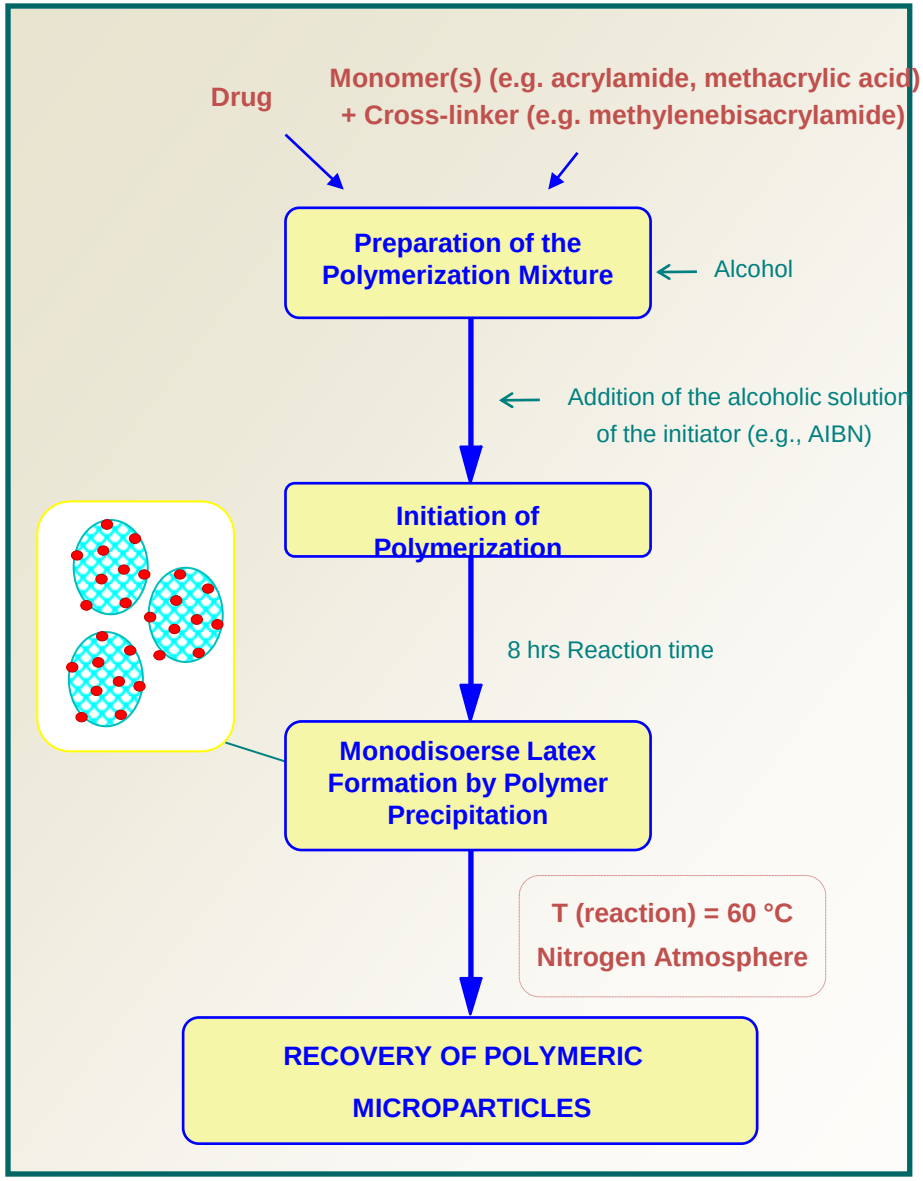
Step 2:

Emulsification of the polymer phase into an aqueous phase containing a suitable stabilizer, thus, forming a o/w emulsion.

Step 3:

Removal of the organic solvent from the dispersed phase by extraction or evaporation leading to polymer precipitation and formation of the microspheres.

POLYMERIZATION:

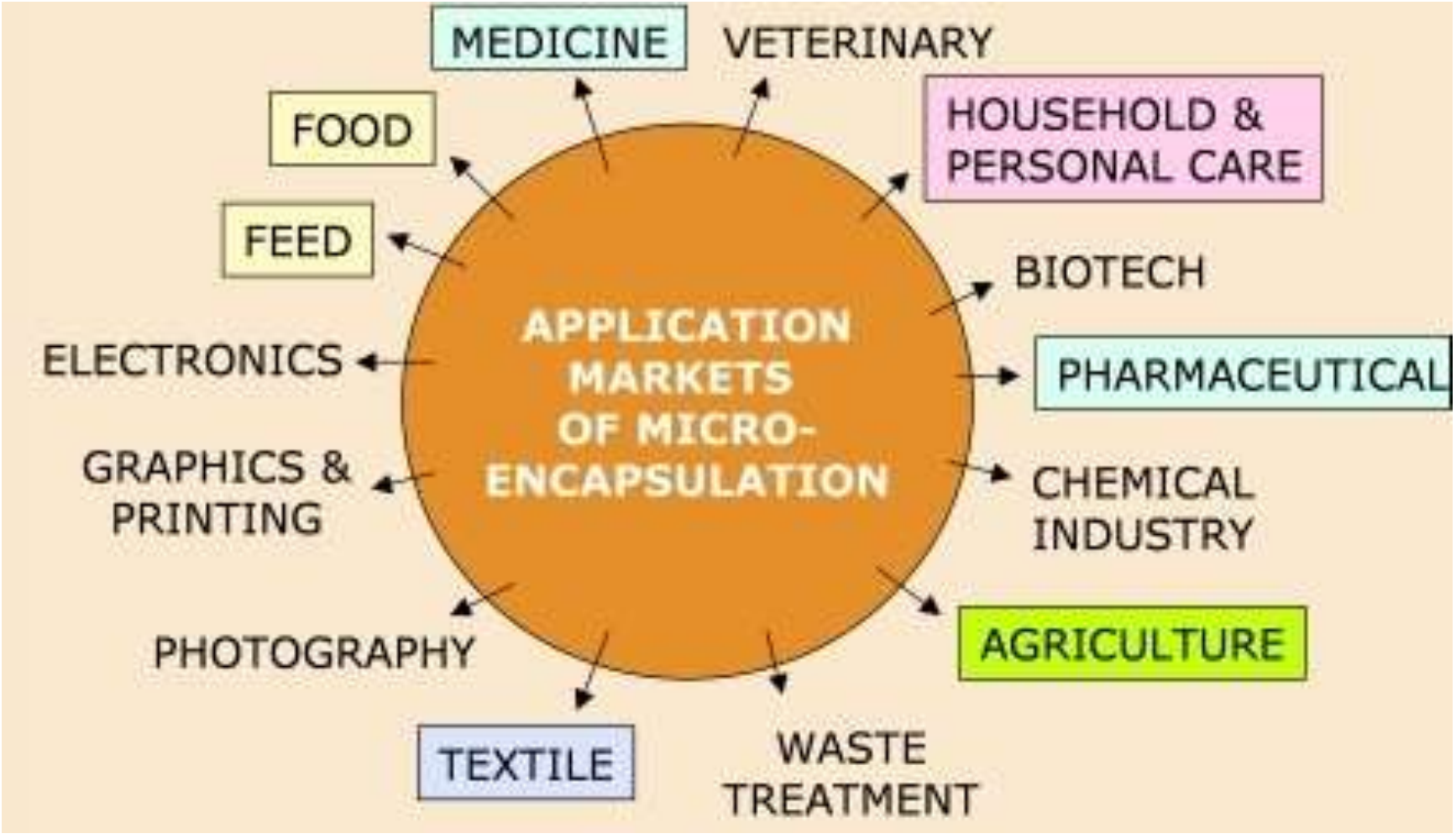


- Monodisperse microgels in the micron or submicron size range.

- Precipitation polymerization starts from a homogeneous monomer solution in which the synthesized polymer is insoluble.

- The particle size of the resulting microspheres depends on the polymerization conditions, including the monomer/co monomer composition, the amount of initiator and the total monomer concentration.

APPLICATION OF MICROENCAPSULATION TECHNIQUES:



CONCLUSION:

- The microencapsulation technique offers a variety of opportunities such as protection and masking, reduced dissolution rate, facilitation of handling, and spatial targeting of the active ingredient.

This approach facilitates accurate delivery of small quantities of potent drugs, reduced drug concentrations at sites other than the target organ or tissue and protection of labile compounds before and after administration and prior to appearance at the site of action.

- In future by combining various other approaches,microencapsulation technique will find the vital place in novel drug delivery system.


Thank You