MICROENCAPSULATION TECHNIQUES

Definition

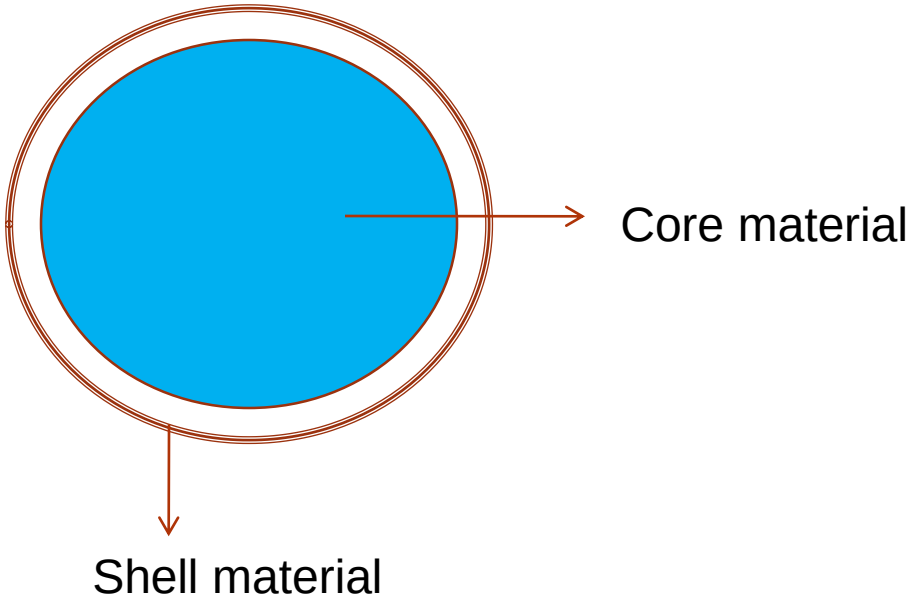
A process by which very tiny droplets or particles of liquid or solid material are surrounded or coated with a continuous film of polymeric material.

- **Particles having diameter between 3 – 800 µm are known as micro-particles.**
- **Particles larger than 1000 µm are known as Macro particles .**

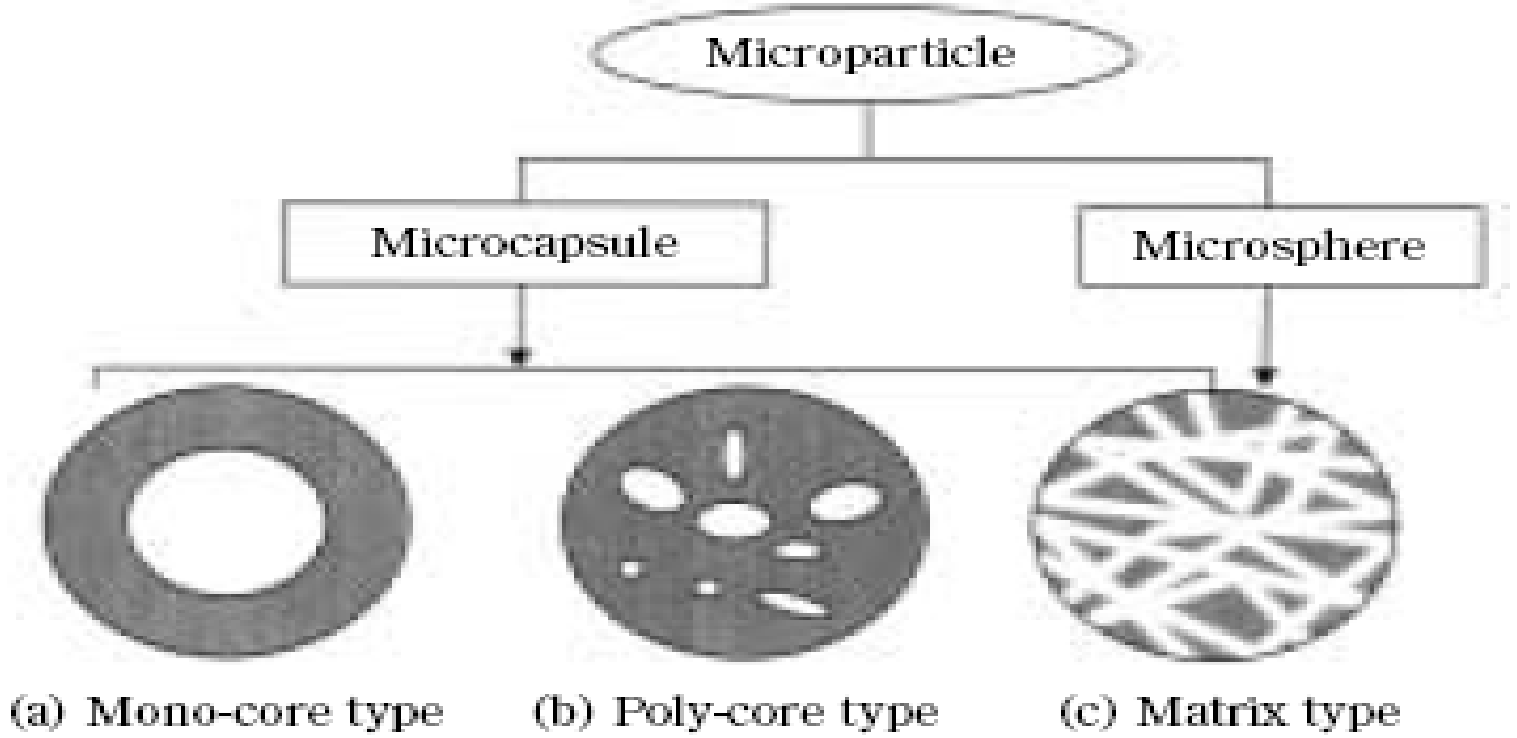
Generally consist of two components

a) Core , internal phase or fill

b) Shell, Coat or membrane.



CLASSIFICATION:

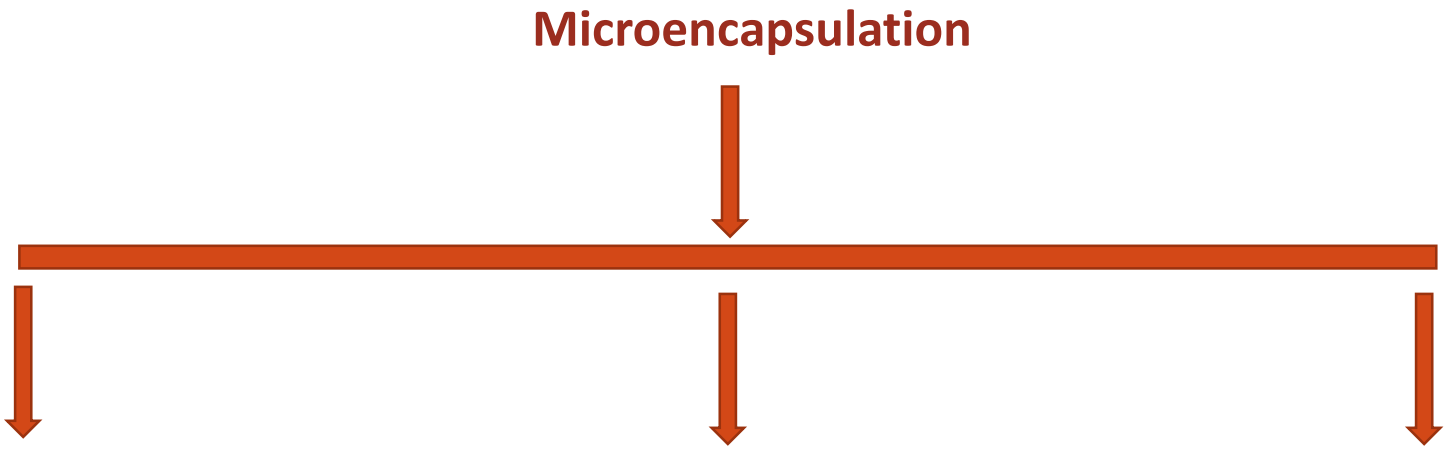


1. ***Microcapsules: The active agent forms a core surrounded by an inert diffusion barrier.***
2. ***Microspheres: The active agent is dispersed or dissolved in an inert polymer.***

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:



Solid

Liquid

Polymers

Waxes

Resins

Proteins

Polysaccharides

Aqueous

Non-aqueous

MICROENCAPSULATION TECHNIQUES:

Physical Methods:

- Air suspension techniques (Wurster)
- Coacervation Process
- Spray Drying & Congealing
- Pan Coating
- Solvent Evaporation
- Polymerization
- Extrusion
- Single & Double Emulsion Techniques
- Supercritical fluid Anti Solvent method (SAS)
- Nozzle Vibration Technology

Chemical Methods:

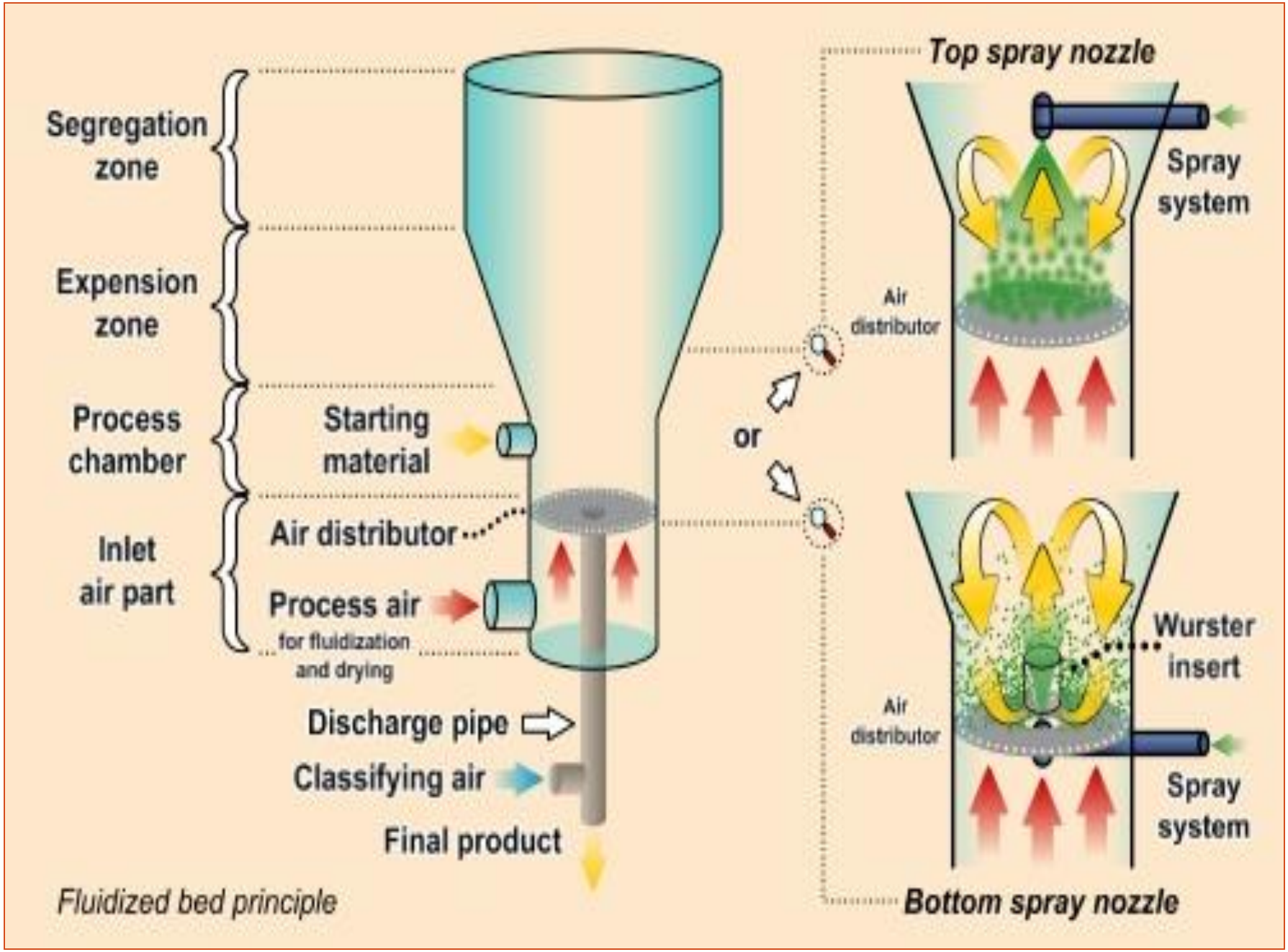
- Interfacial polymerization
- In-situ polymerization
- Matrix polymerization

AIR SUSPENSION TECHNIQUES (WURSTER) PROCESS:

In this process, the drug particles are coated and dried while suspended in an upwardly moving current of air.

Solutions and suspensions of coating materials in both water and volatile organic solvents are employed.

The drying of the coated particles is accomplished at either room or elevated temperatures, depending on the solvent used.


Segregation zone
Expension zone
Process chamber
Inlet air part
Starting material
Air distributor
Process air
for fluidization and drying
Discharge pipe
Classifying air
Final product
Fluidized bed principle
or
Top spray nozzle
Spray system
Air distributor
Wurster insert
Air distributor
Spray system
Bottom spray nozzle

COACERVATION / PHASE SEPARATION

Three steps process.

Step 1: Formation of three immiscible chemical phases

(i) a liquid manufacturing vehicle phase, (ii) a core material phase and (iii) a coating material phase.

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**
- **By adding a salt**
- **By adding a non-solvent**
- **By adding incompatible polymer to the polymer solution**
- **By inducing a polymer-polymer interaction.**

COACERVATION / PHASE SEPARATION

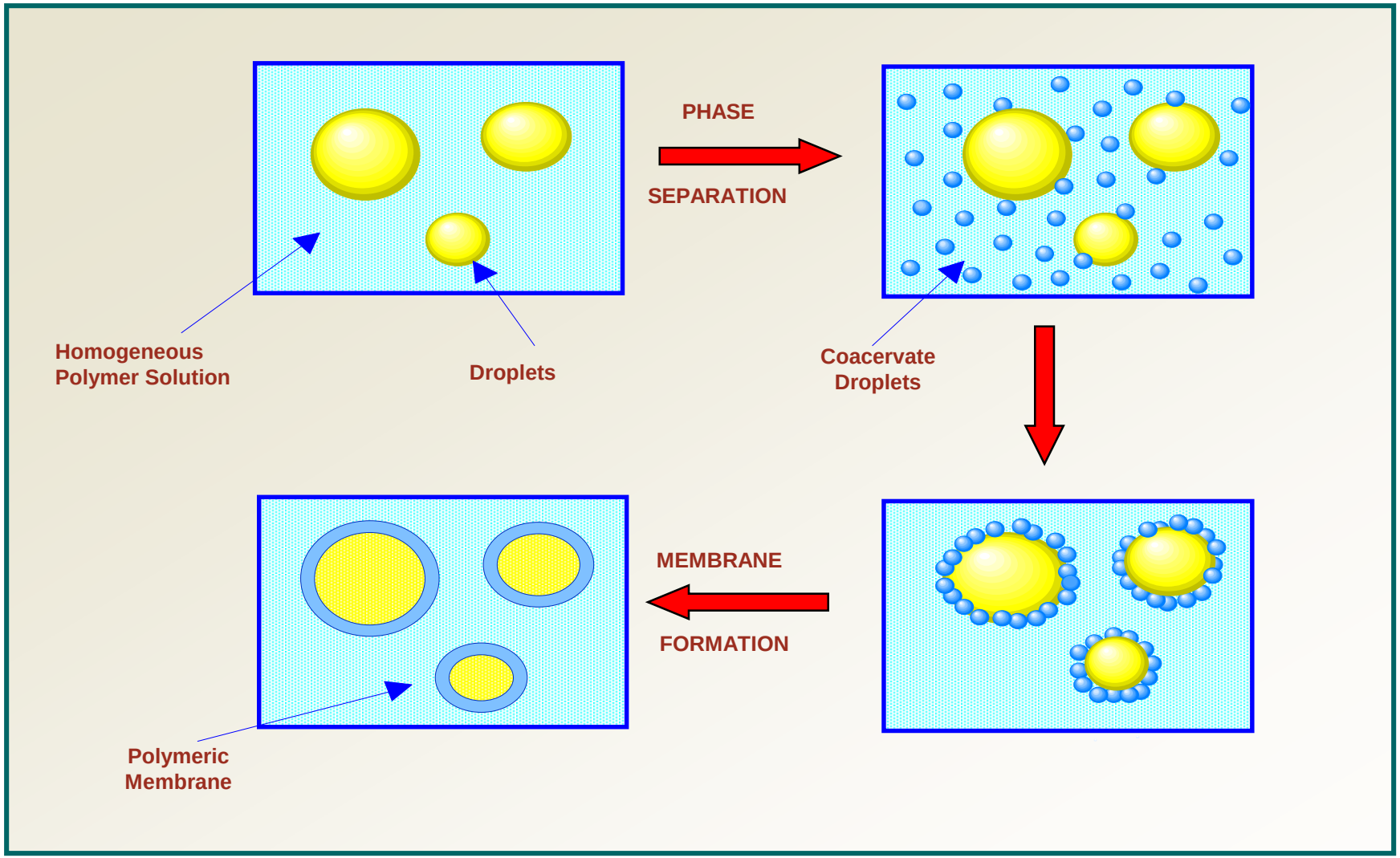
Step 2: Depositing the liquid polymer coating upon the core material

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.

Step 3: Rigidizing the coating

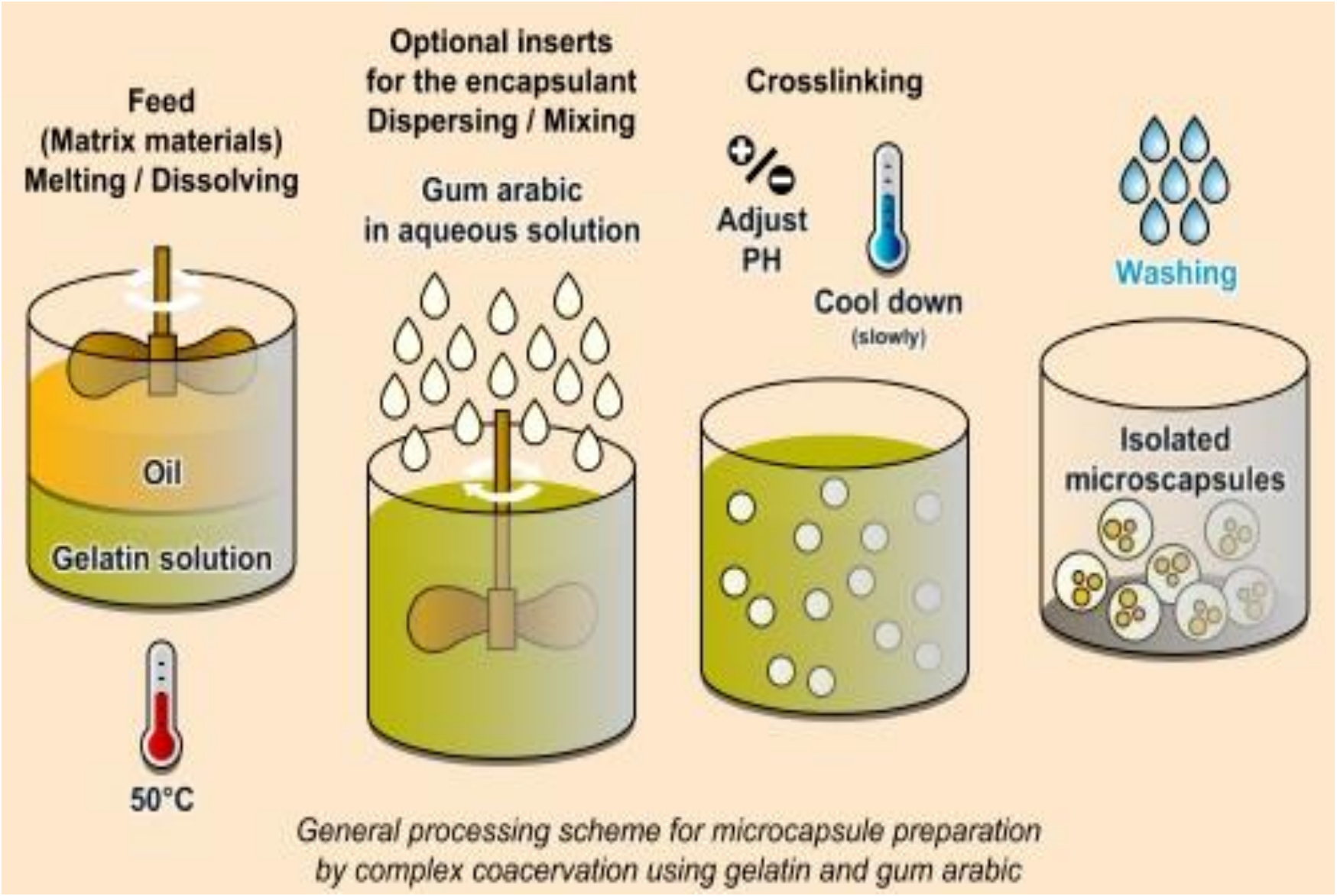
This is usually done by thermal, cross linking or desolvation techniques, to form a self sustaining microcapsule.



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

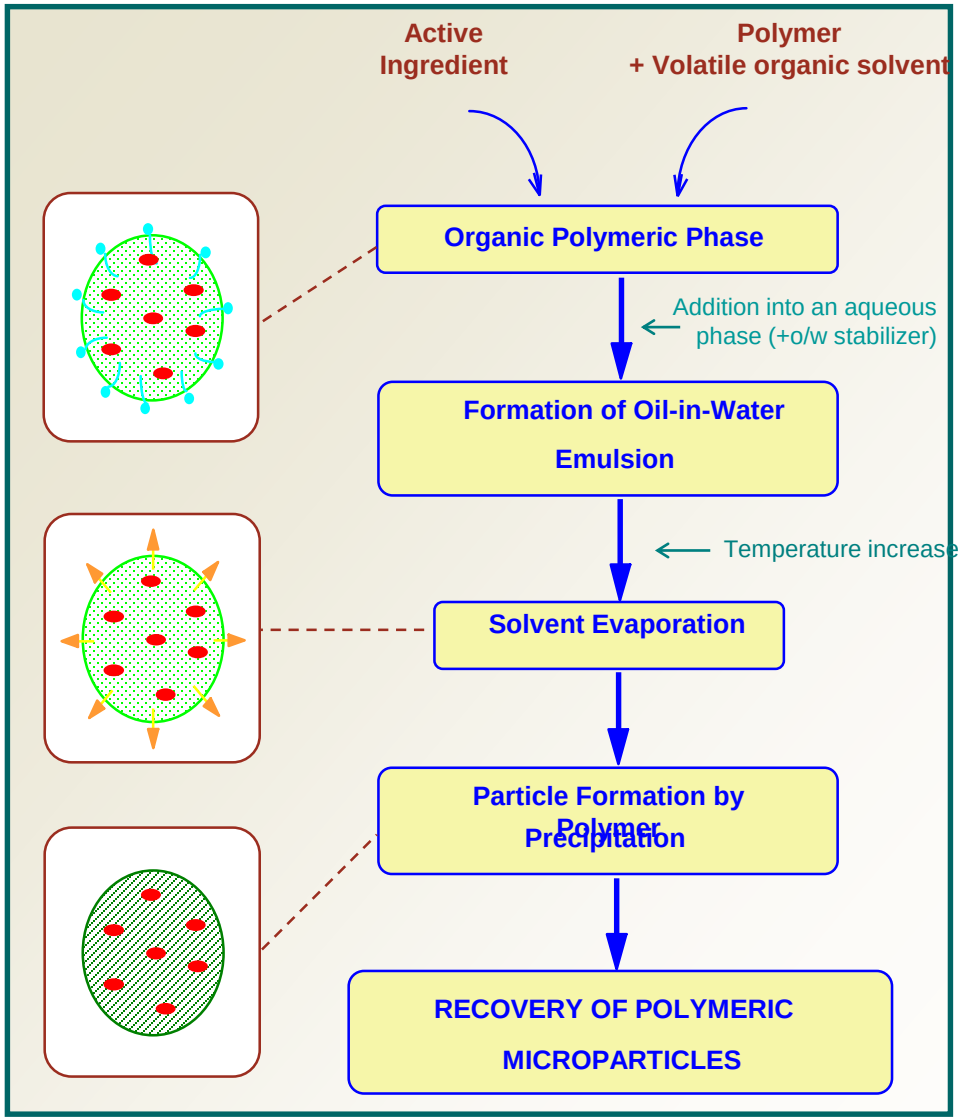
3. Rigidization of coating.

COMPLEX COACERVATION :



General processing scheme for microcapsule preparation by complex coacervation using gelatin and gum arabic

SOLVENT EVAPORATIONS



Step 1:

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

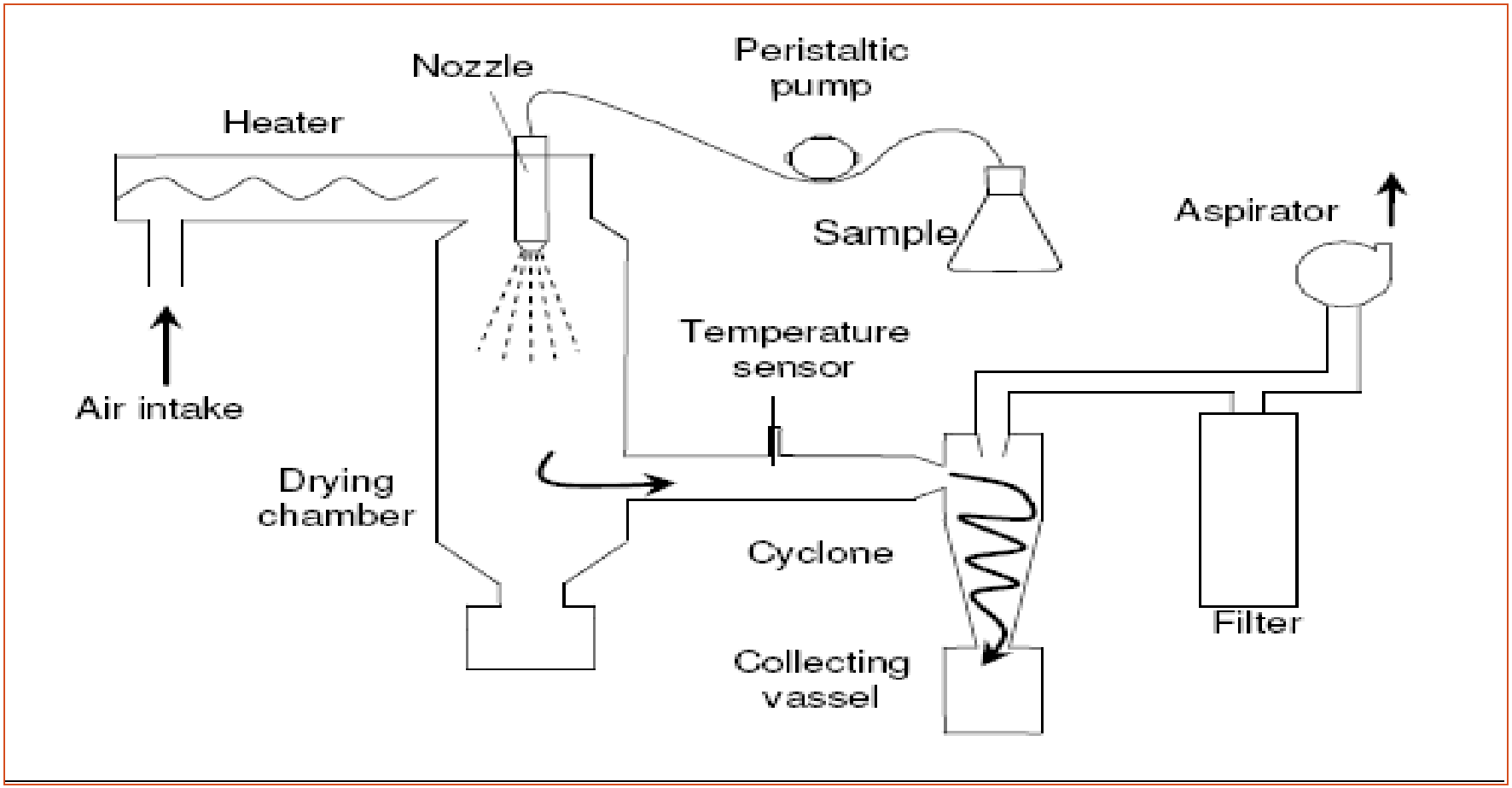
Step 2:

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.

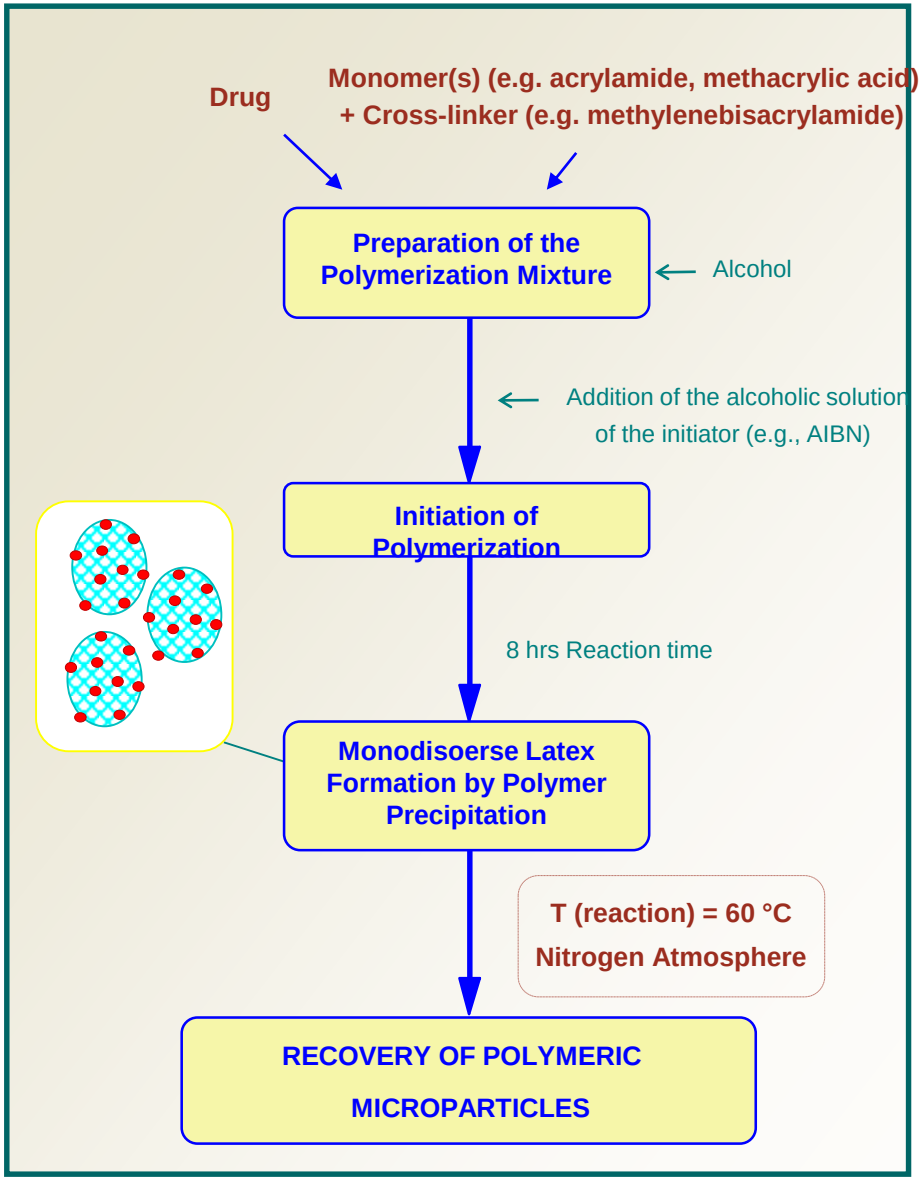
SPRAY DRYING & CONGEALING (COOLING)



Spray drying : Spray = Aqueous Solution / Hot Air

Spray congealing : Spray = Hot Melt / Cold Air

POLYMERIZATION:



- Mono-disperse micro-gels in the micron or submicron size range.

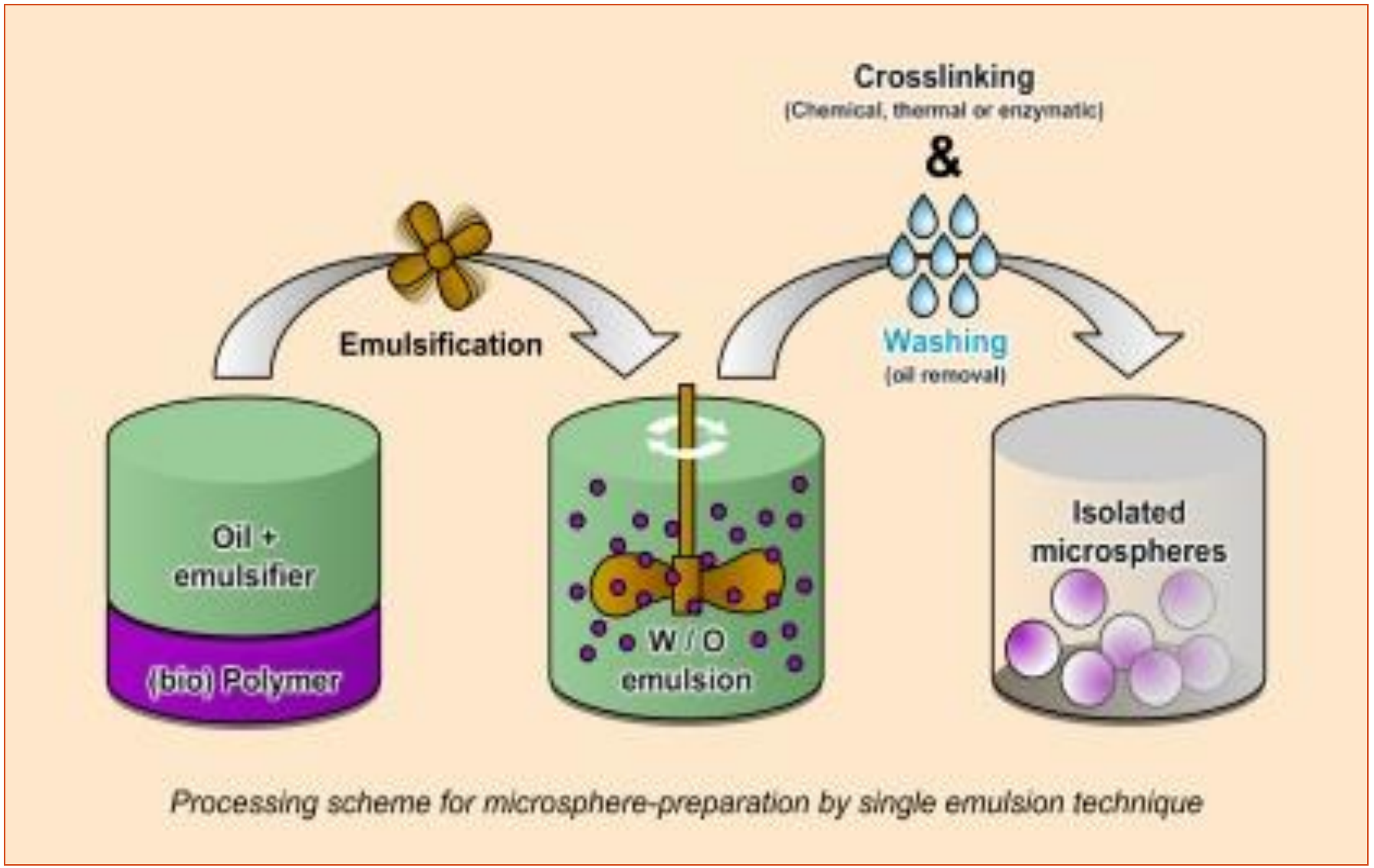
- Precipitation polymerization starts from a homogeneous monomer solution in which the synthesized polymer is insoluble.

- 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.

EXTRUSION:

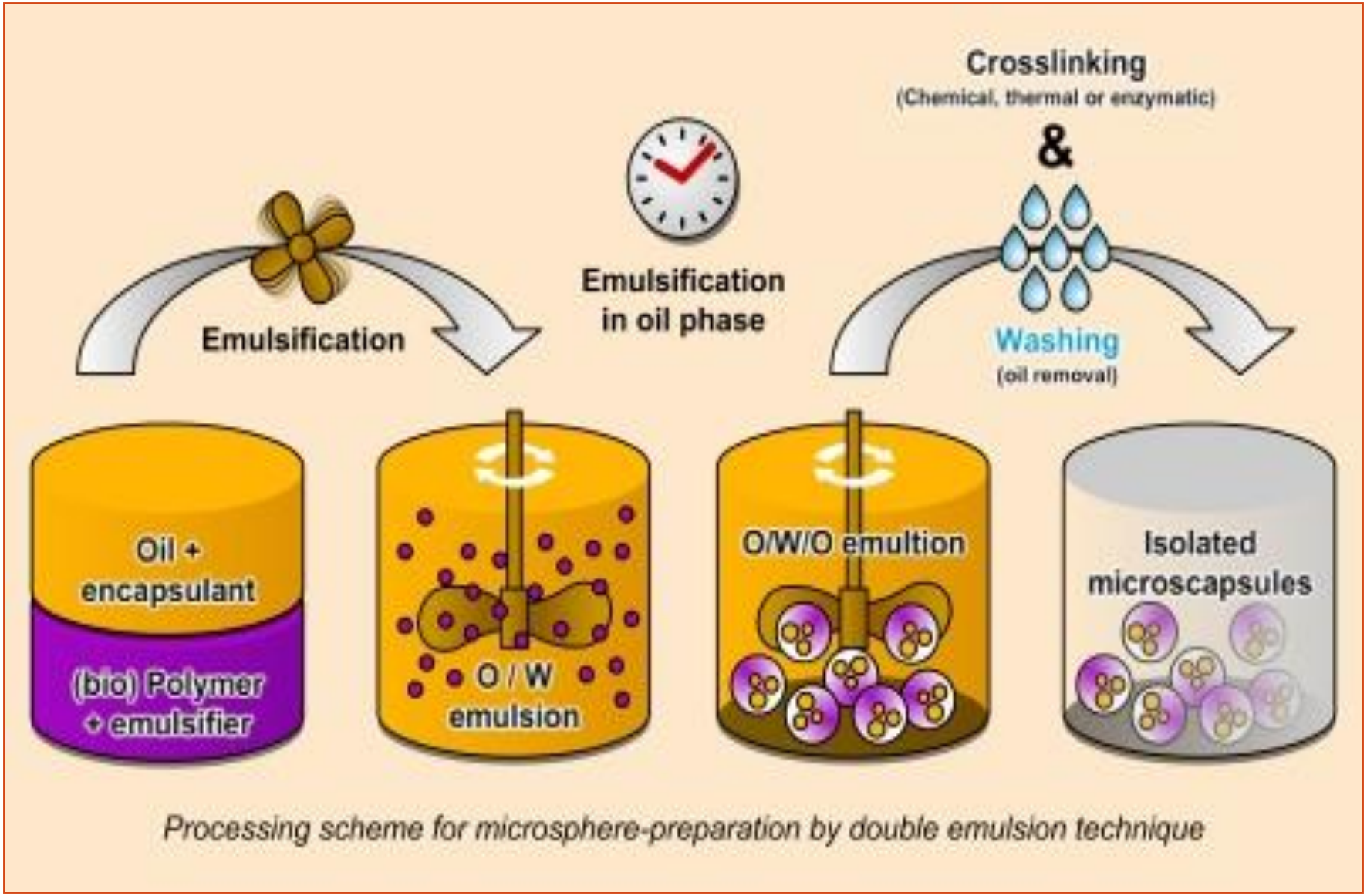
- This method was first patented in 1957.
- The advantage of extrusion is that it completely surrounds the core material with wall material.
- The process involves forcing a core material dispersed in a molten carbohydrate mass through a series of dies, into a bath of dehydrating liquid.
- When contact with the liquid is made, the carbohydrate case hardens to entrap the core material.
- The extruded filaments are separated from the liquid bath, dried using an anti-caking agent such as calcium tri-polyphosphate and sized.
- This process is particularly useful for heat labile substances such as flavours, vitamin-C and colours.

SINGLE EMULSION TECHNIQUE :



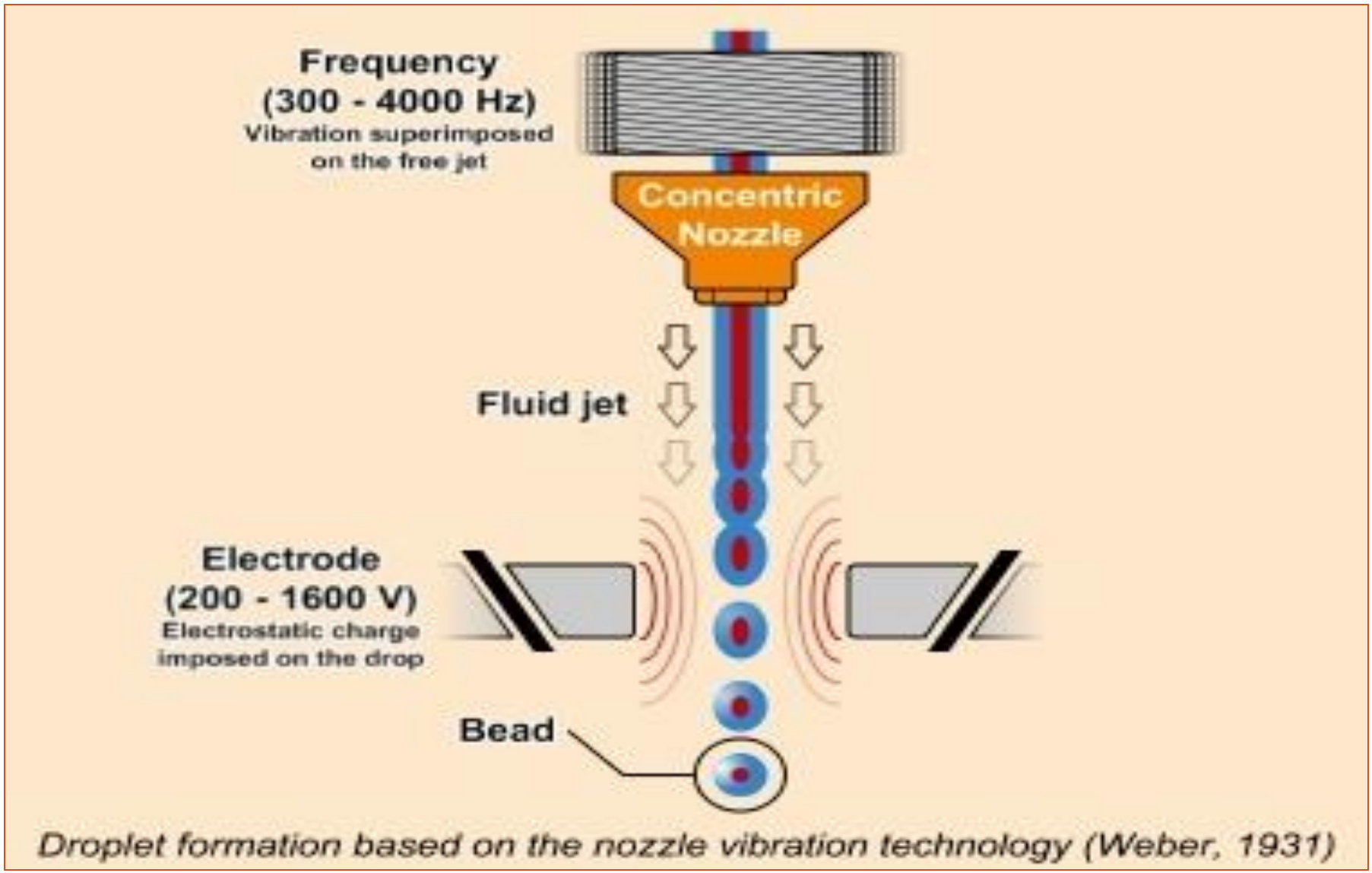
Processing scheme for microsphere-preparation by single emulsion technique

DOUBLE EMULSION TECHNIQUES:



Processing scheme for microsphere-preparation by double emulsion technique

NOZZLE VIBRATION TECHNOLOGY :

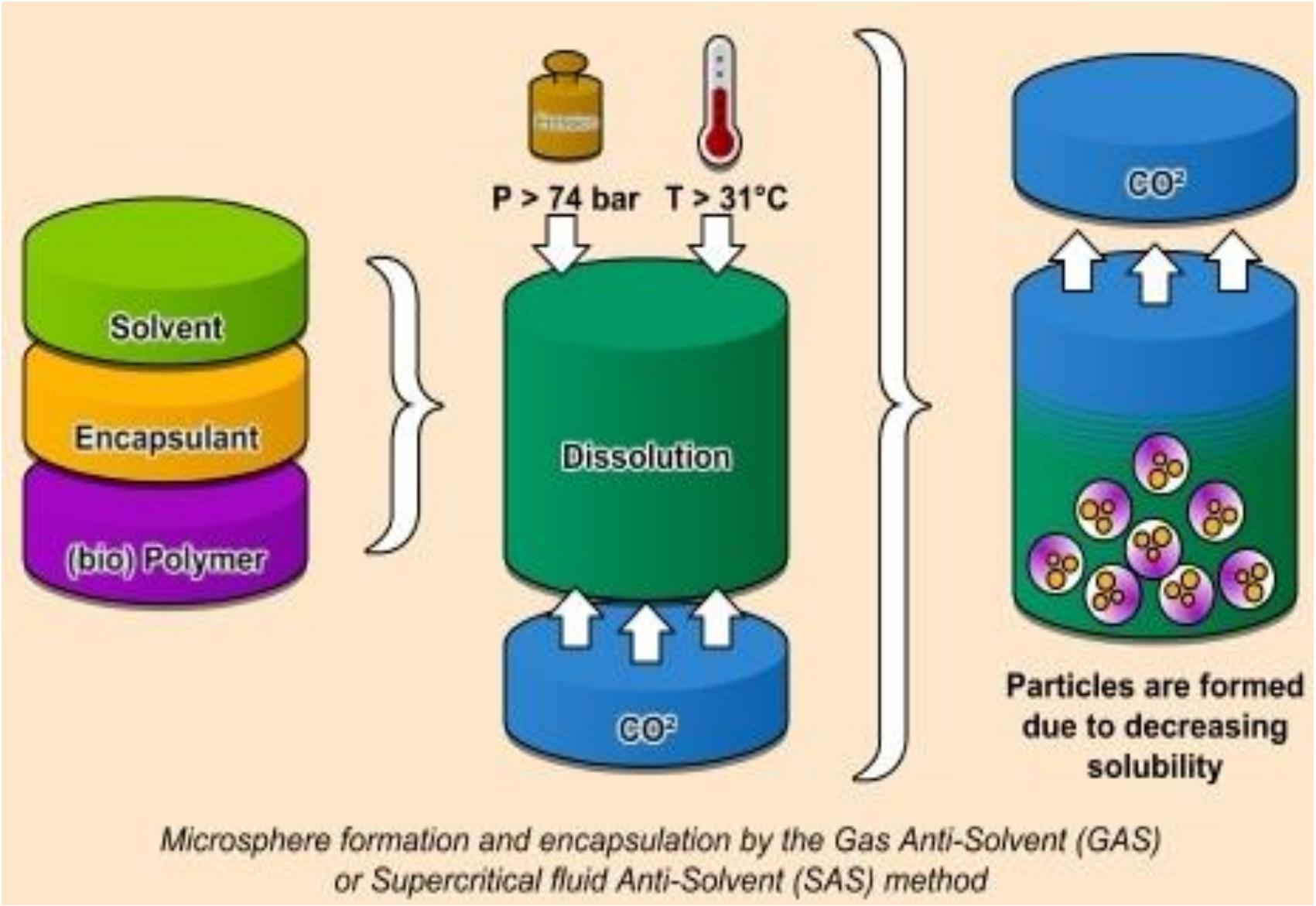


Droplet formation based on the nozzle vibration technology (Weber, 1931)

SAS METHOD :

The solid is dissolved in a conventional solvent. The solution is introduced into a supercritical fluid (mostly CO_2 and water (anti-solvent) leading to a rapid volume expansion of the solution. As a result, the solvent power of the conventional solvent decreases and super-saturation triggers off the precipitation of particles. After the solid has precipitated out fresh anti-solvent is added to flush away the solvent.

SAS METHOD :

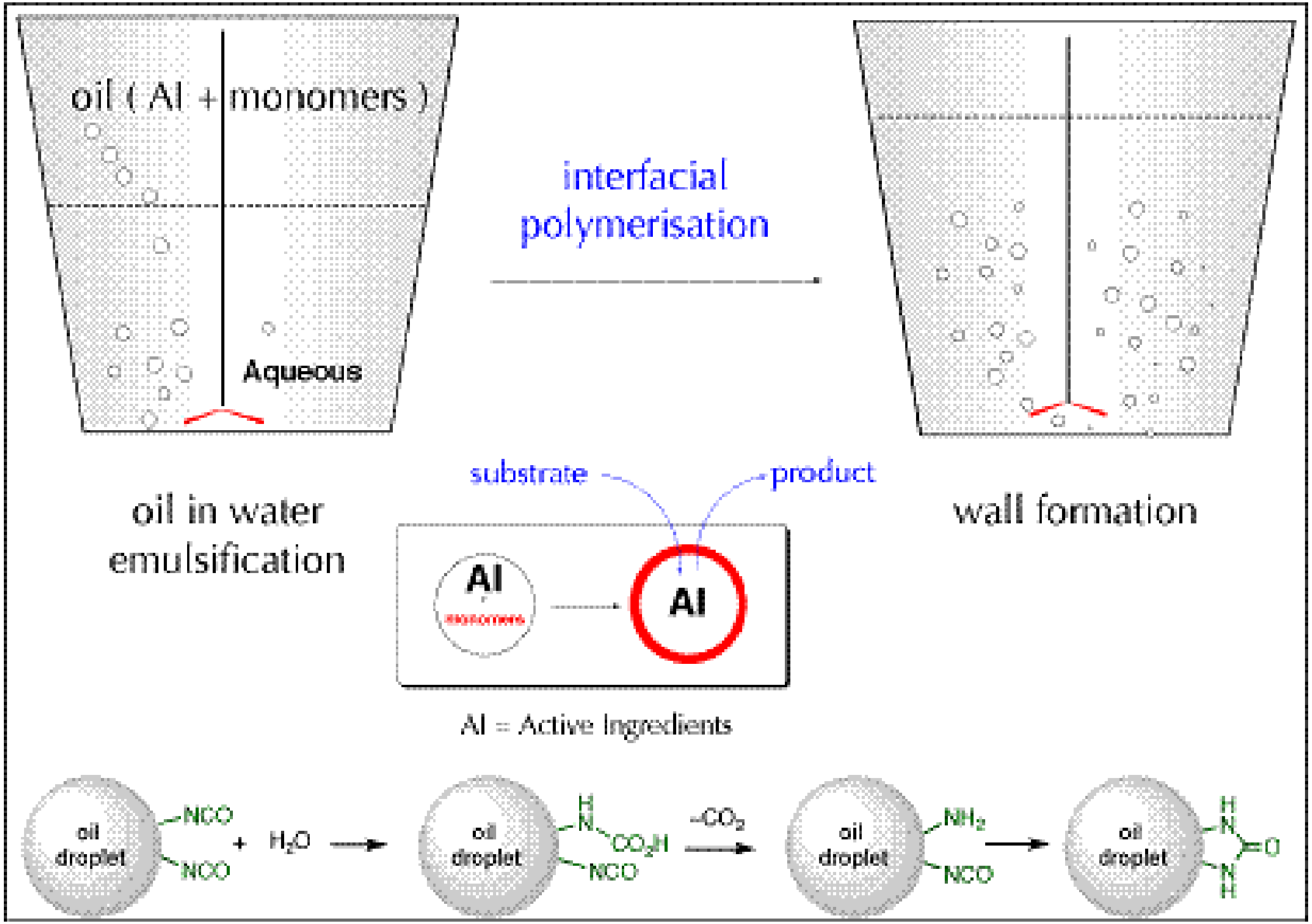


Microsphere formation and encapsulation by the Gas Anti-Solvent (GAS) or Supercritical fluid Anti-Solvent (SAS) method

Interfacial polymerization

A polymerization reaction that occurs at or near the interfacial boundary of two immiscible solutions. This involves dispersing an organic phase (containing poly-functional monomers and/or oligomers) into an aqueous phase (containing a mixture of emulsifiers and protective colloid stabilizers) along with the material to be encapsulated.

The resulting oil-in-water emulsion undergoes interfacial polymerization, with the monomers / oligomers reacting spontaneously at the phase boundary to form microcapsule polymer walls.



Microcapsule manufacture by interfacial polymerisation.

In-situ polymerization

In this process direct polymerization of a single monomer is carried out on the particle surface. In one process, e.g. Cellulose fibers are encapsulated in polyethylene while immersed in dry toluene. Usual deposition rates are about 0.5 µm / min. Coating thickness ranges 0.2-75 µm. The coating is uniform, even over sharp projections.

Matrix polymerization

The core material is imbedded in a polymeric matrix during formation of the particles. A simple method of this type is spray-drying, in which the particle is formed by evaporation of the solvent from the matrix material. However, the solidification of the matrix also can be caused by a chemical change.

APPLICATION OF MICROENCAPSULATION TECHNIQUES: