

# MICROSPHERES

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# MICROSPHERES

- Microspheres are small spherical particles, with diameter 1  $\mu\text{m}$  to 1000  $\mu\text{m}$ .
- They are spherical free flowing particles consisting of proteins or synthetic polymers which are biodegradable in nature.

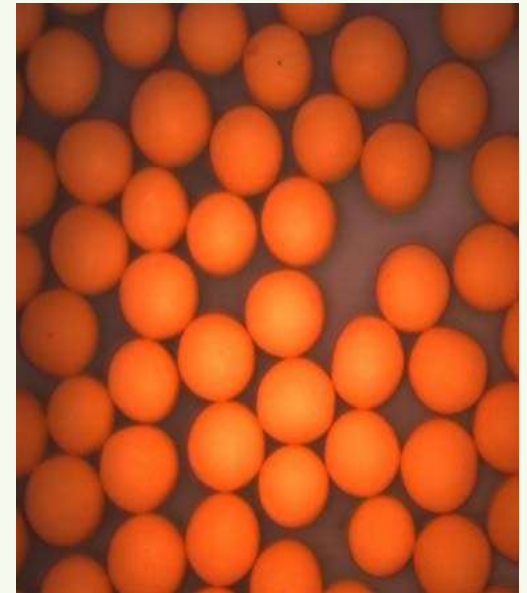
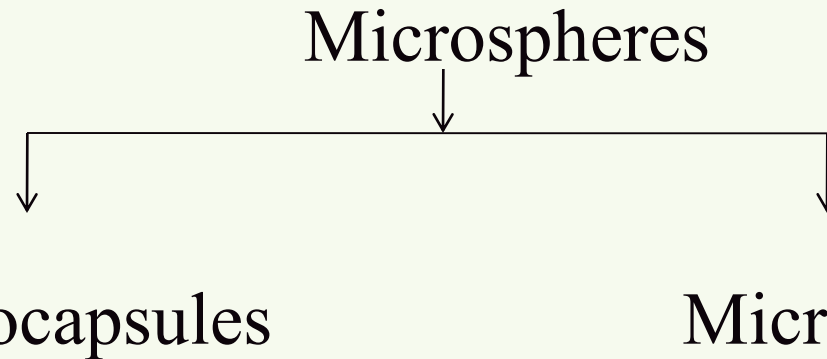


Fig: Microspheres

# CLASSIFICATION



- Microcapsules are those in which entrapped substance is distinctly surrounded by distinct capsule wall.
- Micromatrices in which entrapped substance is dispersed throughout the matrix.

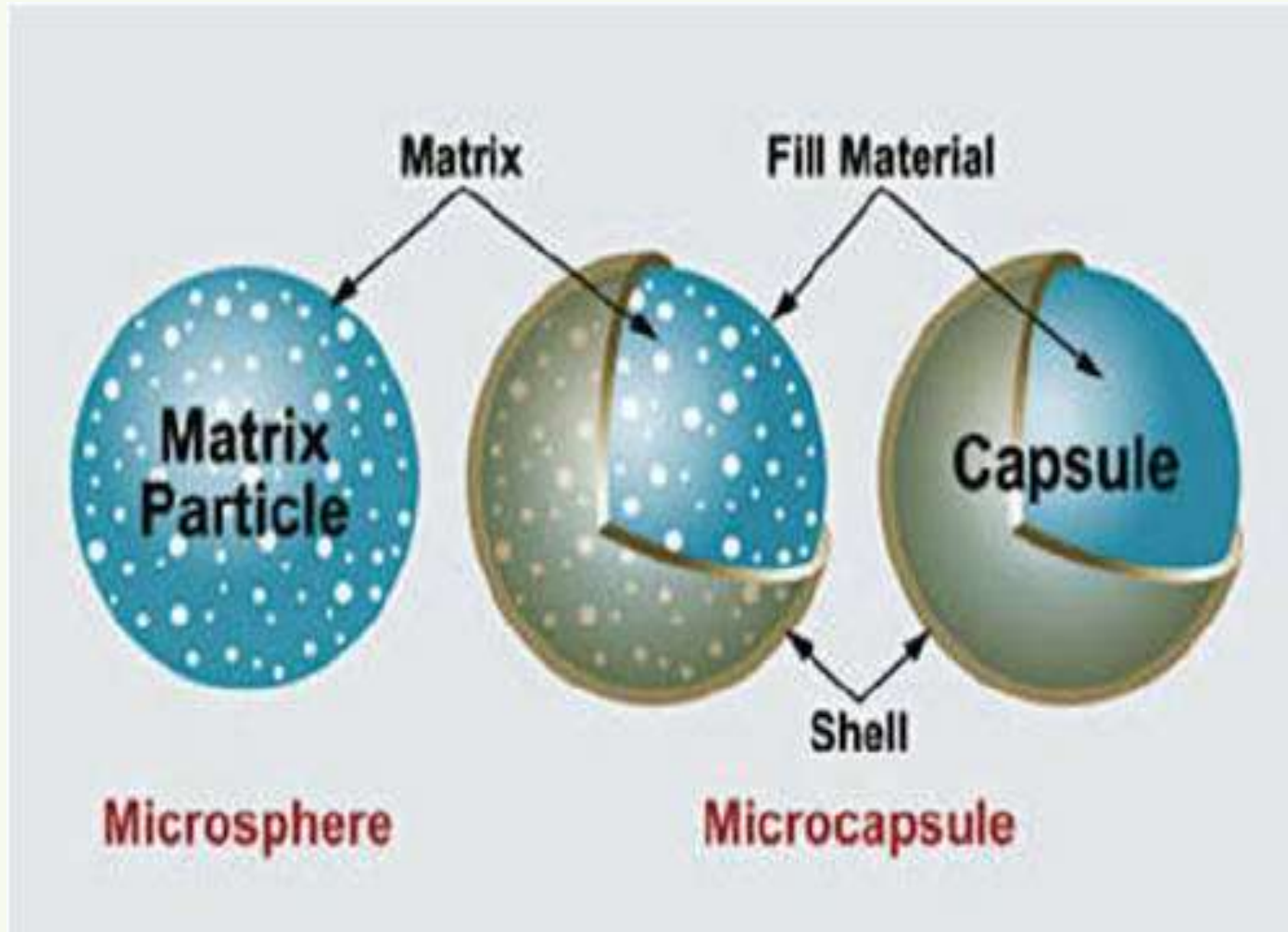


Fig: Microspheres and Microcapsules

# ADVANTAGES

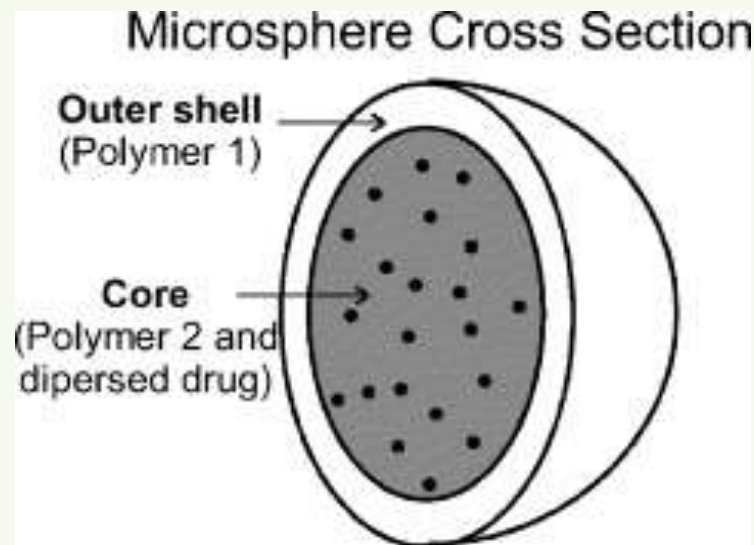
- Improve bioavailability
- Provide constant and prolonged therapeutic effect.
- Provide constant drug concentration in blood .
- Decrease dose and toxicity.
- Protect the drug from enzymatic and photolytic cleavage so it is best for drug delivery of protein.
- Reduce the dosing frequency and thereby improve the patient compliance

# DISADVANTAGES

- The cost is more.
- Reproducibility is less.
- Process conditions like change in temperature, pH, solvent addition, and evaporation/agitation may influence the stability of core particles.
- Degradation of product due to heat, hydrolysis, oxidation, solar radiation or biological agents.

# MICROSPHERES

- The spherical shells of microspheres are usually made up of polymers which are having a diameter in microns or nanometer range , and it is often filled with a drug substance for release as the shell is degraded.



# TYPES OF MICROSPHERES

- Bioadhesive microspheres
- Floating microspheres
- Radioactive microspheres
- Magnetic microspheres
- Polymeric microspheres
  - i) Biodegradable polymeric microspheres
  - ii) Synthetic polymeric microspheres

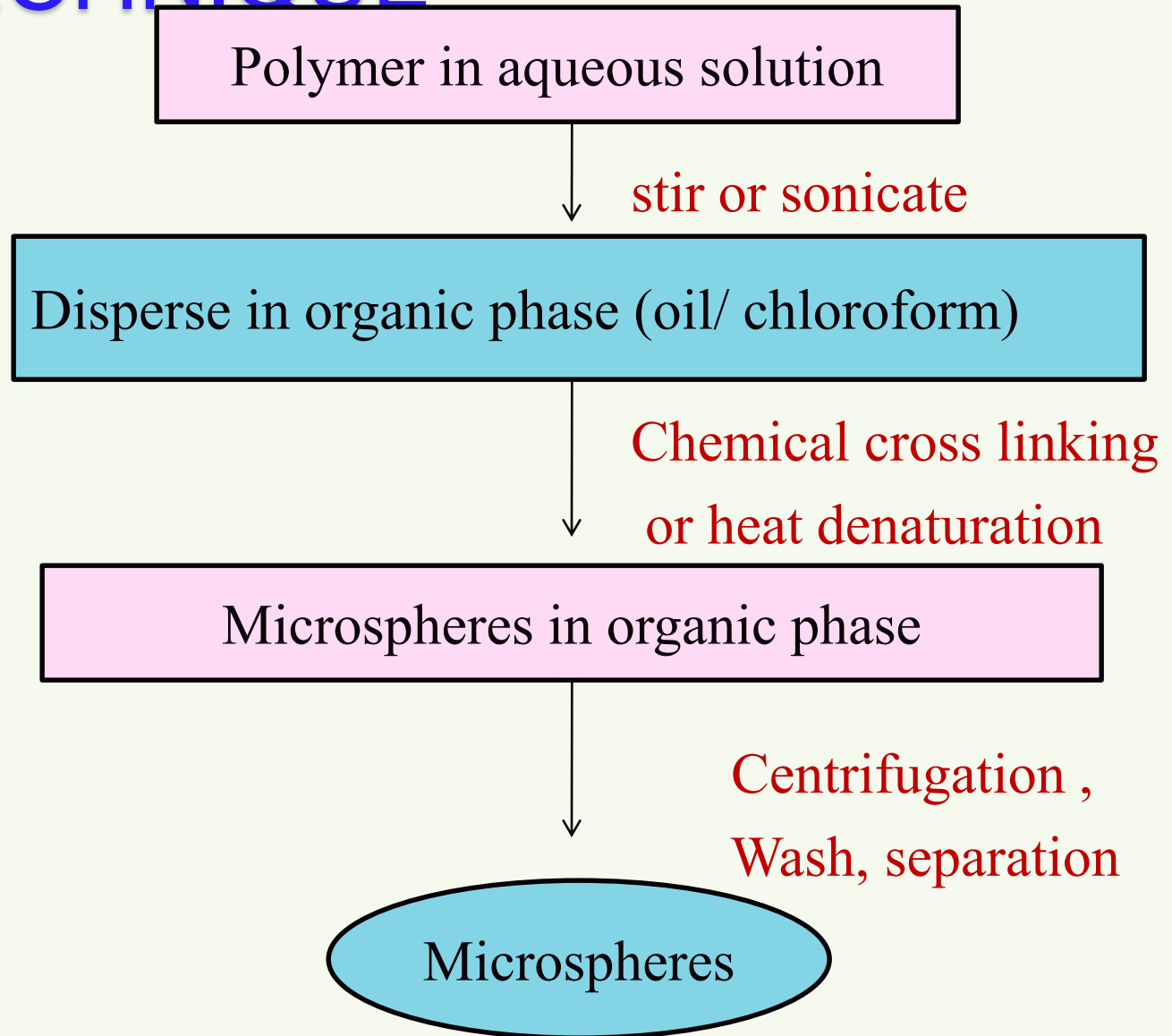


TYPES	DESCRIPTION	APPLICATION
1. Bioadhesive microspheres	Prolonged residence time	Nasal - Gentamycin
2. Floating microspheres	Bulk density less than gastric fluid	NSAIDS , Antibiotics
3. Radioactive microspheres	Deliver high radiation dose to targeted site.	Diagnostic: Liver , spleen
4. Polymeric microspheres	Biodegradable and non biodegradable Swells in aqueous medium	Vaccines: Hepatitis Local: Proteins and hormones
5. Magnetic microspheres	Localize the drug to the disease site	Chemotherapeutic agent to liver

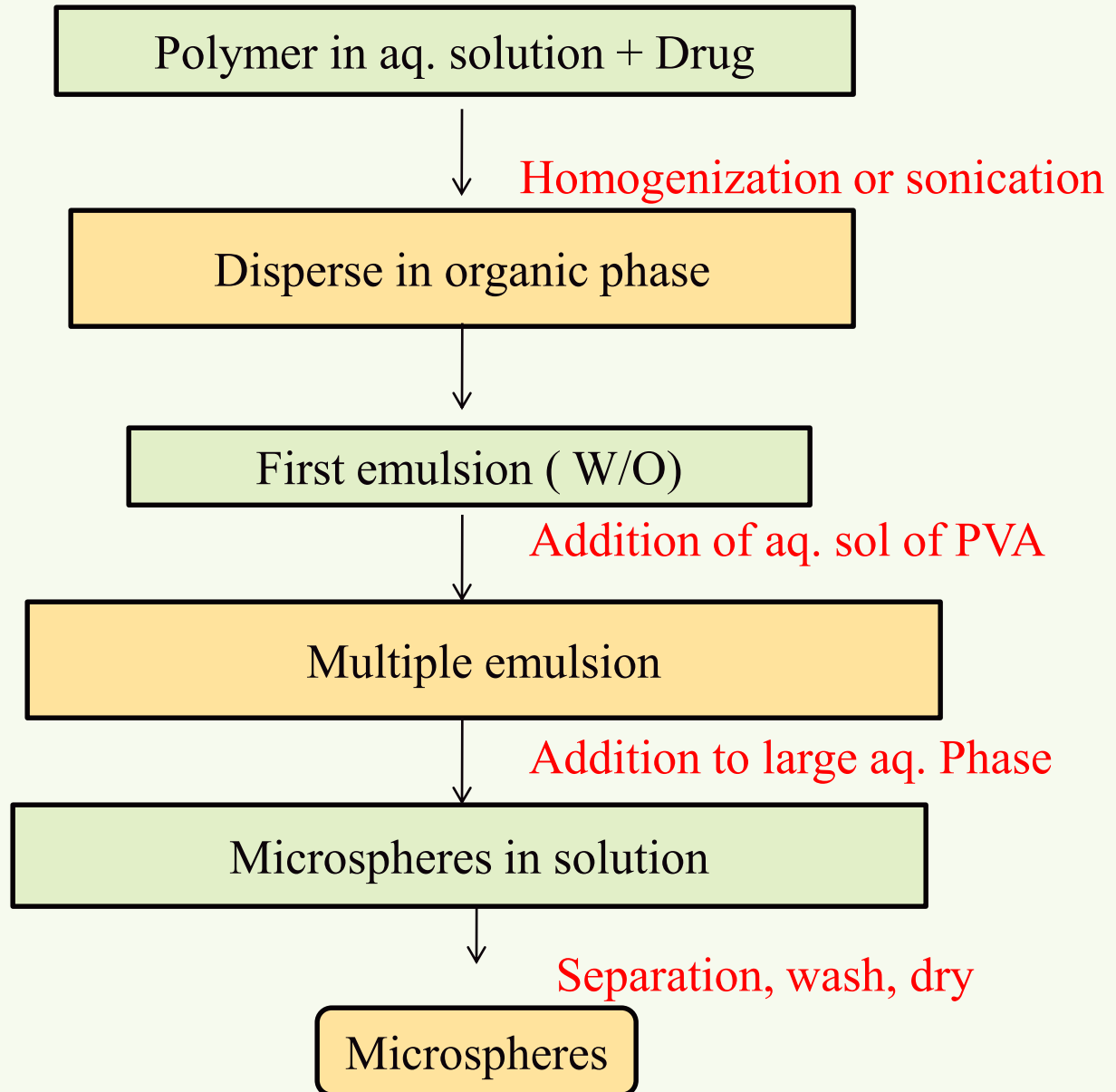
# METHOD OF PREPARATION:

- Single emulsion technique
- Double emulsion technique
- Solvent evaporation
- Phase separation coacervation technique
- Spray drying and spray congealing
- Solvent extraction
- Polymerization

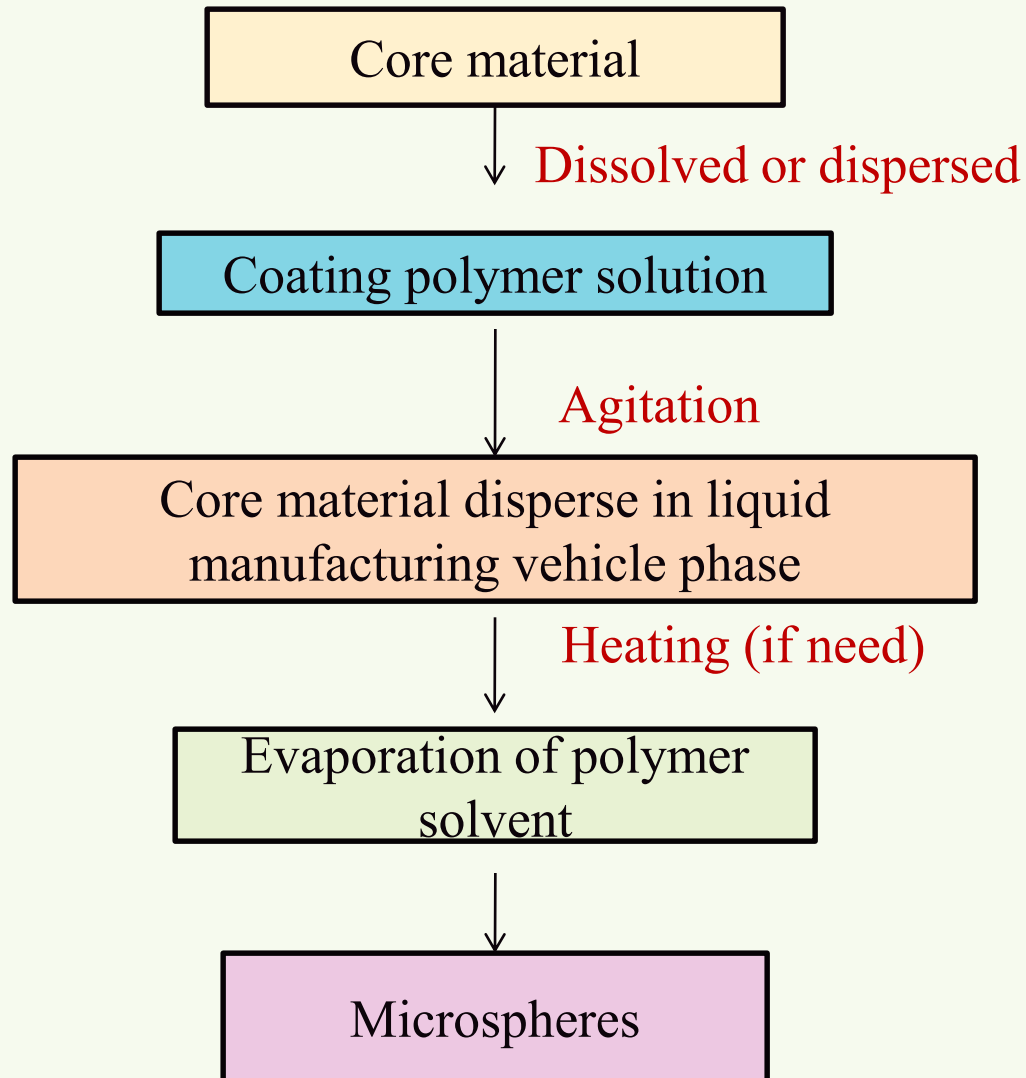
# SINGLE EMULSION TECHNIQUE



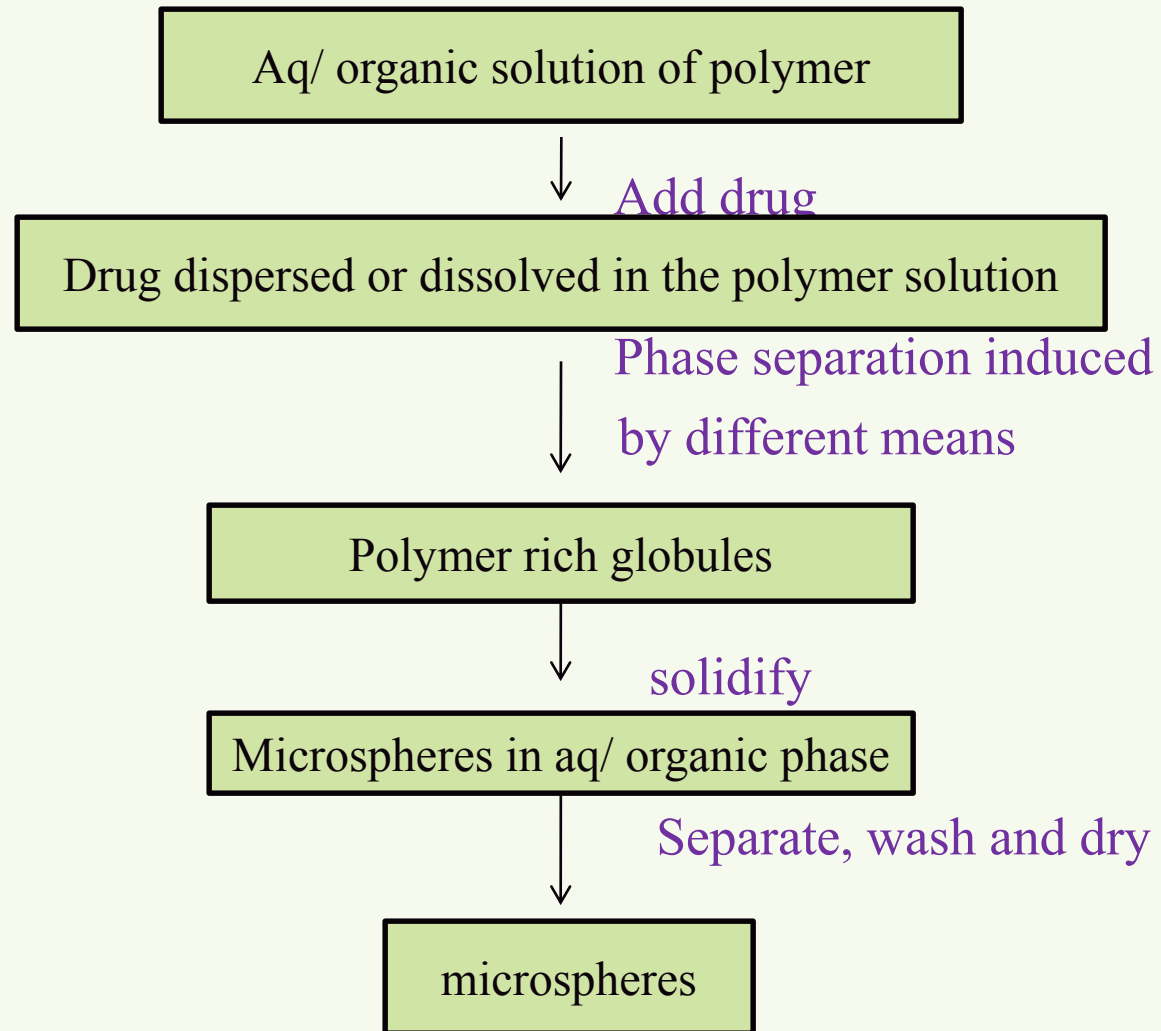
# DOUBLE EMULSION TECHNIQUE



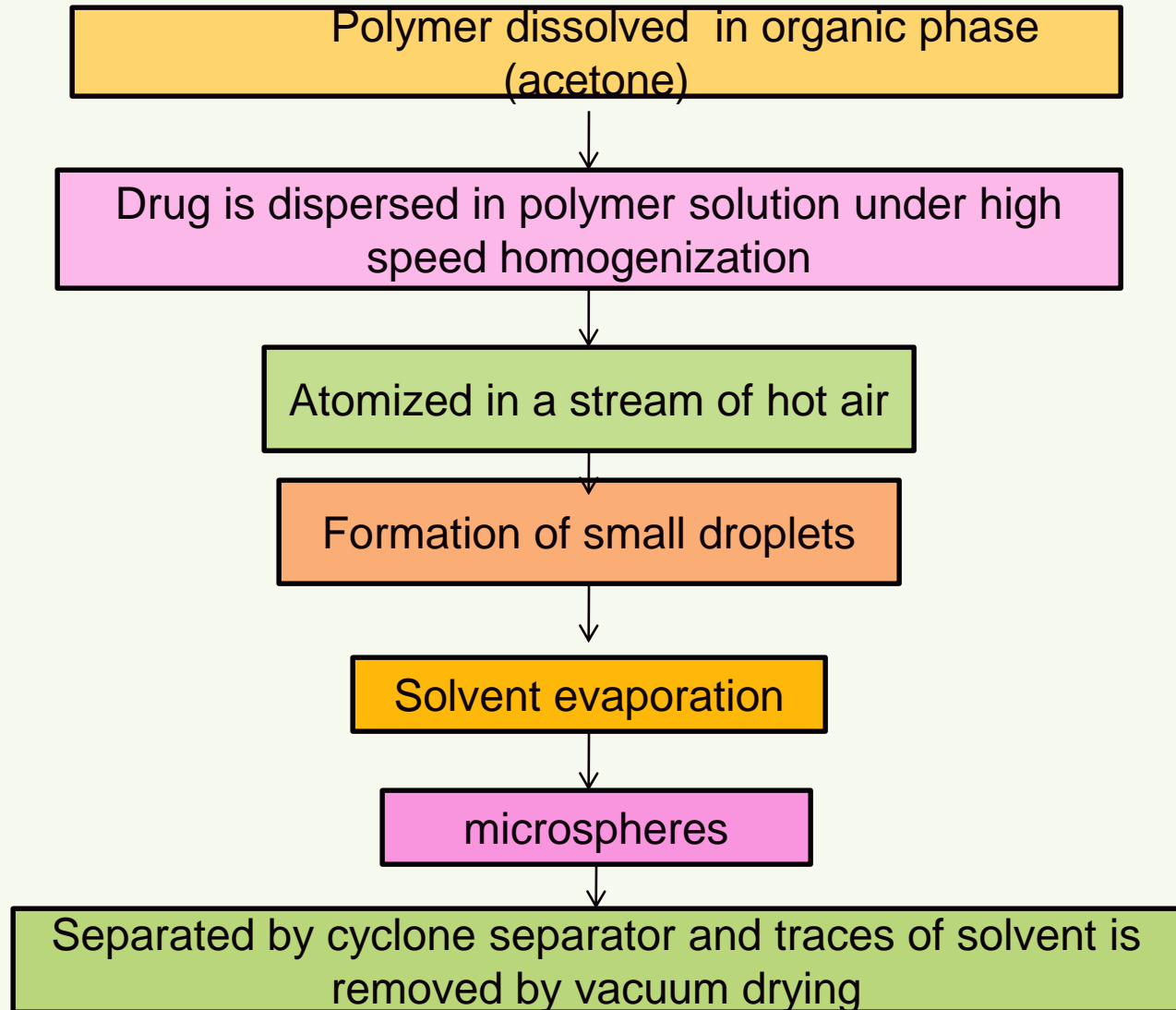
# SOLVENT EVAPORATION



# PHASE SEPARATION COACERVATION TECHNIQUE



# SPRAY DRYING AND SPRAY CONGEALING



# SOLVENT EXTRACTION

Drug is dispersed in organic solvent  
(water miscible organic solvents like isopropanol)



Polymer in organic solvent



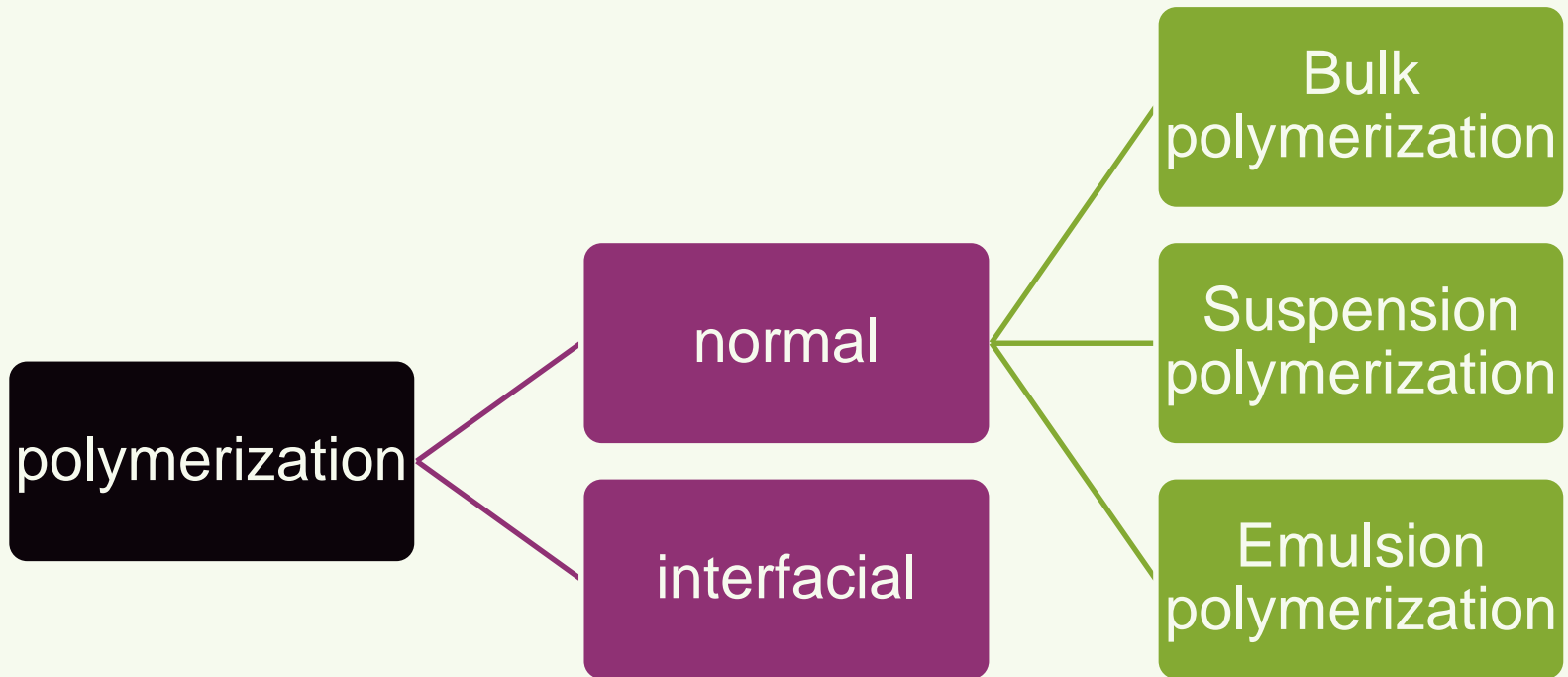
Organic phase is removed by extraction with water



microspheres



# POLYMERIZATION



# BULK POLYMERIZATION

Monomer / mixture of monomer + initiator



Heated to initiate polymerization

Polymer obtained is moulded / fragmented



**Microspheres**

# SUSPENSION POLYMERIZATION

Monomer or composition of monomers are heated and dispersed in water



Droplets  
(vigorous agitation)



Microspheres

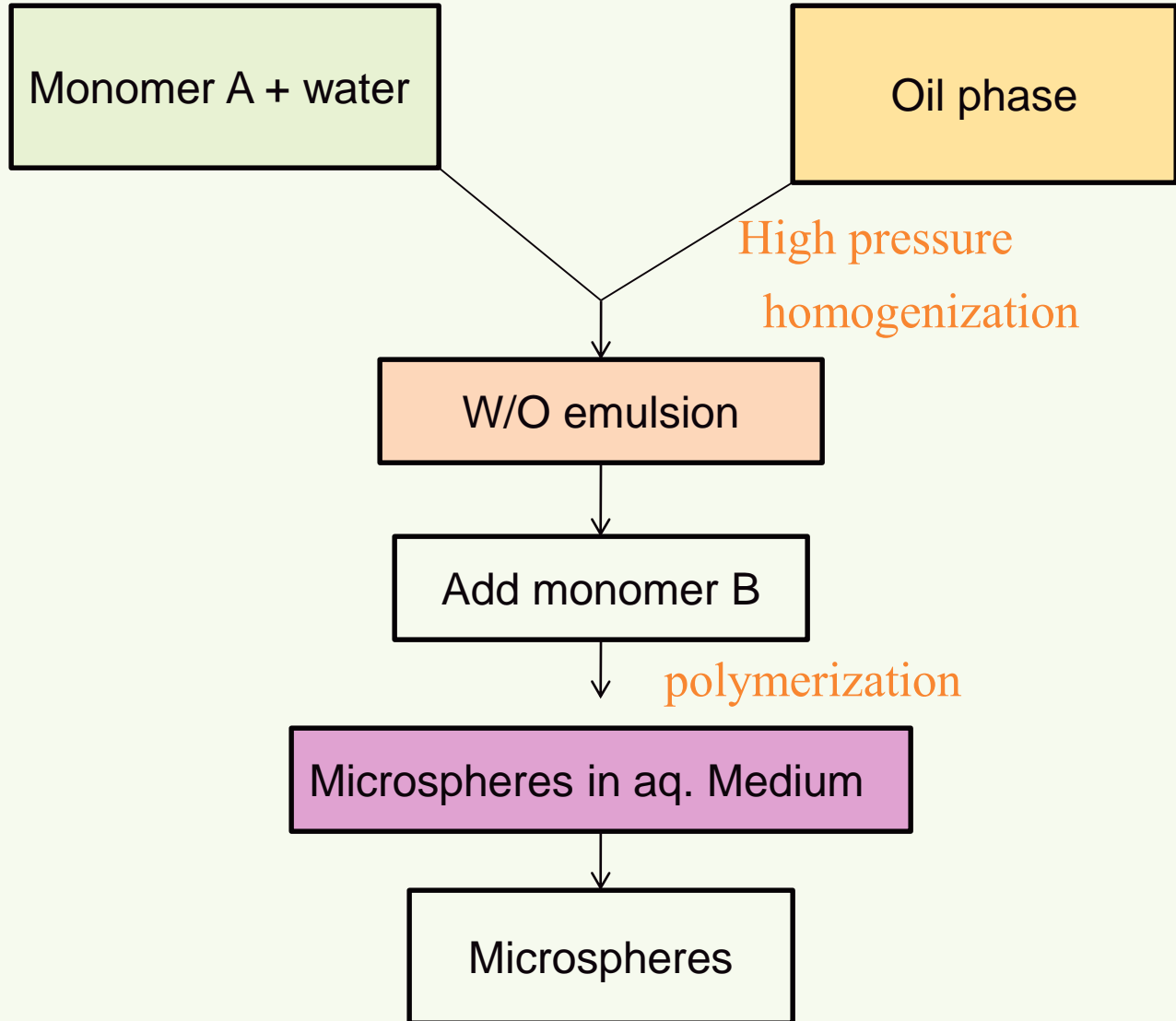
# EMULSION POLYMERIZATION

Monomer + aq. Solution of NaOH +  
initiator ( stir)

Micelles solution of polymer in aq.  
medium

Polymerization occurs , microspheres  
are formed

# INTERFACIAL POLYMERIZATION



# EVALUATION OF MICROSPHERES:


- 1) Particle size and shape:** The most widely used procedures to visualize microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM).
- 2) Degradation behavior:** The surface chemistry of the microspheres can be determined using the electron spectroscopy for chemical analysis (ESCA).

### **3) Angle of repose:**

The powder mass was allowed to flow through the funnel orifice kept vertically to a plane paper kept on the horizontal surface, giving a heap angle of powder on paper. The angle of repose was calculated by the following equation

$$\tan \theta = h/r$$

Where h & r are the height and radius of the powder cone.



**4) Bulk density:** Bulk density was obtained by dividing the mass of powder by the bulk volume in  $\text{cm}^3$ . It was calculated by using equation

$$\text{Bulk density} = \text{mass of microspheres} / \text{bulk volume}$$

**5) Tapped density:** It is the ratio of total mass of the powder to the tapped volume of the powder. It is expressed in  $\text{g/ml}$  and is given by

$$\text{Tapped density} = \text{mass of microspheres} / \text{Tapped volume.}$$



## 6) Drug entrapment efficiency:

It is the percentage of drug that is successfully entrapped with in microspheres

Drug entrapment efficiency can be calculated using following equation,

$$\% \text{ Entrapment} = \text{Actual content} / \text{Theoretical content} \times 100$$

## 7) Swelling index :

It is conducted in a phosphate buffer of pH 6.8. Their diameter is measured periodically by using laser particle size distribution analyzer until they were decreased by erosion and dissolution.

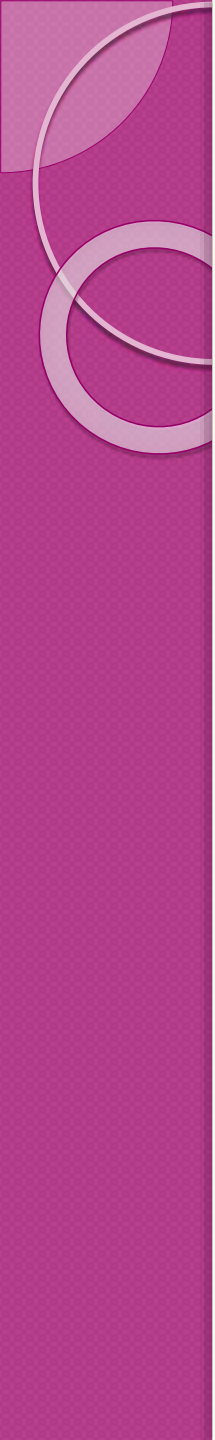
**Swelling index= (mass of swollen microspheres –  
mass of dry microspheres/mass of  
dried microspheres) 100**

## **8) *In vitro* methods:**

- Release studies for different type of microspheres are carried out by using phosphate buffer pH 7.4, mostly by rotating paddle apparatus.
- Agitated with 100 rpm, samples were collected at specific time intervals and replaced by same amount and analyzed.

## **9) Adhesion property:**

- Freshly cut piece of pig intestine is used (5 cm long), clean and wash it with isotonic saline solution.

- 
- Accurate weight of microspheres was placed on mucosal surface, phosphate buffer of pH 6.8 is warmed at 37 °c was peristaltically pumped at a rate of 5 ml/ min over the tissue.
  - The duration of complete washing of microspheres from pig intestine was recorded.

# APPLICATIONS

- Ophthalmic Drug Delivery
- Oral drug delivery
- Gene delivery
- Nasal drug delivery
- Buccal drug delivery
- Gastrointestinal drug delivery
- Transdermal drug delivery
- Colonic drug delivery

# Recent microsphere technology

- Tretinoin microsphere gel 0.04% for acne treatment<sup>®</sup>.
- Metronidazole mucoadhesive microspheres.
- Lupron depot<sup>®</sup> and nutropin <sup>®</sup>genentech's recombinant human growth hormone (rhGH) encapsulated with in poly(D,L-lactide -co-glycolide) PLG microspheres using alkermes proprietary ProLease<sup>®</sup>( but it is withdrawn from the market as its production costs were too high).

# Reference

- Theory and practice in novel drug delivery system by S.P. VYAS.
- **MICROSPHERES: A BRIEF REVIEW** Kadam N. R. and Suvarna V Department of Quality Assurance, SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Vile Parle, Maharashtra.



THANK YOU