SOLVENT EVAPORATION TECHNIQUE

Pharmaceutical technology

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SOLVENT EVAPORATION TECHNIQUE

Definition

Process of microencapsulation in which deposition of coating material or polymer around drug or core material is carried out by the evaporation of volatile solvent in which polymer is present. Actually creation of insufficiency of water for polymer by evaporation of solvent results in precipitation of polymer around core material and formation of microcapsules.

Polymer for microsphere preparation

Polymers which are used as matrices or wall-formers for drug deliver can be classified into 3 types

1. Water soluble polymers
2. Biodegradable polymers
3. Non-biodegradable polymers

In solvent evaporation technique we are mainly concern with biodegradable polymers so we will discuss them.

Biodegradable polymers

Both natural and synthetic polymers are used as matrix material in preparation of biodegradable microspheres.

Examples of commonly used biodegradable polymers are shown in the following table

	Animal proteins	**Animal polysaccharides**	**Plant polysaccharides**
NATURAL POLYMERS	Albumin Gelatin Fibrin Fibrinogen	Chitin Chitosan Hyaluronic acid	Starch Dextrin Dextran
SYNTHETIC POLYMERS	Polylactic acid(PLA) Polyglycolic acid(PGA) Poly (lactic/glycolic acid) (PLGA)	Polyanhydrides	Poly (ortho esters)

Lactic /glycolic acid polymers

PLA, PGA & PLGA (formed by combination of PLA and PGA) are the most commonly used synthetic polymers for microcapsules prepared by solvent evaporation technique.

	PGA	PLA	PLGA
NATURE	Most hydrophilic polymer	Hydrophobic than PGA	Hydrophobic polymer
SOLUBILITY	Insoluble in organic solvents	Soluble in organic solvents	Soluble in organic solvents
STATE	Crystalline	Amorphous	
	Poor candidate for drug release	Good candidate for drug matrix release	

Due to the biocompatibility, biodegradability and predictability of degradation these polymers have following applications in the field of medicine

- They are used in controlled release preparation of anticancer agents, antibiotics, NSAIDS, local anesthetics and contraceptives.
- These polymers are used in the preparation of various dosage forms for drug delivery e.g. microcapsules, microspheres, pellets, nanoparticles and implants.
- Biomaterial applications of these polymers include:
    - Ligament reconstruction
    - Dental and fracture repairs
    - Surgical dressings

Method of preparation of microcapsules by solvent evaporation process:

Two major techniques are used for microencapsulation by solvent evaporation. These includes

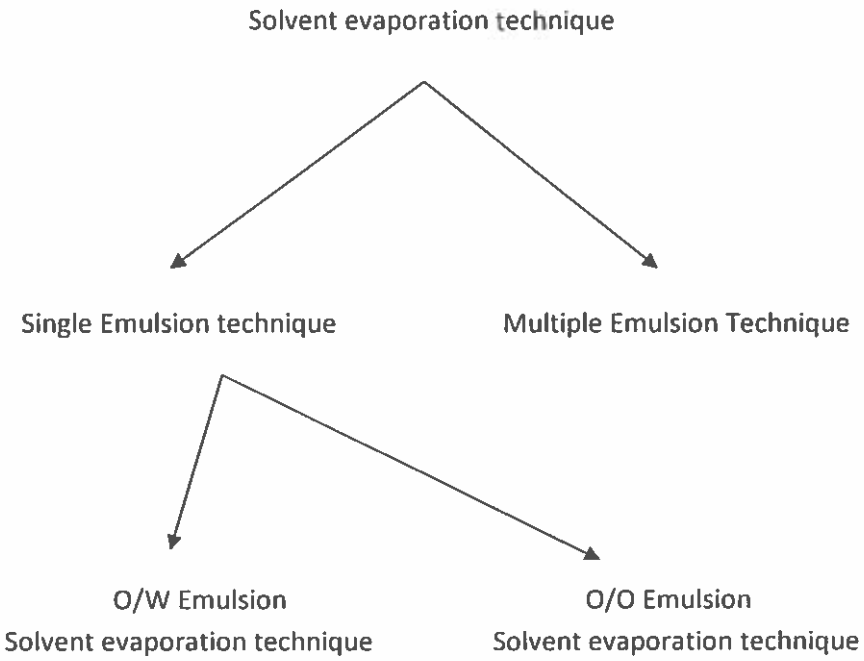
A. Single emulsion solvent evaporation technique
B. Multiple emulsion solvent evaporation technique

Single emulsion solvent evaporation technique

It is further divided into;

- Oil in Water Emulsion solvent evaporation technique
- Oil in Oil Emulsion solvent evaporation technique

It can be shown diagrammatically as:



1. Oil in water emulsion solvent technique (O/W)

This technique is mostly used for the entrapment of **lipophilic drugs** because hydrophilic drugs have increased solubility in water and these drugs can defuse from the organic dispersed phase into aqueous continuous phase, which results in poor entrapping.
In single emulsion technique polymer (PLGA or PLA) is dissolved in the volatile organic solvent (usually methylene chloride or chloroform). Then drug which is present in co-solvent is added to the same organic phase. Then this dispersed phase is emulsified with an aqueous solution containing a suitable emulsifier to form oil in water emulsion.

Then evaporation of organic solvent is carried out

- Either under atmospheric pressure
- Or under reduced pressure
- Or by heating

As the result of solvent evaporation, polymer shrinks around the core & formation of discrete, hardened monolithic type of particle takes place

Commonly used solvents

- Methylene chloride
- Chloroform

Commonly used Emulsifying agents

- Methyl cellulose (MC)
- Hydroxy propyl methyl cellulose (HPMC)
- Tween etc

Drugs commonly encapsulated by this technique

- Steroidal hormone (Testosterone, progesterone)
- Antibiotics (Doxorubicin)
- Local anesthetics

Advantages

O/W emulsion solvent evaporation technique is commonly used due to

- Simplicity of process
- Easy cleaning of final product

Disadvantages

Low encapsulation ability for water soluble drugs. However they can be encapsulate by reducing the solubility of drug in external phase which can be done by modifying the pH of this phase, saturating external phase with drug, or adding electrolytes.

2. Oil in Oil Emulsion Solvent Evaporation Technique O/O

This technique is also referred as w/o emulsification emulsification solvent evaporation technique and it is mostly used for the entrapment of hydrophilic drugs.
In this technique polymer (PLGA) and drugs are added in polar solvent to form dispersed phase. Then this polar (dispersed) phase is added in a lipophilic phase containing oil soluble surfactant to form oil in oil emulsion. Lipophilic phase is mineral oil and surfactant is span.

Commonly used polar solvent

- Acetonitrile etc

Commonly used external phase

- Mineral oil

Commonly used emulsifying agent

- Span (oil soluble surfactant)

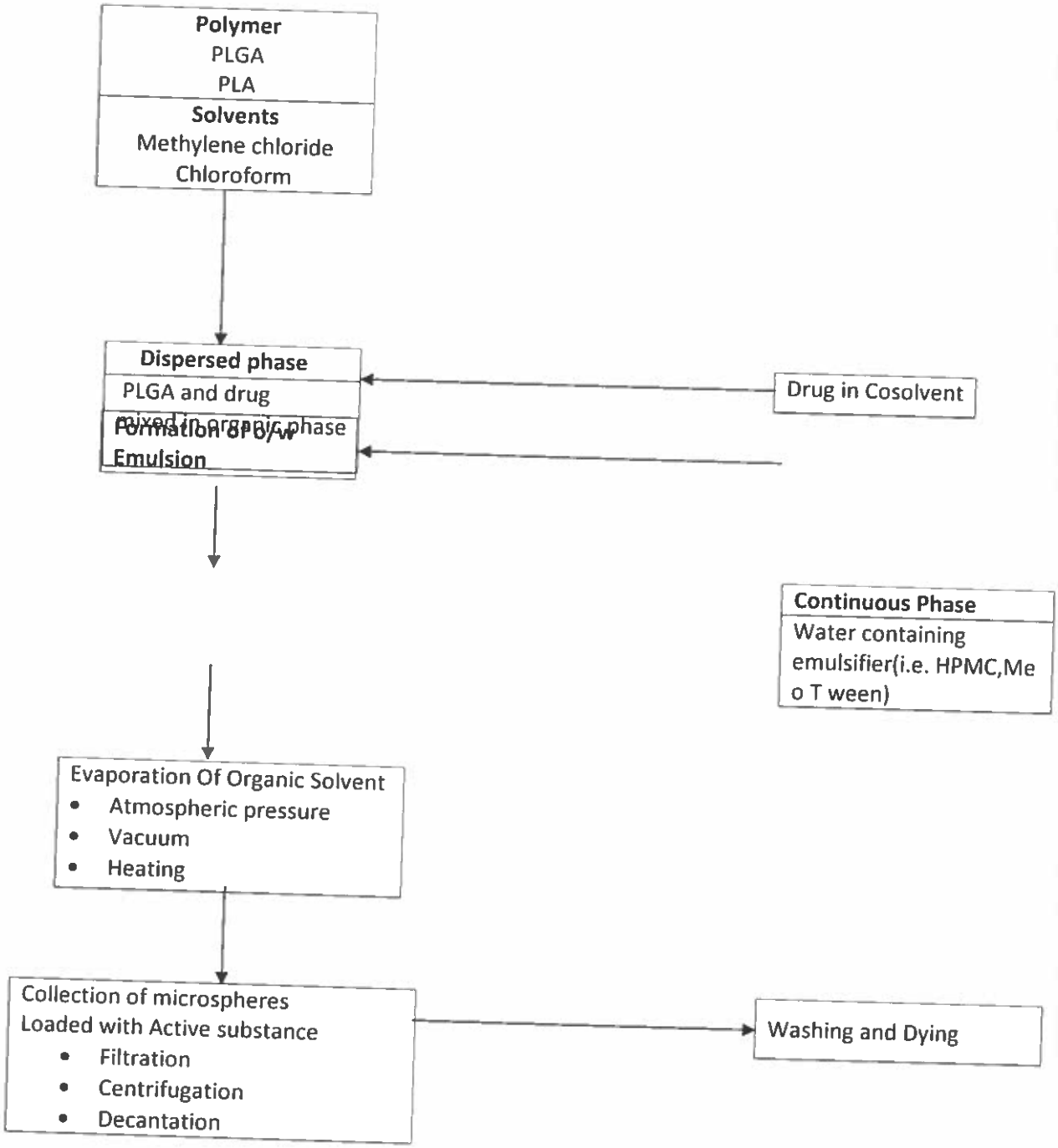
Drugs which can be encapsulated by this technique

- Diphenyl hydramine HCL
- Mitomycin
- Phenobarbital etc

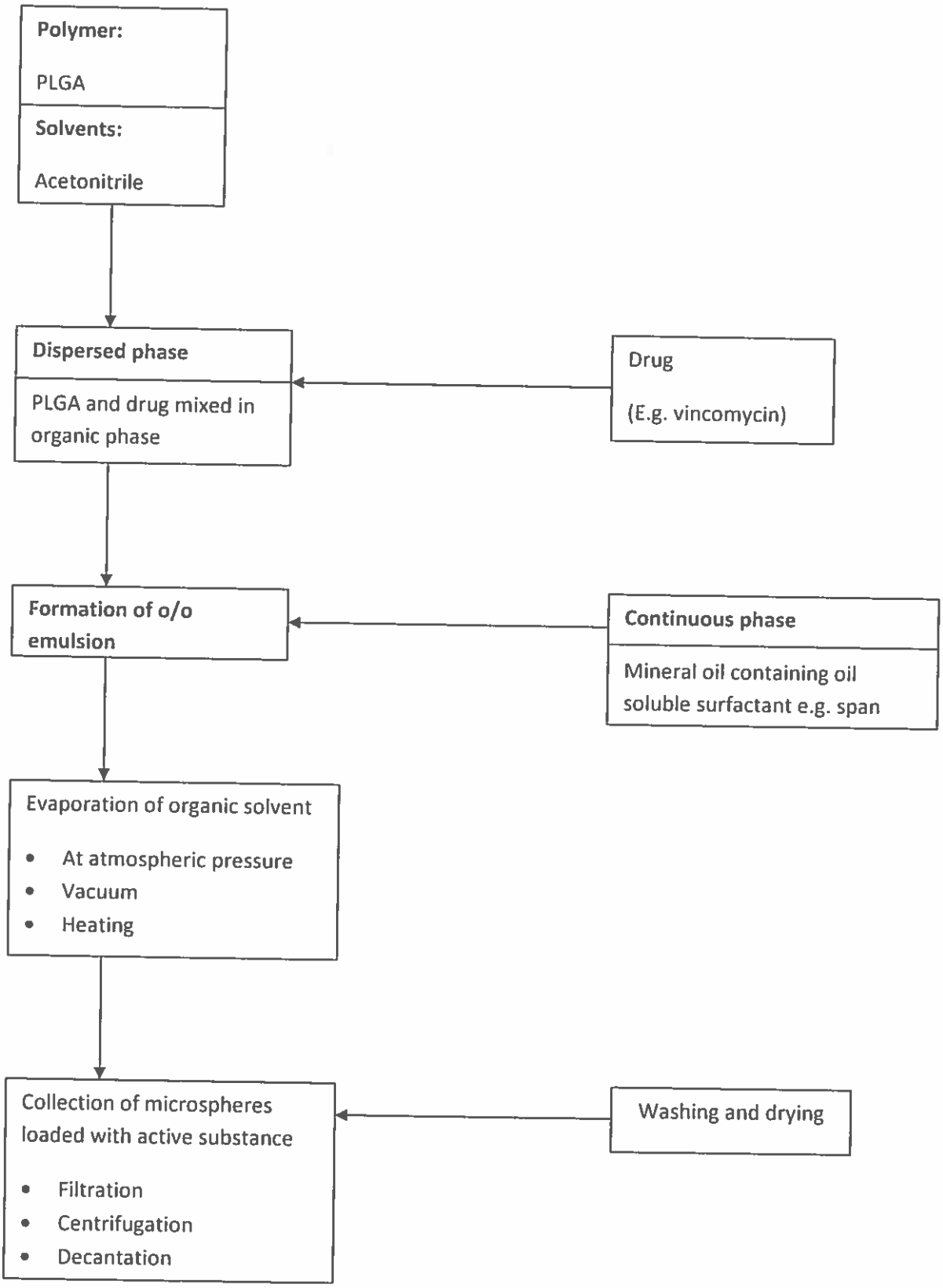
Disadvantages

Disadvantage of using oil as external phase is difficulty in cleaning the final product. The oil has to be removed by using organic solvent such as n-hexane.

Flow chart for preparation of PLGA microspheres by o/w emulsion solvent evaporation technique:



Flow chart for preparation of PLGA microspheres by o/o emulsion solvent evaporation technique



MULTIPLE EMULSION TECHNIQUE (W/O/W)

This drug is commonly used for the entrapment of water soluble drugs, peptides proteins and other macromolecules.

- In this method drug is dissolved in distilled water (inner water phase) and polymer is dissolved in volatile organic solvent which is not miscible with water.
- Then the inner phase is poured either in presence or absence of surfactant in organic phase to form primary emulsion (w/o).
- Then this emulsion is poured under vigorous mixing using mechanical stirrer into an aqueous phase that contains an emulsifier forming a (w/o/w) emulsion.
- The resulting multiple emulsions are continuously stirred and solvent is allowed to evaporate which results in polymer precipitation and ultimately formation of drug loaded microcapsules.
- These microcapsules are ultimately separated by filtration rinse with water in order to removing the emulsifying agent. And then dried under vacuum or freeze dried.

In this case, organic phase act as a barrier between the two aqueous compartments, thus preventing the diffusion of active material from inner aqueous phase into the external aqueous phase.

Drugs Commonly Encapsulated By This Technique

- Proteins
- Peptides
- Nucleic acids

Flow chart for preparation of microspheres by w/o/w emulsion solvent evaporation technique