# MICROENCAPSULATION


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- Micro encapsulation is the means of applying thin coatings to small particles of solids or droplets of liquids and dispersions. The coating of particles ranging from several tenths of a micron to 5000 microns in size.

- Microencapsulation provides the means of converting the liquids to solids, of altering the colloidal and surface properties, of providing environmental protection,

## ADVANTAGES:

- Microencapsulation provides the means of converting liquids to solids.
- Altering colloidal and surface properties.
- Providing environmental protection
- Controlling the release characteristics.

## DISADVANTAGES:

- No single microencapsulation process is adaptable to all core material candidates or product applications.
- Difficulties such as incomplete or discontinuous coating
- Inadequate stability or shelf life of sensitive pharmaceuticals.
- Non reproducible and unstable release characteristics of coated products
- Economic limitations often are encountered in the attempt to apply particular microencapsulation method.

## ➢ Fundamental Considerations:

### ✓ Core Material:

- The core material, defined as the specific material to be coated , can be liquid or solid in nature.
- The solid core can be a mixture of active constituents , stabilizers , diluents, excipients, and accelerants.

**TABLE 13-6.** *Properties of Some Microencapsulated Core Materials*

| *Core Material* | *Characteristic Property* | *Purpose of Encapsulation* |
|---|---|---|
| Acetaminophen | Slightly water-soluble solid | Taste-masking |
| Activated charcoal | Adsorbent | Selective sorption |
| Aspirin | Slightly water-soluble solid | Taste-masking; sustained release; reduced gastric irritation; separation of incompatibles |
| Islet of Langerhans | Viable cells | Sustained normalization of diabetic condition |
| Isosorbide dinitrate | Water-soluble solid | Sustained release |
| Liquid crystals | Liquid | Conversion of liquid to solid; stabilization |
| Menthol/methyl salicylate camphor mixture | Volatile solution | Reduction of volatility; sustained release |
| Progesterone | Slightly water-soluble solid | Sustained release |
| Potassium chloride | Highly water-soluble solid | Reduced gastric irritation |
| Urease | Water-soluble enzyme | Permselectivity of enzyme, substrate, and reaction produ |
| Vitamin A palmitate | Nonvolatile liquid | Stabilization to oxidation |

## Coating Material:

**The selection of a specific coating material depends upon that**

- What are the specific dosage or product requirements- stabilization, reduced volatility, release characteristics , environmental conditions.

- What coating material will satisfy the product objectives and requirements.

- What microencapsulation method is best suited to accomplish the coated product objectives.

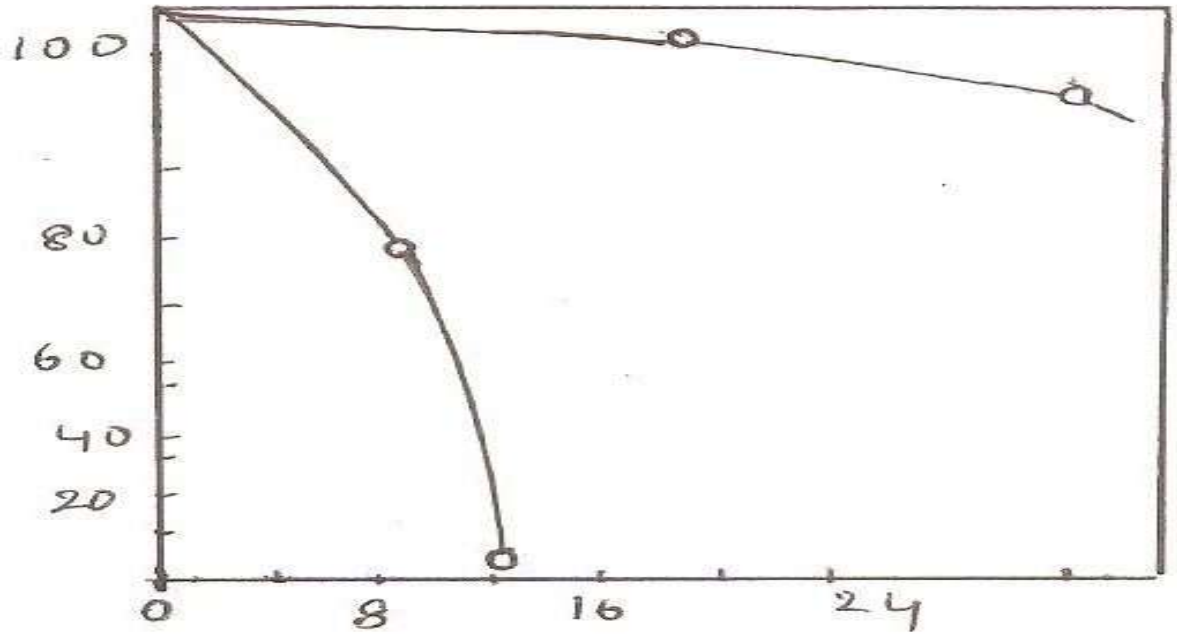
- The coating material should be capable of forming a film that is cohesive with the core material, be chemically compatible and non reactive with the core material and provide a desired coating properties, such as strength, flexibility, impermeability, optical properties, and stability.

- The typical coating properties such as cohesiveness , permeability,moisture sorption, solubility, stability and clarity must be considered in the selection of the proper microcapsule coating material.

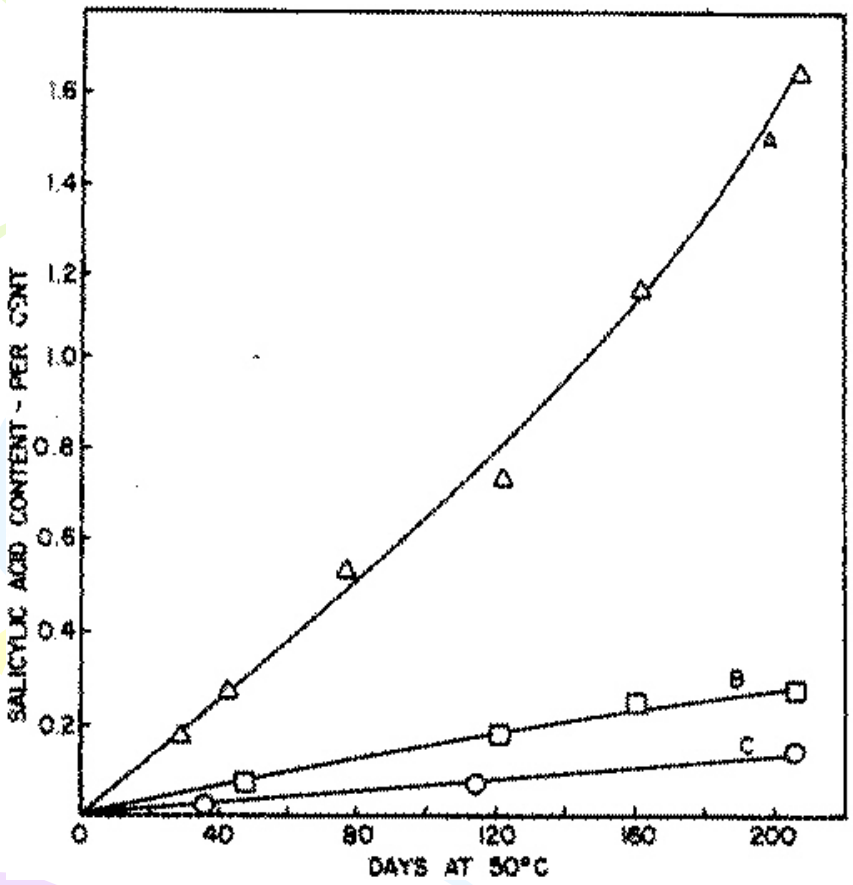
TABLE 13-7. *Representative Coating Materials and Appli*

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

# ➢ Selected Stability , Release And Other Properties:




Stability of microencapsulated vitamin A palmitate corn oil prepared by Phase separation or coacervation technique compared with unencapsulated control

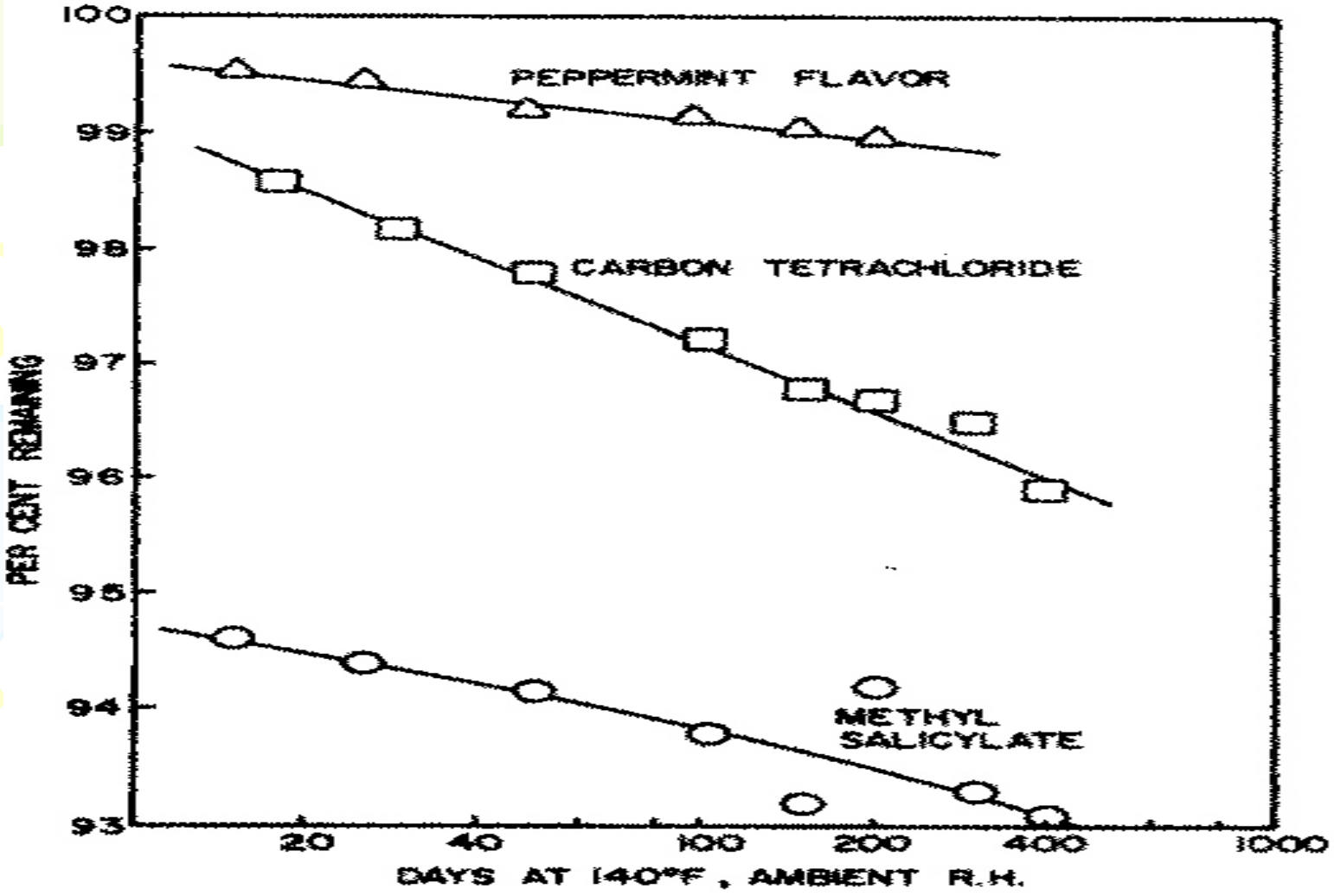



a. Aspirin hydrolysis of chlorpheniramine maleate- aspirin mixture

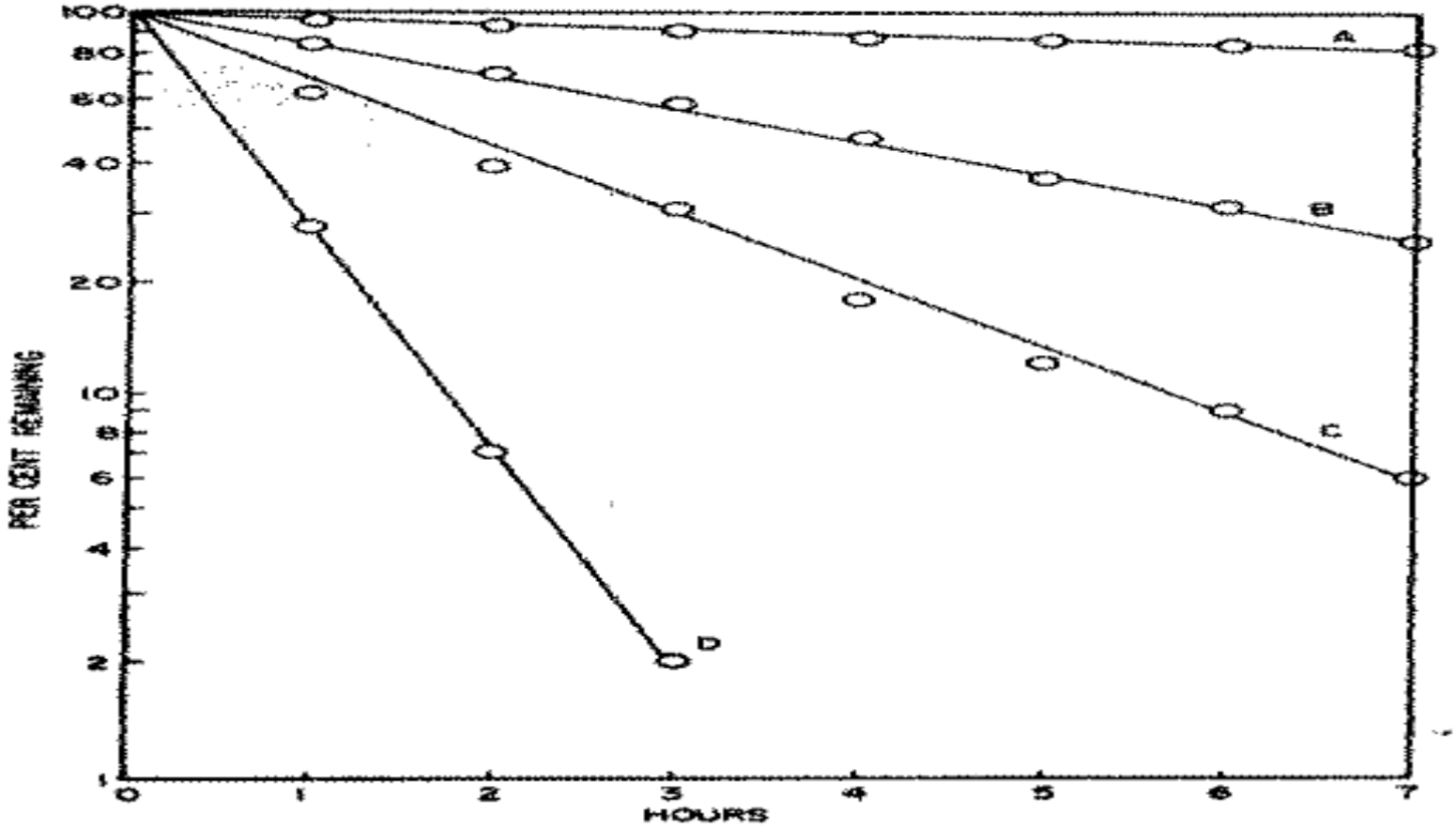
b. Aspirin hydrolysis of microencapsulated mixture.

c. Hydrolysis of aspirin control.

*Stability enhancement of incompatible aspirin mixture by microencapsulation*



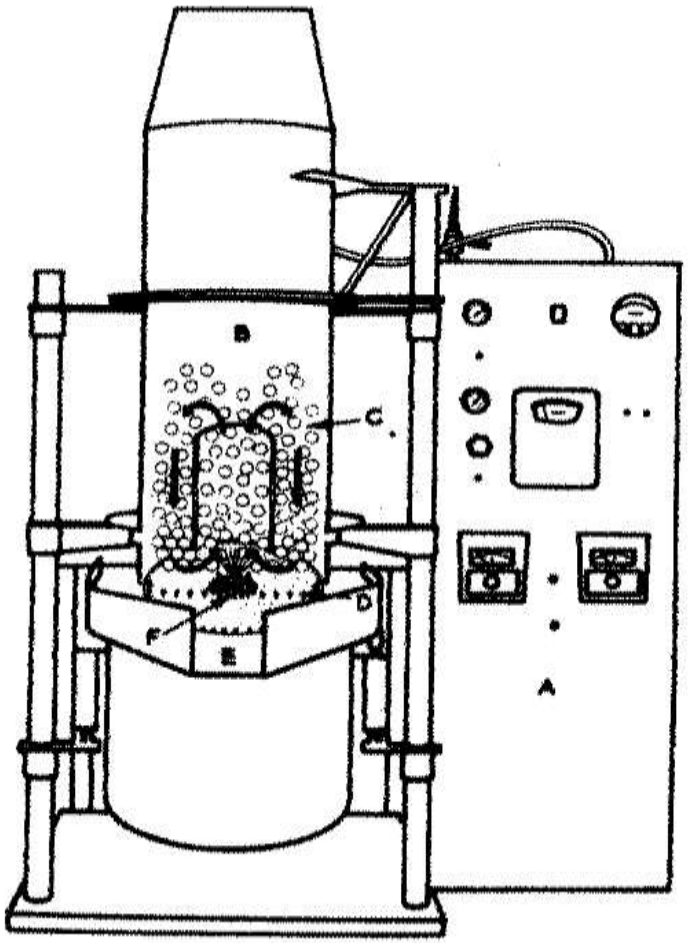

*The above graph shows that the stability of microencapsulated Volatile liquids, prepared by coacervation phase separation*




*Invitro release patterns of crystalline aspirin coated with various amounts of ethyl cellulose using phase separation coacervation techniques.*

## EQUPMENT AND PROCESSING:

- Air suspension.
- Coacervation phase separation.
- Multi orifice-centrifugal process.
- Spray drying and congealing
- Pan Coating.
- Solvent evaporation techniques.
- Polymerization.



WURSTER AIR SUSPENSION APPARATUS

a. Control panel

b. Coating chamber.

c. Particles being treated.

d. Process air flow.

e. Air distribution plate.

f. Nozzle for applying film coatings.

Processing variables that receive consideration for efficient , effective, encapsulation by air suspension include:

- Density, surface area, melting point, solubility, friability, volatility , crystallinity and flowability to the core material.
- Coating material concentration.
- Coating material application rate.
- Volume of air required to support and fluidize the core material.
- Amount of coating material required.
- Inlet and outlet operating temperatures.

## Coacervation Phase Separation:

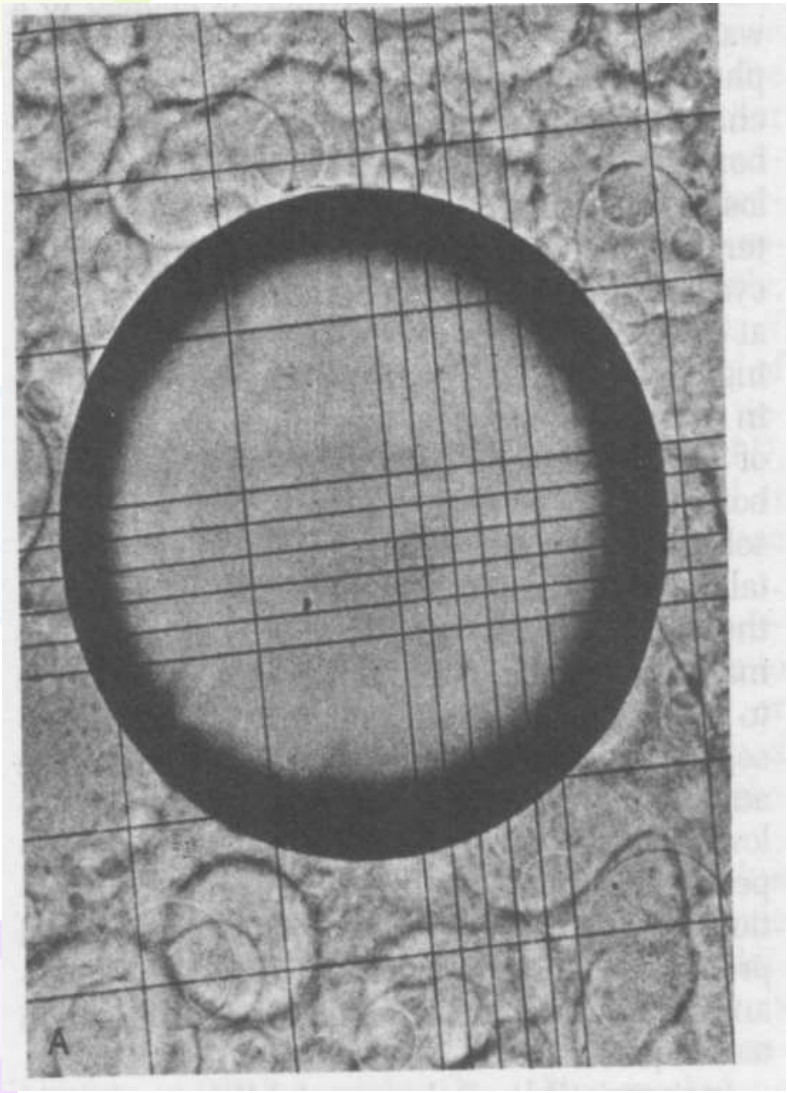
- Microencapsulation by coacervation phase separation is generally attributed to The National Cash Register (NCR) The process consists of three steps

- Formation of three immiscible phases; a liquid manufacturing phase, a core material phase and a coating material phase.

- Deposition of the liquid polymer coating on the core material.

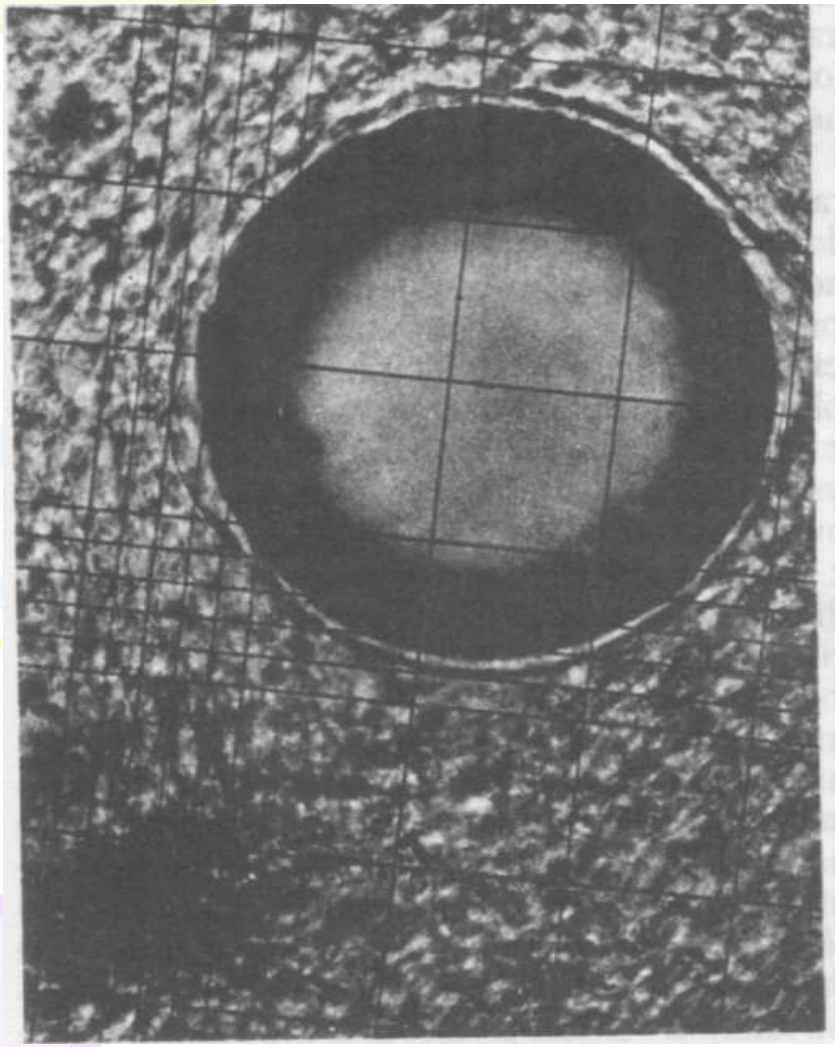
- Rigidizing the coating usually by thermal, cross linking or desolvation techniques to form a microcapsule.

STEP -1




- To form the three phases, the core material is dispersed in a solution of 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 i.e. by changing temperature of polymer solution or by adding the salt, non solvent, or incompatible polymer to the polymer solution.

STEP-11



The deposition of the liquid polymer around the interface formed between the core material and the liquid vehicle phase.

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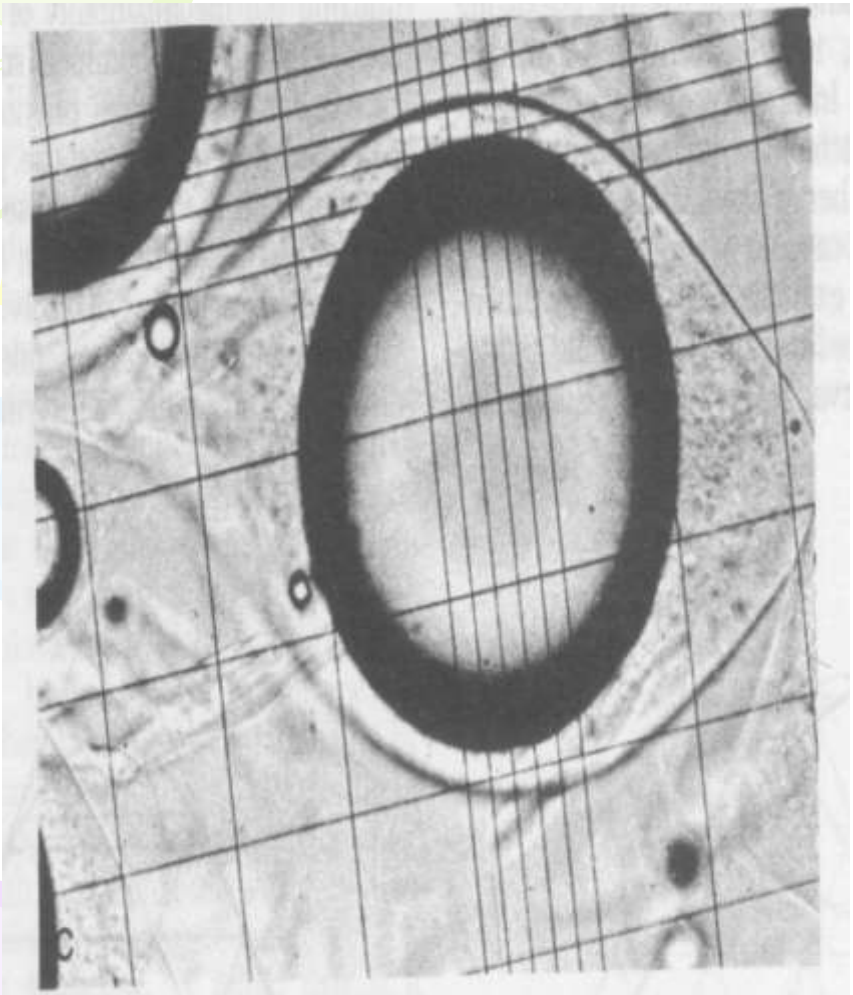
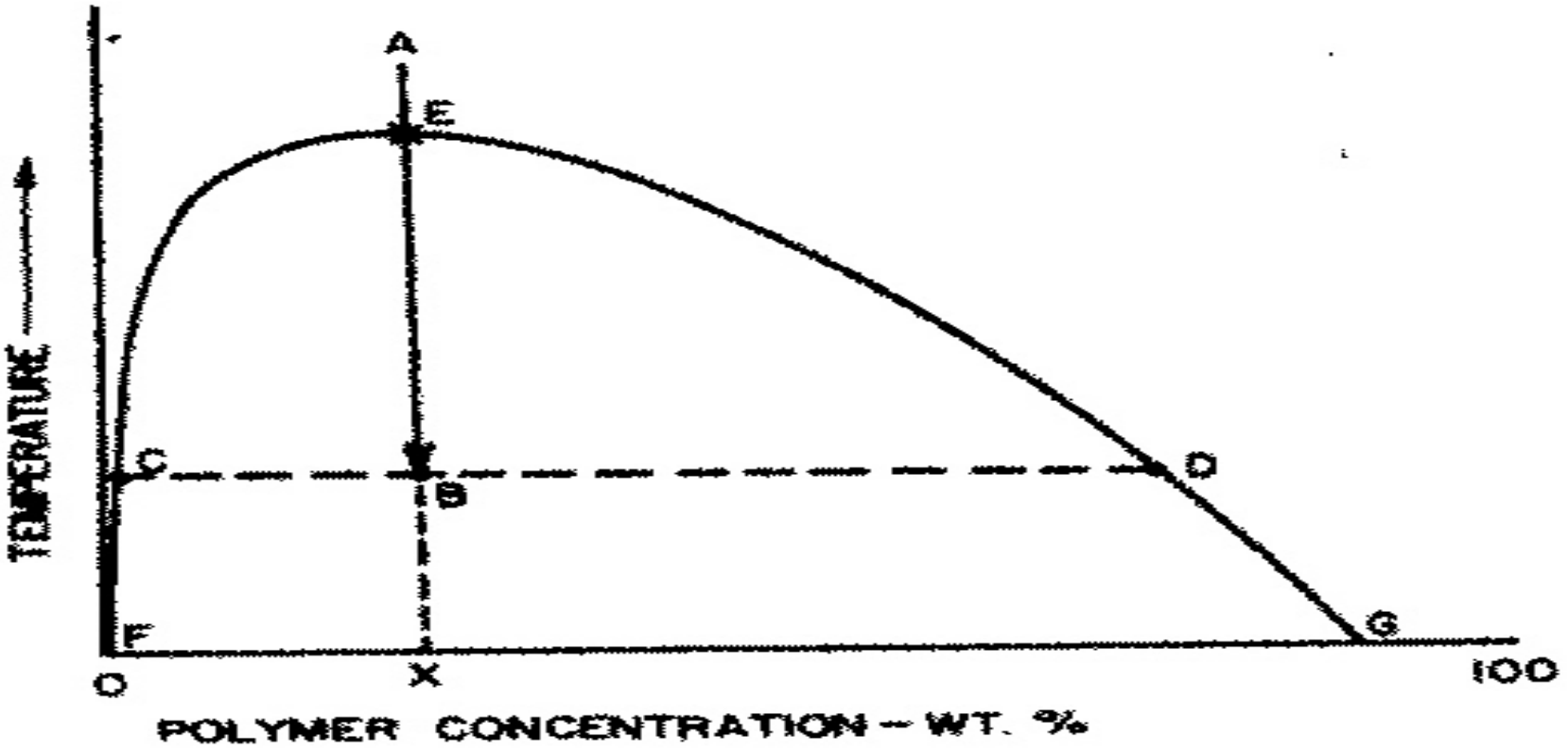
# STEP-III



Step 3. Completed Capsules in Manufacturing Vehicle

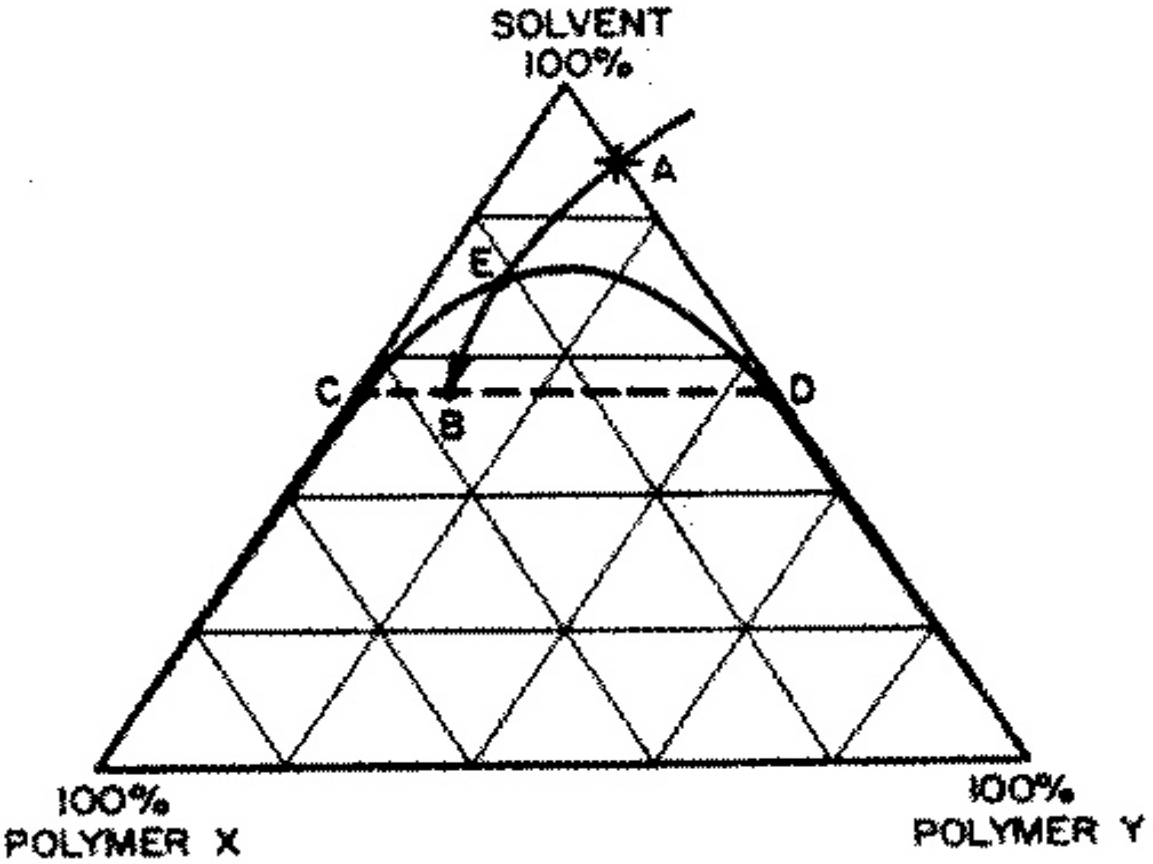
This process involves rigidizing the coating , usually by thermal, cross linking, or desolvation techniques, to form self sustaining microcapsule.

- **Temperature Changes:**



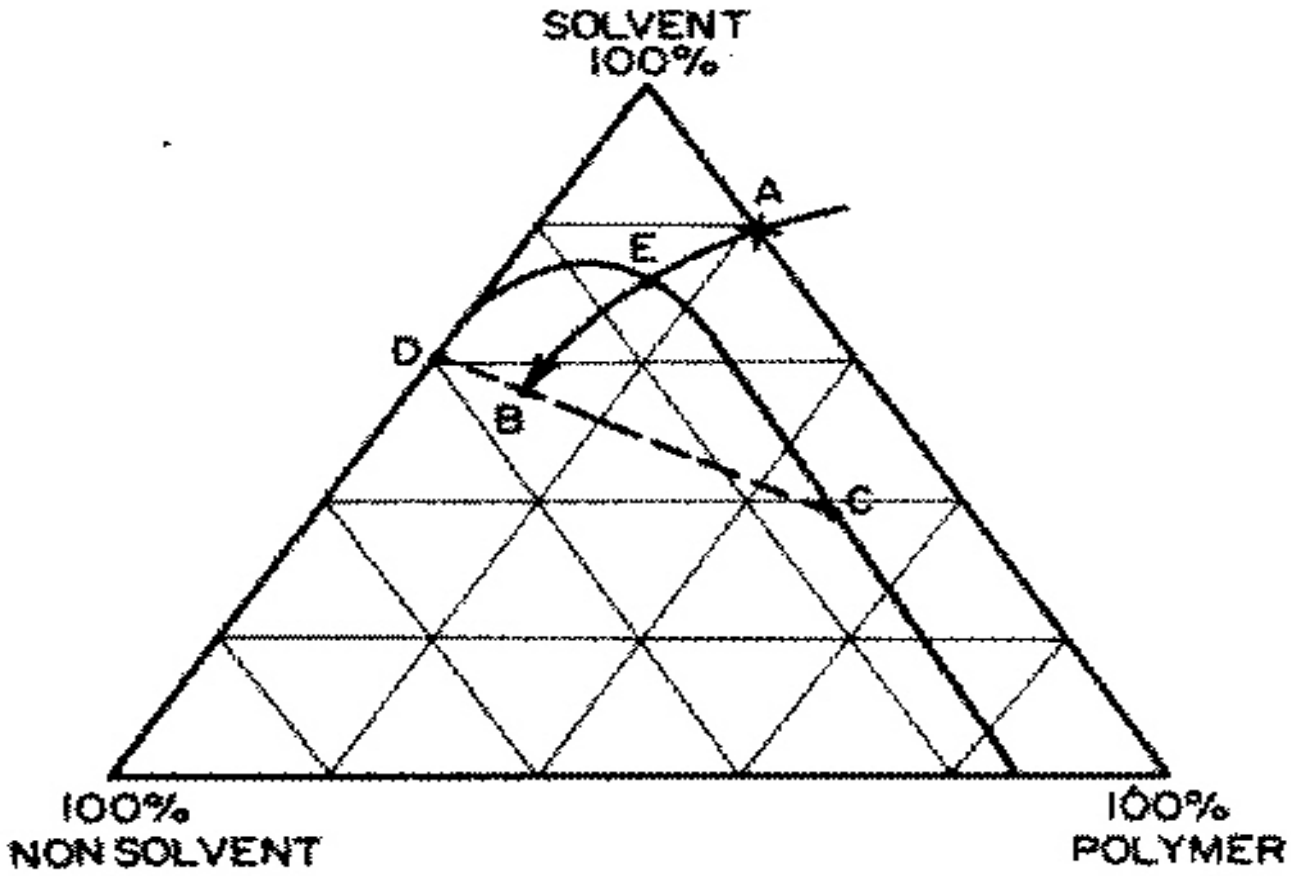

- Ex:N – Acetyl Para Aminophenol coated with EC dissolved in cyclohexane as solvent.

## Incompatible Polymer Addition:



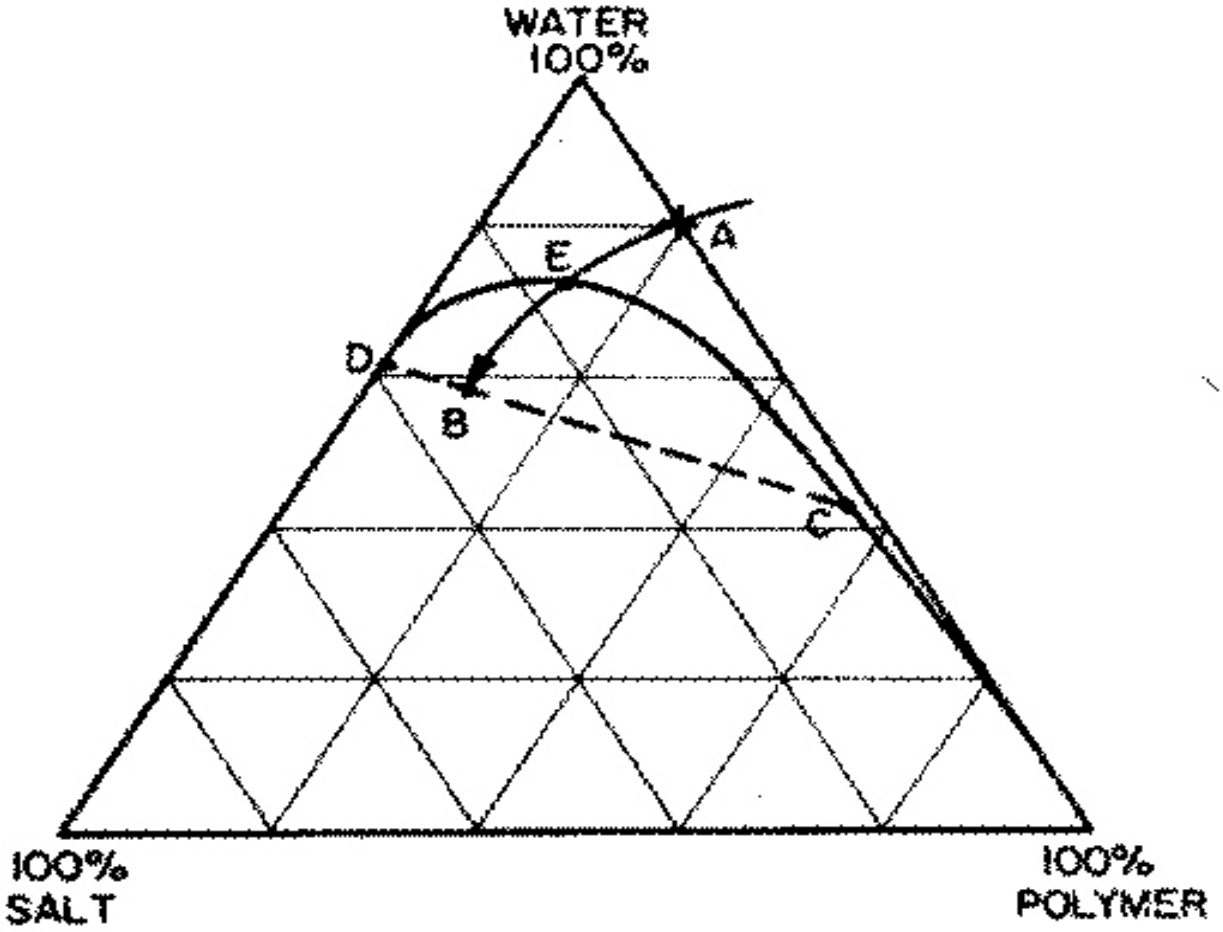

Four Parts of Methylene Blue HCl is coated with two % EC dissolved in toluene is phase separated by the addition of 25 parts of incompatible polymer Polybutadiene

# Non Solvent Addition:




Methyscopolamine Hydrobromide is coated with 5 % W/V of CAB dissolved in methylethyl ketone is phase separated by the addition of 1:2 parts of isopropyl ether as non solvent

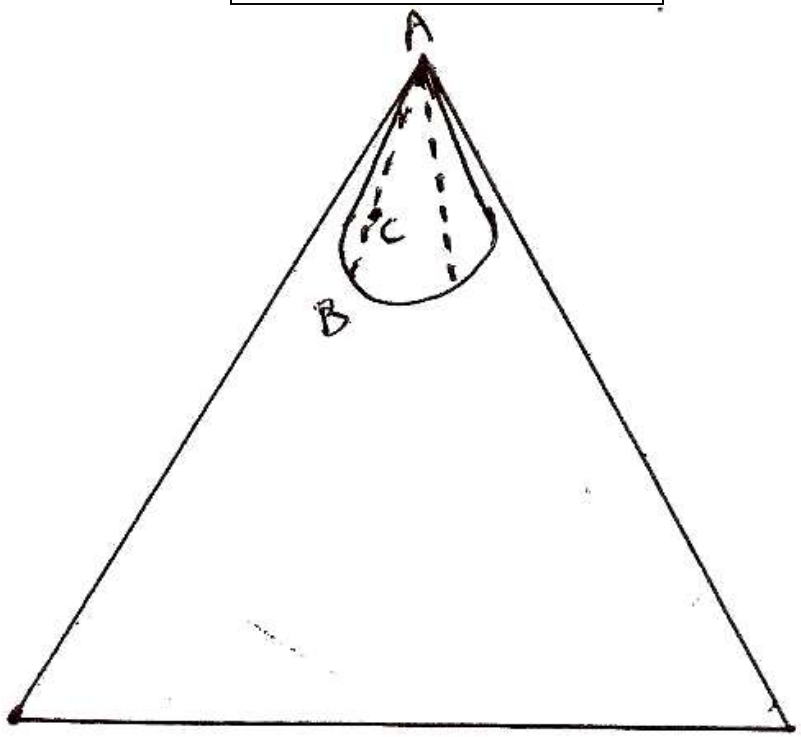
## Salt Addition:




Vitamin A in corn oil is emulsified with 10% Gelatin at $50^0$c is microencapsulated by adding 20% Sodium sulphate as salt solution which is further rigidized by transferring them in to 7% sodium sulphate solution at $19^0$C

## Polymer- Polymer Interaction:

100% water

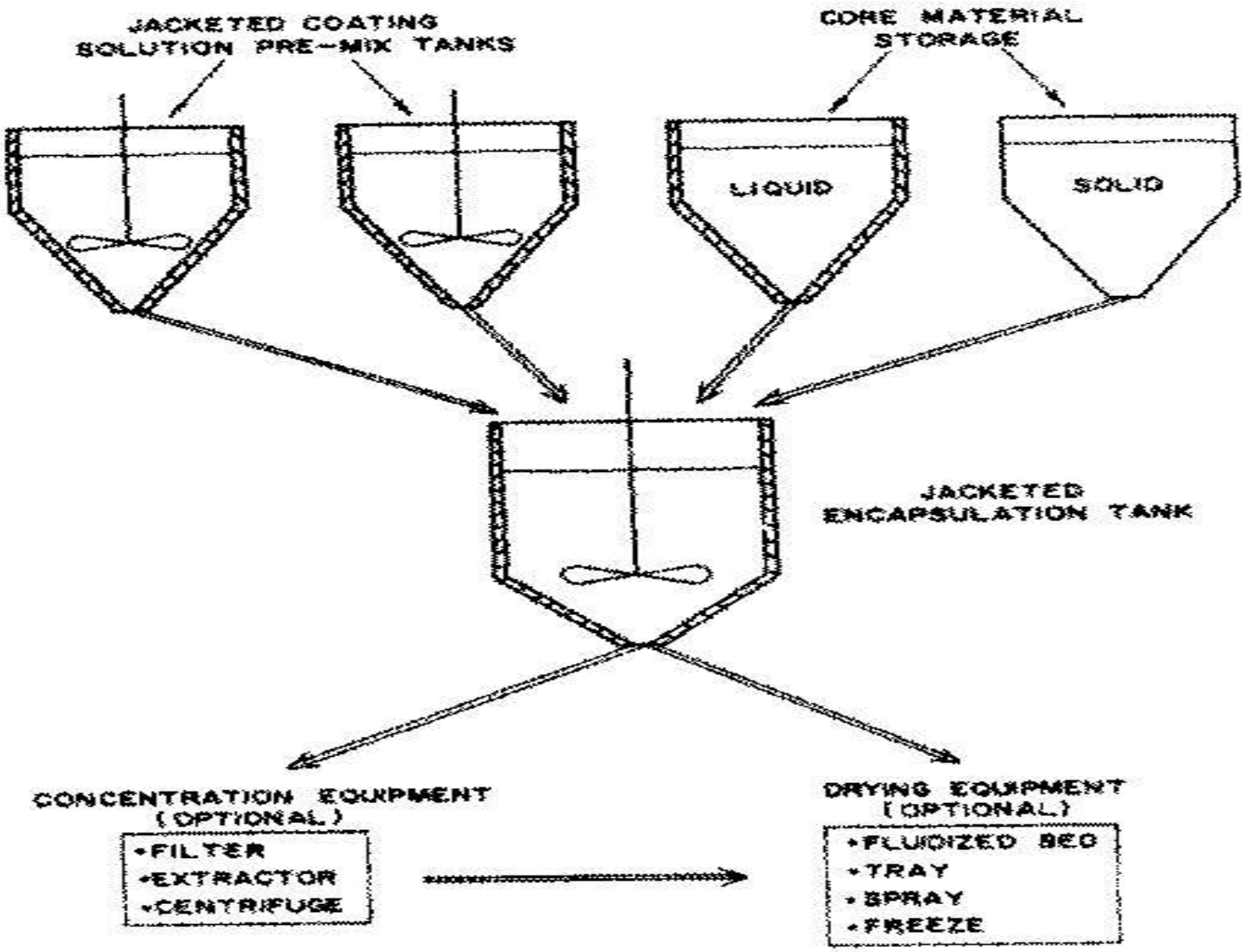



100 % $pe^{+}$

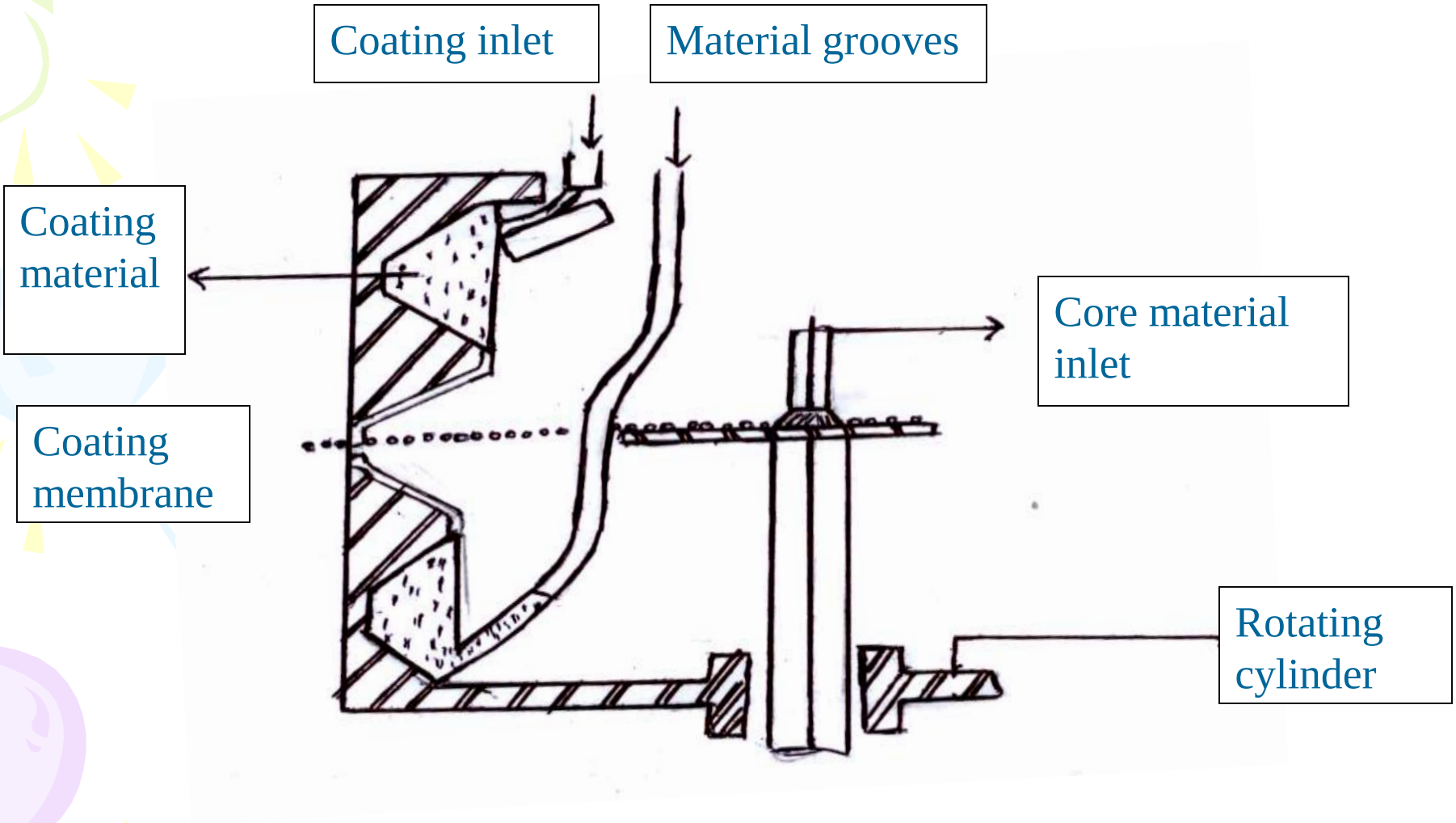
100 % $pe^{-}$

25 % of Methyl Salicylate is emulsified by interacting positively charged 2% Gelatin with negatively charged 2% Gum Arabic at 4.5pH while maintaining the temperature at 40 – 45 $^{0}$C. The microcapsules are rigidized by further stirring at 20-25$^{0}$C.

# Flow diagram of typical phase separation /coacervation process



## ➢ MULTIORIFIC-CENTRIFUGAL PROCESS:



## PAN COATING:

- 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 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 of the coating is effected.

- The principal difference between the two methods, 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 method 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 ten accomplished by sorption extraction or evaporation techniques.

- Microencapsulation by spray drying is conducted by dispersing a core material in a coating solution, in which the coating substance is dissolved and in which the core material is insoluble, and then by atomizing the mixture in to an air stream.

- Micro encapsulation by spray congealing can be accomplished with spray drying equipment, when the protective coating is applied as melt.

- Many solidification is accomplished by spraying the hot mixture in to a cool air stream.

- Waxes, fatty acids, alcohols, polymers & sugars which are solid at room temperature but meltable at reasonable temperatures, are applied to spray congealing techniques.

# SOLVENT EVAPORATION:

- The process involves dissolving microcapsule coating (polymer) in a volatile solvent which is immiscible with the liquid manufacturing vehicle phase. A core material (drug) 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 appropriate size microcapsules. Agitation of system is continued until the solvent partitions into the aqueous phase and is removed by evaporation.

- Factors that must be considered when preparing microcapsules by solvent evaporation techniques include choice of vehicle phase and solvent for the polymer coating, as these choice greatly influence microcapsule properties as well as the choice of solvent recovery techniques.

## POLYMERIZATION:

- The methods involve the reaction of monomeric units located at the interface existing between a core material substance and a continuous phase in which the core material is dispersed.

- Microcapsules having coatings of nylon formed by interfacial polymerization, or colloidan formed by phase separation/coacervation techniques.

## APPLICATIONS:

The applications of microencapsulation include:

- Sustained release or prolonged action medications.
- Taste masked chewable tablets, powders and suspensions.
- Single layer tablets containing chemically incompatible ingredients
- New formulations concepts for creams, ointments, aerosols, dressings, plasters, suppositories and injectables.

# Physicochemical evaluation characterization:

The physico chemical evaluation include:

- **Morphology Of Microspheres.**
- **Particle Size.**
- **Density Determination**
- **Capture Efficiency.**
- **Angle Of Contact.**

# In Vitro Methods :

## ❖ Beaker Method

- The dosage form in this method is made to adhere at the bottom of the beaker containing the medium and stirred uniformly using over head stirrer.
- Volume of the medium used in the literature for the studies varies from 50- 500 ml and the stirrer speed form 60-300 rpm.

## ❖ Dissolution Apparatus

- Standard USP or BP dissolution apparatus have been used to study *in vitro* release profiles using both rotating elements, paddle [20, 21, 22 and basket 23, 24].
- Dissolution medium used for the study varied from 100-500 ml and speed of rotation from 50-100 rpm.

# Thank you