Welcome

TO MY

PRESENTATION

BY

Ass.Prof. Dr. Mohamed Akl

Microencapsulation

Content

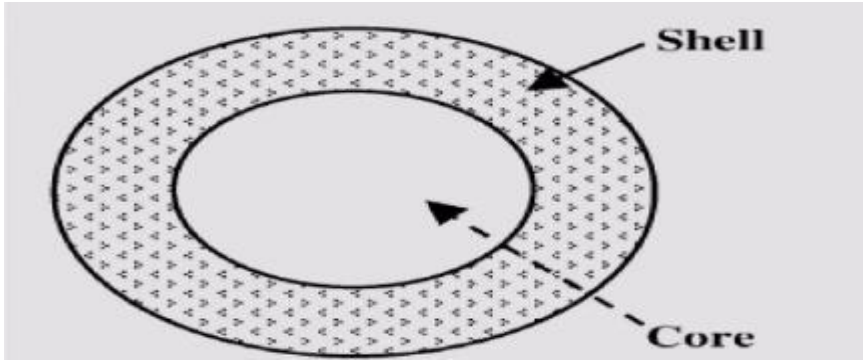
- Introduction
- Core and coating materials
- Reason for Encapsulation
- Techniques of Manufacturing Microcapsule
- Applications
- stability

Introduction

Microencapsulation

Definition: It is the process in which micro-particles of solid,, or liquid material is encapsulated by the application of thin coatings of film-forming material around them to produce capsule in micrometer range.

- Size of resulting product 0.5-2000 μm



Introduction

Fundamental Consideration

- Generally Micro particles consist of two components
  a. Core material.
  b. Coat or wall or shell material

- *Core* material (nucleus): The specific material to be coated. It can be solid (mixture of drugs, stabilizers, diluents, excipients) or liquid [may be dissolved (solution) or dispersed (suspension or emulsion)].

- *Coating* material: It is inert film-forming material coats on core with desired thickness.

Fundamental Consideration

Composition of coating:

- Inert polymer : such-as gelatin and synthetic polymers.
- Other additives may or may not be included e.g Plasticizer. Coloring agent, Release rate enhancers or retardants

The coating material should be:

- Capable of forming a cohesive film on the core material.
- Chemically and physically stable.
- Compatible, non-reactive with the encapsulated material.
- With a desired coating parameters as flexibility, strength, stability and impermeability.

Commonly used coating materials include:

1. Water soluble resins: Gelatin, gum, PVP, MC.
2. Water insoluble resins: EC, cellulose nitrate, silicon, polyethylene, polypropylene, and nylon.
3. Waxes: Paraffin, carnauba wax and spermaceti.
4. Fatty acids: Stearic, palmetic, myristic and lauric acids
5. Fatty alcohols: Stearyl, meristyl and lauryl alcohols.
6. Esters of fatty acids and fatty alcohols: Glyceryl stearate.
7. Enteric- resins: Shellac, zein, CAP, cellulose acetate butyrate.

Aims (reasons) of microencapsulation:

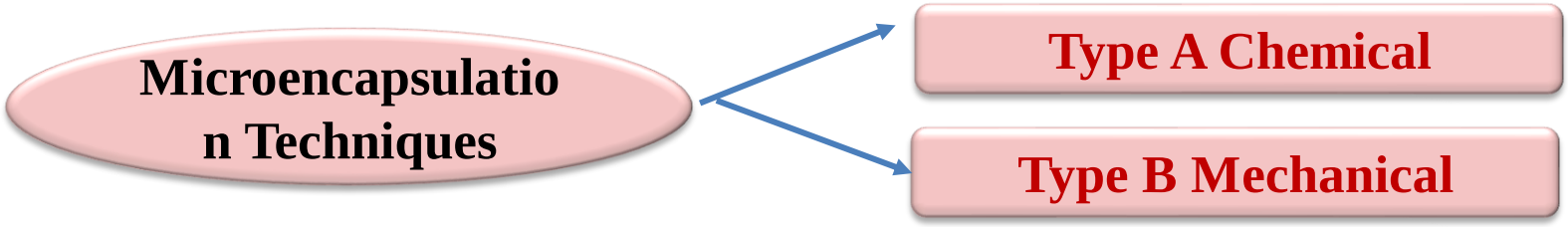
1. To separate reactive or incompatible materials within a tablet or powder mixture, as in case of acetyl salicylic acid (antipyretic) and chlorpheniramine maleate (antihistaminic) .
2. To control and/or prolong the release of the encapsulated drug e.g. applying EC films to microscopic crystals of aspirin.
3. To stabilize the encapsulated materials, as in isolating vitamins from the deteriorating effects of oxygen.

- such as microencapsulation of vitamin A with palmitate oil to retard its degradation.

4. To aid in handling or storage.
5. To improve compressibility.
6. To mask the undesirable taste or odor of the core.

Microencapsulation techniques

Two types of techniques are adopted.



- Capsules produced by type A, or chemical processes, are formed entirely in a liquid-filled stirred tank or tubular reactor.
- Capsules produced by type B, or mechanical processes, utilize a gas phase at some stage of the encapsulation process.

Techniques to Manufacture Microcapsules

The technique of microencapsulation depends on

- The physical and chemical properties of the material to be encapsulated.
- The stability and the biological activity of the drug should not be affected
- Yield and drug encapsulation efficiency should be high.
- Microsphere quality and drug release profile should be reproducible within specified limits.
- Microsphere should not exhibit aggregation or adherence.
- Process should be usable at an industrial scale
- The residual level of organic solvents should be lower than the limit value.

1. Complex coacervation:

- The technique which deals with the system containing more than one colloidal solute.
- It is based on the ability of cationic and anionic water-soluble polymers to interact in water to form a liquid, polymer rich phase called a complex coacervate.
- Four steps carried out under continuous agitation:
  1. Preparation of the dispersion of core material into homogenous coating polymer solution.
  2. Formation of three immiscible chemical phases (i.e. polymer rich phase, solvent phase and dispersed phase)
  3. Deposition of the coating polymer on the core material.
  4. hardening of the coating

1. Complex coacervation:

1st step: Preparation of the dispersion of the core material in an aqueous gelatin (coating polymer) solution. →This is normally done at 40-60 C, a temperature range at which the gelatin solution is melted and liquid.

2nd step: co-acervation of the polymer molecule.

- After a polyanion or -ve charged polymer like gum arabic is added to the system, the pH and concentration of polymer are adjusted between 4.0 and 4.5.

3rd step: Once the liquid coacervate forms the system is cooled to room temperature. The gelatin in the coacervate gels, thereby forming capsules with a very rubbery shell.

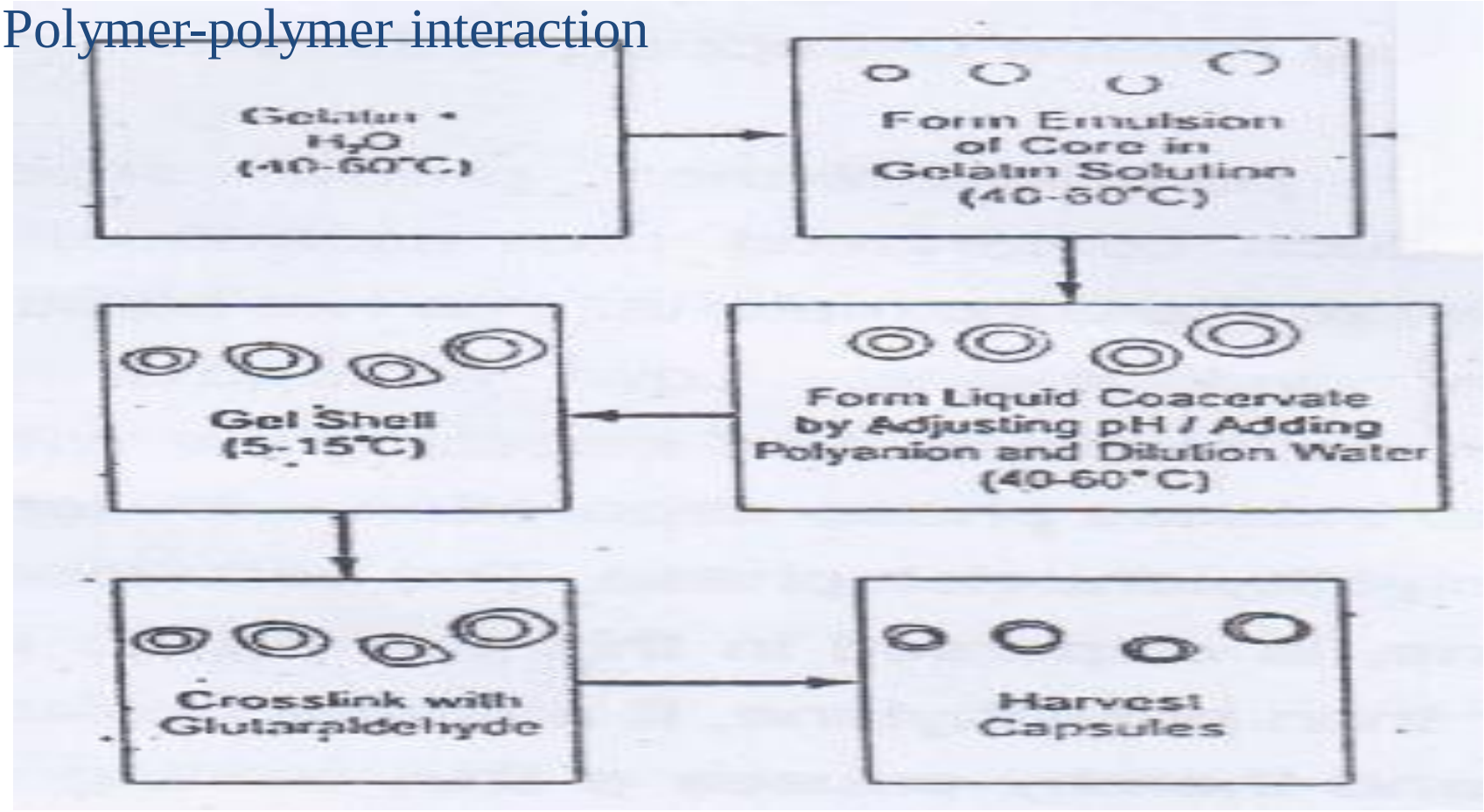
1. Complex coacervation:

- In order to increase the strength of the water-swollen shell and create a gel structure that is not thermally reversible, → the capsules normally are further cooled to approximately 10 C and treated with glutaraldehyde which crosslinks the gelatin by reacting with amino groups located on the gelatin chain.

4th step: Glutaraldehyde-treated capsules can be dried to a free-flowing powder or coated on a substrate and dried,

Method of achieving co-acervation (coating material phase formed by utilizing following methods:)

1. Change in temperature
2. Addition of in compatible polymer
3. Addition of non-solvent
4. Polymer-polymer interaction



2- Polymer-Polymer Incompatibility:

- The process generally does not involve any chemical reaction.
- This technique utilizes a polymer-phase separation phenomenon quite different from complex coacervation.

→In complex coacervation 2-oppositely charged polymers, gelatin + a polyanion, join together→ to form the complex coacervate and both polymers become part of the final capsule shell.

→In contrast, polymer-polymer incompatibility occurs because 2-chemically different polymers dissolved in a common solvent are incompatible and do not mix in solution. →They essentially repel each other and form 2-distinct liquid phases.

- One phase is rich in polymer designed to act as the capsule shell.
- The other is rich in the second, incompatible polymer.

2- Polymer-Polymer Incompatibility:

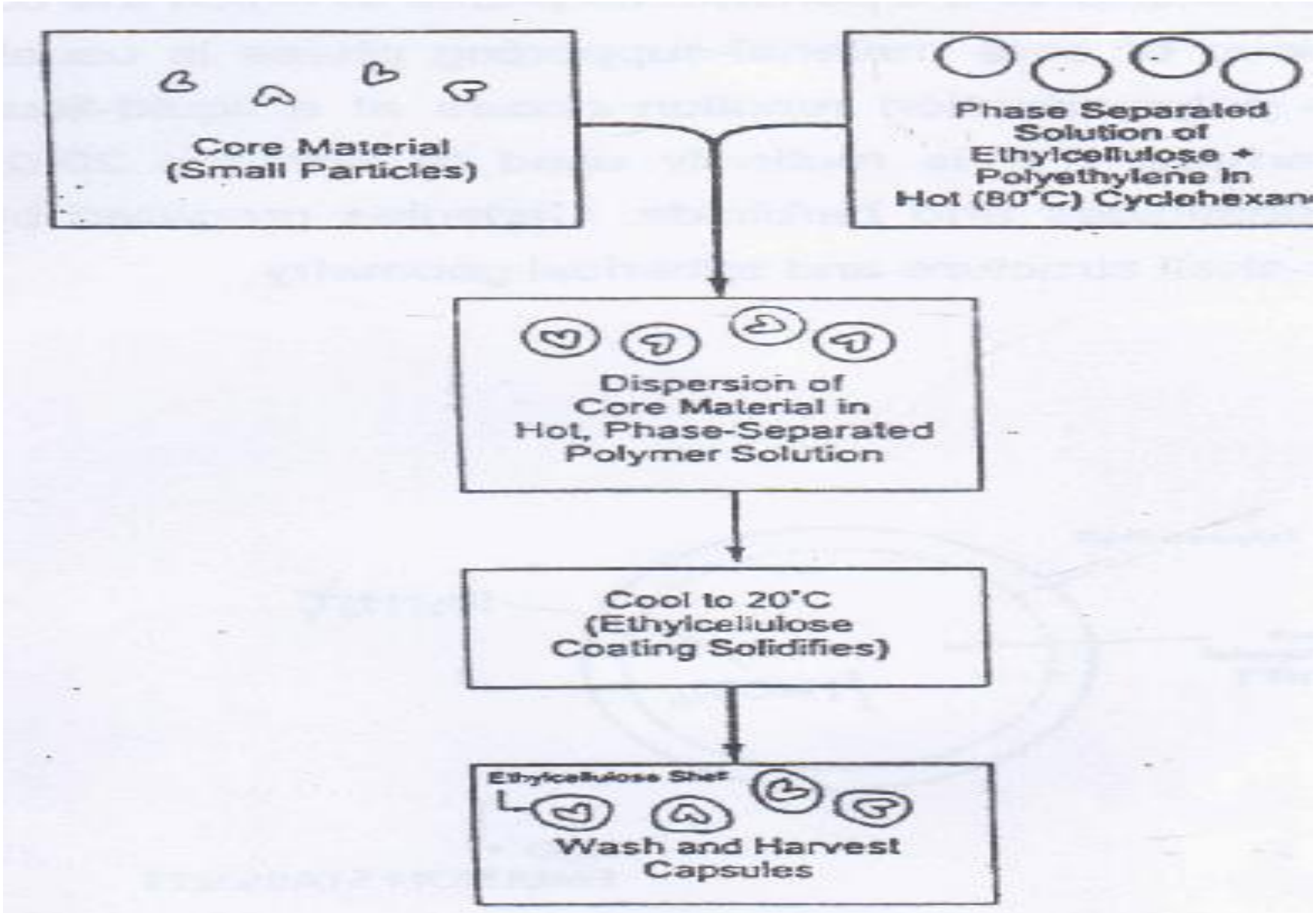
- 1st step is to disperse the core material in a hot solution (80 °C) of ethyl cellulose (coater) in cyclohexane.
- 2nd step→ low molecular weight polyethylene, a polymer soluble in hot cyclohexane and incompatible with EC, is added to the system. → This induces phase separation with formation of an EC-rich phase and polyethylene-rich phase.
- 3rd step: the core material, a solid unaffected by 80 °C cyclohexane, is dispersed in this two-phase system. → Since the EC is more polar than polyethylene, → it adsorbs preferentially on the surface of the core material and thereby causes a thin coating of shell material solution to engulf the particles of core material.

2- Polymer-Polymer Incompatibility:

- **4th Step:** cooling the system to room temperature→ the EC precipitates, → thereby solidifying the EC solution → forming solid microcapsules → collected.

❑ Aspirin and potassium chloride are examples of commercial encapsulated pharmaceutical products prepared in this technique.

2- Polymer-Polymer Incompatibility:



3- Centrifugal Force and Two-Fluid Submerged Noufe Processes:

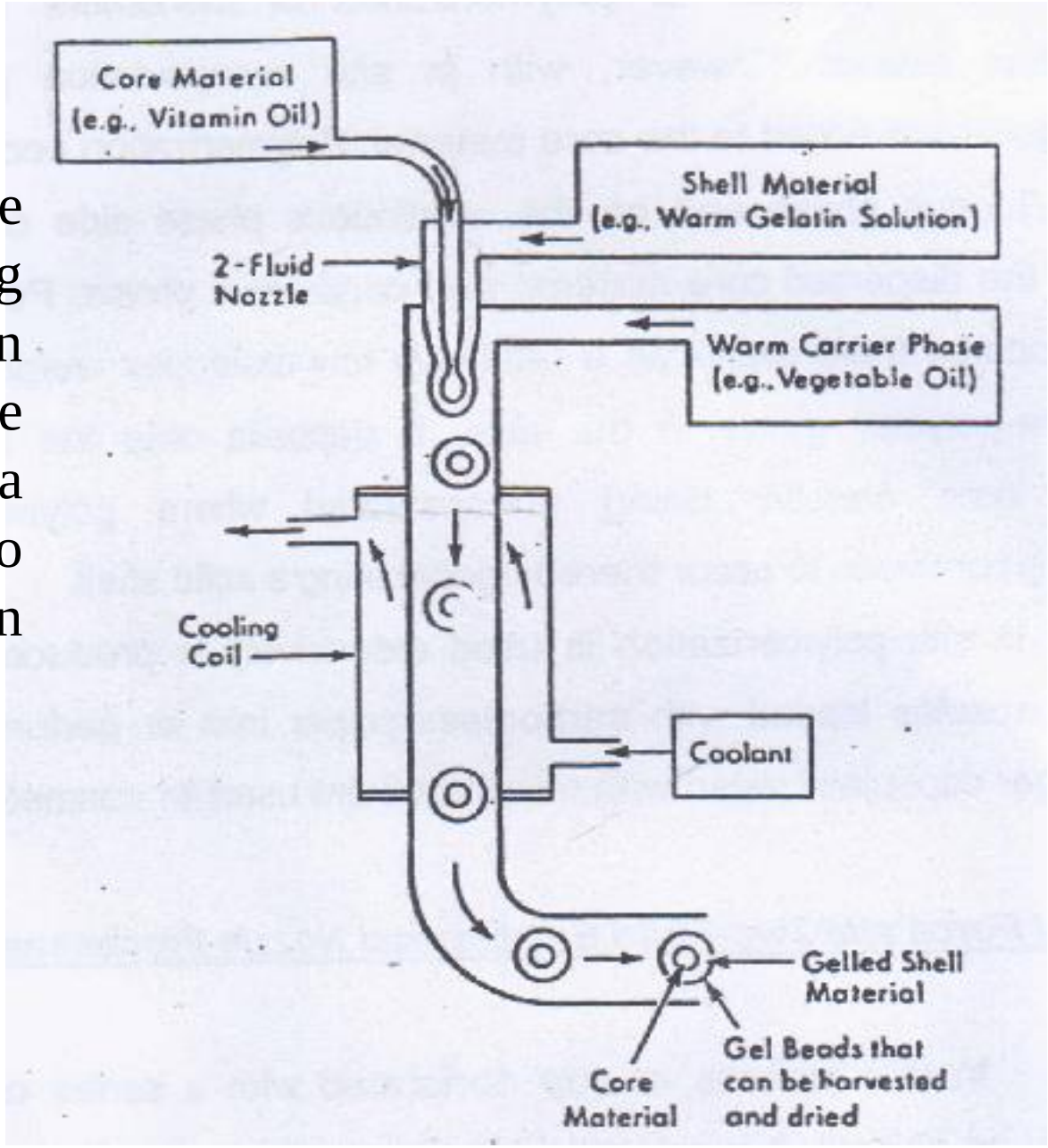
- In one process, a cup perforated with a series of fine holes is immersed in an oil bath. → It is rotated while immersed in the oil, → thereby extruding into the oil phase a stream of droplets of an oil-in-water emulsion.
- The water (outer) phase of this emulsion (O/W) is a concentrated solution of a water-soluble polymer (Gelatin is specific example) that gels on cooling.

→ By controlling the temperature of the oil bath, the external phase of the extruded emulsion droplets is gelled to create oil-loaded gel beadlets → isolated and dried.

- Isolated capsules consist of a number of small oil droplets dispersed throughout a matrix of shell material.

3- Centrifugal Force and Two-Fluid Submerged Noufe Processes:

- Capsules can also be produced by co-extruding an aqueous gelatin solution and an oil to be encapsulated through a two-fluid nozzle into moving fluid stream of an oil solution.



Type B (Mechanical) Techniques:

1. Air suspension technique.
2. Spray drying techniques.
3. Spray congealing technique.
4. Fluidized bed coaters.
5. Centrifugal extrusion.
6. Rotational Suspension Separation
7, Electrostatic deposition technique.
8. Multi-orifice centrifugal process.
9. Pan coating technique.
10. Emulsion-solvent evaporation technique.

Air suspension technique:

- Solid, particulate core materials are dispersed in a supporting air stream.
- The atomized coating solution is sprayed on the air suspended particles of the core material (suspended on upward moving air).
- The supporting air stream, which can be heated, → evaporates the volatile coating solvent, → thus depositing a thin film of coating on the suspended core material.
- Micron or submicron particles can be effectively encapsulated.
- Advantage: Various coating material can be used, Capacity is ↑
- Disadvantage- Applicable only to solid core,

Agglomeration of the particles to some larger size is normally achieved.

Factors controlling the efficiency of air suspension technique:

1. Factors related to the core materials such as: .

a-Density. b- Surface area c- Melting point. d- Solubility. e- Friability. f- Volatility. g- Crystallinity. h- Flowability.

2. Factors related to the coating material, such as:

a. Concentration or melting point (if not a solution).
b. Amount of coating material.

3. Factors related to the technique conditions, such as:

a. Application rate of coating material.
b. Volume of air used to support and fluidize the core material.
c. Inlet and outlet operating technique.

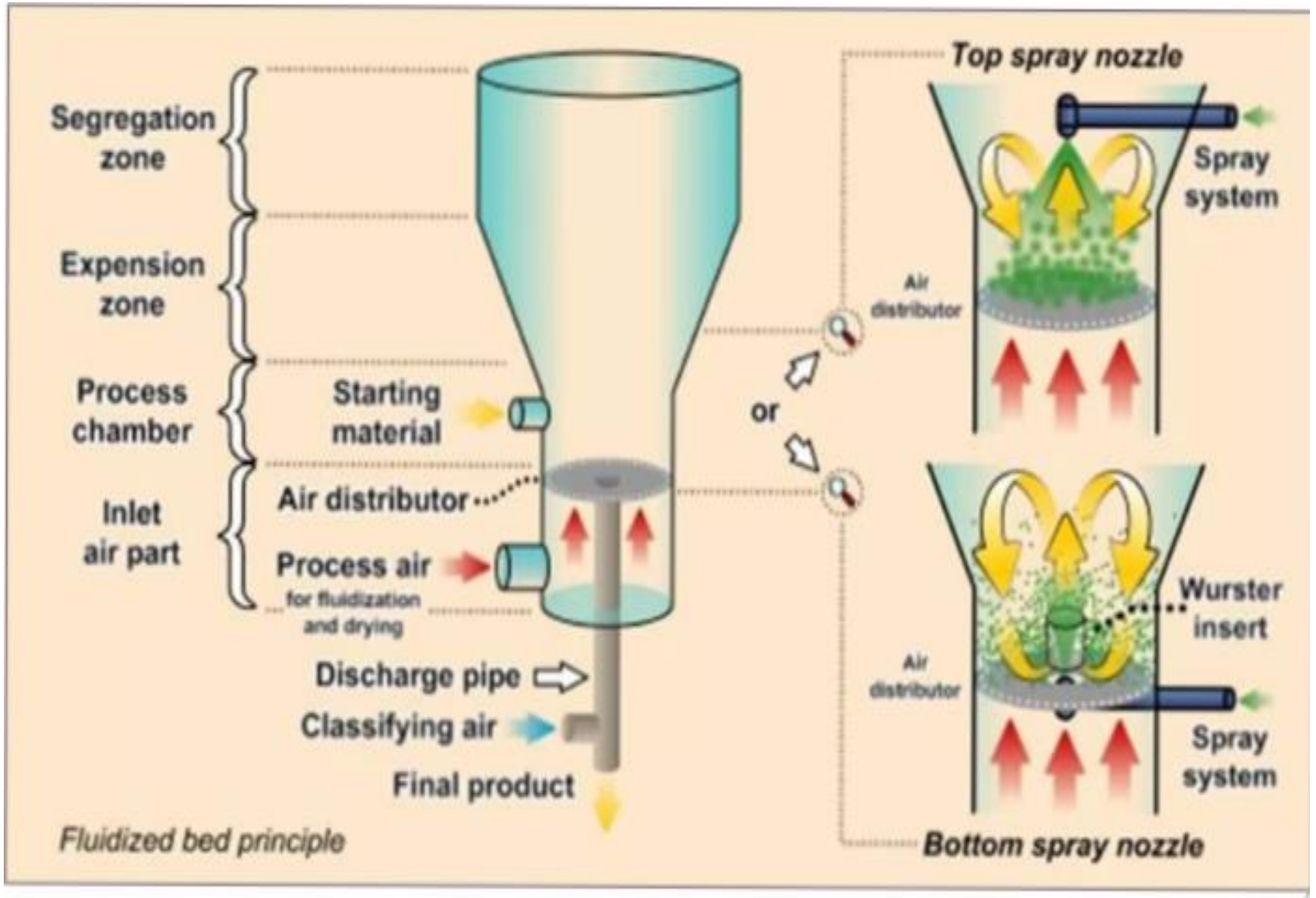


Fig. 4: Air Suspension Apparatus.

Fluidized Bed Coaters

- The fluidized bed coaters are limited to encapsulating solid particles or porous particles into which liquid has been absorbed.
- Fluidized bed coaters function by suspending a bed or column of solid particles in a moving gas stream, usually air.
- A liquid coating formulation is sprayed onto the individual particles, and freshly coated particles are cycled into a zone where the coating formulation is dried either by solvent evaporation or cooling.
- This coating and drying sequence is repeated until a desired coating thickness has been applied .

Fluidized Bed Coaters

Advantages of Fluidized Bed Coating Process:

1. The ability to handle an extremely wide range of coating formulations.
2. They can be used to apply hot melts, aqueous latex dispersions, organic solvent solutions of shell material, and aqueous solutions of shell material.
3. 3- Enteric polymer are insoluble in gastric fluid and soluble in intestinal fluid, so capsules or tablets coated with them can pass intact through the stomach and not disintegrate until reach the intestine.
4. Available in three different types: top spray, tangential spray and bottom spray. These units differ in location of the nozzle

Spray Drying and Spray Congealing

- The encapsulated substance is dispersed in a coating solution that dissolves the coating material but does not dissolve the core material.

Both method has the same principle. → The principal difference between the two methods, is the means by which coating solidification is accomplished

- **Spray Drying:** The coating solidification effected by rapid evaporating of solvent in which coating material is dissolved.
- **Spray Congealing:** The coating solidification is affected by thermally congealing a molten coating material. The removal of solvent is done by sorption, extraction or evaporation technique.

Spray drying techniques:

- The mixture of both materials is atomized into hot air-stream, where the solvent evaporates → shell material solidifies onto the core particles and the dried solid particles are collected.

- Examples for this technique include:

a. Spray drying mostly used for the encapsulation of fragrances, oils and flavours liquid to obtain free flowing powders.

- Gum arabic is usually used as coating material. The rapid rate of water evaporation minimized volatilization of flavor components.

b. Microencapsulation of sulphamethyl-thiadiazol with a solution of castor wax in chloroform.

Spray conqealinq (chilling) technique:

This method can be accomplished by:

- Dispersing the core material in a coat-material melt rather than solution.
- Spraying the hot mixture of core and coating materials into cold air-stream.
- Waxes, fatty acids and alcohols and polymers which are solid at room temperature but melt at reasonable temperature are usually used in this technique

– Example: the preparation of taste-masked vitamin beadiest microencapsulated with digestible waxes.

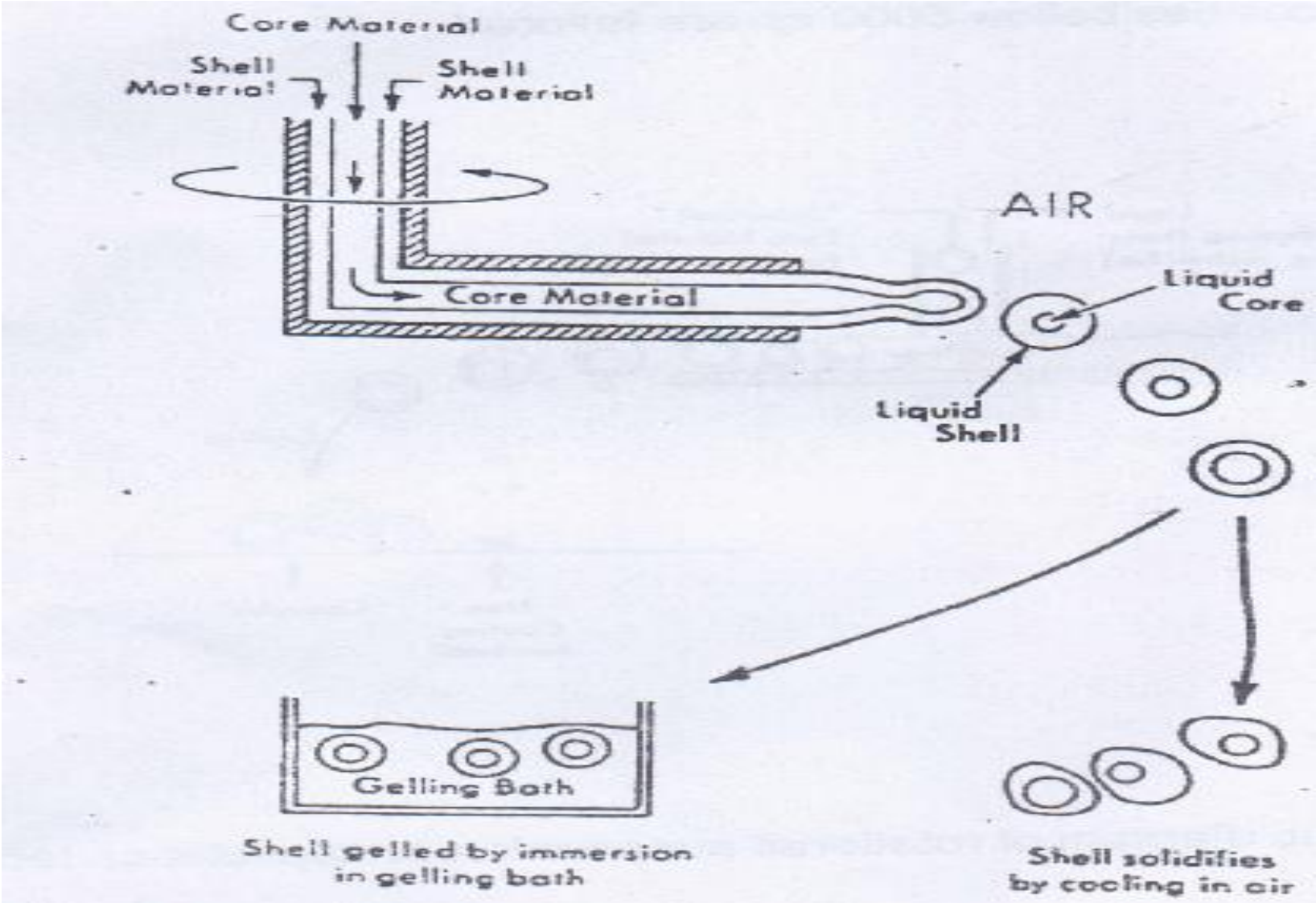
Centrifugal Extrusion

- A dual fluid stream of liquid core and shell materials (two mutually immiscible) is pumped through a rotating extrusion head containing two concentric nozzle and forms spherical droplets under the influence of vibration.
- Each droplet contains a continuous core region surrounded by a liquid shell.
- The shell is then hardened by chemical cross linkings, cooling, or solvent evaporation.
- This process is excellent for forming particles 400–2,000 μm in diameter.
- Since the drops are formed by the breakup of a liquid jet, → the process is only suitable for liquid or slurry.

Centrifugal Extrusion

- A high production rate can be achieved, i.e., up to 22.5 kg of microcapsules can be produced per nozzle per hour per head.
- Different types of extrusion nozzles have been developed in order to optimize the process.
- Heads containing 16 nozzles are available.

Centrifugal Extrusion



A schematic diagram of a centrifugal extrusion process

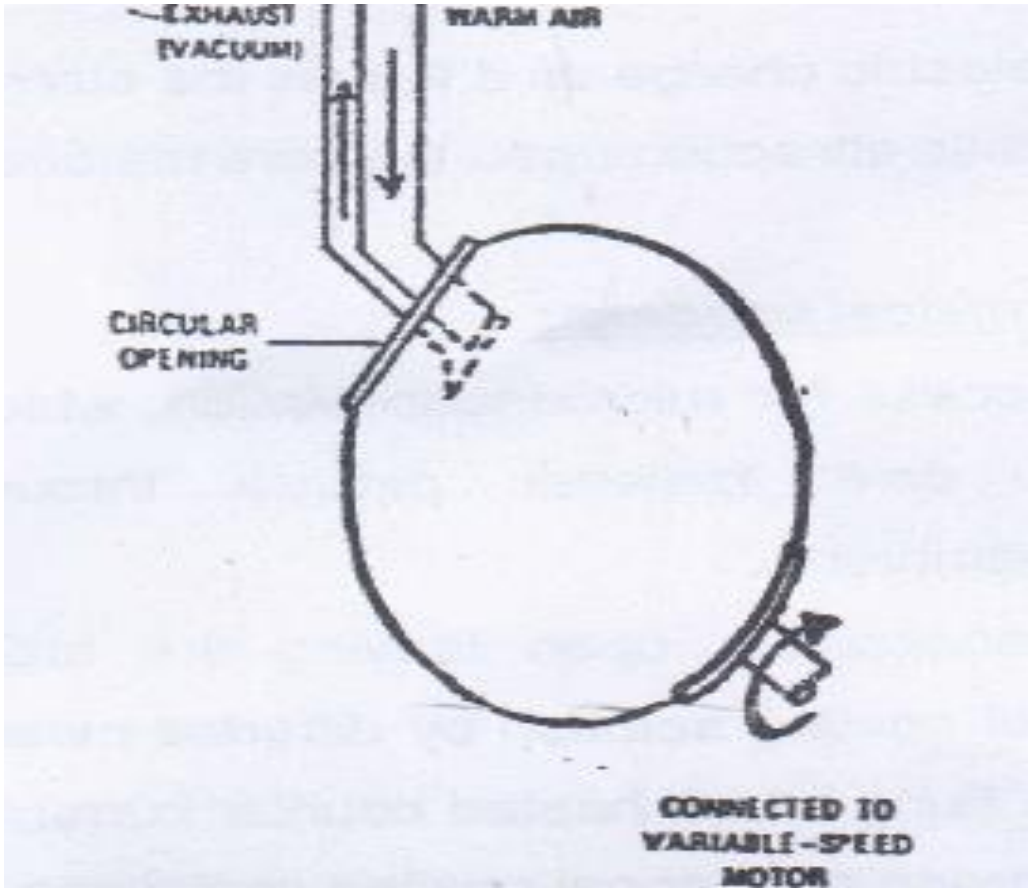
Pan coating:

- Oldest industrial procedures for forming small, coated particles or tablets.
- Suitable for relatively large particles solid particles greater than 600 microns in size are generally coated by pan coating.
- extensively employed for the preparation of controlled release beads
- Solution or atomized spray of the coating material is slowly applied to the solid core material of reasonable particle size (> 600 μm) in the coating pan.
- Hot air or dusting talc is applied to eliminate the solvent of the coating material in the coating pans. .

Pan coating:

- N.B. Core materials (Medicaments) are usually coated onto various spherical seeds such as sugar → and then coated with protective layer of different polymers e. g. preparing of sustained- release pellets in which sugar seeds are coated first with dextroamphetamine sulfate and then with a release-retardant wax-fat coating.

Advantages:	Disadvantages:
➢Suitable to larger particles.	➢Time consuming.
➢Sustained release preparations.	➢High material loss.



Applications of Microcapsules

- Agricultural Applications.
- Catalysis
- Food Industry.
- Pharmaceutical

Pharmaceutical Applications of Microcapsules

1. To reduce gastric and other GIT irritations. eg: Aspirin preparations.
2. Prolonged release dosage forms preparation.
3. Preparation of enteric-coated dosage forms .
4. Replacement of therapeutic agents (not taken orally like insulin), gene therapy and in use of vaccines for treating AIDS, tumors, cancer and diabetes.
5. Delivery of DNA vaccines.
6. Prodrug approach. eg: Minocycline HCl.
7. Biodegradable and biocompatible microparicles preparations. Example: Risperidone or testosterone.

Marketed Microcapsules

Marketed formulations prepared using microcapsules[5]

S.No	Brand Name	Generic Name	Category of drug
1.	Lupin	Cefadroxil	Antibiotic
2.	ZORprin CR	Aspirin	Anti-arthritic
3.	Glipizide SR	Glucotrol	Anti diabetic

References

1. http://www.authorstream.com/Presentation/vivekchauhan-1147305-microencapsulation.
2. Hammad umer et.al," International Journal of Research in Pharmaceutical and Biomedical Sciences" ISSN: 2229- 3701.
3. S. S. Bansode et.al," Institute of Pharmaceutical Education And Research", Volume 1, Issue 2, March –April 2010; Article 008 .
4. Lachman LA, Liberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. Mumbai, India: Varghese Publishing House; 3:414-415.
5. http://www.authorstream.com/Presentation/thokesagar-1295371-shree/


THANK
YOU