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AN OVERVIEW ON MICROENCAPSULATION TECHNIQUES

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1. INTRODUCTION

Microencapsulation is described as a process of enclosing micro sized particles of solid or droplet of liquid or gases in inert shell, which tern isolated and protect from the external environment (Jyothi and Prasanna, 2010).

Microencapsulation is a process by which very tiny droplets or particles of liquid, solid or even gas material is surrounded or coated with a continuous film of polymeric material.

It includes Bioencapsulation which is more restricted to the entrapment of a biologically active substance (from DNA to entire cell or group of cells) generally to improve its performance or enhance its shelf life. In such one of the in using microsphere as carrier for drugs. microsphere containing protein and synthetic polymers and they are biodegradable from and it's ideally having is less 200 am. Microencapsulation process widely employed to modify and delayed drug resale from the different pharmaceutical dosage from in various route administration.

In enclosed material in the Microcapsules referred to as the core, internal Phase, or film, whereas the wall is sometimes called a shell coating. Some materials like lipids and polymers, in such as alginates, may be used in used as mixture to trap material of interest inside. Most Microcapsules have pore with diameter in between few nanometers and few micrometers.

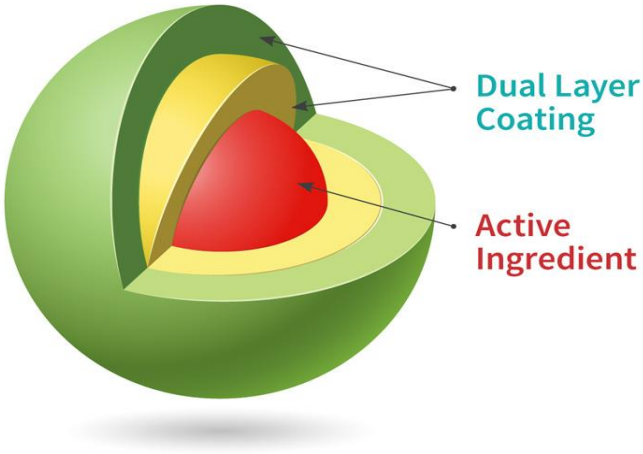


Figure: 1 microencapsulation

The products obtained by the process are called micro particles, microcapsule, microspheres and internal structure of the small particle. Microencapsulation is a technique in which chemicals are released in a controlled manner over a long period. In this process small particles or droplets are confined in a coating to give small capsules or microcapsules. The materials inside the capsules form the core and the outside coating becomes a barrier wall. Hence the core material is isolated from hostile outside environment and can be released either slowly by diffusion through the wall or by rupture of the wall on demand. The microcapsules can then be attached to textiles, conferring various properties to them (Batool, 2008).

The goal of any drug-delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly, and then maintain, the desired drug concentration and deliver the drug at a rate dictated by the needs of the body over an entire period of treatment. (Manzana, *et al.*,2010).

This is a treatment. (The lively aspect of an end has excessive vapor strain or while it wishes to be activated most effective on precise occasions. The pleasant instance of an easy software of microencapsulation is carbonless replica paper. This paper has a skinny coating of microcapsules at the again side. The microcapsules incorporate an ink the again the again. When something is written at the paper, the strain of writing releases the ink from the layer of microcapsules and a replica of the unique writing is created on a sheet stored beneath Neath carbonless replica paper. (Cachinn*ate al.*, 2010).

The coating generally used as coating polymer are given below,

- Ethyl cellulose
- Gelatin
- Polyvinyl alcohol
- Sodium alginate

Many microcapsules however bear little resemblance to these simple spheres. The core may be a crystal, a jagged adsorbent particle, an emulsion, a Pickering emulsion, a suspension of solids, or a suspension of smaller is Microcapsules the Microcapsules even may have multiple walls. The material is enclosed and envelope within the microcapsule are known as the core material or pay loaded material or nucleus and enclosing materials are known as coating material or wall material or shell (member).

There are type depends on size and shape as below: -

1) Microparticles –
2) Microspheres -
3) Microcapsules: - "Microcapsules, refers to microparticles having a core surrounded by the coat or wall of the materials distinctly different from the core or pay load or nucleus and Which may solid, liquid or even gas.

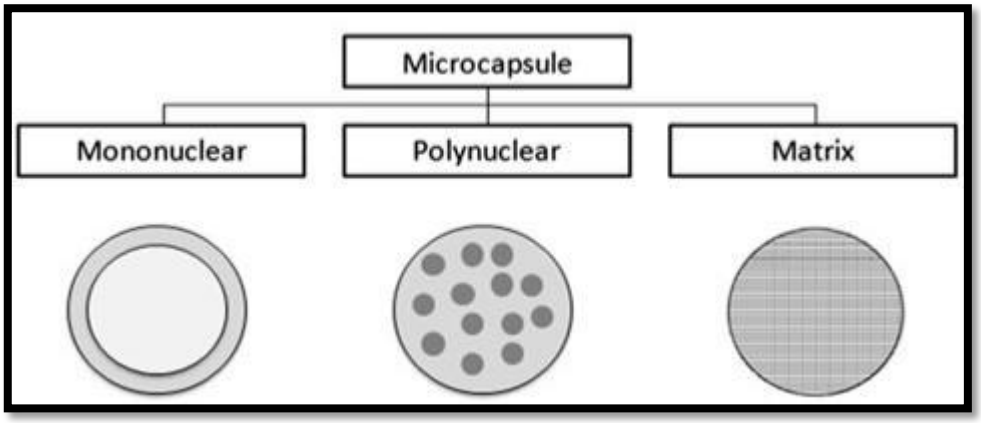


Figure 2 - Classification of microcapsules.

Microcapsules can be classified on three types

1) Mononuclear: - containing the shell around the core.
2) Polynuclear: - Having many cores enclosed with in shell.
3) Matrix type: - Distributed homogeneous into the shell material.

Advantages:

1) Microcapsules received much attention not only for controlled release but also for targeting of anticancer drugs to the tumor.
2) Improve patient compliance.
3) Microencapsulation could deliver the needed ingredients in children in terms of a tasty way by taste masking.
4) Protection from u's, heat, oxidation, acids, or bases.
5) Improve shelf-life property due to preventing derivative reactions like dehydration or oxidation.
6) Increased effectiveness.
7) To decrease the evaporation rate of core material.

8) Converted to the liquid to solid state

9) To increase the bio availability

Disadvantages:

1) Polymer may produce toxic effects

2) More production cost.

3) Difficult to achieve continuous and uniform phases.

4) Possible the cross reaction between core material and she'll material.

5) More skill and knowledge person required.

Core material:

The core material, defined as the specific material to be coated, can be liquid or solid in nature. the composition of the core material can be varied, as liquid core can include dispersed or dissolved material. The solid core be active required. Diluents, excipients and release rate retardants. The ability to vary the core material composition provides definite flexibility and utilization of these characteristics often allows effectual design and development of desired Microcapsule's properties

Composition of core material:

- Drug or active constituent
- Additives like diluents
- Stabilizer.

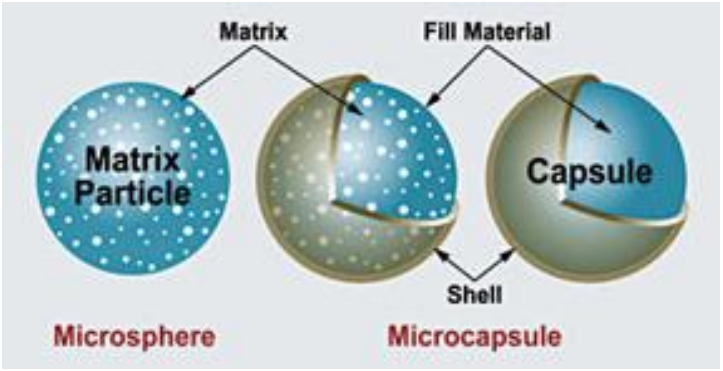


Fig 3: Microsphere and microcapsule

Coating material: The selection of appropriate coating material decides the physical and chemical properties of the resultant microcapsules/ microsphere. while selecting a polymer the product requirements. I.e., stabilization, reduced volatility, release characteristics, environmental condition, etc. it should be taken into consideration. The polymer should be capable of forming a film that cohesive Sisowath the core material. It should be chemically compatible, non-reactive with core material and provide the desired coating properties such bas strength, flexibility, impermeability, stability and optical properties (Mishra, and Goda.2012)

The coating material should be capable of forming a film that is cohesive with the core material; be chemically compatible and nonreactive with the core material; and provide the desired coating properties, such as strength, flexibility, impermeability, optical properties, and stability. The coating materials used in microencapsulation methods are amenable, to some extent, to in situ modification. (Bans ode, and Banerjee. 2010).

Composition of coating material:

- Inert polymer
- Plasticizer
- Coloring agent
- Resins, waxes and lipid.
- Release rate Enhancer or retardants**.**

The selection of a given coating often can be aided by the review of existing literature and by the study of free or cast films, although practical use of free-film information often is impeded for the following reasons:

1. Cast or free films prepared by the usual casting techniques yield films that are considerably thicker than those produced by the microencapsulation of small particles; hence, the results obtained from the cast films may not be extrapolate to the thin microcapsule coatings.
2. The particular microencapsulation method employed for the deposition of a given coating produces specific and inherent properties that are difficult to simulate with existing film-casting methods.

Example of coating material is:

A) Synthetic polymer

B) Natural polymer

A) Synthetic polymer:

(a) Non-biodegradable polymers e.g., Poly methyl methacrylate (PMMA), Acrolein, Glycidyl methacrylate Epoxy polymers

(b) Biodegradable polymers e.g., Lactides, Glycoside's& their co polymers Cyanoacrylates Polyanhydrides. . (Mishra and Jain, 2013)

B) Natural polymers: -

(a) Proteins: albumin, gelatin and collagen

(b) Carbohydrates: -agarose, carrageenan, chitosan, starch

(c) Chemically modified carbohydrates: poly dextran, poly starch. (Mishra and Jain ,2013)

Coating Material Propertie:

- Stabilization of core material.
- Inert toward active ingredients.
- Controlled release under specific conditions.
- Film-forming, pliable, tasteless, stable.
- Non-hygroscopic, no high viscosity, economical.
- Soluble in an aqueous media or solvent, or melting.
- The coating can be flexible, brittle, hard, thin. (Bandanaed Banarjee,2010)

2. HISTORY OF MICROENCAPSULATION TECHNIQUES

The process had its origin in the late 1930 s as a cleaner substitute for carbon paper and carbon ribbons as sought by the business machines industry. The ultimate development in the 1950s of reproduction paper and ribbons that contained dyes in tiny gelatin capsules released on impact by a typewriter key or the pressure of a pen or pencil was the stimulus for the development of a host of microencapsulated materials, including drugs or API (Active pharmaceutical ingredients) .In addition of encapsulation process of highly water soluble drug received much attention .These symptom readerly on polymers that vary with impermeability, dissolution rate of swell\ng .It include Bioencapsulation technique which can be enhance the performance of shelf life of that drug .(Singh. *et al*.,2016) .

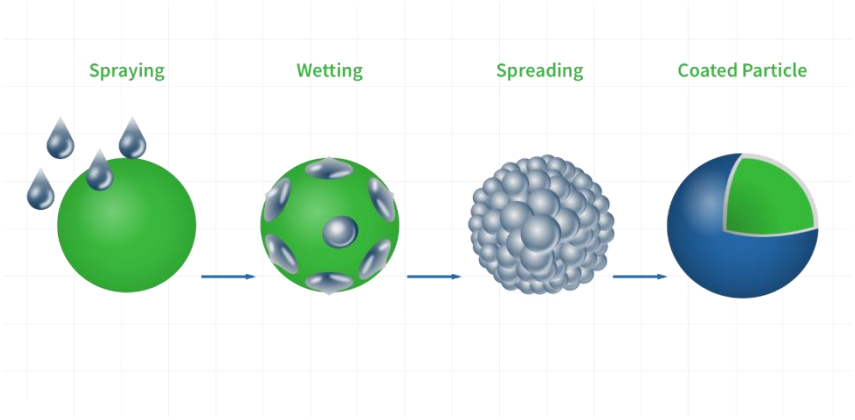


Fig 4. Basic mechanism of microencapsulation process

A well-designed controlled drugs delivery systems system can be overcome some of the problems of conventional therapy and enhance the all-over therapeutic efficacy of the given drug. And to obtain maximum therapeutic efficacy , and it becomes necessary to deliver that agent to the targeted tissue in the optimal amounts of in right period of time there by causing little toxicity and minimal side effects .There are various approaches in delivering a therapeutic substance to the target site in a sustain controlled drug delivery fashion .inside a micrometric wall made of hard or soft soluble film , in order to reduce dosing frequency and prevent the degradation of pharmaceutical drug .(Singh .M.N.*et al.*, 2010)

There are many reasons towards microencapsulation. In some cases, the core must be isolated from its surroundings, as in isolating vitamins from the deteriorating effects of oxygen, retarding evaporation of a volatile core, improving the handling properties of a sticky material or isolating a reactive core from chemical attack. There are several reasons why substances may be encapsulated. ? (Agnihotri. N. *et al.*, 2012).

1) The primary reason for the microencapsulation is found to be either for produce sustained or prolong drug release.

2) Microencapsulation techniques has been widely used for masking taste and odor of many drug the patient compliance.

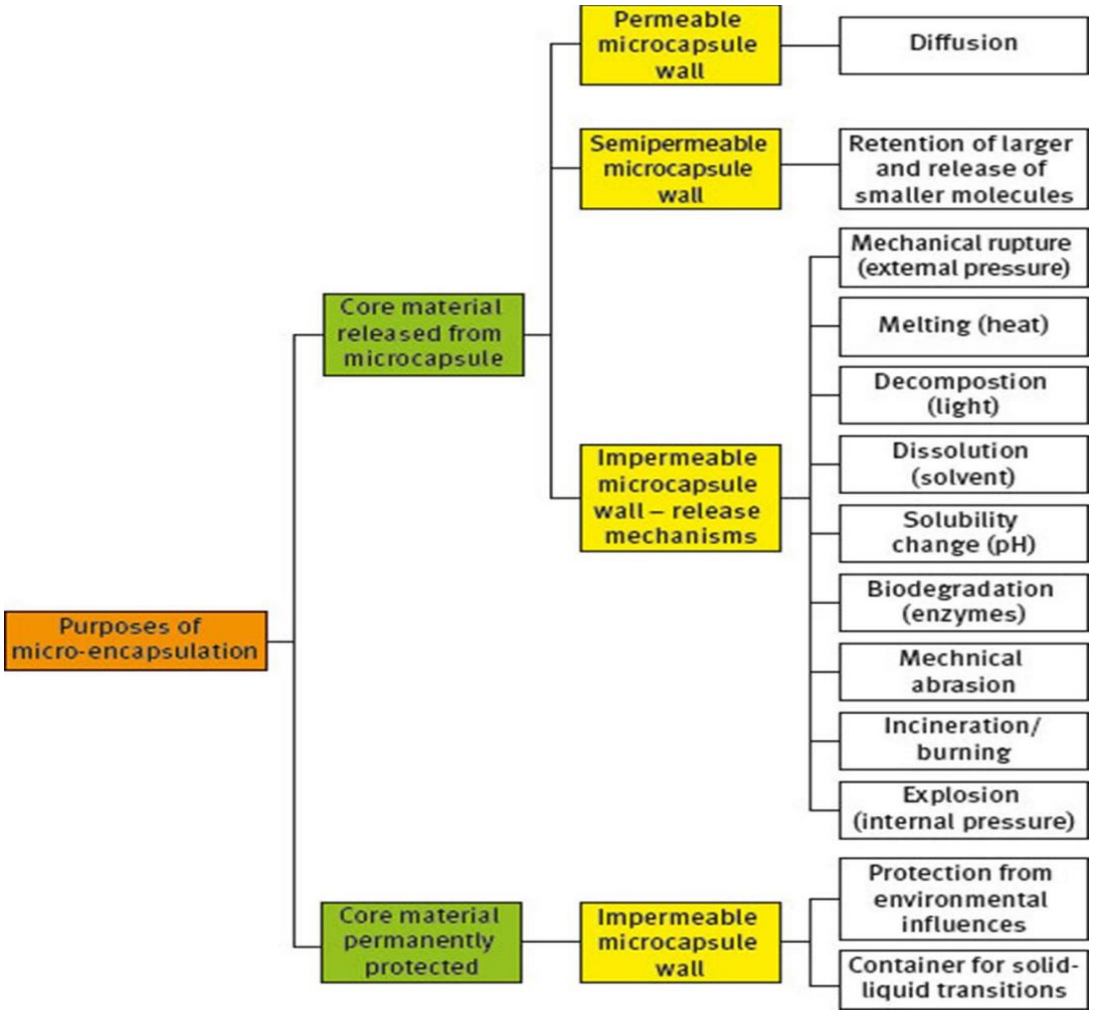
3) This technique can be used for converting liquid drugs in a free-flowing powder.

4) Incomparability among the drug can be prevented microencapsulation process.

5) In general vaporization of many volatile drugs, Ex – methyl salicylate and peppermint oil can be prevented by microencapsulation techniques.

6) The drugs, which are sensitive to oxygen, moisture or light sensitive can be stabilized by microencapsulation.

7) Balkan and Anderson reported that microencapsulated Vitamin A had enhanced stability



Flowchart 1: - Purpose of Microencapsulation

3. TYPES OF DRUG RELEASE MECHANISM

Release mechanism is depended when the aim of microencapsulation application is the isolation of the core from it surrounding the wall must be raptured at the time of use be raptured at the time of use.

A variety of of release mechanism have been proposed for microencapsulation.

i) By chemical reaction

ii) By enzymes attack

iii) By pressure and shear streets

iv) By Hydrolysis

v) By dissolving under particular condition, as an in this case of enteric drug coating

A) Diffusion control system

The rate limiting step is diffusion of drug through Inert water insoluble membrane barrier. These are there two types: -

a) Water penetration control system:

Rate controlling step is penetration of water into the system. It is of two types

1. Swelling control system:

These types of systems are initially dry and when placed in body, absorb Water. Other fluids and it swells. Swelling Increases aqueous solvent content within t Formulation as well as the polymer mesh size**.**

2. Osmotically control system*:*

In this type of system core i.e., osmotically active drug or combination of osmotically inactive drug + osmogene is enclosed within semi permeable membrane made up of biocompatible polymer like cellulose acetate.

B) Dissolution control system: -

In this system the rate controlling step is Dissolution. The drug is embedded in slow Dissolving or erodible matrix or by coating with Slow dissolving substances. It is of two types Encapsulation: The drug particle is coated or encapsulated by micro encapsulation techniques. With slow dissolving materials like cellulose The Dissolution rate depends upon the solubility and Thickness of coating.

Matrix: It is also called as "MONOLITHS". They Employ waxes such as bees wax, hydrogenated Castor oil which control drug dissolution by Controlling rate of dissolution fluid penetration into

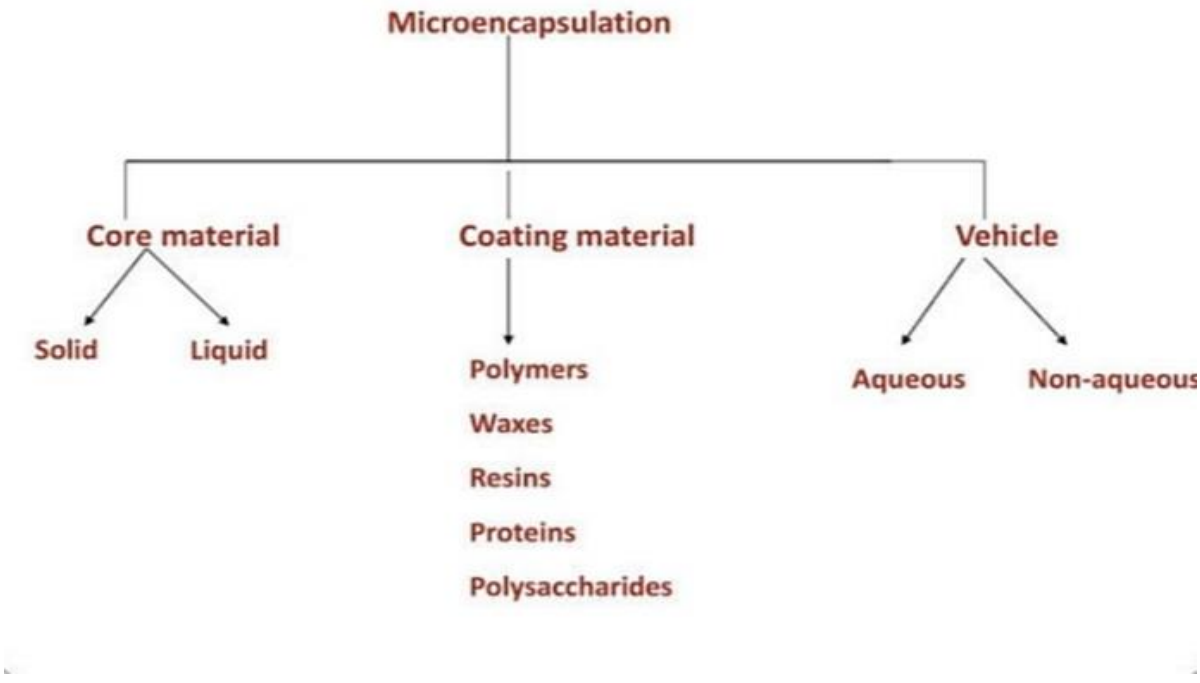
C) Chemically control system:

In this type the polymer is degraded as a result of Hydrolysis into biologically safe and smaller Moieties. It is of two types.

a) Erodible system: Pendent: It consists of linear or homo copolymers attached to the drug. The drug is release from polymer by hydrolysis or enzymatic degradation of the linkages.

b) Hydrogels: Composed of primarily hydrophilic polymers. They are rendered insoluble because of physical or chemical cross links. The physical cross links include crystallites, entanglements, weak association like hydrogen bonds. It provides desirable protection to liable drugs protection and peptides.

Fundamental's consideration:



Flowchart 3: - Fundamental consideration of microencapsulation

4. CHARACTERISTICS OF MICROCAPSULES

1. **Particle size and shape -** The mostly commonly used method to visualize Microcapsules is conventional light microscopy, scanning electron microscopy (SEM). The technique is used to analyze the particle size and shape or structure of Microcapsules.

   In Scanning electron microscopy (SEM) provide a high resolution as compared to the with light microscopy. (Stonehand Prasad. ,2016).

2. **Fourier transforms infrared spectroscopy (FTIR): -** It is used to determine to analyze the degradation of Polymeric matrix of carrier system and also check interaction between polymer and drug system.

3. **Car's index and Hauser's Ratio: -** The angle of repose was determined according to the fixed funnel and cone method. The bulk density of mixed microcapsule Was calculated by determining by Hauser ratio. With the help of poured or tapped bulk densities of known weight of samples using measuring cylinder (Hauser 1967, Car's. 1965).

$$Carrs\ Index = \frac{Tapped\ Density - Bulk\ Density}{Tapped\ Density} X\ 100 \ldots\ldots\ldots\ldots (1)$$

4. **Bulk density: -** Weight accurate microcapsule and then transfer to 100 ml cylinder to obtain apparent volume of between 50 and 100 ml.

$$Bulk\ Density = [\ \frac{Weight\ Of\ Microencapsules\ in\ gm}{Bulk\ Volume\ in\ ml}\ ] \ldots\ldots\ldots\ldots (2)$$

5. **Isoelectric point: -** The micro electrophoresis is an apparatus which is used to measure electrophoresis mobility of Microcapsules by which Isoelectric point can easily be calculated. The mobility is related with surface contained charge, ionizable behavior or ion Behavior or ion absorption nature of Microcapsules. (Singh and Due, 2016)

6. **Contact angle: -** The angle of contact is calculated to determine the wetting property of Microcapsules. with the help of this method, we can easily know about the nature of Microcapsules in terms of hydrophilicity and hydrophobicity. This is measured at solid/air /water surface by placing in a droplet in cell mounted above the objective of inverted microscope. It is measured at 200 c measured of decomposition of Microcapsules (Singh and Due ,2016)

5. MICROENCAPSULATION TECHNIQUES

The selection of microencapsulation method and coating materials are interdependent. Based on the coating material or method applied, the appropriate method or coating materials selected. Coating materials, which are basically film-forming materials, can be selected from a wide variety of natural or synthetic polymers, depending on the material to be coated and characteristics desired in the final microcapsules.

- **Techniques to manufacture microcapsules (Agnihotri. *et al.*, 2012)**

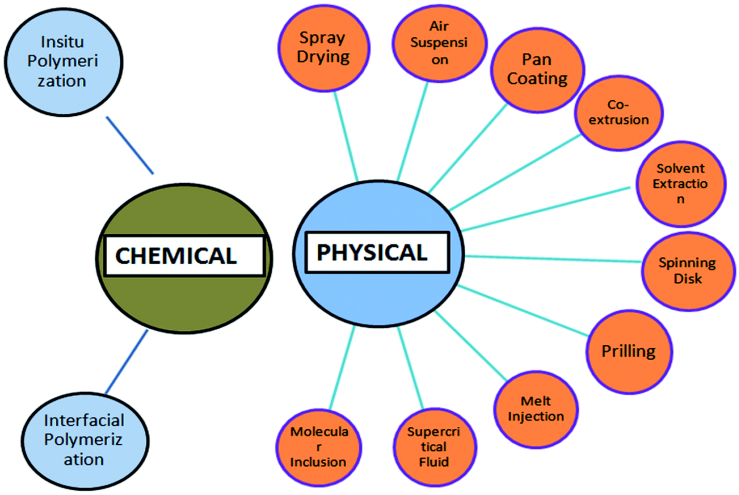
Preparation of microencapsulation should be satisfied certain criteria

- The ability to incorporate reasonable high concentration of drug.
- Stability of the preparation after synthesis with a clinically acceptable shelf life.
- Controlled particle size and displacement in aqueous vehicle for injection.
- Release of active reagent with good control over a wide time scale.
- Biocompatibility with a controlled biodegradable and susceptible to modification.
- The ability to incorporate reasonable high concentration Microencapsulation techniques are as below:

  A. Physical methods or physio mechanical method

  B. Physio chemical method

  C. Chemical method



Flowchart 4 Microencapsulation Technique

A. PHYSICAL METHOD: -

1] Air suspension coating

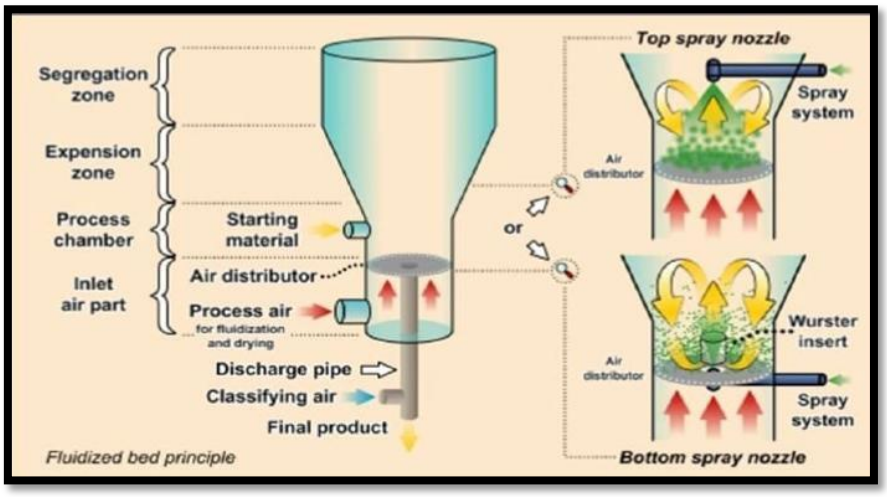


Figure 4. Air suspension technique

Microencapsulation by air suspension technique consists of dispersing of solid, particulate core material is a supporting air stream and the spray coating on the air suspended particle. Within the coating chamber, particles are suspended on upward moving air stream. The design of the chamber and it's operating parameters effect recirculating flow of the particles through the coating zone portion of the chamber, where a. Coating material, usually a polymer solution, is spray applied to the moving particles.

Air suspension coating of particles by solutions or melts gives better control and flexibility. The particles are coated while suspended in an upward moving air stream. They are supported by a perforated plate having different patterns holes inside and outside a cylindrical insert. Just sufficient air is permitted to rise through the outer annular space to fluidize the setting particles. Most the rising air flow inside the cylinder causing particles to rise rapidly. The air suspension process offers a wide variety of coating material candidate for microencapsulation. The process has the capability of applying coating in the form of solvent solutions, aqueous solutions, emulsion, dispersion or hot melts in equipment range in capacity from 1 pound to 990 pound.

Coacervation Process and Coacervation phase separation process: -

Solution of the shell material in Water. Egg. Copolymer Coacervation Gum Arabic solutions 20-30 % Gelatin solutions 20%. (Bans ode and Banerjee., 2010)

Preparation: -

The core material will be added to the solution. The core material should not react or dissolve in water.

Dispersion: -

The core material is dispersed in the solution. The particle Size will be defined by dispersion parameter, as stirring Speed, stirrer shape, surface tension and viscosity. Size Range ca. 2µm – 1200µm.

2] Coacervation: -

Coacervation starts with a change of the pH value of the Dispersion, e.g., by adding H2SO4, HCl or organic acids. The result is a reduction of the solubility of the dispersed phases (shell material)

The shell material (coacervate) starts to precipitate from the solution. The shell material forms a continuous coating around the core droplets.

Cooling and Harding phase droplet's

- The shell material is cooled down to harden and forms the final capsule.
- Hardening agents like formaldehyde can be added to the Process.
- The microcapsules are now stable in the suspension and Ready to be dried process.

Drying phase - The suspension is dried in spray dryer or in fluidized bed dryer.

And spray drying is suitable for heat sensitive product.

Coacervation phase separation: The general outline of the processes consists of three steps carried out under continuous agitation they as follow –

1. Formation of three immiscible phase.
2. Deposition of the coating.
3. Iridization of the coating.

1. **Formation of three immiscible chemical phases**– A Liquid manufacturing vehicle phase, a core material Phase, and a coating material phase. To form the three Phases, the core material 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 the Methods of phase separation-coacervation, i.e., by Changing the temperature of the polymer solution; or by adding a salt, non-solvents, or incompatible polymer to the polymer solution; or by inducing a polymer-Polymer interaction.

2. **Deposition of coating material:** - in these steps consists of depositing the liquid polymer coating upon the core material. This is accomplished by controlled, physical mixing of the material in the manufacturing vehicle.

   Deposition of liquid polymer Coating around the core material occurs.

   If the polymer is adsorbed of the interface between the two phase or between the core material and liquid Phase and this adsorption phenomenon is called a prerequisite coating.

   Iridization of the coating – It involves rigidizing the Coating, usually by thermal, cross-linking, or Desolation techniques, to form a self-sustaining Microcapsule. (Bans ode And Banerjee, .2010)

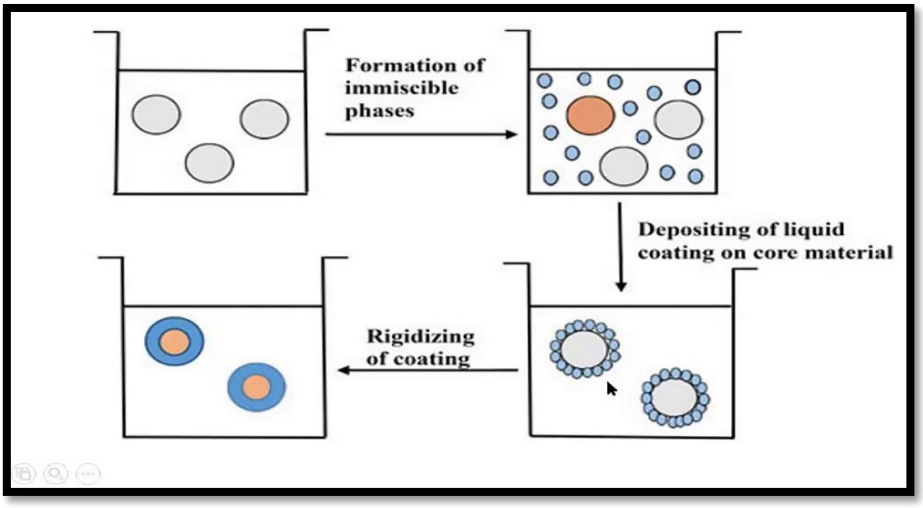


Figure 5. Coacervation process

3] Spray drying process:

In this spray drying process a microcapsule is formed by spraying core and coating material into the chamber which is at high temperature process variables:

Viscosity, uniformity, concentration of core & core material, feed rate of atomization drying rate. (Mishra. angora. 2012)

Some Advantages of spray drying process:

1. It is versatile process.

2. It provides good control of final properties such as particle size, flowability, bulk density and mechanical strength.

3. It is suitable for vitamins, hormones, plasma, serum, dextrin's, chloramphenicol can be encapsulated.

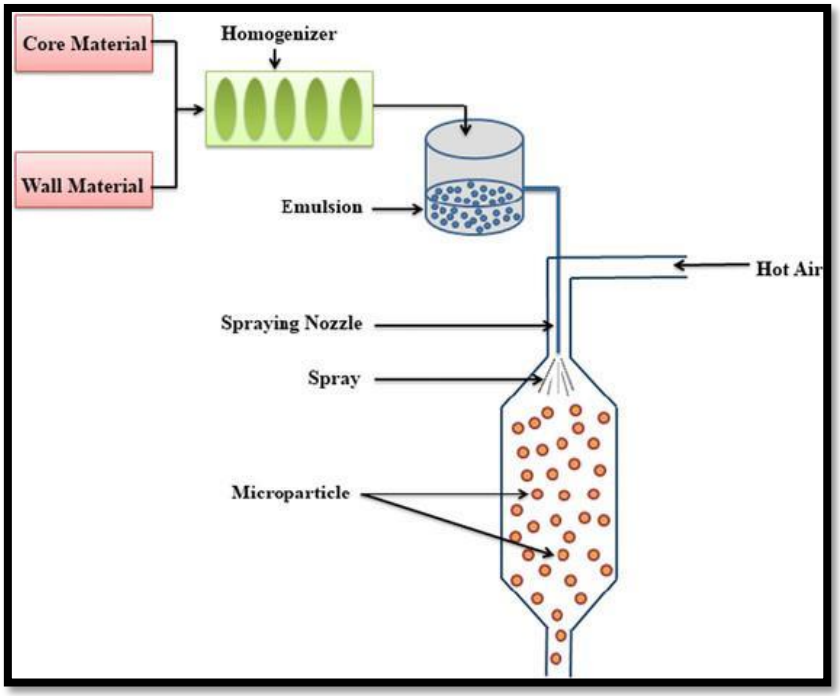


Figure 6. Spray drying process.

4] Pan coating:

The Pan coating process or method used in pharmaceutical industry, is among the oldest industrial procedures forming a small coated particle. The particles are tumbled in a pan or other device while the coating material is applied slowly respect to microencapsulation, solid particles greater than 600 microns in size are generally considered essential for effective coating, and has extensively employed for preparation of controlled release beads.

In medicament are usually coated onto various spherical shape or substrate, such as non-peril sugar seed and then coated with protective layer of the polymer.

In practice, the coating is applied as a solution to the desired solid core material in Coating pan. Usually to remove the coating solvent, warm air passed over the coated material as coating are begin applied in coating pans. (. Shekhar and Madhu, 2012).

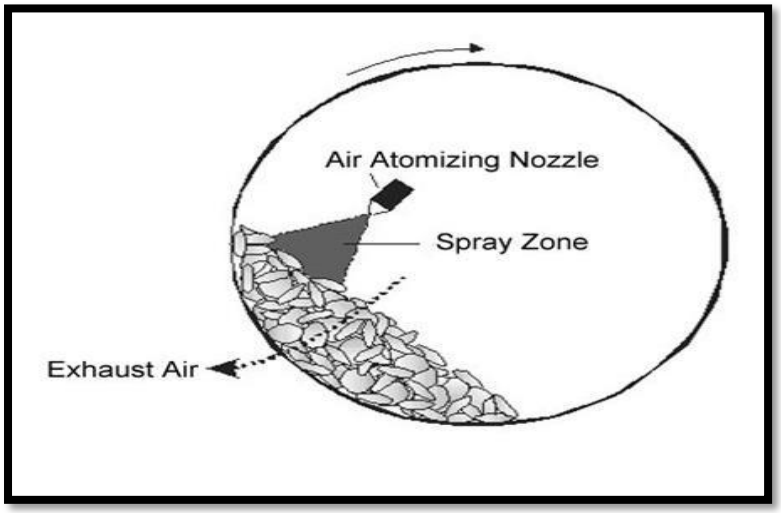


Figure 7. Pan coating.

5] Fluidized bed coating: - (Wurster' coating)

The fluidized bed coating is also known as Suspension coating. This technique is mainly Used in pharmaceutical industries and now it is Also employed in food industries because of it Benefits. The principle involved in fluidized Bed coating is that the liquid coating or wall Material is sprayed on to the particles of core and the rapid evaporation helps in the Formation of a protective layer on the active Material or cores. The Coating materials used in the process are Cellulose derivatives, lipids, Protein derivatives, and starch derivatives. The Particle size in this process is 20 to 1500µThe fluidized bed coating process is three (Saiki ran and Perli,2018)

Types of fluid bed are: -

1. Top spray
2. Bottom spray
3. Tangential spray

1) **Top spray: -** The classification of top spray, bottom spray and tangential spray are based on the direction in which the core material and wall material Sprayed. In top spray the coating material is Sprayed from the top to downwards in order to Meet the core material which is ejecting from the bottom. The core material comes in Contact with the wall material and there will Be formation of protective covering around the Core material. As the wall material is sprayed from the top there is increased encapsulation Efficiency

2) **Bottoms spray:** -Bottom spray Bottom spray fluidized bed coating is also Known as a as Wurster's coaterǁ. The Equipment consists of a coating chamber, cylindrical nozzle and a perforated bottom Plate. The coating material is sprayed from the Bottom such that the particles move upwards.

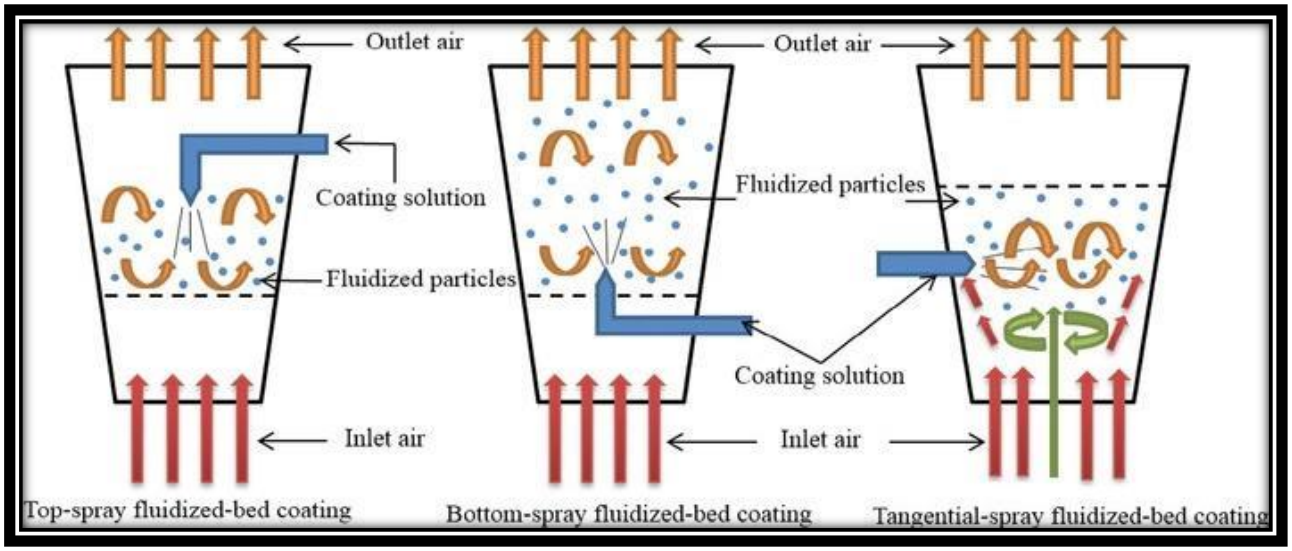


Figure 8. Fluidized bed coating by Top, Bottom, Tangential spray

3) **Tangential spray:** -Tangential spray fluidized bed coating the tangential spray fluidized bed coating Consists of a tangential disc at the bottom of the coating chamber. The disc is raised such that there is a gap between tween the bottom of coating chamber and the disc such that the wall material and core Particles enters into the gap and get Encapsulated.

6] Centrifugal extrusion: -

By using rotating extrusion head containing concentric nozzles, liquids can be encapsulated. In this method, a jet Core is covered by sheath of wall solution. As jet goes through the air it breaks, owing to Rayleigh instability, into the mm Droplets of core, each one coated with the wall solution. The mean diameter of droplets is Within +-10%, they come in a narrow ring. This process is well efficient for forming particles 400-2000 micrometer Diameter.

This process is only be suitable for liquid or slurry. The production rate can be high up to 22.5kg (50lb) of Microcapsules can be produced per nozzle per hour per head (Deo-Nandan, 2016)

B]. Chemical process: -

Solvent evaporation technique: -

Theses technique can be done into liquid manufacturing vehicle (oil in water or o/w) emulsion which can be formed by agitation of two immiscible liquid Phase. In this Microcapsules Coating polymer can dissolved in volatile solvent, which have an immiscible property with liquid manufacturing vehicle Phases. After that, core material is dispersed in coating polymer solution. To obtain desired size of Microcapsules the Core and Coating material dispersed into liquid manufacturing Phase with agitation process. (Singh and Due, 2016)

The solvent evaporation technique to produce Microcapsules in applicable to wide variety of liquid and solid core material. The core material may be either water soluble or water insoluble Material. A variety of film forming polymer can be used as coating.e.g., Evaluation of sucrose ester as alternative surfactant in microencapsulation of protein by the solvent evaporation method

Solvent evaporation method has following advantages.

- Most simple, convenient and easy to carry out in laboratory.
- Less time consuming.
- Required no special apparatus.
- Involve less hazardous chemicals.

C] Polymerization

a) Interfacial polymer: -

In interfacial polymerization, the two reactants in a polycondensation meet at an interface an react rapidly. The basis of this method is classical chotten Baumann reaction between an acid chloride and a Containing active hydrogen atom, such as an amine or alcohol, polyester, polyuria, polyurethane.

Under the right condition, thin flexible walls and from rapidly at the interface. A solution of the pesticides and a diacid chloride are emulsified in water and an aqueous solution containing an Amine and a polyfunctional isocyanate is added. Base is present to neutralize the acid formed during the reaction. (Solution of the pesticides, 2010).

In situ polymerization :

In a few microencapsulation processes, the 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 am /min. Coating thickness ranges 0.2 – 0.75 am. The coating is uniform, even over sharp projections. (Agnihotri and Mishra. R.2012).

Matrix polymer: - In a number of processes, a core material is imbedded in 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. Using this phenomenon, Chang prepares microcapsules Containing protein solutions by incorporating the protein in *the* aqueous diamine phase. Chang has demonstrated the Perm selectivity, by their ability to convert blood urea to Ammonia, the enzyme remaining within the microcapsules When incorporated within an extracorporeal shunt system. Numerous groups are utilizing polymerization techniques to accomplish microencapsulation. Examples are the National Lead Corporation, Errand America. (Mishra. And Goad., 2012).

D] Polymer Encapsulation by Rapid Expansion Of supercritical of Supercritical Fluids: -

Super critical fluid are highly compressed gasses that possess serval advantageous properties both liquid and gases. These fluids have attracted much attention in recent years, the most widely used being supercritical Co2, alkanes (C2 to C4) and nitrous oxide (N2O) They have low hydrocarbon – like solubility for most solute and are miscible with common gas such as hydrogen (H2) and nitrogen. A small change in temperature or pressure causes a large change in density of super critical fluid near the critical point a property which enhances their use in several industrial applications.

Supercritical Co2 widely used for its low critical temperature value, in addition of its nontoxic, nonflammables properties, it's also readily available, highly pure and cost effective.

It has found application in encapsulated active ingredient by polymers. Different core material such as pigment, pesticides, pharmaceuticals ingredients, vitamin, flavors and dyes are encapsulated using this method.

A wide variety of shell material that either dissolve (paraffin wax, acrylate, polyethylene glycol) or do not dissolve (protein and polysaccharide) in supercritical Co2 are used for encapsulating core substance.

The most widely used method are as follows: -

- Rapid expansion of supercritical solutions (RESS)
- Gas Anti- solvent (GAS)
- Particle from gas saturated solution (PGSS)

3) Particles from a gas saturated solution (PGSS): -

This process is carried out by mixing core material and she'll material in supercritical fluid at high pressure. During this process supercritical fluid penetrated the shell material, causing swelling when the mixture is heated above the glass transition temperature the polymer liquefier. Upon releasing the pressure, the shell material is allowed to deposit to allowed to deposit the active ingredient. In this process the core material and she'll material may not be soluble in the supercritical fluid. In pharmaceutical industry, preformed microencapsulation is often used for entrapment of Active material using supercritical fluid under pressure. (Mishra. R and Goad.C.2012)

6. APPLICATION OF MICROENCAPSULATION

There are many reasons why drug and related chemical have been microinsult. The technology has been widely used in the design of controlled release and sustained release dosage form.

1. It has been used to protect drugs from Environmental hazards such as humidity, Light, oxygen or heat. Microencapsulation Does not yet provide a perfect barrier for Materials, which degrade in the presence of Oxygen, moisture or heat, however a great Degree of protection against these factors Can be provided. For example, vitamin A And K have been shown to be protected from the oxygen and moisture through the microencapsulation.

2. The mask the bitter taste of drugs like paracetamol and Nitrofurantoin..

3. Protection of liquid crystal.

4. Drug delivery: controlled release delivery systems.

5. Separation of incompatible substance has been achieved by encapsulation.
6. Beverage production.
7. Quality and safety in food agriculture and environmental sector
8. Protection of molecules from other compounds.
9. Soil inoculation. (Ashish Kumar. 2019)
10. In generally the active moiety of drug is based on the encapsulation purpose.

Active moiety	**Purpose of encapsulation**
Aspirin	Taste masking, sustained release, reduced in gastric irritation.
Paracetamol	Taste masking
Isosorbide dinitrate	Sustained release
Progesterone	Sustained release
Menthol	Sustained release and reduction of volatility
Vitamin A	Stabilization of oxidation
Nifedipine	Prevention of photo instability.

Table 1. Drug and Purpose of Microencapsulation

7. CONCLUSION

Microencapsulation is a packing of active ingredient inside a capsule ranging size from 1µm to the several ranging capsules protect the active ingredient from the surrounding until appropriate time. Then after material escape through the capsule wall by various means, including rupture, dissolution, diffusion or melting. Microencapsulation is the improve drugs performance and enhance its shelf life. Microencapsulation is the most agreeable way of protection and masking reduce rate of dissolution, facilitation of handling and spatial targeting to the active site. These techniques are also beneficial for those drugs which is dissolved into intestine and but not in stomach.

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