Microencapsulation and its various aspects: A Review

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***Abstract*: Microencapsulation is the process which involves wrapping core parties in a continuous layer of coating material that isolates them from the surrounding environment. Microcapsules can be up to 800 µm in size and it is a promising technique for controlled drug delivery. The review will discuss various terms related to microencapsulation, including benefits, need for microencapsulation, particle types, materials required to create microcapsules, drugs released from microcapsules, and factors affecting microencapsulation. Different techniques of the microencapsulation such as physical, chemical, and physiochemical method and characteristics and parameter evaluation of microencapsulation are also included in this review article. This article also provides us with information regarding its application in real life and give better understanding about the different aspects of said topic.**

***Keywords*: Microencapsulation techniques, Physical method, chemical method and application of microencapsulation.**

1. Introduction of microencapsulation

It was Green and Scheicher who invented microencapsulation technology in the 1950[1,2]
Burg de Jon and Kan came up with the microencapsulation procedure[3].
In microencapsulation, continuous film of polymeric material surrounds or coats the small drop or particle of solid, liquid gas.
There is a size range of 1 - 1000 µm in diameter for microencapsulated products[4].
Size of the nanoparticles is <1µm and size of microcapsule is >800µm. Contain 10-90% w/w core[5].
Scanning electron microscopes reveal the structural features of microparticles[6].
A coating protects the sensitive and expensive core from environmental conditions by providing a protective layer[7].
Furthermore, it protects the drug or mainly the protein core from enzymatic cleavage and photolysis[8].
An encapsulated drug should be released in a prescribed manner to prolong or control its effects. The release mechanism is leaching, erosion, or rupture, which depends on moisture, pH, and physical force[9].

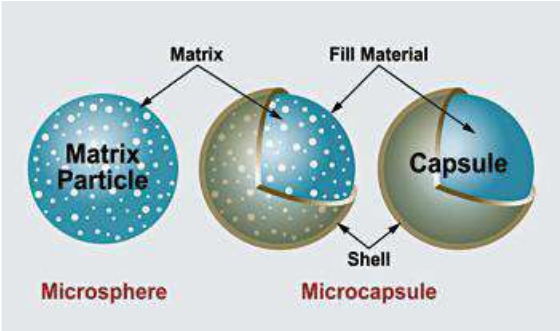
It has the following benefits[10]:

1. Reduces the dosage frequency
2. Increased convenience
3. Acceptance for patients.
4. Target specific.
5. Having high efficiency.
6. Extends the life of compounds.

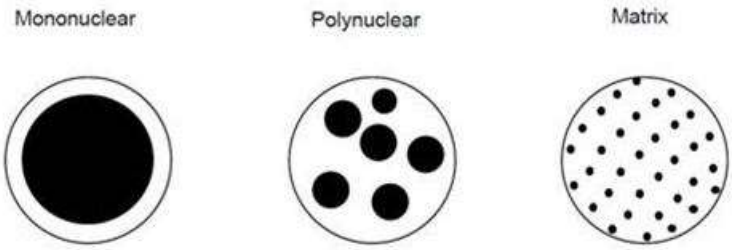
The need for microencapsulation:

- It improves quality by masking unpleasant taste, aroma, and flavors[11,12].
- Sensitive drugs are isolated from moisture light and oxygen by microencapsulation.
- It Increases safety by decreasing microbial growth[13,14].
- It is used to attain sustained or prolonged release of a drug.
- it reduces the toxicity and GI irritation and many major side effects of the drug[15,16].
- It protects the volatile drugs which vaporize at room temperature[17,18].
- It is used to alter the site of absorption.
- It provides enhanced stability to vitamin A palmitate by preventing from oxidation[19].
- Improves handling of sticky compounds and liquids, also converts liquids into free-flowing solid powder.
- Reactive compounds are separated that prevent incompatibility between drugs[20,21].

A. Microcapsules: - core material is surrounded by a layer of coating or shell material. its reservoir system.
B. Microspheres: - core material is distributed in coating material in matrix form[22]



Types of microcapsules:
1. Mononuclear / single core.
2. Polynuclear/ multiple cores.
3. Matrix type[10]



[12]

Fig.2 type of microcapsules

2. Materials required for microencapsulation: -

I. **The core: {internal phase, fill}**

The core is a specific material, it can be liquid or solid. The formation of the core takes place prior to encapsulation.

Table 1: materials required for microencapsulation.

Solid core	Active ingredients, stabilizer, diluents, excipients, release rate influencers e.g., Dextrin, Bases, Herbicides, Pharmaceuticals, Biocides, Minerals[23]
Liquid core	Dissolved or dispersed material e.g., Perfumes, Solvents, Vegetable Oils, Pesticides, Dyes, Catalysts, Bleaches, Cosmetics, Insecticides, Sugars, Salts, Acids, Pigments, Fungicides, Nutrients[24].

II. The coat: (all, shell, coating membrane)

It is the layer of material which coats or covers the core material. Composition of coating may involve Inert polymer, Plasticizer, and Coloring agent[25].

Some desired properties of coating material.

- Controlled release in specific conditions
- Have strength, flexibility, im-permeability, stability, and optical properties.
- Have ability to form cohesive film with core.
- It should be inert, compatible, and stable for core material.
- It should be pliable, tasteless, non-hygroscopic and less viscous[26].

Table 2: - Coating materials

Polymers	Example
A. Natural polymers a. Proteins	Albumin, Gelatin, Collagen, Gluten, casein, peptides[27].
b. Carbohydrates c. Chemically modified carbohydrates	Agarose, chitosan, Starch, Carrageenan, Polystarch, Polydextran, maltodextrins, cyclodextrins[28]
B. Synthetic polymers a. Biodegradable	Lactides, Glycolides and

b. Non-biodegradable	Co-polymers poly alkly cyanoacrylates, poly-anhydrides[29] Polymethyl methacrylate (PMMA), Acrolein, Glycidyl methacrylate, Epoxy polymers[30],[31].
C. Depending upon Solubility a. Water soluble resins	Gelatin, Gum Arabic, starch, poly vinyl pyrrolidine, methyl cellulose, Carboxy methyl cellulose, Hydroxy methyl cellulose, Poly vinyl alcohol, Arabinogalactan, Polyacrylic acid.
b. Water insoluble resins	Ethyl cellulose, Polyethylene, Poly methyl acrylates, poly amide (Nylon), Poly (ethylene vinyl acetate) cellulose nitrates, silicones, poly(lactide-co-glycolides)
D. Waxes and Lipids	Paraffin, carnauba, spermaceti, bees wax, steric acid, stearyl alcohol, Glyceryl stearate, diacylglycerols.
E. Enteric resins	Shellac, cellulose acetate phthalate, Zein[32].

3. Mechanism of drug release: -

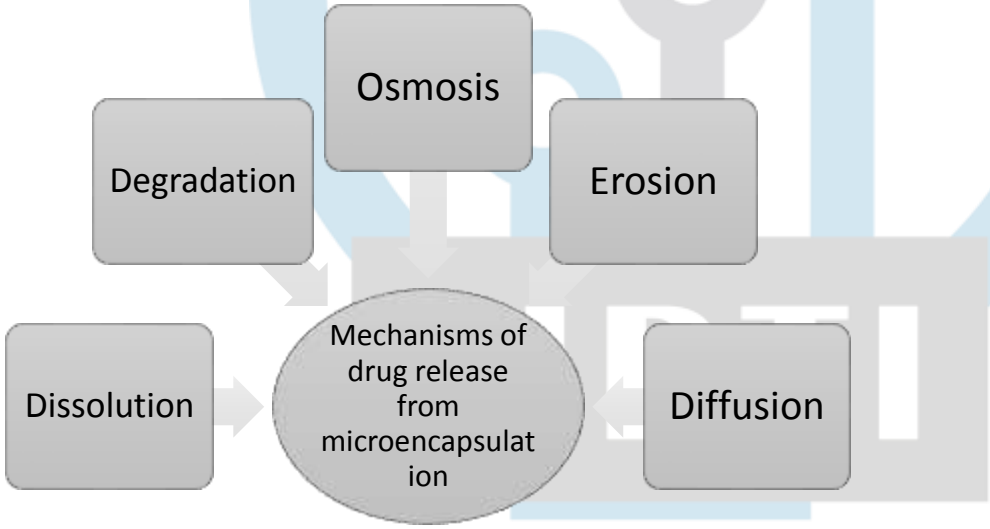


Fig: Type of mechanism of drug release.

a. Degradation:

The drug is dissolved and uniformly distributed in the matrix. The matrix and drug are strongly attached, but on degradation the drug is released. Diffusion takes more time than degradation.

b. Diffusion:

When shell comes in contact with dissolution fluid, it penetrates the shell, dissolves the core, and drug releases or leaks out.

Rate of drug release depends on:

a) Rate of dissolution fluid to penetrate the wall of microcapsules
b) Rate of drug dissolution in dissolution fluid.
c) Rate at dissolved drug leak out and disperse from surface.

It obeys Higuchi's equation,

$Q = [D/J (2A – \varepsilon CS) CS t] ½$

Whereas,

Q is the amount of drug released per unit area of an exposed surface in time t;
D is the diffusion coefficient of the solute in the solution;
A is the total amount of a drug per unit volume;

CS is the solubility of drug in permeating dissolution fluid;
ε is the porosity of the wall of the microcapsule;
J is the tortuosity of the capillary system in the wall.
The above equation can be simplified to Q = vt where, v is the apparent release rate.

c. Dissolution

Polymer coat dissolves as it solubilises in dissolution fluid. Dissolution rate determining in release rate. Coating thickness and solubility of it in dissolution fluid influences rate of drug.

d. Osmosis

Coating wall acts as a semipermeable membrane and allows to create osmotic pressure diffusion outside and inside microcapsules. It takes drug out of microcapsule by small pores in the coating wall.

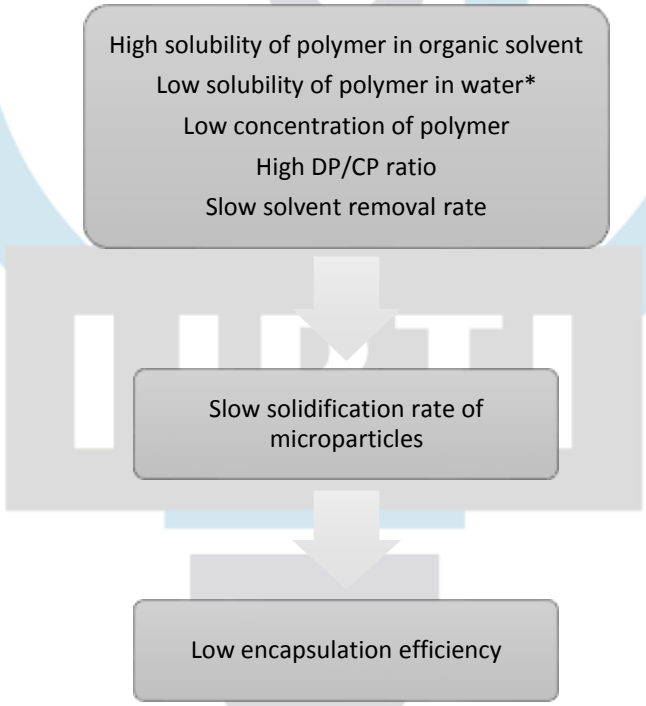
e. Erosion

Change in pH: -
It affects the solubility of the coating material. The material may remain intact in an acidic environment but gets solubilised by changing pH to alkaline environment.
Change in temperature: -
Temperature sensitive release- wall material collapses when exposed to temperature.
Fusion activated release-
Coating material melts in contact with increased temperatures and releases the drug[33],[34],[35].

Some other release mechanisms are there as follows,

a. External pressure which mechanically breaks microcapsules.
b. Internal pressure it allows microcapsule to break wall.
c. Microcapsule wall abrasion, it is used for fragrance release.
d. In Burning when heat increases fire retardants releases[36]

3. Encapsulation efficiency influenced by these:



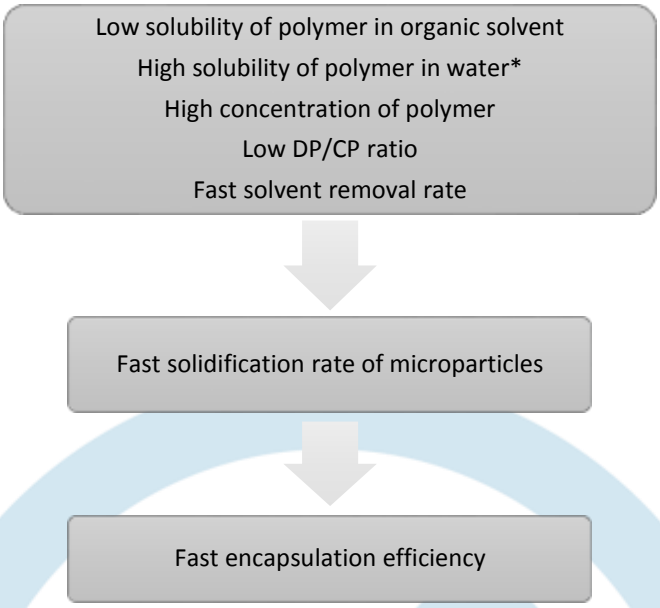


Fig 2: Factors influencing encapsulation efficiency[37].

a. Viscosity of dispersed phase.
b. Volume fraction of dispersed phase to continuous phase.
c. Amount of drug in dispersed phase.
d. Concentration of surfactant.
e. Operating parameters:

Rate of stirring
Temperature,
Pressure [8,12]

4. Techniques for preparation of microencapsulation:

Table 3: Type of preparation methods of microencapsulation[38],[39]: -

Physical methods	Chemical methods	Physio-chemical methods
Air suspension method/ Fluidized bed coating Coacervation method Lyophilisation/freeze drying Multi-orifice centrifugal extrusion process Pan coating Spray drying /spray congealing Spray cooling Spinning disk Super critical fluids-based tech. Vibrational jet technique	Solvent evaporation method Solvent extraction Polymerisation Single emulsion method Double emulsion method Hydrogel microspheres Liposomal entrapment Co-crystallisation	Molecular inclusion complexation Inotropic gelation method Sol-gel method

5. Methods for microencapsulation

A. Physical methods for microencapsulation

i. Air suspension method (Wurster method)/ Fluidized bed coating

Solid core is coated as well as dried. Which is suspended in an upward air stream suspension and solutions of coating material (polymer) in volatile solvent[40].By using air, core material is fluidized and coating material is sprayed over it, in a hot environment. Drying rate is directly proportional to the temperature of the air stream. It efficiently applies a uniform layer of shell material onto the core particles. It has a specific capsule size distribution. It forms microcapsules having a diameter of about 20-1500µm[41].
Different fluidized bed coating methods are: (a) Top spray (b) Bottom spray, and (c) Tangential spray[42].
Advantage: It is Capable to use shell material like polysaccharides, proteins, emulsifiers, fats, enteric coating, powder coatings, etc. The controlled release properties are more versatile with this[43]. Improved control and flexibility compared to pan coating.
Disadvantage: - Process is repeated several times. Agglomeration of particles may occur. It is not suitable for temperature-sensitive compounds[44].

ii. Coacervation method (Salting out)

Affinity of deposition of polymer around the core by changing pH, polarity, temperature, solubility etc. Simple coacervation has single molecule present and coacervation are formed by unavailability of solvent[45]. In complex coacervation ionic or electrostatic interaction between two or more oppositely charged polymers leads to coacervate formation[46]. Formaldehyde is used as a hardening

agent. Coacervation is a phase separation encapsulation process that is most commonly used after spray drying[47]. The microcapsules formed from this method have a size range of about 2-1200µm.
Advantages: High payload. High encapsulation efficiency. It Can be used for heat-sensitive drugs.
Disadvantages: Toxic chemical agents are used. Complex coacervates are highly unstable. Method is complex to perform[48].

iii. lyophilization/freeze drying

It is a multistage process,
a) Freezing,
b) Sublimation (primary drying),
c) Desorption (secondary drying)
d) Storage and it is resulting into dry material[49].
It can be preceded by formation of a matrix or an emulsion of core and coating material that will be sprayed after drying and microcapsules/microspheres will form. Lyophilisation can form microcapsules of a size of about 1-1000 µm.
Advantages: Used for thermosensitive material and aroma.
Disadvantages: It is time consuming. Expensive for processing, storage and transport[50].

iv. Multi-orifice Centrifugal extrusion method

This method is developed by South West Research Institute (SWRI). In this method liquid core material flows through inner tube and coating material (which should be immiscible with core) flows through annular tube around it[51],[52].Vibrational or rotational movement of tubes forms unbroken rope which splits into round droplets after clearing nozzle[53]. Due to effect of surface tension, coating material covers the core material[54],[55]. The wall of droplets solidified by cooling or by gelling bath. The resultant microcapsules may have a size of about 400-2000um. Most of the forming droplets are of ±10% of the mean diameter.
Advantage: Suitable for bioencapsulation
Disadvantages: High temperature, only suitable for liquid or slurry.

v. Pan coating

It is the oldest industrial method of formation of small coated particles. The coating material can be gradually applied or sprayed over core material that are tumbled in pan. Warm air is passed for removal of coating solvent. Sometime, drying oven may use. Microcapsules formed from this method may have diameter about 600-5000 µm.
Advantages: Low-cost equipment
Disadvantages: Core size should be >600 um. It is Difficult to control. It requires high skill[56].

vi. Spray drying /spray congealing

In this method core material is solubilized, dispersed, or emulsified with solution of coating material[57]. It is the continuous conversion of liquid to solid particulate, by spraying feed into hot drying medium. The microcapsules formed from this method have a size of about 5-5000µm[58].
There is very tiny difference between these two methods,
a) Spray drying has rapid evaporation of solvent
b) Spray congealing solidification is completely thermally
Advantages: Versatile, Easy to scale-up. High encapsulation efficiency. Good stability of the finished product. Used for the encapsulation of lipid-soluble vitamins (e.g., b-carotene, vitamins A, D, and E).
Disadvantage: High temperature. Agglomeration of particles may occur; some particles remain uncoated[59].

vii. Spray cooling/spray chilling

It is very similar to spray drying having difference in the use of cooled or chilled air in it[60]**.** In this method atomization of mixture of core material and coating material under cold air current resulted in solidification of droplets in which coating material encapsulates the core material. Spray cooling gives microcapsules having size of about 20-300µm.
Advantage: Used for encapsulating water-soluble vitamins (e.g., ascorbic acid) Thermosensitive materials can be used[61].
Disadvantages: Difficult to control particle size. Formed microcapsules are not stable**.**

viii. Spinning disk

Rotating disk is filled with suspension of core material in liquid coating material. This disk has a spinning action which allows coating material to coat over core particles. By using centrifugal force, coated particles are cast from edge of disk and solidified by cooling. The coated particle has a size range of about 5-1500µm.
Advantages: It is rapid, cost-effective, and relatively simple. It has high production efficiencies[62].

ix. Super Critical Fluids (SCF) based tech

SCF is a solvent at a specific temperature and pressure above its critical point. Various compounds can form this condition including carbon dioxide, water, propane, nitrogen etc. but CO_2 is most commonly used. Use of SCF for several applications by means of co-precipitation and encapsulation[63].SCF-based processes are classified into three categories: -
a) As a solvent: Rapid Expansion of Supercritical Solutions (RESS) and derived processes
b) As an anti-solvent: Supercritical Anti-Solvent (SAS) precipitation and derived processes

c) As a solute: Particles from Gas Saturated Solutions (PGSS) and derived processes.

Advantages: use of the supercritical fluid. Eliminates or reduces the use of toxic organic solvents in the process (3). Prepare microcapsules oriented for inhalation purpose.

Disadvantage: Degradation of thermolabile compounds may occur[64],[65].

x. Vibrational jet technique/Prilling

For this method, basic principle of formation of droplets from a polymer extruded through nozzle using cutting or vibrational forces. Micro granulation or core shell encapsulation is conducted using a laminar flow nozzle and a vibrational nozzle

Advantages: High yields of production. Easy to scale-up.

Disadvantages: High temperature. Risk of orifice clogging[66].

B. Chemical methods for microencapsulation

i. Solvent evaporation method

Coating material (polymer) dissolved in volatile solvent; it should be immiscible with liquid vehicle phase. On the basis of hydrophilicity and hydrophobicity of core material, it is dispersed or dissolved in coating material. The core coating material mixture or dispersion is dispersed in liquid vehicle phase with continuous stirring to obtain specific size of microcapsule. Shrinking of the coat material around the core material occurs which results in hardening of microcapsules. Generally, water insoluble polymers are used. The microcapsules formed by this method may have a diameter of about 0.5-1000μm[67].

Advantages: Easy, simple and convenient. It requires less time. Does not require special apparatus. It has less hazardous chemicals.

Disadvantages: Not suitable for the encapsulation of highly hydrophilic drugs. Lab scale production[68]

ii. Solvent extraction

It is a two-step process. Drug is dispersed in small amounts in a continuous phase. Then, further continuous phase and additional extraction agents are added at sufficient amount to absorb the entire solvent leaching from solidifying microspheres. For, one step process, without emulsification step, the drug/matrix dispersion is immediately homogenized with continuous phase that is capable of dissolving total amount of dispersed phase solvent at once.

Advantages: Used for encapsulation of vitamins, food supplements, oil-soluble substances.

Disadvantages: It requires careful setting of physicochemical parameters for homogenisation[69],[70].

iii. Polymerisation/polycondensation

This new method forms protective microcapsule coatings in situ. Microencapsulation by polymerization has a reaction of core material and continuous phase; both of them may be liquid or gas. The core material is dispersed in a continuous phase. Reactive water-soluble monomer undergoes condensation by nebulizing dispersion or solution of core material with monomer and catalyst. Polymerization occurs over the core material and it is then encapsulated. It gives microcapsules having a size range of about 0.5-1100μm.

Types of polymerization methods:

a) Interfacial polymerization
b) Interfacial cross linking
c) In situ polymerization
d) Matrix polymerization

Advantages: Microcapsules having narrow size distribution can be obtained. It does not require any specific equipment.

Disadvantages: Difficult to control polymerization around the core. Chemicals and free radicals used in this technique are hazardous[71].

iv. Single emulsion method

In this method polymer is dissolved in a volatile solvent, which should be water immiscible. After that drug is dispersed or dissolved in this polymer solution. Followed by emulsification with water and emulsifier. The solvent is removed by extraction or evaporation, resulting in the formation of compact microparticles[72] .

Advantages: It can be used to encapsulate hydrophobic drugs through oil-in water (o/w) emulsification process.

Disadvantages: It Cannot be used for hydrophilic drugs.

v. Double emulsion method

In this method polymer dissolved organic solvent is emulsified with aqueous solution of water-soluble drug and water in oil emulsion is formed by using homogenizer or sonicater. With vigorous stirring, this primary emulsion is emulsified with excess amount of water and forms a W/O/W emulsion. Solvent is removed with extraction or evaporation.

Advantages: Encapsulation of hydrophilic drugs in an aqueous phase with high encapsulation efficiency. It is widely used for the development of protein delivery[17].

vi. Hydrogel Microspheres

In this method, gel-type polymers (Alginate) are dissolved in an aqueous solution and drug is dissolved in that solution mixture. Atomization by using appropriate devices gives microdroplets. These fall into a hardening bath (Calcium chloride) that is slowly stirred.

Advantages: It avoids residual solvent in microsphere. Particle size can be controlled by using size extruders or by varying the flow rate of the solution.

vii. Liposomal entrapment

Liposomes consist of single or multiple lipid bilayer systems in which lipids are concentric around aqueous space. It is the result interaction of a hydrophilic head and a hydrophobic tail between phospholipid in water. The spherical shape of liposomes is gained by using sufficient energy, supplied by solvent evaporation, extrusion, sonication etc.

Advantages: Either hydrophilic or lipophilic material can be encapsulated. It has efficient controlled delivery. It can be used for the delivery of vaccines, hormones, enzymes, and vitamins into the body.[9] High bioavailability, biocompatibility and biodegradability.

Disadvantages: Cost level, Poor physical and chemical stability[59],[65] .

viii. Co-crystallisation

It is also known as co-precipitation**.** It is a new encapsulation method in which sucrose is used as a matrix for incorporation of core materials. A supersaturated sugar syrup is prepared and maintained at optimum temperature to prevent crystallization. Add the core material to this syrup for encapsulation. Mixing the syrup induces agglomeration and nucleation. Agglomerates are discharged from the vessel and these encapsulated products are dried to the desired moisture.

Advantages: Simple and inexpensive. It can be used for encapsulation of food flavors.

The product had good shelf life since the crystals precluded oxygen[73],[74].

C. Physio-chemical methods for microencapsulation

i. Molecular inclusion complexation

It is the encapsulation method, which takes place at the molecular level. Entrapment of guest (active) compound by host (polymer) by using physiochemical forces like hydrogen bonding, van der wall's forces or hydrophobic interaction[65]Cyclodextrin is used as encapsulating agent (9). It has hydrophobic internal part and hydrophilic external part. Apolar guest molecules can be entrapped by apolar internal cavity through hydrophobic interaction. βcyclodextrin protects guest compounds against oxidation, heat degradation, evaporation, and also increases solubility.

Advantage: Very efficient to protect unstable compounds.

Disadvantage: It is restricted to apolar compounds only. β cyclodextrin is expensive. Undesirable release of complexes may occur[75].

ii. Inotropic gelation

It is the physicochemical process in which hardening of droplets occurs by chelating polyelectrolytes with ions (Ca^{++}, Al^{+++}, Zn^{++}). It causes molecules to form an outer film polymer gel layer.

The process of gelation can be external or internal. Dissolved mixture of coating material and core material atomized within ionic solution. Capsules are formed by ionic interaction. Instead of ionic solution, if thermal parameters are used, it will be known as thermal gelation.

Advantages: Low polydispersity, High encapsulation efficiency. It is a water-based technique and avoids organic solvents and temperature**.**

Disadvantages: Higher quantity non-uniform particle size. Limited study about ionic pair combinations and polymers**,** High porosity-promotes intensive burst[76],[77].

iii. Sol-gel method

This method involves adsorption on glass surfaces incorporation in porous glass powder, or entrapment in a polymer matrix. It is a polycondensation reaction between a molecular precursor and a liquid phase; it forms colloidal solution (Sol) and is then subsequently converted to an oxide network (gel). The microcapsules produced by this method have tiny sizes of about 2-20µm.

Advantages: Low cost, low use of chemical Inorganic shell with high thermal conductivity. Simple and safe. Vacuum does not require.

Disadvantages: It may change chemical and biological properties of encapsulated materials due to reduced degree of freedom and interaction with inner surface of pores[78].

6. Characterization of microcapsules: -

a. Particle size and morphology: -

It is determined by different methods

a) Laser diffraction

b) Electron microscopy- Scanning electron microscopy (SEM) it gives both external and internal microstructure in the form of real image. Transmission electron microscopy (TEM) gives shell thickness of microcapsules.

c) Dynamic light scattering – it checks Brownian motion of the particle.

d) Atomic force microscopy and interferometry may be applied for the quantitative characterization of surface coarseness.

e) Confocal laser scanning microscopy (CLSM) is a non-destructive visualization technique that gives information about the structure, surface, and inside of particle[79],[80].

b. Carr's index and Hausner's ratio –

To calculate bulk density of mixed microcapsules Hausner's ratio and Carr's index from by using poured density or tapped density, which are previously measured using measuring cylinders.

Formula for Hausner's ratio-

Hausner's ratio (HR)=ρT/ρB

Whereas,

ρT is tapped density and ρB is bulk density

Formula for Carr's index-

Carr's Index = [Tapped Density-Bulk Density/Tapped Density] ×100[81,82]

c. Bulk density

Weigh accurate microcapsules and then transfer to a 100ml cylinder to obtain apparent volumes of between 50 and 100ml.

Bulk Density (ρρ)= [Weight of Microcapsules (g) (M) / Bulk Volume (ml)(V)]

Whereas,

M = mass of the powder,

Vo = volume of the powder.

To measure density of microspheres multi volume pycnometer is used.

d. Angle of repose-

Angle of repose is measured using fixed funnel and free-standing cone methods. Determination of angle of repose of microcapsules is carried out by,

Angle of repose θ = tan-1 (H/R)

Whereas,

H = Height of the pile;

R = Radius of the pile.[83]

e. Determination of drug loading encapsulation efficiency and microcapsule yield

Encapsulation efficiency is the amount of core material that is encapsulated by coating material against the total amount of core material that was used for encapsulation. The average amount of drug is determined by extraction of drug samples by microencapsulation with methanol. Followed by filtration and appropriate dilution with methanol, the resultant concentration is examined by UV spectrophotometry.

% Drug loading = weight of drug/weight of microcapsules

%Encapsulation efficiency= [%Actual drug content/%theoretical drug content] ×100

%Yield=M/ M_0×100

Whereas,

M = Weight of microcapsules

M_0 = Total expected weight of drug and polymer.

f. Drug release kinetics

To find the mechanism of release of drug from microcapsules. Four models of drug release are used as follows.

a. Zero order kinetics,
b. Higuchi,
c. Korsmeyer-Peppas and
d. Makoid-Banakar[84].

g. Chemical composition of microcapsule shell

To know the chemical composition of the microcapsule shell, three methods are used.

a) Attenuated total reflectance- Fourier Transform Infrared (ATR-FTIR) spectroscopy: - It gives the information about interaction between molecules, outer portion of microcapsule and their component.

b) X-ray photoelectron spectroscopy (XPS): - It is used to analyze microcapsule coat composition. X-ray removes the electrons from the shell.

c) Time-of-Flight Secondary Ion Mass Spectroscopy (ToF-SIMS): - It is qualitative method. It is used to study the outside area of wall microcapsules with depths of 1-2 nm[85].

h. Determination of contact angle

It measures the wetting properties of microcapsules. It is used to measure the quality of a solid surface. It gives information about the nature of microcapsules such as hydrophilicity and hydrophobicity.

It is measures at solid/air/water surface place a droplet in circular cell mounted above objective of inverted microscope.

i. Thickness of coating

Thickness of microcapsules is determined by using the equation:

$$h = r (1-p) d1 / 3[pd2 + (1-p) d1]$$

Whereas:

h =wall thickness of microcapsules,
r = arithmetic mean radius,
d1 = density of core material,
d2= density of coating material,
p = proportion of medicaments in microcapsules.

j. Isoelectric point

To calculate isoelectric point of microcapsules electrophoretic mobility of microcapsules is measured using micro electrophoresis apparatus. The mobility of microcapsules is related to surface charge, ionisable behaviour, and ion absorption nature of microcapsules.

k. In vitro drug release

It may be carried out in different pH conditions like pH 1.2 and pH 7.4 USP rotating basket and paddle apparatus. The sample should be taken out after particular time intervals and replaced with the same medium.
The drug release profile is determined by using the plot of the amount released function of time[86].

l. Porosity

This property depends upon composition of wall material of microcapsule and technique which is used to produce microcapsule. It controls the permeability of volatiles within the capsules and determines the oxidative stability of the core.
Porosity is determined by gas displacement pycnometer and electron microscopy.
Positron emission destruction life-long spectroscopy (PALS) is generally used in studying porous systems, mostly polymers.

m. Surface hydrophobicity

It is a physical property of molecules that are repelled by water. It is based on core material and wall material. In a study, it was found that globular proteins like whey and soy protein, were used as wall materials forms soluble aggregate through surface hydrophobic interaction after high pressure treatment. Hence, surface hydrophobicity is a very critical physical parameter which should be considered.

n. Solubility

Solubility evaluation of microcapsules is used to determine, whether the core material is released in the medium or not. It depends on the core material used for encapsulation.

o. Surface tension

Surface tension is the tendency of a fluid surface to behave as a stretched elastic membrane. The forces causing this are cohesive forces and interfacial forces. It is used to measure the quality of liquid. Surface tension is measured by drop tensiometers.

p. Hygroscopicity

It is the property of microcapsules, that when exposed to an environment with high relative humidity, tend to absorb moisture from the environment. It may affect on stability of microcapsules. This property of the microcapsules can be determined by using the sorption isotherms during storage. The Sorption isotherms of the microcapsules are determined by the gravimetric static method.

q. Mechanical properties

Microcapsules should be mechanically firm at the time of processing and storage. The mechanical properties of the microcapsules include elastic modulus, a rupturing force that is required to rupture the capsule. A study consists of Atomic Force Microscopy combined with Epifluorescence Microscopy was successfully used to determine the mechanical properties and release behaviour of fluorescently filled microcapsules.

r. Heat and light stability

The compounds like vitamins, pigments are sensitive to processes like pasteurization, sterilization, baking etc. Microencapsulation helps to protect or prevent degradation. There are many heat and light sensitive compounds. Microencapsulation increases heat and light stability of compounds[87],[88].

7. Some applications of microencapsulation: -

- It increases absorption and bioavailability of dietary phenolic compounds[89].
- Microencapsulation is used for cell and enzyme immobilization. It allows the reuse of enzymes and provides stability to enzymes[90].
- It increases shelf life of fatty acids and also maintains bioavailability of n-3PUFA (polyunsaturated fatty acids)[91].
- Microencapsulation enhances performance of probiotics during fermentation, downstream processing, and utilisation in commercial products[92].
- It is used for the production of beverages.
- It protects the liquid crystals.
- It has a major role in textiles.
- Microencapsulation in agriculture led to low wastage and greater safety for users as well as the environment.
- Void microspheres that are filled with deuterium in a gaseous phase used to control nuclear fusion.
- When various metals get encapsulated in polyurea, it shows recoverability and recycling benefits.
- Microencapsulation with polymeric system used for delivery of DNA vaccines which gives prolonged, immune response through sustained release of DNA encoding a protein antigen[93].

Conclusion:

As an important component of novel drug delivery systems microencapsulation plays a vital role. With microspheres and microcapsules, this technology allows for the creation of unique carriers. A wide variety of factors contribute to the success of microencapsulation. This microencapsulation can be made using various methods depending on what we need to accomplish from it. It is applicable in various fields such as pharmaceuticals, textiles, food technology, agriculture, etc.

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