ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com
Journal DOI: 10.21474/IJAR01

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

MICROENCAPSULATION AND ITS VARIOUS ASPECTS: A REVIEW.

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Manuscript Info

Manuscript History:

Received: 14 April 2016
Final Accepted: 19 May 2016
Published Online: June 2016

Key words:
Microencapsulation, Microcapsule, Core material, Coating material.

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Abstract

Microencapsulation is a well-established process of enveloping or surrounding one substance into another substance which gives capsules having range from less than one micron to several hundred microns in size. One of the highly efficient method is microencapsulation. The encapsulation efficiency of microcapsules, micro particles or microspheres rely upon various factors like solubility of polymer in solvent, concentration of polymer, solubility of organic solvent in water, rate of solvent removal etc. Substances can be encapsulated in such a way that the core material be confined within capsule shells (coating material) for particular interval of time. This technique has been used in different fields like pharmaceutical, agriculture, textile, food, printing and defence. In case of defence sector this technique has introduced the self-healing composites or chemical decontaminating fabrics. This article covers review on microencapsulation and materials involved, microencapsulation technologies, purposes of microencapsulation, morphology of microcapsules, methodology of microcapsules, release mechanism, application fields with microencapsulated additives in building construction materials.

Introduction:-

Microencapsulation is the process in which substance is enclosing in miniature known as capsule (Krishna et al., 2015). Microencapsulation provide coating of solid, liquid as well as gaseous material by forming a continues film of polymeric material. First research in this field was published by Bungen Berg De Jong and Kan in 1931 (Tiwari et al., 2011). It can help us to convert the liquids into solids, by changing the surface and colloidal properties (Mishra et al., 2013). Microencapsulation provides thin coating to tiny particles of solids or droplets of liquids and dispersions (Preet et al., 2013; Chanana et al., 2013). Microcapsules are spherical in shape having a uniform wall around it (Krishna et al., 2015).

In addition, encapsulation of highly water soluble drugs received much attention. These symptoms rely on polymers that vary with permeability, dissolution rate, degree of swelling or erodibility (Jadupati et al., 2012). It includes bio-encapsulation which can be used to improve the performance or increase its shelf life (Bansode et al., 2010; Agnihotri et al., 2012). Microcapsules provides a constant release of the drug in therapeutic quantity (Patel et al., 2012). It also protect the drug from photolytic or enzymatic cleavage, that's why this is the best method for drug delivery of protein (Tiwari et al., 2011). There are various techniques available to formulate microcapsules, amongst which solvent evaporation method is the best, because it neither requires elevated temperature nor phase separation inducing agent (Singh et al., 2014).

The inner material of microcapsule is referred to as internal phase, core phase or fill, whereas sometimes wall is called shell/coating (Krishna et al., 2015). A large number of core materials has been encapsulated like adhesives, agrochemicals, flavours, live cells and enzymes.

Diameter of microcapsules ranges between few micrometers and a few millimeters (Jadupati et al., 2012). These having size range below 1 micrometer are known as nano particles, nano capsules, nano spheres, particles with 3-800 micrometer diameter are called as micro particles, microcapsules or micro spheres, where 1000 micrometer particle size known as macro particles (Jyothi et al., 2010; Gunjan et al., 2012). The structural features of microcapsules are reveal by scanning electron microscopy (Sachan et al., 2006). Aggregated microcapsules vary in shape and size because of external additional wall (Mishra et al., 2013). Figure-1 shows structure of microcapsule.

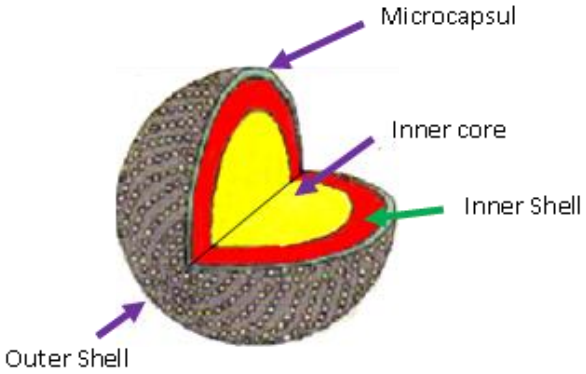

Figure 1:- Structure of microcapsule (Krishna et al., 2015).

Reasons for microencapsulation:-

- It is commonly used enhance the stability and provide release of product in a sustained/prolonged manner.
- This technique is mainly used for taste masking and to improve patient compliance as well as odour of various drugs (Krishna et al., 2015; Dubey et al., 2009).
- Reactive substances are protected from the environment by microencapsulation (Agnihotri et al., 2012; Patel et al., 2012).
- It is helpful to prevent incompatibility between drugs (Preet et al., 2013; Vnekatesan et al., 2009; Boh et al., 2008).
- Liquid drugs can be converted into free flowing powder (Krishna et al., 2015; Gunjan et al., 2012).
- Those drugs, which are vaporize at room temperature or are volatile in nature, can be protected by microencapsulation (Mishra et al., 2013; Venkatesan et al., 2009).
- The rate of drug release can be controlled by formulating microcapsules (Krishna et al., 2015; Umer et al., 2011).
- Alteration in site absorption is also achieve by this technique (Agnihotri et al., 2012; Patel et al., 2012).
- Reduce the side effects of drugs like toxicity or GI irritation (Krishna et al., 2015; Gunjan et al., 2012).
- Moisture, light and oxygen sensitive drugs can be protected by microencapsulation (Mishra et al., 2013; Dubey et al., 2009).

Classification:-

Microcapsules can be classified into three categories;

1. Mononuclear/Single core.
2. Poly nuclear/Multiple core.
3. Matrix type.

Mononuclear type microcapsules contain shell around the core, which poly nuclear having many cores enclosed in the shell. In case of matrix, the core material homogeneously distributed into shell material (Jadupati et al., 2012; Umer et al., 2011).

Due to the presence of additional external wall aggregated microcapsules vary in size and shape. Microstructures of both membrane are also detected by SEM. Figure-2 shows varous type of microcapsule.

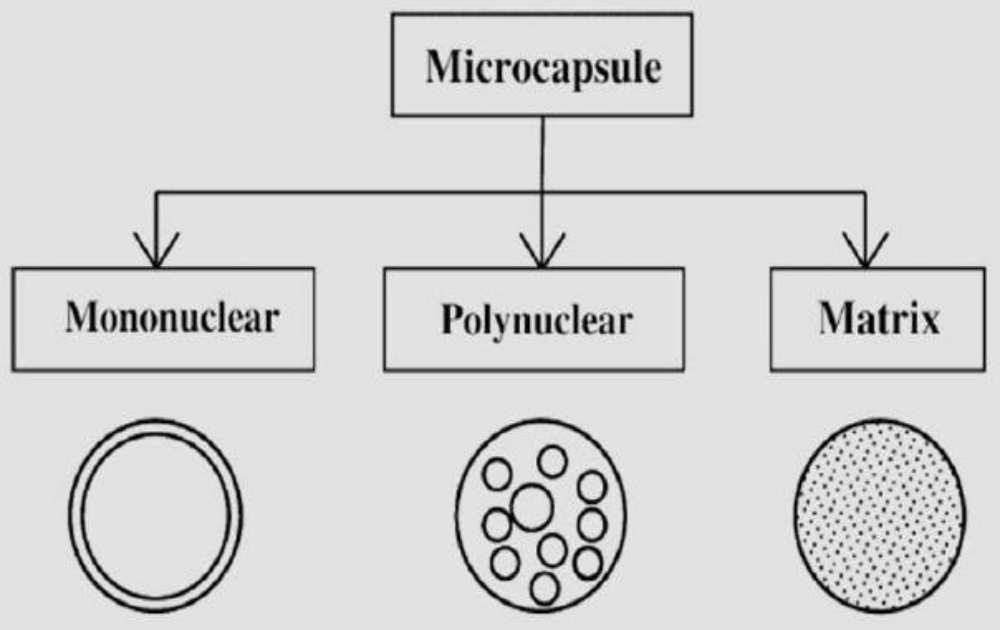

Figure 2:- Types of microcapsules (Preet et al., 2013)

Factors influencing properties of microcapsules:-

Material properties:-

Dispersed phase:-

The polymer used plays a vital role for drug encapsulation which further depends upon-

- Solubility of polymer.
- Concentration of polymer.
- The organic solvent used.
- Solvent removal rate.
- Dispersed and continues phase ratio.
- Nature of drug hydrophilic/hydrophobic.

The encapsulation efficiency micro particle, microcapsule as well as micro sphere is affected by various parameters.

With the increase in concentration of polymer, there will be rise in encapsulation in efficiency of drug and if the disperse phase is too viscous it reduces microcapsules porosity thus sustained the drug release (Krishna et al., 2015).

The rate of solidification of microcapsules rely upon dispersed and continues phase ratio. If the continues phase is large it reveals a high concentration gradient of organic solvent along the boundary phase by diluting the solvent, which gives us fast microcapsules upon solidification. Due to this, the particle size of microcapsules is affected. Thus, enhancement in the volume of continues phase results in increase of the particle size.

The rate of solvent removal is always depend upon temperature, a rapid rise in the temperature results in the formation of thin walled microcapsules. Also enhancement of temperature reduces the size of the core loading to controlled drug release.

Cloud point is defined as the temperature at the onset of cloudiness, the temperature at the inflection point of the transmittance curve, or the temperature at a defined transmittance (e.g., 50%) (Aseyev et al., 2010).The polymer solubility depends on the cloud point (Cs) of organic solvent, higher cloud point of organic solvent results higher solubility of polymer.

Factprs influencing encapsulation efficiency:-

The encapsulation efficiency of micro particles, microcapsule as well as microsphere is affected by various parameters. Figure-3 depicts different factors effecting encapsulation efficiency.

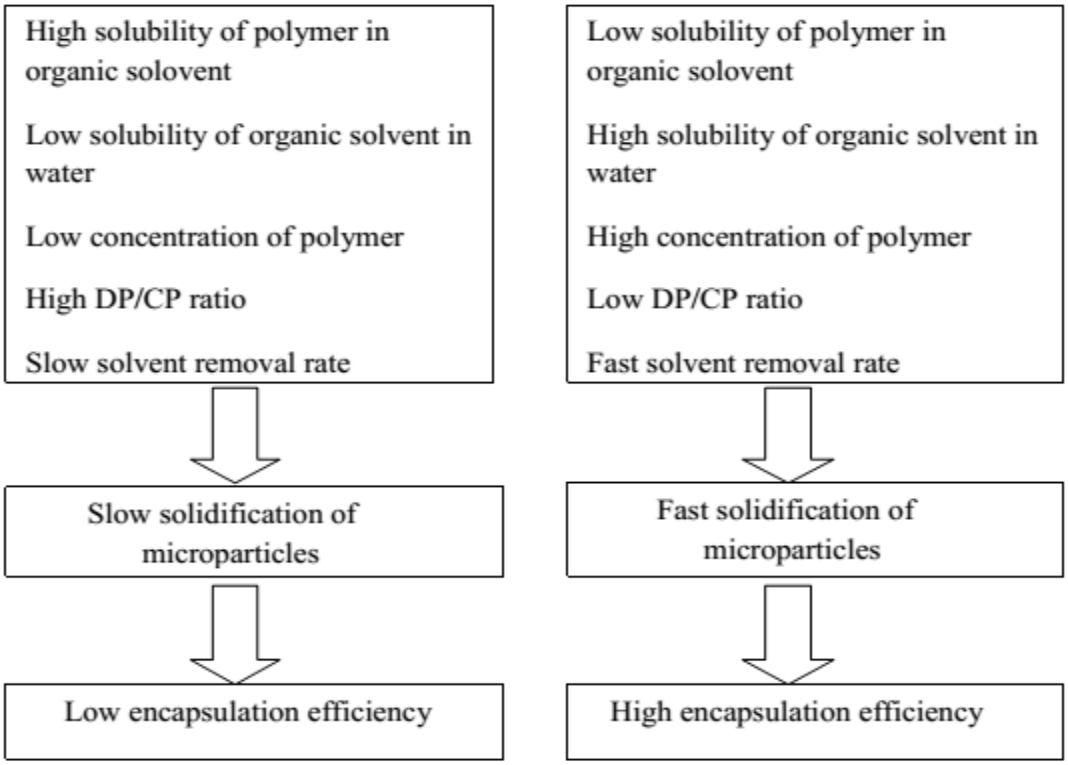

Figure 3-Factors influencing encapsulation efficiency (Jyothi et al., 2010)

- Viscosity of dispersed phase.
- Volume fraction of both dispersed to continues phase.
- Drug quantity in dispersed phase.
- Surfactant concentration.
- Operating parameters.
- Agitation rate/time.
- Temperature.
- Pressure.
- -Geometry of agitator and reactor.

Materials used for microencapsulation:-

Core material:-

It is defined as material to be coated . The liquid core include dissolved materials whereas the solid core belongs to active ingredients, excipients, stabilizers, release rate retardants or diluents (Krishna et al., 2015; Bansode et al., 2010). The core material provides flexibility and allows effective design and development of microcapsules (Mishra et al., 2013; Agnihotri et al., 2012).

Coating material:-

It can be defined as layer of substance which forms a cover over core for production of microcapsules. Desired properties for coating material;

- It should be soluble in aqueous media/solvent and also provide controlled release under specific conditions.
- It should have properties like flexibility, strength, stability, impermeability and optical properties (Krishna et al., 2015; Sri et al., 2012).
- It should be chemical compatible.
- It should have capability to forming a film.
- It should be pilable, tasteless, stable, non hygroscopic, economic and should not have high viscosity (Jadupati et al., 2012; Bansode et al., 2010).

Various coating masterials used in microencapsulation classified as:-

1. Vegetable gums- Gum arabica, agar, carrageenam, dextran sulphate and sodium alginate.
2. Celluloses- Cellulose acetate phthalate, ethyl cellulose, nitrocellulose, cellulose acetate butyrate phthalate, carboxy methyl cellulose (Sri et al., 2012; Poshadri et al., 2010).
3. Homo polymer-Polyvinyl acetate, polystyrene, polyethylene, polyvinyl alcohol, polyvinyl chloride.
4. Copolymer-Acrylic acid copolymers, methacrylic acid co polymers, maleic anhydride polymers.
5. Curable polymers-Nitrated poly styrene, epoxy resins, nitro paraffin (Sachan et al., 2006).
6. Condensation polymers-Poly carbonate, amino resins, nylon, teflon, silicone resins, poly methane.
7. Proteins-Fibrinogen,hemoglobin,collagen,cassein,gelatin,polyaminoacids.
8. Waxes; Paraffin, bees wax, oil, fats, rosin shellac mono glyceride, tristerium (Jadupati et al., 2012; Agnihotri., 2012).

Differnt techniques of microencapsulation:-

Air suspension method:-

This method involves the spraying of coating material in the air and suspending particles and dispersion of core material in air stream. The moving air suspend the particles within the coating chamber. The coating chamber is designed in a specific way that affect the particle flow through coating zone of chamber, where polymer solution coating material is applied to the moving particles (Agnihotri et al., 2012). This cyclic process is repeated several times depending upon the required thickness on the core material. The encapsulated product is air dried. Drying rate is directly proportional to temperature. The various process variables which affect the process are melting point, solubility, surface area, density, melting point, application rate of coating material (Mishra et al., 2013). Table(1) shows formulations prepared by using air suspension method.

Coacervation method:-

It is the method in which core material is dispersed in the solution of coating material. The core material cannot dissolve or react with coating material (Mishra et al.,2013). The particle size rely upon dispersion parameters such as stirrer shape, viscosity, stirrer speed, surface tension. Range of particle size is in between 2 micrometer to 1200 micrometer (Tiwari et al., 2010).

Coacervation phase separation-This technique comprises of three steps:-

Formation of three immiscible phases:-

Three phases involves liquid manufacturing vehicle phase, core material phase, coating material phase. In this, the core material is disperse in solution of coating polymer, the vehicle phase used as solvent for polymer (Tiwari et al., 2010). The microcapsules are formed by one of the methods of phase separation-coacervation i.e by change the temperature of polymer solution or by addition of salt, non solvent, incompatible polymer addition or by polymer polymer attraction (Jadupati et al., 2012; Aulten et al., 2002).

Deposition of the coating:-

In second step depositing the liquid polymer on the core material by controlled mixing of coating material and core material in manufacturing vehicle (Remington et al., 2000). If the polymer absorbed at the interface formed between the core material and liquid phase then coating polymer is deposited on the core material. The deposition of coating material is promoted by deduction in total free energy of system (Mishra et al., 2013).

Rigidization of coating:-

It involves rigidiaztion of coating done by thermal, cross linking or dissolvation techniques, to form a self sustaining microcapsules (Lechman et al., 2009). Table(2) shows formulations prepared by using coacervation method.

Centrifugal extrusion:-

By using rotating extrusion head containing concentric nozzels, 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 droplets of core, each one coated with the wall solution (Jadupati et al., 2012). 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 upto 22.5kg (50lb) of microcapsules can be produced per nozzel per hour per head (Mishra et al., 2013). Table(3) shows formulations prepared by using centrifugal extrusion.

Spray drying and spray congealing:-

These processes are similar in that both involve dispersing the core material into the liquified coating substance and spraying or introducing into core coating mixture, whereby rapid solidification of coating is affected. The basic difference in these two methods is the means by which coating solidification is accomplished. In case of spray drying the coating solidification affected by rapid evaporation of solvent in which coating material is dissolved whereas in case of spray congealing method the coating solidification is accomplished by thermally congealing a molten coating material or by introducing the core material into a non solvent. Removal of non solvent or solvent from the coated product can be done by sorption extraction or evaporation techniques (Preet et al., 2013). Few examples of food ingredients which can be microencapsulated by spray drying are encapsulation of flavors, lipids and cartenoids. A single encapsulating agent cannot hold all ideal wall material properties, now researches focused on gums, proteins as well as carbohydrates (Gharsallaovi et al., 2007). One of the most important step in case of spray drying is the selection of atomiser which put significant effect on size of distribution of final formulation having dried particles (Reo et al., 2007). Table(4) shows formulations prepared by using spray drying and spray congealing.

Pan coating:-

The pan coating method becomes widespread in pharmaceutical industry. Solid particles greater than 600 microns in size are considered for effective coating and process have been employed for controlled release preparation(Preet et al., 2013). Medicaments are coated on various spherical substrates such as nonpareil sugar seeds with various polymers. Generally, the coating can be applied as a solution, or as atomized spray to desired solid core material in coating pan. Coating solvent is removed by passing warm air over coated material (Gunjan et al., 2012; Lechman et al., 2009). Table(5) shows formulations prepared by using pan coating.

Solvent evaporation technique:-

These techniques can be done into liquid manufacturing vehicle (o/w) emulsion which can be formed by agitation of two immiscible liquids. In this process microcapsule coating polymer can be dissolved in volatile solvent, which have an immiscible property with liquid manufacturing vehicle phase. 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 (Venkatsan et al., 2009). The agitation continues till solvent partitions into aqueous phase and aqueous phase is removed by evaporation. Several process variable which affect the process of microencapsulation include method of forming dispersions, evaporation rate of solvent, temperature cycles and agitation rates. Choice of vehicle phase and solvent for polymer coating are the two important factors to be considered for preparing microcapsules by solvent evaporation technique. Water soluble and water insoluble materials can be used as core materials (Jadupati et al., 2012; Lechman et al., 2009). Table(6) shows formulations prepared by using solvent evaporation technique.

Solvent evaporation method has following advantages (Bhogataj et al., 1991; Yuksel et al., 1997; Satturwar et al., 2002; Kim et al., 2002; Anand et al., 2007; Khamanga et al., 2009).

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

Polymerisation:-

Interfacial polymer:-

In this, the two reactants in poly condensation meet at an interface and react rapidly. The basic of this method involves the classical schotten bauman reaction between compound containing acid hydrogen atom and acid chloride, such as amine, polyesters, alcohol, poly urea, polyurethane (Agnihotri et al., 2012). Under the desired conditions thin walls formed rapidly at interface. The solution of pesticide and di-acid chloride get emulsified in water and on aqueous solution containing amine as poly functional isocyanate is added. During the reaction the acid formation can be controlled by the base. Condensed polymer walls rapidly form at interface of the emulsion droplets(Boh et al., 2008).

In-situ polymerization:-

Few microencapsulation processes involving the direct polymerization of a monomer can be carried out on the particle surface. In one process, e.g-cellulose fibers get encapsulated in polyethylene while immersed in dry toluene.

Deposition rates are about 0.5 micrometer/minute. Coating thickness ranges upto0.2-75 micrometer. Over sharp projections coating is uniform (Jadupati et al., 2012; Dubey et al., 2009).

Matrix polymer:-
Mostly the processes involves, a core material imbedded in polymeric matrix. One of the method of this type is spray drying, in which the formation of particle can be done by evaporation of solvent from the matrix material. By chemical change, the solidification of matrix takes place. Table(7) shows formulations prepared by using polymerisation.

Release mechanisms:-

Release mechanisms of drug from microcapsules are:-

Degradation controlled monolithic system:-
The drug is distributed throughout dissolved in matrix. The drug is tightly attached to matrix and can be released on degradation of the matrix. As compared with degradation of the matrix, the diffusion of dug is slow (Shekhar et al., 2010; Jadupati et al., 2012; Patel et al., 2012).

Diffusion:-
It is the most general mechanism in which the dissolution fluid penetrates the shell, dissolves the core and leak through the interstitial channels or pores. Thus, release rely upon (1) the rate at which dissolution fluid penetrates the wall of microcapsules (2) the rate at which drug dissolves in the dissolution fluid (3) the rate at which the dissolved drug disperse from the surface. The kinetics of such drug release obeys higuchi's equation as below (Jadupati et al., 2012; Sachan et al., 2006)

$$Q = [D/J\,(2A - \varepsilon\, CS)\, CS\, t]^{1/2}$$

Q=The amount of drug released per unit area of exposed surface in time 't'.
D=The diffusion coefficient of solute in solution.
A=Total amount of drug per unit volume.
Cs=Solubility of the drug in penetrating dissolution fluid.
ε =The porosity of the wall of microcapsule.
J=The torotuosity of the capillary system in the wall.

Diffusion controlled monolithic system:-
The active agent can be released by diffusion or due to degradation of polymer matrix. Release rate also rely upon where the polymer degrades by homogeneous or heterogeneous mechanism (Gunjan et al., 2012; Umer et al., 2011).

Diffusion controlled reservoir system:-
The active agent is encapsulated in a rate controlling membrane through which the agent diffuses and the membrane erodes only after delivery is completed. In this, release rate can't rely upon degradation of matrix (Agnihotri et al., 2012).

Osmosis:-
The polymer coat acts as a semi permeable membrane and allows formation of an osmotic pressure difference between the inner and outer side of microcapsule and this pressure drives drug solution through small pores in the coat (Patel et al., 2012).

Erosion:-
Erosion of coat occurs due to ph and enzymatic hydrolyses which cause drug release with coat material like glyceryl, mono stearate, beeswax and stearyl alcohol etc (Gunjan et al., 2012; Umer et al., 2011).

Based on different studies concerning the release characteristics;

1. Release rate of drug from microcapsules confining to reservoir type is of zero order.
2. Microcapsules of monolithic type or containing dissolved drug have t1/2 dependent release rates during first half of total drug release and then the drug release rate declines exponentially.
3. If monolithic type microcapsules contains dissolved drug in excess, the release rate is t1/2 dependent throughout the entire drug release.

The path travelled by drug which is monolithic type is not constant, drug at centre travels a large distance as compare than drug at surface. That's why, the rate of release generally decline with time (Shekhar et al., 2010).

Characterization of microcapsules:-

Particle size and shape:-

The most commonly used method to visualize microcapsule is conventional light microscopy, scanning electron microscopy (SEM). These both techniques are used to analyze the shape and structure of microcapsule. SEM provides high resolution as compared with light microscopy. It investigates the microsphere surfaces also allows the investigation of double walled systems. Confocal laser scanning microscopy (CLSM) is referred to as non destructive visualization technique, which gives result not only about structures as well as surface, but also reveals about inside particle (Preet et al., 2013).

Fourier transform-infrared spectroscopy (FTIR):-

It is used to analyze the degradation of polymeric matrix of carrier system, and also check interaction between polymer and drug system.

Carr's index and hausner's ratio:-

The angle of repose was determined according to fixed funnel and cone method. The bulk density of mixed microcapsules was calculated by determining the hausner's ratio or carr's index, with the help of poured or trapped bulk densities of known weight of sample using measuring cylinder (Hausner, 1967; Carr, 1965).

Carr's Index = [Tapped Density-Bulk Density/Tapped Density] ×100
Hausner's ratio (HR)=ρT/ρB where ρT is tapped density and ρB is bulk density (Mishra et al., 2013)

Bulk density:-

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

Bulk Density (ρρ)= [Weight of Microcapsules(g) (M) / Bulk Volume (ml)(V)]
where, M = mass of the powder,
Vo = volume of the powder

Isoelectric point:-

The micro electrophoresis is an apparatus which is used to measure electrophoretic mobility of microsphere by which isoelectric point can easily be calculated. The mobility is related with surface contained charge, ionisable behaviour or ion absorption nature of microcapsules (Preet et al., 2013).

Determination of drug loading, encapsulation efficiency and microcapsule yield:-

The drug content was determined by extraction of 20mg sample of microcapsules with methanol . Following filtration and dilution with methanol, the resultant concentration was checked by UV spectrophotometry.
%loading = weight of drug/weight of microcapsules
%Encapsulation efficiency= [%Actual drug content/%theoretical drug content] ×100
%Yield=M/ M0 ×100
M = Weight of microcapsules
M0 = Total expected weight of drug and polymer (Mishra et al., 2013; Agnihotri et al., 2012).

Contact angle:-

The angle of contact is calculated to determine the wetting property of microcapsule. 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 a droplet in circular cell mounted above the objective of inverted microscope. It is measured at 200c within a minute of decomposition of microcapsules (Preet et al., 2013).

In vitro drug release studies:-

It can be carried out in various ph conditions like ph 1.2 and ph 7.4 using USP rotating basket and paddle apparatus. The sample should be taken out after particular time intervals and is replaced by same medium. The release profile is determine using the plot of amount released function of time (Preet et al., 2013).

Advantages:-

- Microcapsules received much attention not only for controlled release but also for targeting of anticancer drugs to the tumour (Patel et al., 2012; Umer et al., 2011).
- Studies on macrophage uptake of the microcapsules have demonstrated their potential in targeting drugs to pathogens residing intracellularly.
- Microorganism and enzyme immobilization.
  - Enzymes encapsulated in cheeses to accelerate ripening and flavor development (Preet et al., 2013).
  - The microorganism encapsulation has been used to improve stability of starter cultures (Chanana et al., 2013; Sachan et al., 2006).
- Improve texture, processing and less wastage, control hygroscopy, enhance flow ability as well as solubility (Preet et al., 2013; Agnihotri et al., 2012).
- To deliver the drug to the target site with specificity, if modified and to maintain the desired concentration at the site of interest without untoward effects (Sachan et al., 2006).
- Microencapsulation could deliver the needed ingredients in children in terms of a tasty way by taste masking.
- Protection from u.v, heat, oxidation, acids, or bases (Preet et al., 2013).
- The size, surface charge, hydrophilicity of microcapsules have been found important in calculating the fate of particles in vivo .
- Masking the taste or odours.
- Solid biodegradable microcapsules have potential throughout the particle matrix for the controlled release of drug.
- Improve shelf life property due to preventing degradative reactions like dehydration or oxidation .

Table 1:- Formulations by air suspension method.

Sr. no	Drug	Polymer	Method	Purpose	Reference
1)	Ibuprofen	Ethyl cellulose	Air suspension method	MDTs By Pellets	Hossein Sedighikamal et al., 2015
2)	Carbamazepine	Eudragit RSPO Eudragit S100	Air suspension method	Controlled release tablets	Tehrani et al., 2000
3)	Salbutamol	Eudragit RS 30 D	Air suspension method	Controlled release pellet preparation	Govender et al., 1997
4)	Chlorpheniramine	Eudragit NE 30 D	Air suspension method	Controlled release by microcapsules	Mathir et al., 1997

Table 2:- Formulations by coaservation technique.

Sr.no	Drug	Polymer	Method	Purpose	Reference
1)	Mirtazapine	EE100	Coaservation phase separation	Taste masking ODTs	Simay et al., 2015
2)	Metronidazole	Eudragit RS 30D	Coaservation	Microspheres	Irin Dewan et
3)	Lamivudine	Gelatin	Coaservation phase separation	Microspheres	Pyneedi et al., 2014
4)	Hydroxyzine HCL	Ethyl cellulose	Coaservation phase separation	Microspheres	Christianne et al., 2013
5)	Bacillus coagulans	Hypromellose	Coaservation phase separation	Mucoadhesive microspheres	Alli et al., 2011
6)	Nitrofurantoin	Eudragit RS100 Eudragit RL 100	Coaservation phase separation	Micropellets	Baidya et al., 1999

Table 3:- Formulations by extrusion spheronisation method.

Sr.no	Drug	Polymer	Method	Purpose	Reference
1)	Glimepiride	Polyacrylamide grafted guar gum	Extrusion spheronization method	Pellets	Gowrav et a., 2015
2)	Omeprazole	Microcrystalline cellulose PVP K 30 PEG 6000 Sodium Lauryl Sulphate	Extrusion spheronization method	Pellets	Sabiha et al., 2014
3)	Ibuprofen	Eudragit RS Avicel	Extrusion spheronization method	Pellets	Garekani et al., 2013
4)	Metformin HCL	Aquacoat WG Avicel 955 MCC	Electro co-extrusion	Pellets	Gouldson et al., 1997

Table 4:- Formulations by spray drying and congealing.

Sr.no	Drug	Polymer	Method	Purpose	Reference
1)	Prednisolone	Eudragit EPO Eudragit E100	Spray drying	Taste masking microparticles	Witold et al., 2015
2)	Etravirine	Soluplus	Spray drying	Solubility	Ramesh et al., 2015
3)	Ranitidine	Alginate	Spray drying	Prolonged releaase microspheres	Marta et al., 2015
4)	Prochlorperazine	Chitosan	Spray drying	Mucoadhesive microspheres	Shah et al., 2015
5)	Metronidazole	Sodium alginate	Spray drying	Microspheres	Szekalska et al., 2015
6)	Chlorthalidone	Eudragit L 30 D-55 Opadry Kollicoat	Spray drying	Microcapsules	Marcoet al., 2015
7)	Carboplatin	Gelatin	Spray drying	Microspheres	Harsha et al., 2014
8)	Ganciclovir	Gelatin	Spray drying	Microspheres	Tuanhilp et al., 2014
9)	Isoflavon	Gelatin	Spray drying	Microspheres	Pannizon et al., 2014
10)	Vanomycin	PLGA	Spray drying	Microspheres	Elisabetta et al., 2004

Table 5:- Formulations by pan coating.

Sr.no	Drug	Polymer	Method	Purpose	Reference
1)	Matoprolol tartrate	Methocel K 100 HPMC 15.000 Eudragit NE 30D	Pan coating	Modified release pellets	Todoran et al., 2014
2)	Ketoprofen	Ethyl cellulose	Pan coating	Pellets	Subhabrota et al., 2011
3)	Methylene blue	PVP	Pan coating	Microcapsules	Deasy et al., 2011
4)	Phenylpropanolamine HCL	Polivinyl acetate copolymer	Pan coating	Microcapsules	Hamed et al., 1992

Table 6:- Formulations by solvent evaporation method.

Sr.no	Drug	Polymer	Method	Purpose	Reference
1)	Dexamethason	PLGA (5050) (25KDa) PLGA (9010) (113KDa)	Solvent evaporation method	Microspheres for minimize burst release	Bing GU et al., 2015
2)	Theophylline	Eudragit S100	Solvent diffusionmethod	Microspheres GRTs	Kedar et al., 2015
3)	Quercitine dihydrate	Eudragit S100	Solvent evaporation method	Mucoadhesive microspheres	RC Jat et al., 2015
4)	Captopril	Carbopol 934 HPMC	Solvent evaporation method	Gastroretentive mucoadhesive formulation	Usrete et al., 2015
5)	5-Fluorouracil	PEG	Solvent evaporation method	Microspheres	Ganguly et al., 2015
6)	Leflunomide	PLA PLC HPMC	Solvent evaporation method	Microspheres	Setoughy et al., 2015
7)	Zidovudine	EC Eudragit RS 100 Methocel k4M Methocel k15M	Solvent evaporation method	Microspheres	Tania et al., 2015
8)	Famotidine	Eudragit S 100	Solvent evaporation method	Floating microspheres	Rishikesh et al., 2014
9)	Nifedipine	Ethyl cellulose	Solvent evaporation method	Microspheres sustained release	Patitapabana et al., 2014
10)	Acetazolamide	Eudragit RS 100	Solvent evaporation method	Microspheres	Marwah et al., 2014
11)	Cefpodoxime proxetil	Ethyl cellulose HPMC	Solvent evaporation method	Microspheres	Dedania et al., 2014
12)	Aceclofenac	Eudrgit RS 100 Eudragit RL 100 HPMC K 100M	Solvent evaporation method	Microspheres	Irin Dewan et al., 2014
13)	Ondansetron hydrochloride	Eudragit E 100	Solvent evaporation method	Taste masked microspheres	Vandana et al., 2014
14)	Didanosine	Ethyl cellulose Cellulose acetate phthalate	Solvent evaporation method	Microspheres	Sethi et al., 2013
15)	Metformin hydrochloride	Dillenia indica Abelmoschus esculentus	Solvent diffudion technique	Controlled release microspheres	Hemanta et al., 2013

Table 7:- Formulations by polymerisation.

Sr.no	Drug	Polymer	Method	Purpose	Reference
1)	Cyhalothrin	Silica N isopropyl Acrylamide Bis acrylamide	Radicle polymerisation	Microcapsules	Yong XU et al., 2015
2)	N- heptadecane	Polystyrene	Emulsion polymerisation	Microcapsules	Ahmet Sari et al., 2014
3)	Tramadole	Ethylene glycol dimethacrylate	Precipitation polymerisation	Micro-Nano particles	Seifi M et al., 2014
4)	Doxorubicin	Chitoson	Emulsion polymerisation	Co-encapsulation	Duan et al., 2012
5)	Ketoprofen	N-[tris(hydroxymethyl)methyl] acrylamide gelatin	Inverse suspension polymerisation	Microspheres	Zhou C et al., 2012
6)	Levofloxacin Peflofloxacin	Gelatin	Emulsion polymerisation	Micro-nano particles	Madan J et al., 2010
7)	5-Fluorouracil	Guar gum	Emulsion polymerisation	Microspheres	Kaushik et al., 2009
8)	Di ammonium hydrogen phosphate	Polyurethane urea	Interfacial polymerisation	Microcapsules	Saihi et al., 2006

Conclusion and future trends:-

The research goes widespread in the area of microencapsulation which has huge potential to provide raw material advantages traits resulting in superior products. The most widely used is solvent extraction/evaporation based technique using beaker/stirrer for production of large amount of microcapsule in an economic or well controlled manner (Freitas et al., 2005). Microencapsulation is the most agreeable way of protection and masking, reduce rate of dissolution, facilitation of handling and spatial targeting of active ingredient (Li et al., 2008; Sachan et., 2006). This technique is also beneficial for those drugs which dissolves into intestine not in the stomach. This technology provides simple immobilization or entrapment to sophisticated and precise microcapsule formation (Li et al., 2008). This field also goes vast in nutraceuticals, food ingredients as well as live probiotic bacterial cells. The delivery of viable microencapsulated probiotic bacterial will become more importance in future. In future trend of microcapsules, multiple delivery may be developed like co-encapsulating prebiotics and probiotics as well as nutraceuticals. In the field of food processing industry storage, preservation and microencapsulation play vital role to protect viability and enhance the survival of bacteria for adverse environmental conditions (Mishra et al., 2013; Preet et al., 2013).

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