MICROENCAPSULATION : A REVIEW

S. S. Bansode*, S. K. Banarjee, D. D. Gaikwad, S. L. Jadhav, R. M. Thorat
Vishal Institute of Pharmaceutical Education and Research, Ale, Pune-412411.
*E-mail : rupali.78@rediffmail.com

ABSTRACT

The review of Microencapsulation is a well-established dedicated to the preparation, properties and uses of individually encapsulated novel small particles, as well as significant improvements to tried-and-tested techniques relevant to micro and nano particles and their use in a wide variety of industrial, engineering, pharmaceutical, biotechnology and research applications. Its scope extends beyond conventional microcapsules to all other small particulate systems such as self assembling structures that involve preparative manipulation. The review covers encapsulation materials, physics of release through the capsule wall and / or desorption from carrier, techniques of preparation, many uses to which microcapsules are put.

Key-words: Microencapsulation, Core Materials, Coating Materials.

INTRODUCTION

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

Microencapsulation includes Bioencapsulation which is more restricted to the entrapment of a biologically active substance (from DNA to entire cell or group of cells for example) generally to improve its performance &/or enhance its shelf life[1].

Microencapsulation provides the means of converting liquids to solids, of altering colloidal and surface properties, of providing environmental protection and of controlling the release characteristics or availability of coated materials. Several of these properties can be attained by macropackaging techniques; however, the uniqueness of microencapsulation is the smallness of the coated particles and their subsequent use and adaptation to a wide variety of dosage forms and not has been technically feasible[2].

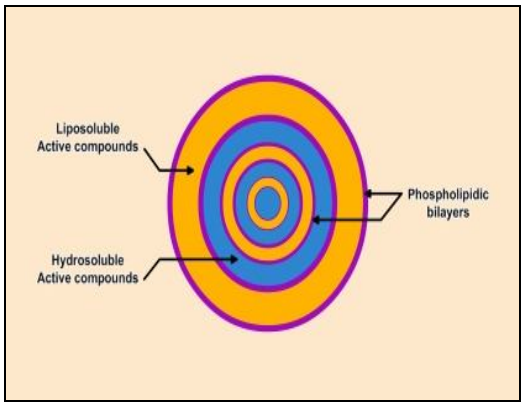

Figure 1: Microencapsulation process

REASONS FOR MICROENCAPSULATION

- The primary reason for microencapsulation is found to be either for sustained or prolonged drug release.
- This technique has been widely used for masking taste and odor of many drugs to improve patient compliance.
- This technique can be used for converting liquid drugs in a free flowing powder.
- The drugs, which are sensitive to oxygen, moisture or light, can be stabilized by microencapsulation.
- Incompatibility among the drugs can be prevented by microencapsulation.
- Vaporization of many volatile drugs e.g. methyl salicylate and peppermint oil can be prevented by microencapsulation.
- Many drugs have been microencapsulated to reduce toxicity and GI irritation including ferrous sulphate and KCl.
- Alteration in site of absorption can also be achieved by microencapsulation.
- Toxic chemicals such as insecticides may be microencapsulated to reduce the possibility of sensitization of factorial person.
- Bakan and Anderson reported that microencapsulated vitamin A palmitate had enhanced stability[3].

RELEASE MECHANISMS

Mechanisms of drug release from microspheres are

1. Degradation controlled monolithic system : -

The drug is dissolved in matrix and is distributed uniformly throughout. The drug is strongly attached to the matrix and is released on degradation of the matrix. The diffusion of the drug is slow as compared with degradation of the matrix.

2. Diffusion controlled monolithic system : -

Here the active agent is released by diffusion prior to or concurrent with the degradation of the polymer matrix. Rate of release also depend upon where the polymer degrades by homogeneous or heterogeneous mechanism.

3. Diffusion controlled reservoir system : -

Here the active agent is encapsulated by a rate controlling membrane through which the agent diffuses and the

membrane erodes only after its delivery is completed. In this case, drug release is unaffected by the degradation of the matrix.

4. Erosion : -

Erosion of the coat due to pH and enzymatic hydrolysis causes drug release with certain coat material like glyceryl mono stearate, beeswax and steryl alcohol etc[3].

CORE MATERIALS

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 the liquid core can include dispersed and/or dissolved materials. The solid core be active constituents, stabilizers, diluents, excipients, and release-rate retardants or accelerators. The ability to vary the core material composition provides definite flexibility and utilization of this characteristics often allows effectual design and development of the desired microcapsule properties [2].

COATING MATERIALS

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.

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.
3. The coating substrate of core material may have a decisive effect on coating properties. Hence, the selection of a particular coating material involves consideration of both classic free-film data and applied results.

COATING MATERIAL PROPERTIES

1. Stabilization of core material.
2. Inert toward active ingredients.
3. Controlled release under specific conditions.
4. Film-forming, pliable, tasteless, stable.
5. Non-hygroscopic, no high viscosity, economical.
6. Soluble in an aqueous media or solvent, or melting.
7. The coating can be flexible, brittle, hard, thin etc.

Examples of coating materials:

1. Water soluble resins – Gelatin, Gum Arabic, Starch, Polyvinylpyrrolidone, Carboxymethylcellulose, Hydroxyethylcellulose, Methylcellulose, Arabinogalactan, Polyvinyl alcohol, Polyacrylic acid.

2. Water insoluble resins – Ethylcellulose, Polyethylene, Polymethacrylate, Polyamide (Nylon), Poly (Ethylene-Vinyl acetate), Cellulose nitrate, Silicones, Poly(lactide-co-glycolide).

3. Waxes and lipids – Paraffin, Carnauba, Spermaceti, Beeswax, Stearic acid, Stearyl alcohol, Glyceryl stearates .

4. Enteric resins – Shellac, Cellulose acetate phthalate, Zein[2].

TECHNIQUES TO MANUFACTURE MICROCAPSULES

1. Physical methods

1.1 Air-suspension coating

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 of holes inside and outside a cylindrical insert. Just sufficient air is permitted to rise through the outer annular space to fluidize the settling particles. Most of the rising air (usually heated) flows inside the cylinder, causing the particles to rise rapidly. At the top, as the air stream diverges and slows, they settle back onto the outer bed and move downward to repeat the cycle. The particles pass through the inner cylinder many times in a few minutes methods.

The air suspension process offers a wide variety of coating materials candidates for microencapsulation. The process has the capability of applying coatings in the form of solvent solutions, aqueous solution, emulsions, dispersions or hot melts in equipment ranging in capacities from one pound to 990 pounds. Core materials comprised of micron or submicron particles can be effectively encapsulated by air suspension techniques, but agglomeration of the particles to some larger size is normally achieved [4].

1.2 Coacervation Process

Solution of the shell material in water.

Example: Copolymer coating

Gum arabic solution 20-30%

Gelatin solution 20%

Preparation

The core material will be added to the solution. The core material should not react or dissolve in water (maximum solubility 2%)

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

Coacervation

• Coacervation starts with a change of the pH value of the dispersion, e.g. by adding H_2SO_4, 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 hardening phase

• 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.

Drying phase

• The suspension is dried in a spray dryer or in a fluidized bed drier.

• Spray Drying is a suitable method for heat sensitive Products.

• The atomized particles assume a spherical shape. The rapid the coating material keeps the core material below 100°C, even if the temperature in the drying chamber is much greater.

• Microencapsulation makes the spray drying process easier for sticky products like fruit pulp or juice, with a high content of invert sugar[5.]

Coacervation-Phase Separation

The general outline of the processes consists of three steps carried out under continuous agitation:

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, nonsolvent, or incompatible polymer to the polymer solution; or by inducing a polymer-polymer interaction.
2. Deposition of the coating – It 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 if the liquid polymer coating around the core material occurs if the polymer is adsorbed at the interface formed between the core material and the liquid vehicle phase, and this adsorption phenomenon is a prerequisite to effective coating. The continued deposition of the coating material is promoted by a reduction in the total free interfacial energy of the system, brought about by the decrease of the coating material surface area during coleasance of the liquid polymer droplets.
3. Rigidization of the coating – It involves rigidizing the coating, usually by thermal, cross-linking, or desolvation techniques, to form a self-sustaining microcapsules [2]

eg. Coacervation Microencapsulation of Talc Particles with Poly (methyl methacrylate) by Pressure-Induced Phase Separation of CO_2-Expanded Ethanol Solutions[6.]

1.3 Centrifugal extrusion

Liquids are encapsulated using a rotating extrusion head containing concentric nozzles. In this process, a jet of core liquid is surrounded by a sheath of wall solution or melt. As the jet moves through the air it breaks, owing to Rayleigh instability, into droplets of core, each coated with the wall solution. While the droplets are in flight, a molten wall may be hardened or a solvent may be evaporated from the wall solution. Since most of the droplets are within ± 10% of the mean diameter, they land in a narrow ring around the spray nozzle. Hence, if needed, the capsules can be hardened after formation by catching them in a ring-shaped hardening bath. This process is excellent for forming particles 400–2,000 µm (16–79 mils) in diameter. Since the drops are formed by the breakup of a liquid jet, the process is only suitable for liquid or slurry. A high production rate can be achieved, i.e., up to 22.5 kg (50 lb) of microcapsules can be produced per nozzle per hour per head. Heads containing 16 nozzles are available[4.]

1.4 Pan coating

The pan coating process, widely used in the pharmaceutical industry, is among the oldest industrial procedures for forming small, coated particles or tablets. The particles are tumbled in a pan or other device while the coating material is applied slowly[4.]

The pan coating process, widely used in the pharmaceutical industry, is among the oldest industrial procedures for forming small, coated particles or tablets. The particles are tumbled in a pan or other device while the coating material is applied slowly with respect to microencapsulation, solid particles greater than 600 microns in size are generally considered essential for effective coating, and the process has been extensively employed for the preparation of controlled - release beads. Medicaments are usually coated onto various spherical substrates such as nonpareil sugar seeds, and then coated with protective layers of various polymers.

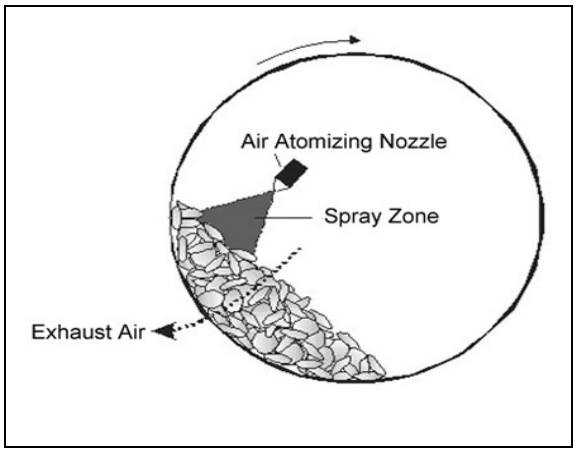

Figure 2: Representation of a typical pan coating

In practice, the coating is applied as a solution, or as an atomized spray, to the desired solid core material in the coating pans. Usually, to remove the coating solvent, warm air is passed over the coated materials as the coatings are being applied in the coating pans. In some cases, final solvent removal is accomplished in a drying oven [2]

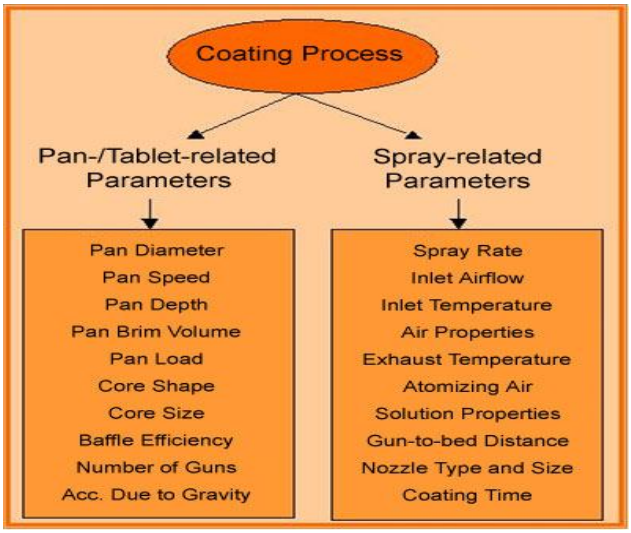

Figure 3 : List of variables affecting pan coating process [7]

1.5 Spray–drying

Spray drying serves as a microencapsulation technique when an active material is dissolved or suspended in a melt or polymer solution and becomes trapped in the dried particle. The main advantages is the ability to handle labile materials because of the short contact time in the dryer, in addition, the operation is economical. In modern spray dryers the viscosity of the solutions to be sprayed can be as high as 300mPa.s

Spray drying and spray congealing processes are similar in that both involve dispersing the core material in a liquified coating substance and spraying or introducing the core - coating mixture into some environmental condition, whereby, relatively rapid solidification (and formation) of the coating is effected. The principal difference between the two methods, is the means by which coating solidification is accomplished. Coating solidification in the case of spray drying is effected by rapid evaporation of a solvent in which the coating material is dissolved. Coating solidification in spray congealing methods, however, is accomplished by thermally congealing a molten coating material or by solidifying a dissolved coating by introducing the coating - core material mixture into a nonsolvent. Removal of the nonsolvent or solvent from the coated product is then accomplished by sorption, extraction, or evaporation techniques.

In practice, microencapsulation by spray drying is conducted by dispersing a core material in a coating solution, in which the coating substance is dissolved and in which the core material is insoluble, and then by atomizing the mixture into air stream. The air, usually heated, supplies the latent heat of vaporization required to remove the solvent from the coating material, thus forming the microencapsulated product. The equipment components of a standard spray dryer include an air heater, atomizer, main spray chamber, blower or fan, cyclone and product collector.

Microencapsulation by spray congealing can be accomplished with spray drying equipment when the protective coating is applied as a melt. General process variables and conditions are quite similar to those already described, except that the core material is dispersed in a coating material melt rather than a coating solution. Coating solidification (and microencapsulation) is accomplished by spraying the hot mixture into a cool air stream. Waxes, fatty acids and alcohols, polymers and sugars, which are solids at room temperature but meltable at reasonable temperatures, are applicable to spray congealing techniques. Typically, the particle size of spray congealed products can be accurately controlled when spray drying equipment is used, and has been found to be a function of the feed rate, the atomizing wheel velocity, dispersion of feed material viscosity, and variables[2].

Airflow

The initial contact between spray droplets and drying air controls evaporation rates and product temperatures in the dryer. There are three modes of contact:

1.5.1. Co-current

Drying air and particles move through the drying chamber in the same direction. Product temperatures on discharge from the dryer are lower than the exhaust air temperature, and hence this is an ideal mode for drying heat sensitive products. When operating with rotary atomizer, the air disperser creates a high degree of air rotation, giving uniform temperatures throughout the drying chamber. However, an alternative non-rotating airflow is often used in tower or FILTERMAT®-type spray dryers using nozzle atomizers with equal success.

1.5.2. Counter-current

Drying air and particles move through the drying chamber in opposite directions. This mode is suitable for products which require a degree of heat treatment during drying. The temperature of the powder leaving the dryer is usually higher than the exhaust air temperature.

1.5.3. Mixed-flow

Particle movement through the drying chamber experiences both co-current and counter-current phases. This mode is suitable for heat stable products where coarse powder requirements necessitate the use of nozzle atomizers, spraying upwards into an incoming airflow, or for heat sensitive products where the atomizer sprays droplets downwards towards an integrated fluid bed and the air inlet and outlet are located at the top of the drying chamber.

eg. Study on microencapsulation of lycopene by spray-drying[8].

2. Chemical process

2.1 Solvent Evaporation

This technique has been used by companies including the NCR Company, Gavaert Photo - Production NV, and Fuji Photo Film Co., Ltd. to produce microcapsules. The processes are carried out in a liquid manufacturing vehicle. The microcapsule coating is dissolved in a volatile solvent, which is immiscible with the liquid manufacturing vehicle phase. A core material to be microencapsulated is dissolved or dispersed in the coating polymer solution. With agitation, the core coating material mixture is dispersed in the liquid manufacturing vehicle phase to obtain the appropriate size microcapsule. The mixture is then heated (if necessary) to evaporate the solvent for the polymer. In the case in which the core material is dispersed in the polymer solution, polymer shrinks around the core. In the case in which core material is dissolved in the coating polymer solution, a matrix - type microcapsule is formed. Once all the solvent for the polymer is evaporated, the liquid vehicle temperature is reduced to ambient temperature (if required) with continued agitation. At this stage, the microcapsules can be used in suspension form, coated on to substrates or isolated as powders.

The solvent evaporation technique to produce microcapsules is applicable to a wide variety of liquid and solid core materials. The core materials may be either water - soluble or water - insoluble materials. A variety of film - forming polymers can be used as coatings [2]

eg. Evaluation of Sucrose Esters as Alternative Surfactants in Microencapsulation of Proteins by the Solvent Evaporation Method[9.]

2.2. Polymerization

A. Interfacial polymer

In Interfacial polymerization, the two reactants in a polycondensation meet at an interface and react rapidly. The basis of this method is the classical Schotten Baumann reaction between an acid chloride and a compound containing an active hydrogen atom, such as an amine or alcohol, polyesters, polyurea, polyurethane. Under the right conditions, thin flexible walls form rapidly at the interface. A solution of the pesticide 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. Condensed polymer walls form instantaneously at the interface of the emulsion droplets.

B. 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 0.5µm/min. Coating thickness ranges 0.2-75µm. The coating is uniform, even over sharp projections.

C. Matrix polymer

In a number of processes, a core material is imbedded in a 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 permselectivity, 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, Eurand America [4].

APPLICATION[10-11]

1. Cell immobilization: In plant cell cultures, Human tissue is turned into bio-artificial organs, in continuous fermentation processes.

2. Beverage production

3. Protection of molecules from other compounds:

4. Drug delivery: Controlled release delivery systems.

5. Quality and safety in food, agricultural & environmental sectors.

6. Soil inoculation.

7. In textiles**:** means of imparting finishes.

8. Protection of liquid crystals.

CONCLUSION

Microencapsulation means packaging an active ingredient inside a capsule ranging in size from one micron to several millimeters. The capsule protects the active ingredient from its surrounding environment until an appropriate time. Then, the material escapes through the capsule wall by various means, including rupture, dissolution, melting or diffusion. Microencapsulation is both an art and a science. There's no ONE way to do it, and each new application provides a fresh challenge. Solving these riddles requires experience, skill and the mastery of many different technologies.

REFERENCES

1. http://www.gate2tech.org.
2. Leon, L., Herbert A. L., Joseph, L. K; " The Theory And Practice Of Industrial Pharmacy", 3rd edition, 1990, Varghese Publishing House,412, 428.
3. James, S., "Encylopedia of Pharmaceutical Techonology ", 3rd edition,Vol-, 1325-1333.
4. Jackson, L. S., Lee., K., (1991-01-01), " Microencapsulation and the food industry "(htm) Lebennsmittel-Wissenschaft Techonologie. Rerrived on 1991-02-02.
5. http://www.buchi.com.
6. http://www3.interscience.wiley.com.
7. Pandey P, Turton R, Joshi N, Hammerman E, Ergun J, " AAPS Pharma Sci. Tech."; 2006, 7(4).
8. http://www.niroinc.com
9. Youan, B. C., Hussain, A., Nguyen, N.T., "AAPS Pharma Sci.", 2003, 5(2).
10. Alfonso, R. G., "Remington: The Science of Practice Of Pharmacy", Vol-2, Lippincott Willarms And Wilkins, 890-891.
11. Nelson, G., "International Journal of Pharma." 2002, 242(1-2): 55-62.

****