Review Article

A REVIEW ON MICROENCAPSULATION

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ABSTRACT

The review of Microencapsulation is about the preparation, properties and uses of microcapsules in various fields like 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. In this review an overview on encapsulation materials, mechanism of release through the capsule wall and / or desorption from carrier, techniques of preparation, many uses to which microcapsules are included.

Keywords: Microencapsulation, microcapsules, self assembling structures.

INTRODUCTION

Microencapsulation is the process of enclosing a substance inside a miniature capsule. Extremely tiny droplets, or particles of liquid or solid material, are packed within a second material or coated with a continuous film of polymeric material for the purpose of shielding the active ingredient from the surrounding environment. These capsules, which range in size from one micron to seven millimetres, release their contents at a later time by means appropriate to the application. The ingredients to be coated are referred to as core, internal phase (IP), encapsulate or fill, whereas terms applied to the coating of the microcapsules include the wall, shell, external phase or membrane. All three states ie. solid, liquid and gases, may be encapsulated and affect the size and shape of the capsules. If a solid or a crystalline material is used as the core, the resultant capsule may be irregularly shaped. However, if the core material is a liquid, simple spherical capsules, containing a single droplet of encapsulate, may be formed. The capsulated particles produce their required effect when their core material is released. There are four typical mechanisms by which the core material is released from a microcapsule:

Mechanical rupture of the capsule wall

Dissolution of the wall

Melting of the wall

Diffusion through the wall.

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].

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 odour 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]

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 can 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.

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 enable to some extent, to *insitu* 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:

- 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.
- 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.
- 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

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

Examples of coating materials:

Water soluble resins- Gelatin, Gum Arabic, Starch, Polyvinylpyrrolidone, Carboxymethyl-cellulose, Hydroxyethylcellulose, Methylcellulose, Arabinogalactan, Polyvinyl alcohol, Polyacrylic acid.

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

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

Enteric resins – Shellac, Cellulose acetate phthalate, Zein.

Techniques to Manufacture Microcapsules

Physical methods

Air-suspension coating [4]

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.

Coacervation Process

The core material will be added to the solution. The core material should not react or dissolve in water (maximumsolubility 2%). 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 2µm - 1200µm. 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.

• The shell material is cooled down to harden and forms the final capsule.

Coacervation-Phase Separation [5, 6]

The general outline of the processes consists of three steps carried out under continuous agitation: 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. 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 coatings, rigidizing the coating, usually by thermal, cross-linking, or desolvation techniques, to form a self-sustaining microcapsules.

Centrifugal extrusion [7]

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.

Pan coating [8]

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. 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.

Spray–drying [9, 10, 11]

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 liquefied coating substance and spraying or introducing the core-coating mixture into some environmental condition, whereby, relatively rapid solidification (and formation) of the coating is affected. 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.

Chemical process

Solvent Evaporation [12]

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.

Polymerization

Interfacial polymer [13]

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.

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.

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.

Factors Influencing Encapsulation Efficiency

The encapsulation efficiency of the microparticle or microcapsule or microsphere will be affected by different parameters

High solubility of the polymer in organic solvent.

Low solubility of organic solvent in water.

Low concentration of polymer.

High DP/CP ratio.

Low solvent removal rate.

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Slow solidification of microparticles.

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Low encapsulation efficiency.

Low solubility of the polymer in organic solvent.

solubility of organic solvent in water.

High concentration of polymer.

Low DP/CP ratio.

High solvent removal rate.

↓

Fast solidification of microparticles.

↓

High encapsulation efficiency.

Release Mechanisms

Mechanisms of drug release from microcapsules are

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.

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.

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.

Erosion

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

Applications of Microencapsulation [14, 15]

Some of the applications of microencapsulation can be described in detail as given below:

1. Prolonged release dosage forms. The microencapsulated drug can be administered, as microencapsulation is perhaps most useful for the preparation of tablets, capsules or parenteral dosage forms.
2. Microencapsulation can be used to prepare enteric-coated dosage forms, so that the medicament will be selectively absorbed in the intestine rather than the stomach.
3. It can be used to mask the taste of bitter drugs.
4. From the mechanical point of view, microencapsulation has been used to aid in the addition of oily medicines to tabletted dosage forms. This has been used to overcome problems inherent in producing tablets from otherwise tacky granulations. This was accomplished through improved flow properties. For example, the non-flowable multicomponent solid mixture of niacin, riboflavin, and thiamine hydrochloride and iron

phosphate may be encapsulated and made directly into tablets.

5. It has been used to protect drugs from environmental hazards such as humidity, light, oxygen or heat. Microencapsulation does not yet provide a perfect barrier for materials, which degrade in the presence of oxygen, moisture or heat, however a great degree of protection against these elements can be provided. For example, vitamin A and K have been shown to be protected from moisture and oxygen through microencapsulation.
6. The separations of incompatible substances, for example, pharmaceutical eutectics have been achieved by encapsulation. This is a case where direct contact of materials brings about liquid formation. The stability enhancement of incompatible aspirin-chlorpheniramine maleate mixture was accomplished by microencapsulating both of them before mixing.
7. Microencapsulation can be used to decrease the volatility. An encapsulated volatile substance can be stored for longer times without substantial evaporation.
8. Microencapsulation has also been used to decrease potential danger of handling of toxic or noxious substances. The toxicity occurred due to handling of fumigants, herbicides, insecticides and pesticides have been advantageously decreased after microencapsulation.
9. The hygroscopic properties of many core materials may be reduced by microencapsulation.
10. Many drugs have been microencapsulated to reduce gastric irritation.
11. Microencapsulation method has also been proposed to prepare intrauterine contraceptive device.
12. In the fabrication of multilayered tablet formulations for controlled release of medicament contained in medial layers of tabletted particles

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 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.

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