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FUNDAMENTALS OF MANUFACTURING, APPLICATIONS AND DRUG RELEASE IN MICROCAPSULES

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ABSTRACT

This review of Microencapsulation is 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 application. 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: Micro encapsulation, Nano particles, Drug Release.

1.INTRODUCTION

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

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. Alteration in site of absorption can also be achieved by microencapsulation.

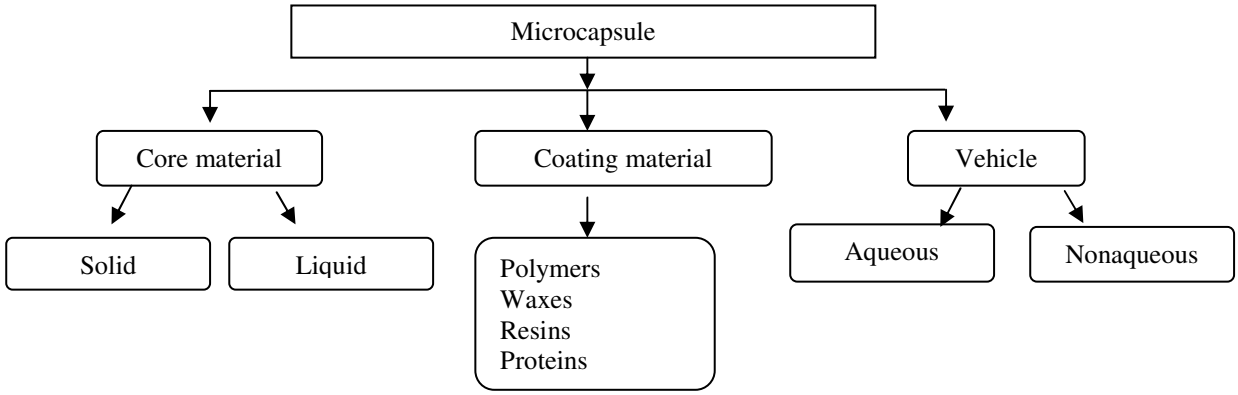

Fig.1. Schematic diagram showing principal constituents of a microcapsule

Classification of microcapsules: Generally micro particles are made up of two components
a.Core material, b.Coat or shell or wall material.

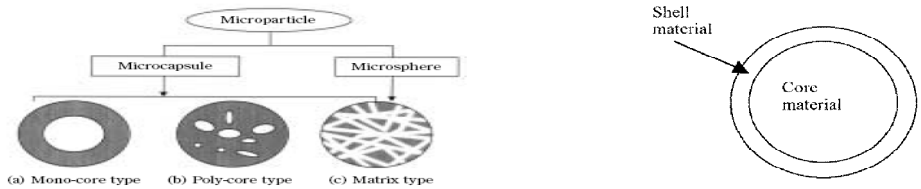

Fig.2. Schematic diagram showing different types of microcapsules

Mechanism of release of drug from the microcapsule: Mechanisms of drug release from microcapsules 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 materials like glyceryl mono stearate, beeswax and steryl alcohol etc.

Techniques of manufacturing microcapsules: The different techniques involved in the manufacturing of micro capsules are broadly classified into physical methods, physiochemical methods and chemical methods.

Physical methods:

1. 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.

2. Air-suspension coating: Micro-encapsulation by air suspension is a technique that gives improved control and flexibility compared to pan coating. Solid, particulate core material is supported in a rising air stream and spray coating applied to the air suspended particles. The design of the coating chamber is arranged so that the solid particles pass up through the coating zone, then disperse into slower moving air and sink back to the base of the coating chamber, making repeated passes through the coating zone until the desired thickness of coating is achieved. Drying of the coated particles takes place simultaneously by the passage of hot air for suspending the particles.

3. Centrifugal extrusion: Liquids are encapsulated using a rotating extrusion 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**.** 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 22.5kg of microcapsules can be produced per nozzle per hour per head. Heads containing 16 nozzles are available.

4. Vibrational nozzle: Core-Shell encapsulation or Micro Granulation (matrix-encapsulation) can be done using a laminar flow through a nozzle and an additional vibration of the nozzle or the liquid. The vibration has to be done in resonance of the Rayleigh instability and leads to very uniform droplets. The liquid can consist of any liquids with limited viscosities e.g. solutions, an emulsion, suspensions, melts etc. The solidification can be done according to the used gelatin system with an internal gelation (e.g. sol-gel processing, melt) or an external (additional binder system, e.g. in a slurry). The process works very well for generating droplets between 100–5,000 µm , The units are deployed in industries and research mostly with capacities of 1–10,000 kg per hour at working temperatures of 20–1500 °C (68–2732 °F).

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 are the ability to handle thermolabile materials because of the short contact time in the dryer; in addition, the operation is economical.

Physico-chemical methods

Coacervation: Currently, two methods for coacervation are available, namely simple and complex processes. The mechanism of microcapsule formation for both processes is identical, except for the way in which the phase separation is carried out. In simple coacervation a desolvation agent is added for phase separation, whereas complex coacervation involves complexation between two oppositely charged polymers.

The process consists of three steps:

1. Formation of three immiscible phases: Solvent, Core material phase, Coating material phase.
2. Deposition of the coating material on the core material.
3. Stiffening the coating usually by thermal, cross linking or desolvation techniques to form a microcapsule.

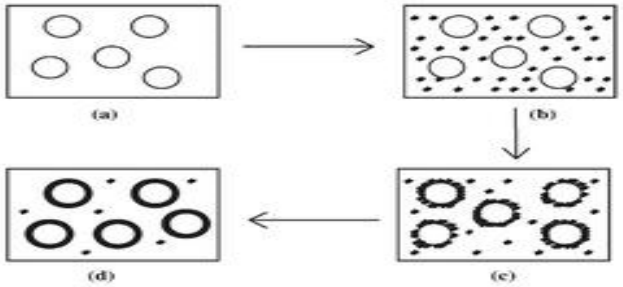

Fig.3. Schematic diagram representing the various steps in coacervation
(a) Core material dispersion in solution of shell polymer, (b) Separation of coacervate from solution,
(c) Coating of core material by micro droplets of coacervate,
(d) Coalescence of coacervate to form continuous shell around core particles.

Chemical methods:

1.Interfacial polycondensation: In Interfacial polycondensation, 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.

2.Interfacial cross-linking: Interfacial cross-linking is derived from interfacial polycondensation, and was developed to avoid the use of toxic diamines, for pharmaceutical or cosmetic applications. In this method, the small bifunctional monomer containing active hydrogen atoms is replaced by a biosourced polymer, like a protein. When the reaction is performed at the interface of an emulsion, the acid chloride reacts with the various functional groups of the protein, leading to the formation of a membrane. The cross-linked protein microcapsules are biocompatible and biodegradable, and the presence of the protein backbone renders the membrane more resistant and elastic than those obtained by interfacial polycondensation. The method is very versatile, and the properties of the microcapsules (size, porosity, degradability, mechanical resistance) can be easily tuned by varying the preparation parameters. A carbohydrate can be added to the protein, for the modulation of particle biodegradability.

3.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 0.2–75 μm. The coating is uniform, even over sharp projections.

2.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 science. There's no one way to do it, solving these riddles requires experience, skill and the mastery of many different technologies.

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