MICROENCAPSULATION

Abstract

Microencapsulation is a procedure that surrounds tiny particles or droplets with a covering to create miniature capsules with beneficial qualities. There are various applications of microencapsulation in pharmaceutical field. This article describes the microencapsulation and its methods such as Air suspension, Coacervation phase separation, Multiorifice-centrifugal process, Spray drying and congealing, Pan coating Solvent evaporation, Polymerization and application of it.

Keywords:Microencapsulation, Microcapsules /Microspheres, Microencapsulation methods, Applications.

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I. INTRODUCTION

Microencapsulation is a process in which any type of materials like solids, liquids or in some cases gases may be enclosed as a core material in microscopic polymeric layer which act as a coating layer.

Micro-encapsulation is a method in which particles are coated with polymeric coating layers, resulting in a capsule-like structure that is beneficial for a variety of pharmacological qualities. Microcapsules look like a tiny sphere particles in which drug molecule entrapped by a suitable coating polymer. Here, drug molecule known as a core and polymeric layer known as a coating layer. These microcapsules having capacity of sustained drug release, so it leads to dose reduction, reduction in frequency and reduce toxicity of pharmaceuticals. Some well known polymers such as alginate very widely used as a coating material in the formulation of microcapsules. Size of microcapsules pores diameter is found in range from few micrometers to millimeters.[1]

Advantages: [2]

1. Targeted and specific drug delivery is possible with microencapsulation.
2. Controlled drug delivery is possible with matrix type of microcapsules. From the polymeric matrix drug is continuously release in a controlled manner.
3. Microcapsules widely used in the cancer treatment due to its targeted and site specific action.
4. Increase bioavailability.
5. Improve patient compliance.
6. Mask the unwanted taste.
7. Protect the drug from the GI fluid.

Disadvantages

1. Possible cross reaction between core and shell material.
2. Difficult to achieve continuous and uniform film.
3. Shelf life of hygroscopic drugs is reduced.
4. Production costs are high.

II. MICROCAPSULES / MICROSPHERES: [3]

Microcapsule is one type of capsule which is micron in size or we can say that microcapsules are controlled drug delivery system in which drug is continuously release in a controlled manner for a long period of time at a target site from the inner core of drug. Inner core of drug is surrounded by polymeric layer which is known as coating layer. Coating layer is prepared from the natural, synthetic and semi-synthetic polymers. Microcapsules are free flowing powder its size rangeing between 1-1000 µm. Now a days microcapsules are made up from biodegradable polymers.

Ideal characteristics of microcapsule

1. Microcapsules have capacity to entrap high amount of drug.
2. Microcapsules have higher capacity compare to other particulate system such as liposome, niosome etc.
3. Drug release in a controlled manner for a long period of time from the microcapsules.
4. Microcapsules have a very high biocompatibility with a controlled degradability.
5. Microcapsules are highly susceptible for any type of chemical modification.

III. MICROPARTICLES

Microparticles are tiny particles in which drug remain entrap by polymeric layer. Same like microcapsules in case of microparticles entrap drug behave like core material and polymeric layer behave as a coating layer. From this entrapment drug is release in controlled manner for a long period of time at a particular site of action. Core material of drug is either in a solid or liquid form. Coating layer made from waxy polymers.

Microparticles are matrix systems which is sphere in shape. Drug is uniformly distributed inside polymeric matrix. Microparticles are also available in a form of reservoir systems in which drug is separately entrap as a core material and surrounded by matrix polymers. Microparticles are always in sphere in shape but microcapsules are available in both spherical and non-spherical shape.

IV. METHODS OF MICROCAPSULATION

Microencapsulation is a process which is divided into three steps namely dissolution of drug ina suitable solvent, using suitable approach drug is entrapped into suitable polymeric matrix and, finally drug is attached to a microparticles matrix. Based on the selection of method different particulate systems like microparticles, microspheres and microcapsules can be obtained. Different types of microcapsules shown in figure 1.

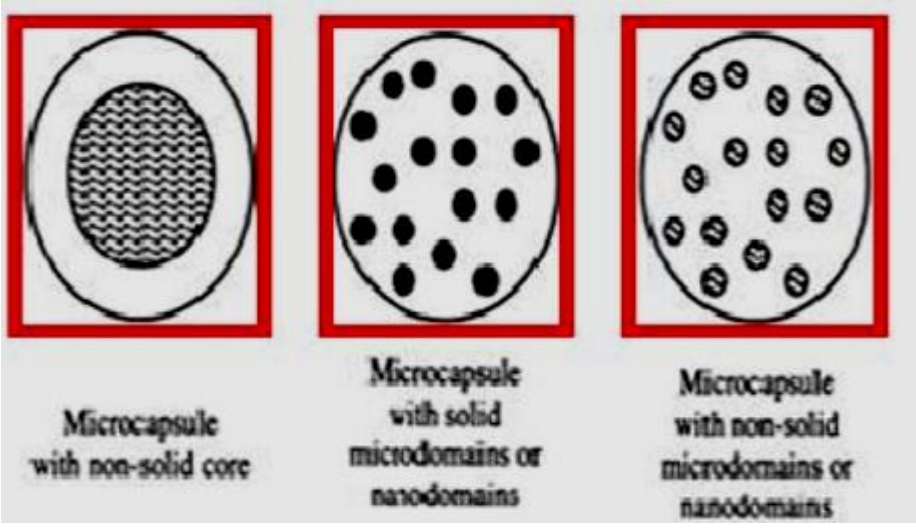

Figure 1: Different types of Microcapsules

Microcapsules delivered a drug by various route for the treatment of chronic diseases. They are used in the delivery of vaccines and also used in case of gene therapy. Compare with other controlled release dosage form microparticles offer more protection of encapsulated core material against any type of degradation and drug release in a controlled manner starting from few hours to up to months.

V. CRITERIA FOR THE FORMULATION OF MICROENCAPSULATION

For the formulation of microparticles and microcapsules pharmaceuticals required some suitable criteria. Here, some ideal criteria list out which are required for the formulation of microcapsules.

1. Selected coating polymer should possess ability to incorporate higher amount of drug material as a core.
2. Prepared microcapsules should possess enough stability after synthesis with a suitable half-life.
3. Microcapsules should possess controlled particle size and easily dispersed in a vehicle for parenteral drug delivery system.
4. Drug release should be in a controlled manner for a long period of time.

VI. COMPONENTS OF MICROCAPSULES: [4, 8]

1. **Core material:** The core material is always an API (Active Pharmaceutical agent) which is to be coated. It can be a solid and liquid.

2. **Coating material:** The selection of appropriate coating material decides the physical and chemical properties of the resultant microcapsules/microspheres. Generally hydrophilic polymers, hydrophobic polymers (or) a combination of both are used for the microencapsulation process. A number of coating materials have been used successfully; examples of these include gelatin, polyvinyl alcohol, ethyl cellulose, and cellulose acetate phthalate and styrene maleic anhydride.

VII. MICROENCAPSULATION METHODS

Microcapsules are prepared by following seven methods.

Air suspension
Coacervation phase separation
Multiorifice-centrifugal process
Spray drying and congealing
Pan coating
Solvent evaporation techniques
Polymerization

1. **Air suspension:** In this air suspension technique first drug materials in a form of particulates, suspended into air. Later solution of coating polymer prepared and sprays it on the air suspended drug particles. Drug particles remain in upward position within the

air stream inside coating chamber. Spray gun attached within the coating chamber in such way that coating solution continuously sprays on the air suspended particles. While each cycle drug particles passing through coating zone and received coat of polymeric solution. This process repeated several hundred times till desire thickness obtained. Simultaneously air stream dry the coating layer while drug is encapsulated. Drying rate is depending on flow rate of air stream inside the chamber. [5-7, 8, 9]

2. **Coacervation phase separation:** Microencapsulation by coacervation phase separation techniques divide in three main steps:

- **Preparation of three chemical phases:** In this technique three phases namely 1) vehicle phase, 2) drug solution as a core phase, and 3) polymer solution as a coating phase prepare. For the preparation of drug solution drug is dissolve into prepare vehicle phase. In a suitable organic solvent, the polymer was dissolved. The coating solution's temperature can be changed to create a polymer solution, or non-solvent can be added.

- **Deposition of the coating:** In this second step after preparation of all three phases, deposition of coating solution on drug solution takes place. This is occurring by continuous mixing of both the solution into the vehicle. Physically both the phases at higher rotation speed mixed with each other. While continuous mixing coating polymer starts deposition on the surface of drug particles. This adsorption becomes preliminary step for effective coating. For complete coating on drug particles free interfacial energy of the system reduced and due to this, coating polymer completely cover surface of drug particles. Later on drug completely entrap inside coating layer.

- **Rigidization of the coating:** In this step, hard layer of coating polymer forms surrounding drug particle. Hardening is often accomplished using heat and cross-linking processes to generate microcapsules. E.g. Coacervation Pressure-Induced Phase Separation of CO-Expanded Ethanol Solutions for Talc Particle Microencapsulation with Polymethylmethacrylate. [5, 6, 8, 9]

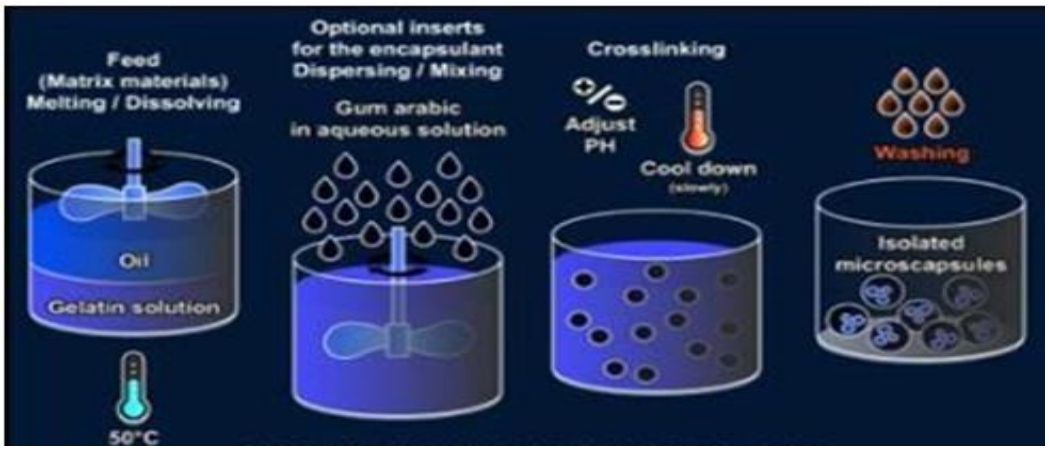

Figure 2: Steps of Coacervation phase separation

3. **Multi – orifice centrifugal process:** Southwest Research Institute invented the multi-orifice centrifugal method (SWRI). Making microcapsules involves a mechanical technique. The mechanical microencapsulation created by this technology uses centrifugal forces to enclose the microencapsulation membrane around a core material particle. The processing factors include the cylinder's rotational speed, the flow rates of the core and coating materials, and the concentration, viscosity, and surface tension of the core material. The Multi-orifice Centrifugal method (as depicted in figure 3) can be used to microencapsulate liquids and solids of various sizes with a variety of coating materials The product that has been encapsulated can be delivered as a slurry in the hardening mediator to create a dry powder. These procedures produce between 50 and 70 pounds/hour.. [5, 6, 8-10]

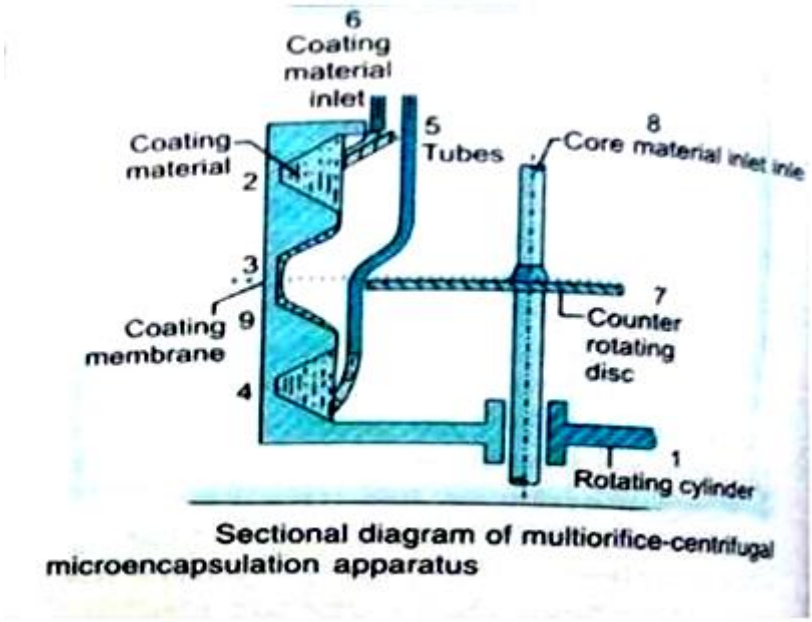

Figure 3: Multi – Orifice Centrifugal Apparatus

4. **Spray drying and congealing:** The active substance must be dissolved or suspended in a melt of polymer solution before spray drying (as depicted in Figure 4), which turns it into dried particle form. The main advantages using spray dryer is that it can be used for encapsulating the labile materials due to its short contact time in the dryer as well as the operation is also economical. In contemporary spary dryers, the solution that needs to be sprayed has a high viscosity of 300mPa.

   Both the spray drying and congealing methods include dispersing the core material into a liquid coating material and spraying the coating mixture under specific environmental conditions, which causes the coating to solidify and results in the production of a dry encapsulated particle.

   These both processes only differ in principle by which the coating solidification is accomplished. In Spray drying method the coating solidification is done by rapid evaporation of a solvent, while in Spray congealing method the coating solidification is

thermally congealed in a molten coating material or by use of a non-solvent. Further the removal of the non-solvent or solvent from the coated product can be done using sorption, extraction, or evaporation techniques. [6, 8, 9]

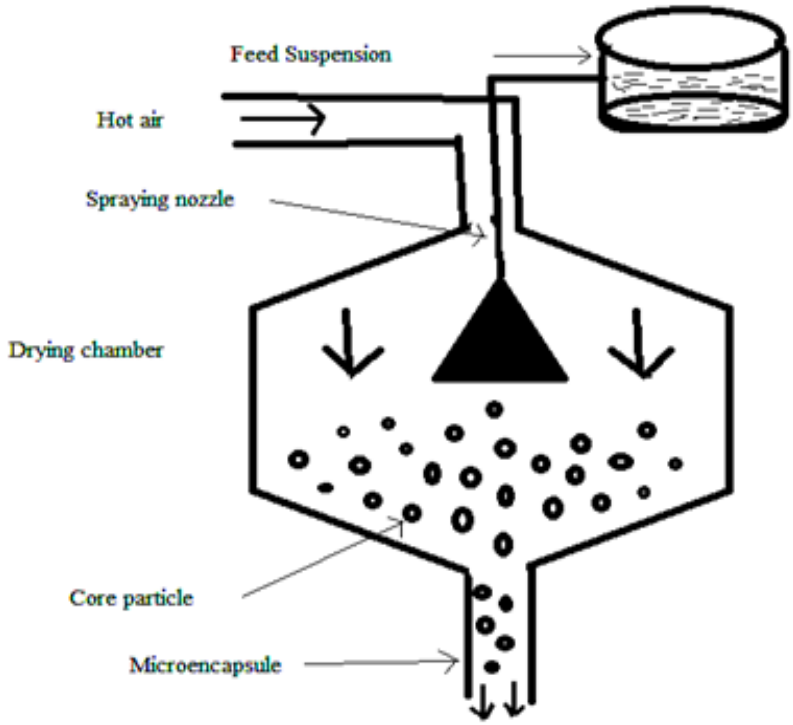

Figure 4: Spray Drying and Congealing Process

5. **Polymerization:** Polymerization processes are used in a relatively recent microencapsulation technology to create protective microcapsule coverings in situ. The processes include the reaction of monomeric units that are present at the interface between a substance that makes up the core of the material and a continuous phase in which it is disseminated. A liquid-liquid, liquid-gas, solid-liquid, or solid-gas interface is where the polymerization reaction takes place since these are the two phases that often support the continuous or core material phase. [6, 8-10]

6. **Pan coating:** Pan Techniques for microencapsulating of relatively big particles have become widely used in the pharmaceutical industry. For efficient coating in the context of microencapsulation, solid particles bigger than 600 microns in size are typically regarded as necessary, and this method has been extensively utilised for the creation of controlled release beads. Medications are typically covered with protective coatings made of different polymers and coated onto a variety of spherical substrates, such as nonpareil sugar seeds. The required solid core material in the coating pan is coated using a solution or an atomized spray. Warm air is typically circulated over the coated components when the coating is placed inside coating pans to remove the coating solvent. The last solvent removal is sometimes carried out in a drying oven. [6-9]

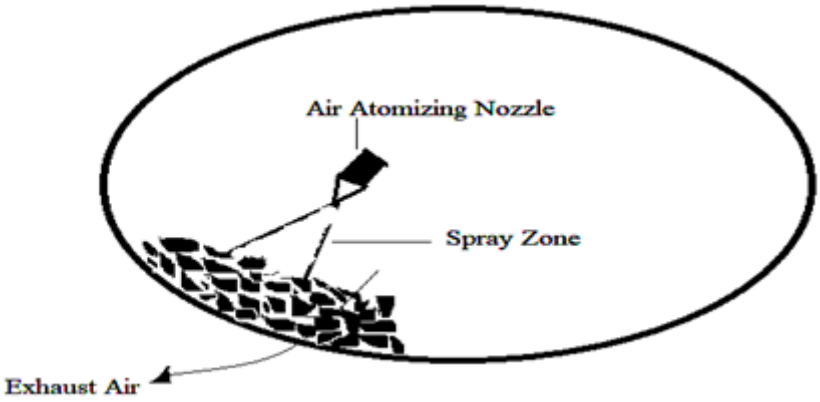

Figure 5: Pan Coating Process

7. **Solvent evaporation:** Similar to suspension cross linking, solvent evaporation/solvent extraction creates microcapsules, however in this instance the polymer is often hydrophobic polyester. The core material is dissolved/dispersed along with the polymer in a water-immiscible volatile organic solvent, such as DCM or chloroform. To create small polymer droplets containing encapsulated material, the resultant solution is added dropwise in a stirring aqueous solution containing a suitable stabiliser such as poly (vinyl alcohol) or polyvinylpyrrolidine, etc. The appropriate polymer microcapsules are created when the droplets get harder over time. This hardening procedure is carried out either by solvent extraction or solvent evaporation removal (by heat or reduced pressure) (with a third liquid which is a precipitant for the polymer and miscible with both solvent and water Solvent extraction produces microcapsules with larger porosities than solvent evaporation. Figure 6 depicts a schematic illustration of the solvent evaporation process of microencapsulation. For the creation of drug-loaded microcapsules made of biodegradable polyesters such polylactide, poly (lactide-co-glycolide), and polyhydroxybutyrate, the solvent evaporation/solvent extraction approach is more advantageous. [6, 8]

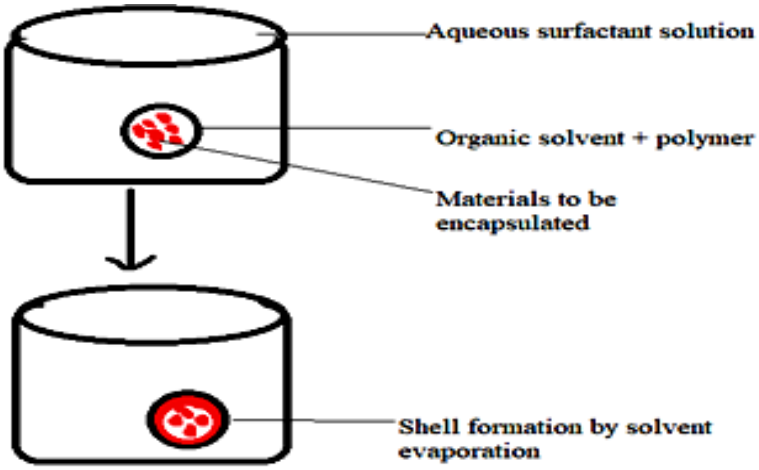

Figure 6: Solvent Evaporation Process

VIII. APPLICATIONS OF MICROCAPSULATION

1. To mask the bitter taste of drugs like Paracetamol, Nitrofurantoin etc.
2. Many medications have been microencapsulated to lessen irritations of the gastrointestinal system. According to reports, sustained release aspirin preparations generate much less G.I. haemorrhage than traditional preparations. A liquid can be converted to a pseudo-solid for easy handling and storage. eg. Eprazinone.
3. Hygroscopic properties of core materials may be reduced by microencapsulation eg. Sodium chloride.
4. Carbon tetra chlorides and a number of other substances have been microencapsulated to reduce their odor and volatility.
5. To protect the core materials against atmospheric impacts, such as Vit. A Palmitate, microencapsulation has been used.
6. Encapsulation has been used to separate incompatible substances.[6]

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