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MICROENCAPSULATION: PROCESS, TECHNIQUES AND APPLICATIONS

Sangita Kumari*[1], Govind Shukla[1], A. Sambasiva Rao[2]

[1]Assistant Professor, [2]Principal, Sri Indu Institute of Pharmacy,
Seriguda, Ibrahimpatnam, R.R. Dist., Hyderabad, Andhra Pradesh, India.

ABSTRACT

Microencapsulation is a process in which tiny particles or a coating to give small capsules with many useful properties surrounds droplets. 'Small is better' would be an appropriate motto for the many people studying microencapsulation. In its simplest form, a microcapsule is a small sphere with a uniform wall around it. The material inside the microcapsule is referred to as the core, internal phase, or fill, whereas the wall is sometimes called a shell, coating, or membrane. Most microcapsules have diameters between a few micrometers and a few millimeters. The reasons for microencapsulation are countless. Microencapsulation system offers potential advantages over conventional drug delivery systems and also established as unique carrier systems for many pharmaceuticals. Although significant advances have been made in the field of microencapsulation, still many challenges need to be rectified during the appropriate selection of core materials, coating materials and process techniques.

Key words: Microcapsules, Microencapsulation, Microspheres, Gelatin, Coating material.

INTRODUCTION

Microencapsulation is a process in which tiny particles or a coating to give small capsules with many useful properties surrounds droplets. 'Small is better' would be an appropriate motto for the many people studying microencapsulation. In its simplest form, a microcapsule is a small sphere with a uniform wall around it. The material inside the microcapsule is referred to as the core, internal phase, or fill, whereas the wall is sometimes called a shell, coating, or membrane. Most microcapsules have diameters between a few micrometers and a few millimeters [1]. Gelatin is a common wall-forming material but synthetic polymers like polyvinyl alcohol, ethyl cellulose, polyvinyl chloride and other materials also may be used. One of the advantages of microencapsulation is that the administered dose of a drug is subdivided into small units that are spread over a large area of the gastrointestinal tract, which may enhance absorption by diminishing localized drug concentration [2,3]. Custom-made microspheres and microcapsules are provided to customers in the food, pharmaceutical, cosmetic, consumer and personal care products, agricultural, veterinary medicine, industrial chemicals, biotechnology, biomedical and sensor industries.

Features of Microcapsule

Microencapsulation is the packaging of small droplets of liquid or particles with a thin film [4]. Typically, the lowest particle size of microcapsules is 1µm and the largest size is 1mm. Microcapsules consist of a core and a wall (or shell). The configuration of the core can be a spherical or irregular particle, liquid-phase suspended solid, solid matrix, dispersed solid and aggregates of solids or liquid forms [5].

Classification

Microcapsules can be classified on three basic

Corresponding Author :- **Sangita Kumari** Email:- sangita.mpharm@gmail.com

categories according to their morphology as follows,
1. Mononuclear
2. Polynuclear and
3. Matrix types

Mononuclear (core-shell) microcapsules contain the shell around the core, while polynuclear capsules have many cores enclosed within the shell. In matrix encapsulation, the core material is distributed homogeneously into the shell material. In addition to these three basic morphologies, microcapsules can also be mononuclear with multiple shells, or they may form clusters of microcapsules.

Reasons for Encapsulation

The reasons for microencapsulation are countless. In some cases, the core must be isolated from its surroundings, as in isolating vitamins from the deteriorating effects of oxygen, retarding evaporation of a volatile core, improving the handling properties of a sticky material or isolating
a reactive core from chemical attack [6]. There are several reasons why substances may be encapsulated [7,8].
1. To protect reactive substances from the environment
2. To convert liquid active components into a dry solid system
3. To separate incompatible components for functional reasons
4. To mask undesired properties of the active components
5. To protect the immediate environment of the microcapsules from the active components
6. To control release of the active components for delayed (timed) release or long-acting (sustained) release

MATERIALS AND METHODS FOR Microencapsulation

Preparation of microspheres should satisfy certain criteria, like basic understanding of the general properties of microcapsules, such as the nature of the core and coating materials, the stability and release characteristics of the coated materials and the microencapsulating methods

Core Material

The core material defined as the specific material to be coated can be liquid or solid in nature. The composition of the core material is varied, as the liquids core can include dispersed and/or dissolved material. The solid core can be a mixture of active constituents, stabilizers, diluents, recipients and release-rate retardants or accelerators. The ability to vary the core material composition provides definite flexibility and utilization of this characteristic often allows effectual design and development of the desired microcapsule properties.

Coating Materials

The selection of a specific coating material is a lengthy list of candidate materials presents the following questions to be considered by the research:

- What is the specific dosage or product requirement - stabilization, reduced volatility, release characteristics, environmental conditions, etc.?
- What coating material will satisfy the objectives and requirements?
- What micro encapsulation method is best suited to accomplish the coated product objectives?

The selection of the appropriate coating material, dictates, to a major degree, the resultant physical and chemical properties of the micro capsules. 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 typical coating properties such as cohesiveness, permeability, moisture sorption, solubility, stability and clarity must be considered in the selection of the proper microcapsule coating material. 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 micro encapsulation of small particles, hence, the results obtained from the cast films may not be extrapolatable to the thin microcapsule coatings.
- The particular micro encapsulation method employed for the deposition of a given coating produces specific arid inherent properties that are difficult to simulate with existing film casting methods.
- The coating substrate or core material may have a decisive effect on coating material properties. The thickness that can be applied to small spherical particles be thinness of micro-encapsulation coatings, although not necessarily limiting, must be of prime consideration just as the smallness of microcapsules allows unique properties and formulations to be accomplished, the thinness of the resultant coatings also can present unique problems.

Manufacturing techniques of Microcapsules

Microcapsules as bulk materials, in either dry powder or dispersed form, can be processed into final product applications using common equipment such as V-blenders, tablet machines, granulators, homogenizes, kneaders, hard gelatin capsule filling machines, or coating equipment if deposition onto a substrate is desired [9]. There are many factors to consider when selecting the encapsulation process and also various techniques are available for the encapsulation of core materials. Broadly

the methods are divided into two types (Figure 2), such as physical and chemical methods.

Characterization of Reservoir (Solvent Exchange Method): A newer Microencapsulation Technique

On the other hand, it has been noticed that most proteins undergo inactivation events such as degradation and aggregation within the micro particles during the manufacturing process as well as the release period [10-11]. For this reason, the protein release is typically incomplete despite substantial degradation of the polymer. Protein inactivation in the micro particle system is largely due to extensive exposure of the protein to damaging environments, such as large interfacial area between aqueous and organic phases (w/o), hydrophobic polymers, and their acidic degradation products [12,13], one of the recent examples includes encapsulating proteins in hydro gels prior to polymeric microencapsulation, which was found to be effective in preserving the protein stability and controlling the release rate [14]. In addition to the formulation approaches, improvement of microencapsulation techniques has also been attempted. The anhydrous microencapsulation process is one of the examples [15]. Recently, a new microencapsulation technique called the solvent exchange method has been developed in an attempt to address the above problems [16]. Briefly, the new method produces reservoir-type microcapsules by inducing collision between drug-loaded aqueous drops and polymer dissolved organic solvent drops. The micro scaled liquid drops can be generated by different equipment such as ink-jet nozzles [17] and ultrasonic atomizers [18]. Protein release from traditional polymeric micro particles is typically triphasic. The three phases are,

1. An initial burst-release of surface-bound and poorly encapsulated protein,
2. A second phase consisting of diffusion release and/or an induction period that does not release protein,
3. Release due to the degradation of the polymer matrix [19].

Physical study of Microcapsules

The size and shape of the prepared microparticles can be determined by light and scanning electron microscope. Microcapsule solvation can be predicted using following formula;

Microcapsule Solvation (%)=(M1/M2)x 100

M1 - Microcapsules weighed immediately
M2 - After drying to a constant weight
Bulk density is determined by following formula;

Bulk Density= Sample Weight/Sample Volume

Tap density is measured by employing the conventional tapping method using 10 ml measuring cylinder and the number of tapings will reduced to 100 as it is sufficient to bring about a plateau condition. Taped density is calculated by following formula;

Tapped Density= Wt. of Microcapsules/Vol. of Capsules after 100

Compressibility index can be calculated using following formula;

Ci= (initial vol.- final vol.)/ initial vol.x100

Hausnner's ratio, another index of flow ability of microcapsules, is calculated by following formula;

Hausnner's ratio = Volume before taping / Volume after taping

Angle of repose is measured by passing microcapsules through a funnel on the horizontal surface. The height (h) of the heap formed was measured and radius (r) of cone base is also determined. The angle of repose (θ) is calculated by following formula;
Where *r* is the radius and *h* is the height [20]

$$\theta = \tan^{-1} h / r$$

Mechanisms of Drug Release

Major mechanisms of drug release from microcapsules are as follows,

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 [21].

APPLICATIONS OF MICROENCAPSULATION

There are many reasons why drugs and related chemicals have been microencapsulated. The various applications of microencapsulation are presented below (Figure 3). The technology (microencapsulation) has been used widely in the design of controlled release and sustained release dosage forms [22,23]. It includes,

1. To mask the bitter taste of drugs like Paracetamol, Nitrofurantoin etc.
2. To reduce gastric and other gastro intestinal (G.I) tract irritations, For eg., sustained release Aspirin preparations have been reported to cause significantly less G.I. bleeding than conventional preparations.
3. A liquid can be converted to a pseudo-solid for easy handling and storage, eg., Eprazinone.
4. Hygroscopic properties of core materials may be reduced by microencapsulation eg., Sodium chloride.
5. Carbon tetra chlorides and a number of other substances have been microencapsulated to reduce their odor and volatility.
6. Microencapsulation has been employed to provide protection to the core materials against atmospheric effects, e.g., Vitamin- A Palmitate.
7. Separation of incompatible substance has been achieved by encapsulation.
8. Physicochemical evaluation characterization: The characterization of the microparticulate carrier is an important phenomenon, which helps to design a suitable carrier for the proteins, drug or antigen delivery. These microspheres have different microstructures. These microstructures determine the release and the stability of the carrier [24].
9. Sieve analysis: Separation of the microspheres into various size fractions can be determined by using a mechanical sieve shaker [25].

Advantages

- Reliable means 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.
- Solid biodegradable microspheres have the potential throughout the particle matrix for the controlled release of drug.
- Microspheres received much attention not only for prolonged release, but also for targeting of anticancer drugs to the tumour.
- The size, surface charge and surface hydrophilicity of microspheres have been found to be important in determining the fate of particles in vivo.
- Studies on the macrophage uptake of microspheres have demonstrated their potential in targeting drugs to pathogens residing intracellularly [26].

Table 1. Core material and its characteristics

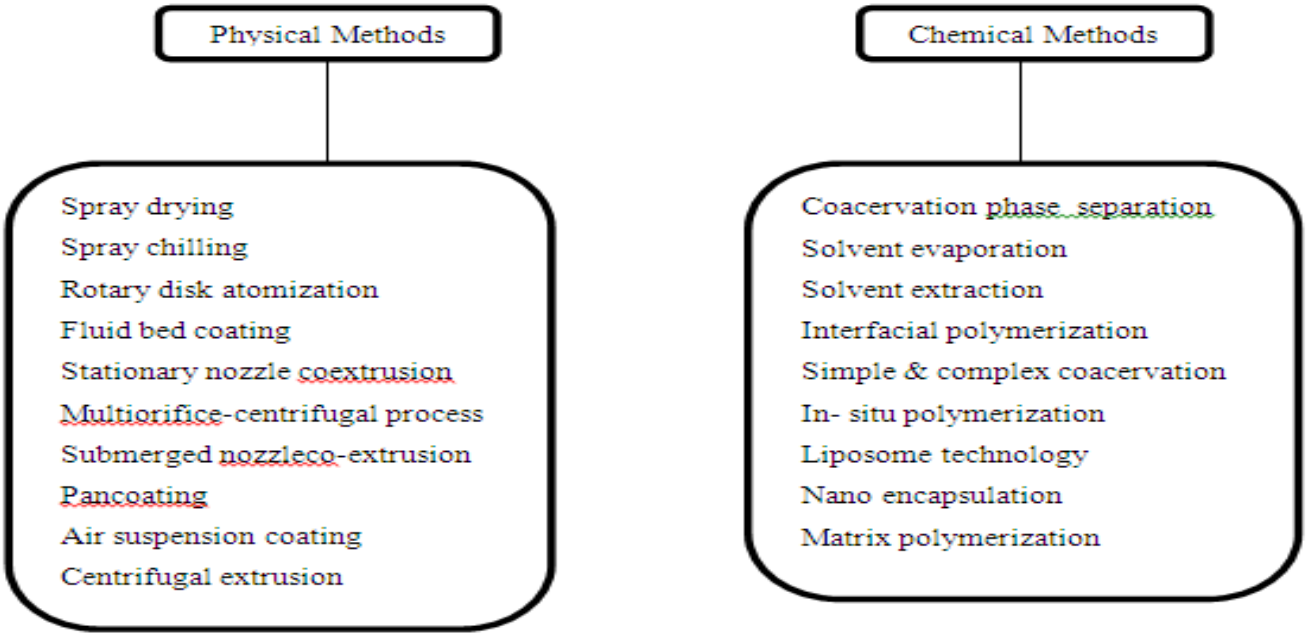
Core Material	Characteristic Property	Purpose of Encapsulation	Final Product Form
Acetaminophen	Slightly water soluble solid	Taste-masking	Tablet
Activated Charcoal	Adsorbent	Selective sorption	Dry Powder
Aspirin	Slightly water soluble solid	Taste-masking; sustained release; reduced gastric irritation; separation of incompatibles	Tablet or capsule
Islet of Langer Hans	Viable cells	Sustained normalization of diabetic condition	Injectable
Isosorbide dinitrate	Water-soluble solid	Sustained release	Capsule
Liquid crystals	Liquid	Conversion of liquid to solid; stabilization	Flexible film for thermal mapping of anatomy
Menthol/methyl salicylate camphor mixtur	Volatile solution	Reduction of volatility; sustained release	Lotion
Progesterone	Slightly water-soluble solid	Sustained release	Varied
Potassium chloride	Highly water-soluble solid	Reduced gastric irritation	Capsule
Urease	Water-soluble enzyme	Perm selectivity of enzyme, substrate, and reaction products	Dispersion
Vitamin-A Palmitate	Nonvolatile liquid	Stabilization to oxidation	Dry powder

Table 2. Representative Coating Materials and Applicable Microencapsulation Process

Coating Materials	Multi-orifice centrifugal	Phase separation coacervation	Pan Coating	Spray Drying	Air Suspension	Solvent Evaporation
Water-soluble resins						
Gelatin	**x**	**x**	**x**	**x**	**x**	**x**
Gum arabic		**x**	**x**	**x**	**x**	**x**

Starch		x	x	x	x	
Polyvinylpyrrolidione	X	x	x	x	x	
Carboxymethylcellulose		x	x	x	x	
Hydroxyethylcellulose		x	x	x	x	x
Methyl cellulose		x	x	x	x	
Arabinogalactan		x	x	x	x	
Polyvinyl alcohol	X	x	x		x	x
Polyacrylic acid		x	x	x	x	X
Water-insoluble resins						
Ethyl cellulose		X	x	x	x	x
Polyethylene	x				x	X
Polymethacrylate					X	x
Polyamide (Nylon)					x	X
Poly [Ethylene-vinyl acetate]	X	x	x	x		x
Cellulose nitrate	x	x	x	x		X
Silicones			x	X		
Poly (Lactide-coglycolide)		x	x			x
Waxes and lipids						
Paraffin	x	x	x	x	X	
Carnauba			x	x	X	
Spermaceti		x	x	x	X	
Beeswax			X	x	x	
Stearic acid			x	X		
Stearyl alcohol			X	x	x	
Glyceryl stearates			x	x	X	
Enteric resins						
Shellac		X	x	x	x	
Cellulose acetate phthalate		x	x	x	x	X
Zein		x		X		

Fig 1. Manufacturing Techniques BOF Microcapsules



CONCLUSION

Microencapsulation system offers potential advantages over conventional drug delivery systems and also established as unique carrier systems for many pharmaceuticals (targeted drug delivery systems). Although significant advances have been made in the field of microencapsulation, still many challenges need to be rectified during the appropriate selection of core materials, coating materials and process techniques.

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