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MICROENCAPSULATION TECHNOLOGY

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ABSTRACT

Microparticulate drug delivery systems provide tremendous opportunities for designing new controlled and delayed release oral formulations, thus extending the frontier of future pharmaceutical development. The Microparticulate offers a variety of opportunities such as protection and masking, reduced dissolution rate, facilitation of handling, and spatial targeting of the active ingredient. It is the process by which individual particles or droplets of solid or liquid material (the core) are surrounded or coated with a continuous film of polymeric material (the shell) to produce capsules in the micrometer to millimeter range, known as microcapsules. Microencapsulation technology can protect active materials against environment, stabilize them, prevent or suppress volatilization. Microencapsulation technology can provide new forms and features and many polymeric drug delivery systems, biodegradable polymers have been used widely as drug delivery systems because of their biocompatibility and biodegradability. Microencapsulation is a powerful technique to achieve targeted delivery and on-demand release of different active ingredients. Many synthetic and natural biodegradable polymers present exciting opportunities in tailor-making the micro particle formulations for long-term drug release with specific release rates. Hence finally concluded that continuous knowledge up gradation is required in order to make desired drug delivery system and minimization of problems associated with physicomechanical techniques and complete knowledge about selection of raw materials and method for their microencapsulation to get desire goal of study.

Key words: Microencapsulation technology, targeted delivery, protection, masking.

INTRODUCTION

Microencapsulation is a rapidly expanding technology. It is the process of applying relatively thin coatings to small particles of solids or droplets of liquids and dispersions. 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. Microencapsulation is receiving considerable attention fundamentally, developmentally and commercially. The term microcapsule is defined as a spherical particle with size varying from 50nm to 2mm, containing a core substance. Microspheres are in strict sense, spherical empty particles. However the terms microcapsule and microsphere are often used synonymously. The microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature, and ideally having a particle size less than 200µm. Solid biodegradable microcapsules incorporating a drug dispersed or dissolved throughout the particle matrix have the potential for the controlled release of drug. These carries received much attention not only for prolonged release but also for the targeting of the anticancer drug to the tumour. The concept of miroencapsulation was initially utilized in carbonless copy papers. More recently it has received increasing attention in pharmaceutical and biomedical applications. The first research leading to the development of micro encapsulation procedures for pharmaceuticals was published by Bungenburg de Jong and Kass in 1931 and dealt with the preparation of gelatin spheres and the use of gelatin coacervation process for coating. In the late 1930s, Green and co-workers of National cash register co. Dayton, Ohio, developed the gelatin coacervation process. Since then may other coating materials and processes of application have been developed by the pharmaceutical industry for the microencapsulation of medicines. Over the last 25 years pharmaceutical companies for microencapsulated drugs have taken out numerous patents.

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.

Microparticles offer various significant advantages as drug delivery systems, including:

i. An effective protection of the encapsulated active agent against (e.g. enzymatic) degradation
ii. The possibility to accurately control the release rate of the incorporated drug over periods of hours to months.
iii. An easy administration (compared to alternative parenteral controlled release dosage forms, such as macro-sized implants).
iv. Desired, pre-programmed drug release profiles can be provided which match the therapeutic needs of the patient.

Microparticulate drug delivery systems are an interesting and promising option when developing an oral controlled release system.Microcapsules are finally dispersed in various dosage forms, such as hard gelatin capsules, which may be enteric coated, soft gelatin capsules, or suspensions in liquids, all of which allow dispersion of individual microcapsules on release.Microcapsules continue to be of much interest in controlled release because of relative ease in design and formulation and partly on the advantages of microparticulate delivery systems. The latter include sustained release from each individual microcapsule and offer greater uniformity and reproducibility. Additional advantage over monolithic systems containing multiple doses is the greater safety factor in case of a burst or defective individual in subdivided dosage forms. Finally, it has been argued that multiple particle systems are distributed over a great length of gastro-intestinal tract, which should result in, (a) lowered local concentrations and hence reduced toxicity or irritancy, and (b) reduced variability in transit time and absorption rate

Basic consideration of microencapsulation technique: Microencapsulation often involves a 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 microencapsulation methods. The intended physical characters of the encapsulated product and the intended use of the final product must also be considered.

a. 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 can be varied as the liquid core can include dispersed and/or dissolved material. The solid core can be a mixture of active constituents, stabilizers, diluents, excipients and release rate retardants or accelerators.

b. Coating materials: The coating material should be capable of forming a film that is cohesive with the core materials, be chemically compatible and non reactive with the core material and provide the desired coating properties such as strength, flexibility impermeability, optical properties and stability. The total thickness of the coatings achieved with microencapsulation techniques is microscopic in size.

c. **Stability, release and other properties**: Three important areas of current microencapsulation application are the stabilization of core materials, the control of the release or availability of core materials and separation of chemically reactive ingredients within a tablet or powder mixture. A wide variety of mechanisms is available to release encapsulated core materials; such as disruption of the coating can occur by pressure, shear or abrasion forces, permeability changes brought about enzymatically etc., improved gastro tolerability of drugs can be obtained by microencapsulation.

d. **Physical character of the final product**: Microcapsules should have desirable physical properties like ability to flow, to be compacted or to be suspended and the capsule wall must be capable of resisting the pressure during compression etc.

e. **coating materials:** A number of different substances both biodegradable as well as non-biodegredable have been investigated for the preparation or microcapsules. These materials include the polymers of natural and synthetic origin and also modified natural substances. Some of the polymers used in the preparation of the microcapsules are classified and listed below.

SYNTHETIC POLYMERS

Non-biodegradable

1. PMMA
2. Acrolein
3. Glycidyl methacrylate
4. Epoxy polymers

Biodegradable

1. Lactides and glycolides and their copolymers
2. Polyalkyl cyano acrylates
3. Polyanhydrides
4. Corbopol

NATURAL MATERIALS

A. Proteins
B. Albumins
C. Gelatin
D. Collagen
E. Carbohydrates
F. Starch , Agarose
G. Carrageenan
H. Chitosan
I. Chemically modified carbohydrates
J. DEAE cellulose
K. Poly (acryl) dextran
L. Poly (acryl) starch

METHODS OF MICROENCAPSULATION

Preparation of microecapsules as prolonged action dosage form can be achieved by various techniques under following headings.

1. Coacervation phase separation
    a. By temperature change
    b. By incompatible polymer addition
    c. By non-solvent addition
    d. By salt addition
    e. By polymer-polymer interaction
    f. By solvent evaporation
2. Multi orifice centrifugal process.
3. Pan coating
4. Air suspension coating
5. Spray drying and spray congealing
6. Polymerization
7. Melt dispersion technique

1. Coacervation phase separation: Microencapsulation by coacervation phase separation is generally attributed to the national cash register (NCR) corporation and the patents of green et.al. The general outline of the processes consists of three steps carried out under continuous agitation.

1. Formation of three immiscible chemical phases
2. Disposition of the coating, and
3. Rigidization of the coating

a. By thermal change: phase separation of the dissolved polymer occurs in the form of immiscible liquid droplets, and if a core material is present in the system, under proper polymer concentration, temperature and agitation conditions, the liquid polymer droplets coalesce around the dispersed core material particles, thus forming the embryonic microcapsules. As the temperature decreases, one phase becomes polymer-poor (the microencapsulation vehicle phase) and the second phase. (The coating material phase) becomes polymer-rich.
b. By incompatible polymer addition: it involves liquid phase separation of a polymers coating material and

microencapsulation can be accomplished by utilizing the incompatibility of dissimilar polymers existing in a common solvent.

c. By non-solvent addition: a liquid that is a non-solvent for a given polymer can be added to a solution of the polymer to induce phase separation. The resulting immiscible liquid polymer can be utilized to effect microencapsulation of an immiscible core material.

d. By salt addition: there are two types of coacervation: simple and complex. Simple coacervation involves the use of only on colloid, e.g. gelatin in water, and involves removal of the associated water from around the dispersed colloid by agents with a greater affinity for water, such as various alcohols and salts. The dehydrated molecules of polymer tend to aggregate with surrounding molecules to form the coacervate. Complex coacervation involves the use of more than one colloid. Gelatin and acacia in water are most frequently used, and the coacervation is accomplished mainly by charge neutralization of the colloids carrying opposite charges rather than by dehydration.

e. By polymer-polymer interaction: the interaction of oppositely charged poly electrolytes can result in the formation of a complex having such reduce solubility that phase separation occurs.

f. By solvent evaporation: the processes are carried out in a liquid manufacturing vehicle. The microcapsule coating is dispersed in a volatile solvent, which is dispersed in volatile solvents, 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 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 dissolved in the coating polymer solution, matrix type microcapsules are formed. The solvent evaporation technique to product microcapsules is applicable to a wide variety of core materials. The core materials may be either water soluble or water insoluble materials.

2. **Multiorifice centrifugal process**: The South-West research institute (SWRI) has developed a mechanical process for producing microcapsules that utilizes centrifugal forces to hurl, a core material particle through an enveloping microencapsulation membrane therapy effecting mechanical microencapsulation. Processing variables include the rotational speed of the cylinder, the flow rate of the core and coating materials, the concentration and viscosity of the coating material an the viscosity and surface tension of the core material. This method is capable of microencapsulating liquids and solids of varied size ranges, with diverse coating materials.

3. Pan coatings: The microcapsulation of relatively large particles by pan coating method are generally considered essential for effective coating. The coating is applied as a solution or as an automized spray to the desired solid core passed over the coated materials during coatings is being applied in the coating pans.

4. Air suspension coating: The process consists of the dispersing of solid particulate core materials in a supporting air stream and the spray coating of the air suspended particles. Within coating chambers, particles are suspended on an upward moving air stream. The design of the chamber and its operating parameters effect a re-circulating flow of the particles through the coating zone portion of the chamber, where is a coating material, usually a polymer solution is spry-applied to the moving particles.

5. Spray drying and spray congealing: Spray drying and spray congealing processes are similar in that both involve dispersing the core material in liquefied coating substance and spraying or introducing the core coating mixture into some environmental condition, whereby relatively rapid solidification of the coating is effected. The principle difference between the two methods is the means by which coating solidification is accomplished. Coating solidification in the case of spray during is effected by rapid evaporation of solvent in which the coating material is dissolved. Coating solidification in spray congealing method, however, is accomplished by thermally congealing a molten coating material or by solidifying the 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.

6. Polymerization: The method involves the reaction of monomeric unit located at the interface existing between a core material and a continuous phase in which the core material is dispersed. The continuous or core material supporting phase is usually a liquid or gas and therefore the polymerization reaction occurs at a liquid-liquid, liquid-gas, solid-liquid or solid-gas interface e.g., microcapsules containing protein solutions by incorporating the protein in the aqueous diamine phase.

7. Melt-dispersion technique: In this technique the coating material is melted by heating upto 80^{o}C. The drug is suspended in it and then emulsified in water containing emulsifying agent at 80^{o}C under stirring. Microcapsules are formed as the temperature of the system reaches to room temperature.

CONCLUSION

Microencapsulation is one of the quality preservation techniques of sensitive substances and a method for production of materials with new valuable properties. Microencapsulation is process of enclosing micron sized particles in a polymeric shell.Significances of microencapsulation For Sustained or prolonged drug release For Masking test and odour of many drugs Converting liquid into free flowing properties Drugs which are sensitive to Light,oxygen, moisture they are easily stabilized. Microencapsulation technologies are applied in any area of the industry. It can be found in: Cell immobilization, Beverage production, Protection of molecules from other compounds, Drug delivery, Quality and safety in food, agricultural & environmental sectors, pharmaceuticals etc.

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