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Review on Microencapsulation Drug delivery Systems

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A B S T R A C T

Microencapsulation is a well-designed controlled or sustained drug delivery system. The advantageous of this system to overcome the some problems in conventional therapy and to enhance the therapeutic efficacy and bioavailability of given drug. It is the 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. Microencapsulation is a process whereby small discrete solid particles or small liquid droplets are surrounded and enclosed by an intact shell. Many different active materials like drugs, pesticides, flavours, enzymes, vitamins and catalysts have been successfully encapsulated microcapsules made from a variety of polymeric and non polymeric materials like poly(ethylene glycol), poly(methacrylate), poly(styrene), cellulose, poly (lactide), poly(lactide-co-glycolide), gelatin and acacia, etc. It is a new technology that has wide applications in pharmaceutical industries, agrochemical, food industries and cosmetics. As it is better drug delivery system than conventional drug delivery system with minimum side effect and having targeted action. The present review focused on advanced techniques and applications of microencapsulation drug delivery system.

Keywords: Microencapsulation, Controlled drug delivery, Therapeutic efficacy, Conventional therapy, Microcapsules

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

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. It may be defined as the process of surrounding or enveloping one substance within another substance on a very small scale, yielding capsules ranging from less than one micron to several hundred microns in size. It is mean of applying thin coating to small particle of solid or droplet of liquid & dispersion[1]. Microencapsulation is a process by which solids, Liquids or even gases may be enclosed in microscopic particles by formation of thin coatings of wall material around the substances, the Particle size was 50-5000 micron and it contain two phases Core material, Coating material. The product obtained by this process is called as micro particles, microcapsules, microsphere, coated granules, and pellets. The Particles having diameter between 3 - 800µm are known as micro particles or microcapsules or microspheres. Particles larger than 1000µm are known as Macroparticles[2].

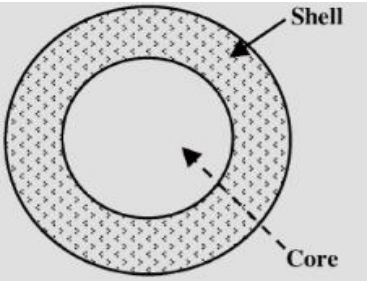

Fig 1: Schematic representation of microencapsulation

Reasons for Microencapsulation

- To protect reactive substances from the environment.
- To convert liquid active components into a dry solid system.
- To separate incompatible components for functional reasons.
- To protect the immediate environment of the microcapsules from the active components.
- Isolation of core 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.
- Isolating a reactive core from chemical attack.
- For safe handling of the toxic materials.
- To get targeted release of the drug.
- To control release of the active components for delayed (timed) release or long-acting (sustained) release.
- The problem may be as simple as masking the taste or odor of the core.
- To Increase of bioavailability.
- To produce a targeted drug delivery.
- Protects the GIT from irritant effects of the drug.
- Extension of duration of activity for an equal level of active agent.

Formulation considerations

Generally Micro particles consist of two components[3,4].

Core material: The solid core can be mixture of active constituents, stabilizers, diluents, excipients and release-rate retardants or accelerators. The material to be coated. It may be liquid or solid or gas. Liquid core may be dissolved or dispersed material.

Composition of core material:

Drug or active constituent
Additive like diluents
Stabilizers

Coat or wall or shell material: Compatible, non-reactive with core material. Provide desired coating properties like strength, flexibility, impermeability, optical properties, and non hygroscopicity, tasteless and stable.

Coating Material

It is a inert substance which coats on core with desired thickness. Coating material composition of inert polymer, plasticizer, coloring agent, resins, waxes and lipids and release rate enhancers or retardants.

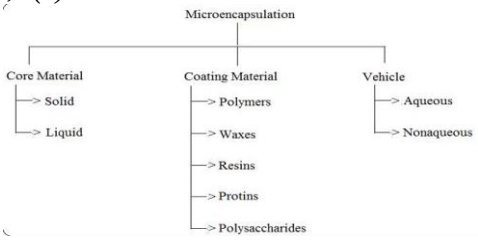

Fig 2: Formulation of Microencapsulation

Mechanisms behind the drug release

There are various mechanisms of drug release that are proposed for microencapsulation[5].

i. The coating is dissolved away from around the core such as when a liquid flavoring oil is used in a dry powdered beverage mix.
ii. A compressive force in terms of a 2 point or a 12 point force breaks open the capsule by mechanical means.
iii. The coating melts away from the core releasing the core in an environment such as that occurring during baking
iv. The capsule is broken open in a shear mode such as that in a waring blender or a Z-blade type mixer.
v. The core diffuses through the coating at a slow rate due to the influence of an exterior fluid such as water or by an elevated temperature.

Methods of preparation

Preparation of microspheres should satisfy certain criteria:

- The ability to incorporate reasonably high concentrations of the drug.
- Stability of the preparation after synthesis with a clinically acceptable shelf life.
- Controlled particle size and dispersability in aqueous vehicles for injection.
- Release of active reagent with a good control over a wide time scale.
- Biocompatibility with a controllable biodegradability.
- Susceptibility to chemical modification.

2. Microencapsulation methods

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

Air suspension: Microencapsulation by air suspension technique consist of the dispersing of solid, particulate core materials in a supporting air stream and the spray coating on the air suspended particles. Within the coating chamber, particles are suspended on an upward moving air stream. The design of the chamber and its operating parameters effect a recirculating flow of the particles through the coating zone portion of the chamber, where a coating material, usually a polymer solution, is spray applied to the

moving particles. During each pass through the coating zone, the core material receives an increment of coating material. The cyclic process is repeated, perhaps several hundred times during processing, depending on the purpose of microencapsulation the coating thickness desired or whether the core material particles are thoroughly encapsulated. The supporting air stream also serves to dry the product while it is being encapsulated. Drying rates are directly related to the volume temperature of the supporting air stream[6].

Coacervation phase separation:

This process of microencapsulation is generally referred to The National Cash Register (NCR) Corporation and the patents of B.K. Green. This process consists of three steps-

a) Formation of three immiscible phases; A liquid manufacturing phase, a coremateriał phase and a coating material phase.

b) Deposition of the liquid polymercoating on the core material.

c) Rigidizing of the coating material.

Step-1: The first step of coacervation phase separation involves the formation of three immiscible chemical phases: a liquid vehicle phase, a coating material phase and a core material phase. The three phases are formed by dispersing the core material in a solution of coating polymer, the vehicle phase is used as a solvent for polymer. The coating material phase consists of a polymer in a liquid phase, is formed by using one of the of phase separation-coacervation method, i.e. .by changing the temperature of the polymer solution, by adding a solution, or by inducing a polymer- polymer interaction[7,8].

Step-2:

It involves the deposition of the liquid polymer coating upon the core material. This is done by controlled mixing of liquid coating material and the core material in the manufacturing vehicle. The liquid coating polymer deposited on the core material if the polymer is adsorbed at the interface formed between the core material and liquid phase. The reduction in the total free interfacial energy of the system help to promote the deposition of the coating material, brought by the decrease of the coating material surface area during coalescence of the liquid polymer droplets.

Step-3:

In the last step rigidizing of the coating material done by the thermal, cross linking desolvation techniques, to forms a self-supporting microcapsule. Microencapsulation by coacervation phase separation process.

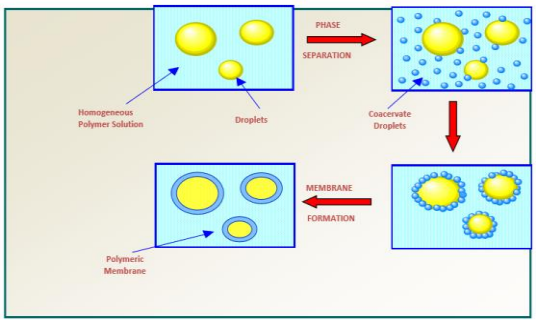

Fig 3: Mechanism of Co-Acervation

Multiorifice-centrifugal process:

The Southwest Research Institute (SWRI) has developed a mechanical process for producing microcapsules that utilizes. Centrifugal forces to hurl a core material particle trough an enveloping microencapsulation membrane thereby 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 and surface tension of the core material. The multiorifice-centrifugal process is capable for microencapsulating liquids and solids of varied size ranges, with diverse coating materials. The encapsulated product can be supplied as slurry in the hardening media or as a dry powder. Production rates of 50 to 75 pounds per our have been achieved with the process[9].

Spray drying and spray congealing:

Spray drying and spray congealing methods have been used for many years as microencapsulation techniques. Because of certain similarities of the two processes, they are discussed together. 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 of the coating is affected. The principal difference between the two methods, for purpose of this discussion, 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 method however is accomplished by thermally congealing a molten coating material or b solidifying a dissolved coating b introducing the coating core material mixture into a nonsolvent. Removal of the nonsolvent or solvent from the coated product is ten accomplished by sorption extraction or evaporation techniques.

Pan coating:

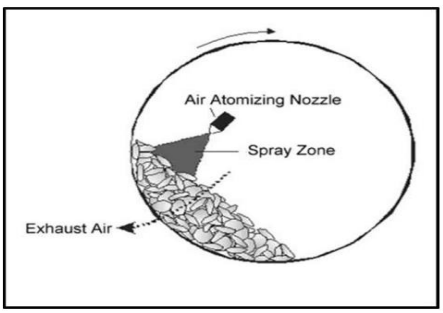

Fig 4: Schematic representation of Pan coating

The microencapsulation of relatively large particles by pan methods has become wide spread in the pharmaceutical industry. With respect to microencapsulation, solid particles greater than 600 microns in size are generally considered essential for effective coating and there process has been extensively employed for the of controlled release preparation. Medicaments are usually coated onto various spherical substrates such as nonpareil sugar seeds and the coated with protective lagers of various polymers. In

practice, the coating is applied as a solution or as an atomized spray to the desired solid core material in the coating pan. Usually, to remove the coating solvent, warm air is passed over the coated materials as the coatings are being applied in the coating pans.

Solvent evaporation techniques:

Solvent evaporation techniques are carried out in a liquid manufacturing vehicle (O/W emulsion) which is prepared by agitation of two immiscible liquids. The process involves dissolving microcapsule coating (polymer) in a volatile solvent which is immiscible with the liquid manufacturing vehicle phase. A core material (drug) 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 appropriate size microcapsules. Agitation of system is continued until the solvent partitions into the aqueous phase and is removed by evaporation. This process results in hardened microspheres which contain the active moiety. Several methods can be used to achieve dispersion of the oil phase in the continuous phase. The most common method is the use of a propeller style blade attached to a variable speed motor. Various process variables include methods of forming dispersions, Evaporation rate of the solvent for the coating polymer, temperature cycles and agitation rates. Important factors that must be considered when preparing microcapsules by solvent evaporation techniques include choice of vehicle phase and solvent for the polymer coating, as these choices greatly influence microcapsule properties as well as the choice of solvent recovery techniques. 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[1,11].

Electrostatic deposition:

This method is suitable for both solid and liquid droplets. Core and coating material are imparted electric charges by means of high voltage. Core is charged and placed in coating chamber and coating material is charged in solution when it leaves the atomizer device prior to spray as a mist. Since both are oppositely charged coating material gets deposited on core due to electrostatic attraction.

Vacuum deposition:

This is not a popular technique. Coating material is vaporized in chamber in which core material is present. Coating material gets deposited on core particles. Core particles are moved on conveyor system and they encounter hot vapours of coating material which gets deposited on them.

Polymerization:

A relatively new microencapsulation method utilizes polymerization techniques to form protective microcapsule. The methods involve the reaction of monomeric units located at the interface existing between a core material substance and a continuous phase in which the core material is dispersed[14].

Interfacial polymerization (IFP):

The capsule shell will be formed at the surface of the droplet or particle by polymerization of the reactive monomers. The substances used are multifunctional monomers. Generally used monomers include multifunctional isocyanates and multifunctional acid chlorides. These will be used either individually or in combination. The multifunctional monomer dissolved in liquid core material it will be dispersed in aqueous phase containing dispersing agent. A reactant multifunctional amine will be added to the mixture. This results in rapid polymerization at interface and generation of capsule shell takes place. A polyurea shell will be formed when isocyanate reacts with amine, polynylon or polyamide shell will be formed when acid chloride reacts with amine. When isocyanate reacts with hydroxyl containing monomer produces polyurethane shell.

In situ polymerization: IFP is the capsule shell formation occurs because of polymerization of monomers. In this process no reactive agents are added to the core material. Polymerization occurs exclusively in the continuous phase and on the continuous phase side of the interface formed by the dispersed core material and continuous phase. Initially a low molecular weight prepolymer will be formed, as time goes on the prepolymer grows in size. It deposits on the surface of the dispersed core material there by generating solid capsule shell.

3. Evaluation of Microencapsulation

Characterization: The characterization of the micro particulate 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.

Sieve analysis:

Separation of the microspheres into various size fractions can be determined by using a mechanical sieve shaker (Sieving machine, Retsch, Germany). A series of five standard stainless steel sieves (20, 30, 45, 60 and 80 mesh) are arranged in the order of decreasing aperture size. Five grams of drug loaded microspheres are placed on the upper-most sieve. The sieves are shaken for a period of about 10 min, and then the particles on the screen are weighed[16,17].

Particle size:

Particle size determination approximately 30 mg microparticles is redispersed in 2–3 ml distilled water, containing 0.1% (m/m) Tween 20 for 3 min, using ultrasound and then transferred into the small volume recirculating unit, operating at 60 ml/ s. The microparticle size can be determined by laser diffractometry using a Malvern Mastersizer X (Malvern Instruments, UK).

Polymer solubility in the solvents:

Solution turbidity is a strong indication of solvent power. The cloud point can be used for the determination of the solubility of the polymer in different organic solvents.

Viscosity of the polymer solutions:

The absolute viscosity, kinematic viscosity, and the intrinsic viscosity of the polymer solutions in different solvents can be measured by a U-tube viscometer (viscometer constant at 40 0C is 0.0038 mm2/s /s) at 25 ±

0.1˚C in a thermostatic bath. The polymer solutions are allowed to stand for 24 h prior to measurement to ensure complete polymer dissolution.

Bulk density:

The microspheres fabricated are weighed and transferred to a 10-ml glass graduated cylinder. The cylinder is tapped using an auto trap (Quantach- rome, FL, USA) until the microsphere bed volume is stabilised. The bulk density is estimated by the ratio of microencapsulated product weight to the final volume of the tapped microsphere bed[18].

Capture efficiency:

The capture efficiency of the microspheres or the percent entrapment can be determined by allowing washed microspheres to lyse. The lysate is then subjected to the determination of active constituents as per monograph requirement. The percent encapsulation efficiency is calculated using following equation:

% Entrapment = Actual content/Theoretical content x 100

Angle of contact: The angle of contact is measured to determine the wetting property of a micro particulate carrier. It determines the nature of microspheres in terms of hydrophlicity or hydrophobicity. This thermodynamic property is specific to solid and affected by the presence of the adsorbed component. The angle of contact is measured at the solid/air/water interface. The advancing and receding angle of contact are measured by placing a droplet in a circular cell mounted above objective of inverted microscope. Contact angle is measured at 200C within a minute of deposition of microspheres.

Morphology of Microspheres: The surface morphologies of microspheres are examined by a scanning electron microscope (XL 30 SEM Philips, Eindhoven, and The Netherlands). The microspheres are mounted onto a copper cylinder (10 mm in diameter, 10 mm in height) by using a double-sided adhesive tape. The specimens are coated at a current of 10 mA for 4 min using an ion sputtering device (JFC-1100E, Jeol, Japan).

Density Determination:

The density of the microspheres can be measured by using a multi volume pychnometer. Accurately weighed sample in a cup is placed into the multi volume pychnometer. Helium is introduced at a constant pressure in the chamber and allowed to expand. This expansion results in a decrease in pressure within the chamber. Two consecutive readings of reduction in pressure at different initial pressure are noted. From two pressure readings the volume and density of the microsphere carrier is determined.

In Vitro Methods:

There is a need for experimental methods which allow the release characteristics and permeability of a drug through membrane to be determined. For this purpose, a number of in vitro and in vivo techniques have been reported. In vitro drug release studies have been employed as a quality control procedure in pharmaceutical production, in product development etc. Sensitive and reproducible release data derived from physico chemically and hydro dynamically defined conditions are necessary. The influence of technologically defined conditions and difficulty in simulating in vivo conditions has led to development of a number of in vitro release methods for buccal formulations; however no standard in vitro method has yet been developed. Different workers have used apparatus of varying designs and under varying conditions, depending on the shape and application of the dosage form developed.

Beaker Method

The dosage form in this method is made to adhere at the bottom of the beaker containing the medium and stirred uniformly using overhead stirrer. Volume of the medium used in the literature for the studies varies from 50500 ml and the stirrer speed form 60-300 rpm.

Dissolution Apparatus:

Standard USP or BP dissolution apparatus have been used to study in vitro release profiles using both rotating elements, paddle [20, 21, 22 and basket 23, 24]. Dissolution medium used for the study varied from 100-500 ml and speed of rotation from 50-100 rpm.

4. Conclusion

The very much popular microencapsulation technique is the most convenient way of protection and masking, reduced dissolution rate, facilitation of handling, and spatial targeting of the active ingredient.This approach facilitates accurate delivery of small quantities of potent drugs; reduceddrug concentrations at sites other than the target organ or tissue; and protection of labile compounds before and after administration and prior to appearance at the site of action.Although significant advantage 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. The microencapsulation approach also beneficial for those drugs which required to dissolved into the intestine not in the stomach. Therefore, in future it is developed safe and efficient particular system.

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