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MICROENCAPSULATION: A REVIEW

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ABSTRACT

The review of Microencapsulation is a well-established 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 applications. 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. 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. Its scope extends beyond conventional microcapsules to all other small particulate systems such as self assembling structures that involve preparative manipulation. 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.

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. Microen capsulation is receiving considerable attention fundamentally, developmentally and commercially. The term microcapsule is defined as a spherical particle with size. Carying from 50nm to 2mm, containing a core substance .microspheres are in strict sense, spherical empty particle. However the term 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 200um. 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 application

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, 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. Several of these properties can be attained by macropackaging techniques; microencapsulation is the smallness of the coated particles and their subsequent use and adaptation to a wide variety of dosage forms and not has been technicallyfeasible.!1-5

Reasons for Microencapsulation

1. The primary reason for microencapsulation is found to be either for sustained or prolonged drugrelease.
2. This technique has been widely used for masking taste and odour of many drugs to improve

patientcompliance.

3. This technique can be used for converting liquid drugs in a free flowingpowder
4. The drugs, which are sensitive to oxygen, moisture or light, can be stabilized by microencapsulation.
5. Incompatibility among the drugs can be prevented bymicroencapsulation.
6. Vaporization of many volatile drugs e.g. methyl salicylate and peppermint oil can be prevented bymicroencapsulation.
7. Many drugs have been microencapsulated to reduce toxicity and Gl irritation including ferrous sulphate andKCl.

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.

Coating material properties

Stabilization of core material. Inert toward active ingredient. Controlled release under specific condition. Film-forming,pliable,tasteless,stable. Non-hygroscopic, no high viscosity, economical. Solube in an aqueous media or solvent or melting. The coating can be flexible, brittle, hard, thin etc.

Examples of coating material

Water soluble resins - gelatin, gum, arabic, starch, polyvinylpyrrolidone, carboxymethylcellulose, hydroxyethylcelluloe, methylcelluloe ,arabinogalactan ,polyviny alchol, polyacrylicacid.

Water insoluble resins - Ethylcellulose, Polyethylene, Polymethacrylate, Polyamide (Nylon), Poly (Ethylene Vinyl acetate), cellulose nitrate, Silicones, Poly lactideco glycolide.

Waxes and lipids - Paraffin, Carnauba, Spermaceti, Beeswax, Stearic acid, Stearyl alcohol, Glyceryl stearates

Enteric resins - Shellac, Cellulose acetate phthalate, Zein

RELEASE MECHANISMS

A variety of release mechanisms have been proposed for microcapsules [6]: A compressive force in terms of a 2 Point or a 12 point force breaks open the capsule by mechanical means. The capsule is broken open in a shear mode such as that in a waring blender or a Z-blade type mixer. The wall is dissolved away from around the core such as when a liquid flavoring oil is used in a dry powdered beverage mix.

The wall melts away from the core releasing the core in environment such as that occurring during baking The core diffuses through the wall at a slow rate due the influence of an exterior fluid such as water or by an elevated temperature.

MULTIORIFIC-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 particle trough an enveloping microencapsulation membrane thereby effecting mechanical icroencapsulation Processing variables include the rotational speed of the cylinder, the flow rate of the core & cutter 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 s a dry powder. Production rates of 50 to 75 pounds per our have been achieved with the process

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 reparation of controlled release beads. 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 In some cases, final solvent removal is accomplished in drying oven.

SPRAY AND DRYING 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 effected. 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 a molten coating material or b dissolved coating

SOLVENT EVAPORATION

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 choice 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

POLYMERIZATION

A relatively new microencapsulation method utilizes polymerization techniques to from protective microcapsule coatings in situ. 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. 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

Drug/Core material	Characteristic property	Purpose of encapsulation	Final product form
Actaminophen	slightly water soluble solid	Taste masking	Tablet
Aspirin	Slightly water soluble solid	Taste masking, sustained release	Tablet capsule
Islet of langerhans	Viable cells	Sustained normalization diabetic condition	Injectable
Isosorbide Dinitrate	water soluble solid	Sustained release	Capsules
Menthol	Volatile solution	Reduce of volatility	Lotion
Progrestone	Highly water	Sustained release	Varied
Potassium Chloride urease	water soluble solid	Permselectivity of enzyme, substrate, and reaction products	Dipersion
Vitamin a	Non volatile liquid	Stabilization oxidation	Dry Powder

Applications of Microencapsulation

Some of the application of microencapsulation are shown in (Table 4) and illustrated as below Microencapsulation can be used to prepare enteric-coated dosage forms, so that the medicament can be selectively absorbed in the intestine rather than the stomach. It can be used to mask the taste of bitter drugs. From the mechanical point of view microencapsulation has been used to aid in the

addition of oily medicines to tableted dosage form. This has been used to overcome problems inherent in producing tablets from tacky granulations. This was accomplished through improved flow properties. For example, the nonflowable multicomponent solid mixture of niacin, riboflavin, thiamine hydrochloride, and iron phosphate may be encapsulated and compress directly into tablets. It has been used to protect drugs from environmental hazards such as humidity light, oxygen or heat. Microencapsulation does not yet provide a perfect barrier for materials, which degrade in the presence of oxygen, moisture or heat, however a great degree of protection against these factors can be provided. For example, vitamin A and K have,been shown to be protected the of through improvedflow

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hygroscopic properties of many core materials be used to can insecticides and pesticides reduced by be may microencapsulation. Many drugs have been microencapsulated to reduce gastric irritation. In the fabrication of multilayered tablets for controlled release of the medicament contained in medial layers of tableted particles (Simon, 1996; Thies, 1983).

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 untowardeffects.

Solid biodegradable microspheres have the potential throughout the particle matrix for the controlled release of drug.

Microspheres attention not only for prolonged release, but also for targeting of anticancer drugs to the tumour.

The size, received much surface charge and hydrophilicity microspheres have been found to be important in determining the fate of surface of particles in vivo.

Studies on the macrophage uptake of microspheres have demonstrated their potential in targeting drugs to pathogens residing intracellularly

Single emulsion method

This method has been primarily used to encapsulate hydrophobic drugs through oil-in- water (o/w) emulsification process. The polymer is dissolved in a water-immiscible, volatile organic solvent such as dichloromethane, and the drug is dissolved or suspended in the polymer solution. The resulting mixture is emulsified in a large volume of water in the presence of an emulsifier (Jain, 2000; Hombreiro et al 2000; Passerini and Craig, 2002). The solvent in the emulsion is removed by either evaporation at elevated temperatures or extraction in a large amount of water, resulting in formation of compact microparticles. The rate of solvent removal is reported to affect the final morphology of microparticles. The solvent removal rate is determined by the temperature of the medium, the solubility characteristics of the polymer, and the solvent used (Hombreiro et al 2000; Passerini and Craig, 2002; Arshady, 1991). This method, however, is only available for the hydrophobic drugs because the hydrophilic drugs may diffuse out or partition from the dispersed oil phase into the aqueous phase, leading to poor encapsulation efficiencies (Hombreiro et al 2000; Arshady1991).

In hydrophilic drugs (e.g. Peptides and proteins), an oil-in-oil (o/o) emulsification method has recently received (Carrasquillo, 2001; Jiang and Schwendeman, 2001a, 2001b). In this method, the miscible organic solvents are employed to dissolve the drug and polymer, whereas hydrophobic oils are used as a continuous phase of the o/o emulsion. The microparticles are obtained by removing the organic solvents through evaporation or extraction process

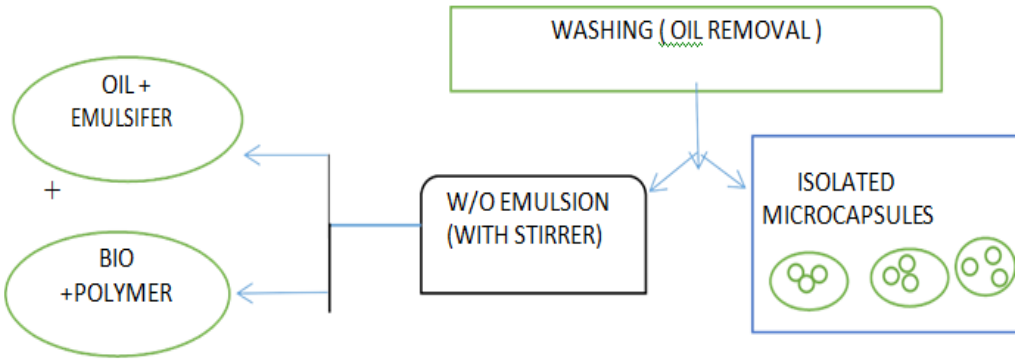

Fig.1: Single emulsion method

Double emulsion method

Most water-soluble drugs have been encapsulated by water-in-oil-in-water (w/o/w) methods. The aqueous solution of the water- soluble drug is emulsified with polymer- dissolved organic solution to form the water-in- oil (w/o) emulsion. The emulsification is carried out using either high speed homogenizers or sonicators. This primary emulsion is then transferred into an excess amount of water emulsifier under vigorous stirring, thus forming a w/ol/w emulsion. In the subsequent procedure, the solvent is removed by either evaporation or extractionprocess. One advantage of this method is encapsulation of hydrophilic drugs in an Madatuion aqueous phase with the high encapsulation efficiency. For this reason, the w/o/w emulsion system has been used widely for the development of protein delivery systems (Sinha and Trehan, 2003; Crotts and Park, 1998; Okochi and Nakano, 2000). The characteristics of the microspheres prepared by the double emulsion method are dependent on the properties of the polymer (such as composition and molecular weight), the ratio of polymer to drug, the concentration and nature of the emulsifier, temperature, and the

stirring/agitation speed during the emulsification process and depicted in (Crotts and Park, 1998; Okochi and Nakano,2000)

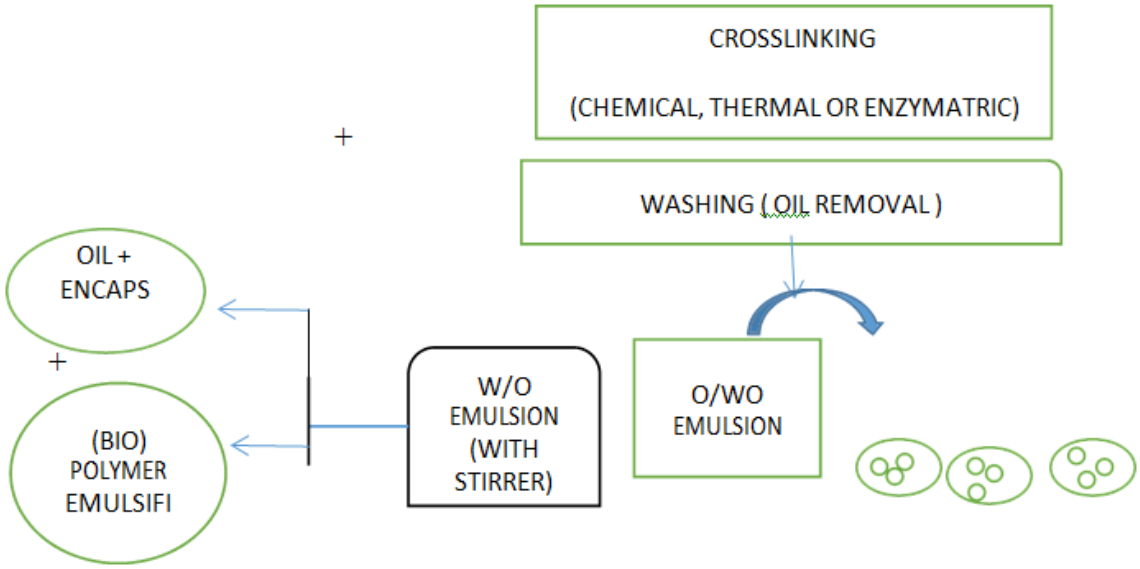

Fig.1: Double emulsion method

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 a science.

There's no ONE way to do it, and each new application provides a fresh challenge. Solving these riddles requires experience, skill and the mastery of many different technologies.

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