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A REVIEW: MICROENCAPSULATION

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ABSTRACT

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), and (iv) Desired, pre-programmed drug release profiles can be provided which match the therapeutic needs of the patient. This article gives an overview on the general aspects and recent advances in drug-loaded microparticles to improve the efficiency of various medical treatments. An appropriately designed controlled release drug delivery system can be a foot ahead towards solving problems concerning to the targeting of drug to a specific organ or tissue, and controlling the rate of drug delivery to the target site. The development of oral controlled release systems has been a challenge to formulation scientist due to their inability to restrain and localize the system at targeted areas of gastrointestinal tract. Microparticulate drug delivery systems are an interesting and promising option when developing an oral controlled release system. The objective of this paper is to take a closer look at microparticles as drug delivery devices for increasing efficiency of drug delivery, improving the release profile and drug targeting. In order to appreciate the application possibilities of microcapsules in drug delivery, some fundamental aspects are briefly reviewed.

Keywords: Drug Delivery Systems, Microcapsules, Controlled Release, Microencapsulation.

I. INTRODUCTION

The word ‘capsule’ implies a core and shell structure, and the term ‘microcapsules’ states the membrane enclosed particles or droplets dispersed in solid matrix lacking a distinctive external wall phase as well as intermediate types[1].Microencapsulation is a process by which solids, liquids or even gases may be enclosed in microscopic particles formation of thin coatings of wall material around the substances. The process had its origin in the late 1930s as a cleaner substitute for carbon paper and carbon ribbons as sought by the business machines industry. The ultimate development in the 1950s of reproduction paper and ribbons that contained dyes in tiny gelatin capsules released on impact by a typewriter key or the pressure of a pen or pencil was the stimulus for the development of a host of microencapsulated materials, including drugs[2,3]. 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. Microencapsulation includes Bioencapsulation which is more restricted to the entrapment of a biologically active substance (from DNA to entire cell or group of cells for example) generally to improve its performance &/or enhance its shelf life[4]. 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; however, the uniqueness of 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 technically feasible[5]. A well designed controlled drug delivery system can overcome some of the problems of conventional therapy and enhance the therapeutic efficacy of a given drug. To obtain maximum therapeutic efficacy, it becomes necessary to deliver the agent to the target tissue in the optimal amount in the right period of time there by causing little toxicity and minimal side effects. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. One such approach is using microspheres as carriers for drugs. Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers which are biodegradable in nature and ideally having particle size less than 200 μm[6,7].These micro-capsules have a number of benefits such as converting liquids to solids, separating reactive compounds, providing environmental protection, improved material handling properties. Active materials are then encapsulated in micron-sized capsules of barrier polymers (gelatin, plastic, wax ...)[8].

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Microparticles: "Microparticles" refers to the particles having the diameter range of 1-1000 µm, irrespective of the precise exterior and/or interior structures.

Microspheres: "Microspheres" particularly refers to the spherically shaped microparticles within the broad category of microparticles.

Microcapsules: "Microcapsules" refers to microparticles having a core surrounded by the coat or wall material(s) distinctly different from that of the core or pay-load or nucleus, which may be solid, liquid, or even gas.

Classification: - Microencapsulation mainly classified into three categories they are as follow

1. Mononuclear: -Mononuclear which contain the shell around the core & in second category. Monochord microcapsules have a single hollow chamber within the capsule
2. Polynuclear: -Polynuclear in which capsules have many core enclosed within the shell & in third category. The polycore microcapsules have a number of different sized chambers within the shell.
3. Matrix: - matrix encapsulation in which the core material is distributed homogenously into the shell material. The matrix type microparticle has the active ingredients integrated within the matrix of the shell material.

However, the morphology of the internal structure of a microparticle depends largely on the selected shell materials and the microencapsulation methods that are employed[9,10].

II. THE NEED FOR MICROENCAPSULATION

- It improves quality by masking unpleasant taste, aroma, and flavors[11,12].
- Sensitive drugs are isolated from moisture light and oxygen by microencapsulation.
- Reactive compounds are separated that prevent incompatibility between drugs[13,14].
- Improves handling of sticky compounds and liquids, also converts liquids into free-flowing solid powder.
- It protects the volatile drugs which vaporize at room temperature[15,16].
- it reduces the toxicity and GI irritation and many major side effects of the drug[17,18].
- It Increases safety by decreasing microbial growth[19,20].
- It provides enhanced stability to vitamin A palmitate by preventing from oxidation[21].

III. COMPOSITION OF MICROCAPSULES

Coating materials A wide variety of coating materials are available for microencapsulation. Some patent innovative coating polymers have also been developed for some special applications particularly among the bioadhesives and mucoadhesives. However, many traditional coating materials are satisfactory for the use in the gastrointestinal tract. They include inert polymers and pH sensitive ones as carboxylate and amino derivatives, which swell or dissolve according to the degree of cross-linking[22-26].

The selection of appropriate coating material decides the physical and chemical properties of the resultant microcapsules/ microspheres. While selecting a polymer the product requirements i.e. stabilization, reduced volatility, release characteristics, environmen-tal conditions, etc. should be taken into consideration. The polymer should be capable of forming a film that is cohesive with the core material. It should be chemically compatible, non-reactive with the core material and provide the desired coating properties such as strength, flexibility, impermeability, optical properties and stability[27-31].

IV. EXAMPLE OF CORE MATERIAL

Synthetic polymers:

a. Non-biodegradable polymers e.g. Polymethyl methacrylate (PMMA), Acrolein,Glycidyl methacrylate Epoxy polymers[38,39].

b. Biodegradable polymers e.g. Lactides, Glycolides & their co polymers[40]Poly alkyl cyanoacrylates Polyanhydrides.

Natural polymers

(a) Proteins: albumin, gelatin and collagen[41].

(b) Carbohydrates: agarose, carrageenan, chitosan, starch[42].

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(c) Chemically modified carbohydrates: poly dextran, poly starch[43].

Core materials The core material is the material over which coating has to be applied to serve the specific purpose. Core material may be in form of solids or droplets of liquids and dispersions. The composition of core material can vary and thus furnish definite flexibility and allow effectual design and development of the desired microcapsule properties. A substance may be microencapsulated for a number of reasons. Examples may include protection of reactive material from their environment, safe and convenient handling of the materials which are otherwise toxic or noxious, taste masking, means for controlled or modified release properties means of handling liquids as solids, preparation of free flow powders and in modification of physical properties of the drug[28,32-37].

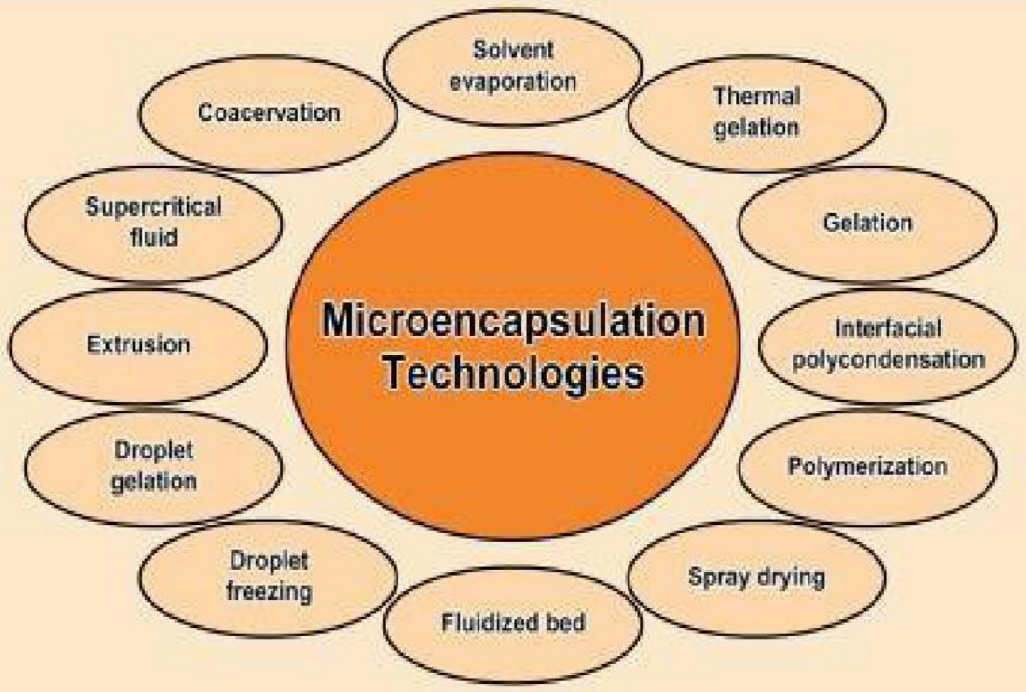

Fig 1: Microencapsulation technologies

Examples of coating materials:

1. Water soluble resins – Gelatin, Gum Arabic, Starch, Polyvinylpyrrolidone, Carboxymethylcellulose, Hydroxyethylcellulose, Methylcellulose, Arabinogalactan, Polyvinyl alcohol, Polyacrylic acid.
2. Water insoluble resins – Ethylcellulose, Polyethylene, Polymethacrylate, Polyamide (Nylon), Poly (EthyleneVinyl acetate), Cellulose nitrate, Silicones, Poly(lactideco-glycolide)
3. Waxes and lipids – Paraffin, Carnauba, Spermaceti, Beeswax, Stearic acid, Stearyl alcohol, Glyceryl stearates .
4. Enteric resins – Shellac, Cellulose acetate phthalate, Zein[44].

Techniques to manufacture microcapsules:

A) Physical method:

a) Pan coating

The pan coating process, widely used in the pharmaceutical industry, is among the oldest industrial procedures for forming small, coated particles or tablets. The particles are tumbled in a pan or other device while the coating material is applied slowly. In pan coating, solid particles are mixed with a dry coating material and the temperature is raised so that the coating material melts and encloses the core particles, and then is solidified by cooling; or, the coating material can be gradually applied to core particles tumbling in a vessel rather than being wholly mixed with the core particles from the start of encapsulation.[46]

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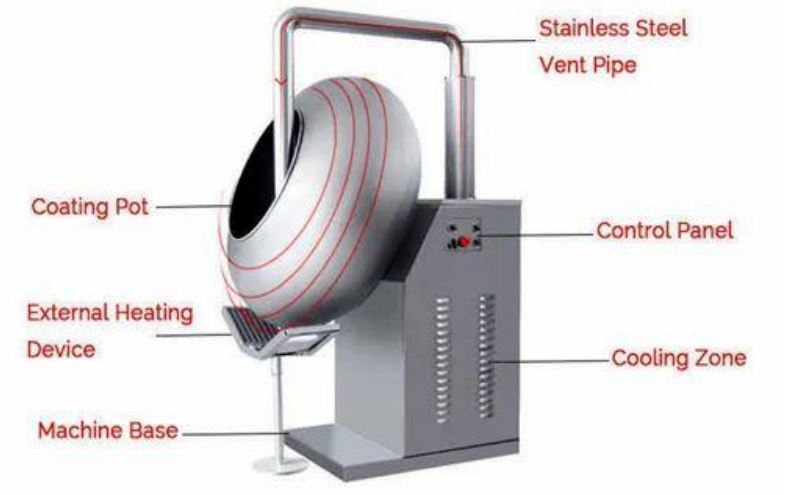

Fig 2: Pan Coating

b) Air-suspension coating

Microencapsulation by air suspension is a technique that gives improved control and flexibility compared to pan coating, via changing the times the core particles pass through the coating zone [47]. In this process, the solid particles are coated and dried while suspended in an upward moving air stream. Solutions and suspensions of coating materials in both water and volatile organic solvents are employed. However, this technique was developed for pharmaceutical industry [48], food industry [49], and cosmetic products [50] and is not suitable for encapsulating PCMs.

B) Chemical method

The most important chemical technique used for microencapsulation of PCMs is the in situ polymerization, which includes interfacial, emulsion and suspension polymerization, although there are some other methods [51,52].illustrates and compares the different types of polymerization methods used to form PCM microcapsules that are discussed below in more details.

a) In situ Polymerization

Like IFP the pill shell formation happens because of polymerization of monomers brought to The encapsulation reactor. In this method no reactive retailers are brought to the core material.Polymerization happens completely within side the continuous segment and at the non-stop segment side of the interface shaped with the aid of using the dispersed core material and non-stop segment.Initially a low molecular weight prepolymer will be shaped, as time is going at the prepolymer grows In size.It deposits at the floor of the dispersed middle material there with the aid of using producing strong pill shell.[53]

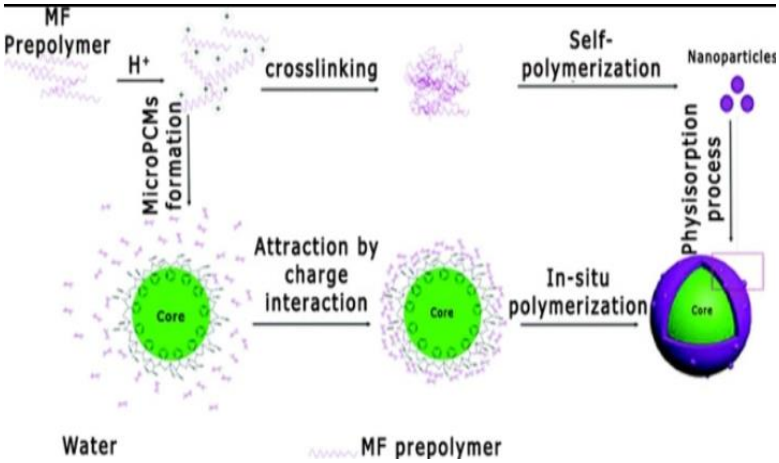

Fig 3: In situ polymerization

b) Interfacial polymerization

The materials used are multifunctional monomers, which include multifunctional isocyanates multifunctional

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acid chlorides.These can be used both personally or in combination.The multifunctional monomer dissolved in liquid center material.A coreactant multifunctional amine can be delivered to the mixture. Base is delivered to neutralize the acid fashioned all through the reaction.This effects in speedy polymerization at interface and era of pill shell [54]

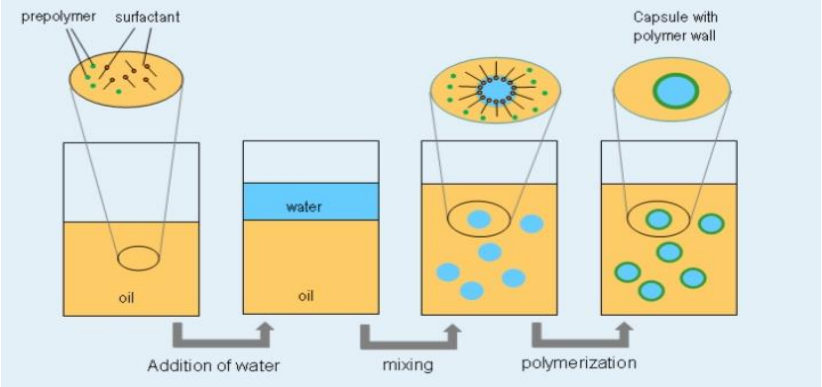

Fig 4: Interfacial polymerization

V. APPLICATION

1. Cell Immobilization:

In plant cell cultures microencapsulation, by mimicking cell natural environment, improves efficiency in production of different metabolites used for medical, pharmacological and cosmetic purposes. Human tissue are turned into bioartificial organs by encapsulation in natural polymers and transplanted to control hormonedeficient diseases such as diabetes and severe cases of hepatic failure. In continuous fermentation processes immobilization is used to increase cell density, productivity and to avoid washout of the biological catalysts from the reactor. This has already been applied in ethanol and solvent production, sugar conversion or wastewater treatment

2. Beverage Production:

Today beer, wine, vinegar and other food drinks production are using immobilization technologies to boost yield, improve quality, change aromas, etc...

3. Protection of Molecules from Other Compounds:

Microencapsulation is often a necessity to solve simple problem like the difficulty to handle chemicals (detergents dangerous if directly exposed to human skin) as well as many other molecule inactive or incompatible if mixed in any formulation. Moreover, microencapsulation also allows preparing many formulations with lower chemical loads reducing significantly processes' cost.

4. Drug Delivery:

After designing the right biodegradable polymers, microencapsulation has permitted controlled release delivery systems. These revolutionary systems allow controlling the rate, duration and distribution of the active drug. With these systems, microparticles sensitive to the biological environment are designed to deliver an active drug in a sitespecific way (stomach, colon, specific organs). One of the main advantages of such systems is to protect sensitive drug from drastic environment (pH,) and to reduce the number of drug administrations for patient.

5. Quality and safety in food, agricultural & environmental sectors:

Development of the "biosensors" has been enhanced by encapsulated bio-systems used to control environmental pollution, food cold chain (abnormal temperature change). [55,56]

VI. CONCLUSION

Microencapsulation way packaging an lively factor inside a tablet ranging in length from one micron to numerous millimeters. The tablet protects the lively factor from its surroundings till the suitable time. Then, the fabric escapes via the tablet wall by numerous way, which include rupture, dissolution, melting or diffusion. Microencapsulation is each an artwork and a science. There's no one manner to do it, and every new application

affords a clean challenge. Solving those riddles calls for experience, talent and the mastery of many different technologies.

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