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A Review on Microcapsules

Azagheswari, Binil Kuriokase, Sathireddy Padma and S. Padma Priya

Department of Pharmaceutics, College of Pharmacy,
Mother Theresa Postgraduate and Research Institute of Health Sciences

Abstract: Microcapsule system is one of the novel drug delivery system found applications in many areas of science and technology. Microencapsulation technology is an innovator in the encapsulation science. This technology forms a basis for the development of various micro and nano drug loaded capsules. This review paper will address the detail about the microencapsulation technology, commonly used microencapsulation methods in the formulation of microcapsules, their advantages and disadvantages and its wider applications in pharmaceuticals, cosmetics, agricultural industry, food technologies and textiles industry. This paper also described about the evaluation techniques, release mechanism of microcapsules and also the recent development in the drug loaded microcapsules.

Key words: Microcapsules · Microencapsulation · Application in Pharmaceuticals

INTRODUCTION

Conventional dosage forms are rapidly absorbed, with the ascending and descending portions of the concentrations versus time curve reflecting primarily the rate of absorption and elimination, respectively. In this oral dosage form, drug must be taken several times which results in fluctuating drug levels in plasma. This drawback can be overcome by formulation of sustained/controlled release dosage forms which provides drug release in an amount sufficient to maintain the therapeutic drug level over extended period of time, with release profiles sustained by the special technological construction and design of the system[1].

The objectives of sustained/ controlled release drug delivery include two important aspects namely spatial placement and temporal delivery of drug. Spatial placement relates to targeting a drug to a specific organ or tissue, while temporal delivery refers to controlling the rate of drug delivery to the target tissue. Several technical advancements have been made recently to sustain the duration of therapeutic activity and /or targeting the delivery of drug to a tissue[2].

Different types of sustained release dosage forms can be classified as the following [3,4].

- Single unit [matrix tablets, coated tablets and spansules]
- Multiple units [granules, microcapsules and microspheres]
- Inert- insoluble matrix
- Hydrophilic gel matrix [bio adhesive, erodible, non-erodible]
- Ion – exchange resins

Among the different types of SRDDS, microcapsules played the vital role in the development of dosage form for treating different ailments. Microcapsules are produced by microencapsulation technique. This technique has been widely employed in the design of controlled release and sustained release dosage forms. The use of microencapsulation for the production of sustained release dosage forms has been introduced by Smith, Nine and French in the early 1950's[5].

Depending upon manufacturing process various types of products are obtained in microencapsulation. These products are,

- *Microcapsules*: Mono or multinuclear materials enclosed by a coat or membrane are called as microcapsules.

Corresponding Author: Azagheswari, Department of Pharmaceutics, College of Pharmacy, Mother Theresa Postgraduate and Research Institute of Health Sciences.

- *Microspheres*: Mono or multinuclear materials embedded in spherical coating matrix are called microspheres.

Microcapsules developed for use in medicine consists of solid or liquid core material containing one or more drugs enclosed in coating material. The core may also be referred as nucleus and the coating as wall or sheet [6, 7].

Microencapsulation [8, 9]: Microencapsulation is a process of incorporating drugs into small size multiparticulate units. This technique involve coating of particles ranging dimensionally from several tenth of a micrometer to about 5000 micrometer.

Fundamentals of microencapsulation.

- Core materials
- Coating materials

Core Materials [10]: The core material can be liquid or solid in nature. The composition of the core material can be varied as liquid core which can be include dispersed and/or dissolved material and the solid core can be diluents, recipients and release rate retardants or accelerators. The shape of core should be uniform and regular. In order to obtain uniform coating on regular spherical particles, polymer type, shape and size of the core material are to be considered.

Coating Materials [11]: The selection of a specific coating material is dependent upon under to increase segmental mobility, imparts flexibility, reduce brittleness and increase resistance of the film coating to Failure produced by mechanical stress, substances such as phthalate esters, fatty acid esters and glycol derivatives.

Types of polymers used in the coating [12].

Natural:

- Protein - Albumin, Gelatin, Collagen
- Carbohydrates - Starch, Agarose, Chitosan
- Waxes - Beeswax, carnauba wax, Paraffin wax.

Synthetic: Poly (lactic acid), Poly (glycolic acid), Poly (hydroxyl butyrate), Poly Amines (nylons), Polyphosphazenes.

Additives [13]:

- *Solvents*: In the microencapsulation process the coating of film formers can be given to cores using a suitable organic (or) inorganic solvent. Solvents like methanol, ethanol, water, ethyl ether are example of solvent used for microencapsulation.
- *Plasticizers*: Plasticizers are normally added to polymeric film formers, particularly those used in pan coating and air suspension coating procedures, in or common type of plasticizers.
- *Surfactants*: Various anionic, cationic and non-ionic surfactants are sometimes added to film coating formulations that are to be sprayed or poured into the surface of cores in order to aid wetty and even spreading of the film coating solution. Interfacial polymerization and Emulsion polymerization involve the use of surfactants.
- *Anti-tactic agents*: To reduce adhesion and friction between surfaces during coating particularly in pan technology. Fatty acids such as stearic acids are more frequently used.
- *Colorants*: Colorants are added to the coating system prior to application by pan or air suspension technology to facilitate the visual observation of buildup of coating and to reduce the risk of accidental contamination of one batch of prepared microcapsules with another. The uniformity of mixing of batches of microcapsules having different release rates was denoted by colour when filled into outer hard gelatin capsules shells.

Microcapsules [14-16]: Microcapsules are characteristically free flowing powders consisting of proteins or systemic polymers, which are biodegradable in nature and ideally having a particle size less than 200 μm. Microcapsules of biodegradable and non-biodegradable polymers have been investigated for sustained and controlled fashion.

Characteristics:

- Microcapsules are spherical, empty particles.
- Microcapsules are free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature.
- They have a particle size less than 200 μm.
- Microcapsules also act as carriers for the targeting of the anti-cancer drug to the tumor.

- Microcapsules incorporate reasonably high concentration of drug.
- Stability of the microcapsules is high.
- Microcapsules are easily dispersible in aqueous vehicle for injection.
- Release of active agent with good control over wide time scale.
- Microcapsules have increase therapeutic efficiency, bioresorbability and target ability
- Microcapsules have good control of content release and also protect the drug

History of Microcapsules [17, 18]: In the year 1931, the micro encapsulating procedure for pharmaceuticals was published by Bunger Burg De Jong & Kars involved in the preparation of gelatine spheres. In the year 1950s when Green and Schleicher produced microencapsulated dyes by complex coacervation of gelatin and arabic gum for the manufacture of carbonless copying paper. The technologies developed for carbonless copy paper paved the way for the development of various microcapsule products in later years.

In 1960s, microencapsulation of cholesteric liquid crystal by complex coacervation of gelatin and acacia was reported to produce a thermo sensitive display material. Later, Fergason developed nematic curvilinear aligned phase (NCAP), a liquid crystal display system by microencapsulation of nematic liquid crystals.[19]

Thus the development of microcapsules revolutionised the modern drug delivery system.

Classification of Microcapsules [20]: Microcapsules can be classified on the basis of their size or morphology.

Micro/Nanocapsules: Microcapsules range in size from one micron (one thousandth of mm) to few mm. Microcapsules whose diameter is in the nanometre range are referred to as nanocapsules to emphasize their smaller size.

Morphology of Microcapsules [21]: Microcapsules can be classified into three basic categories as monocored, polycored and matrix types.

Monocored microcapsules have a single hollow chamber within the capsule. The polycore microcapsules have a number of different sized chambers within the shell. The matrix type micro particle has the active ingredients integrated within the matrix of the shell material. However, the morphology of the internal structure of a micro particle whose diameter is in the nanometre range is referred to as nanocapsule to emphasize their smaller size.

Important Feature of Microcapsules [22]: The most significant feature of microcapsules is their microscopic size that allows for a huge surface area. The total surface area is inversely proportional to the diameter. This large surface area is available for sites of adsorption and desorption, chemical reactions, light scattering, etc.

Techniques of Microcapsule Preparation [23, 24]: Microcapsule preparation by microencapsulation can be broadly divided into two main categories.

The first category includes the methods in which starting materials are monomers/prepolymers. In these methods chemical reactions are also involved along with microsphere/microcapsule formation.

The second category consists of those methods in which starting materials are polymers. Hence, in these methods no chemical reactions are involved and only shape fabrication took place.

The choice of the microencapsulation method depends on the nature of the polymeric/monomeric material used. Thus appropriate combination of starting materials and synthesis methods can be chosen to produce microencapsulated products with a wide variety of compositional and morphological characteristics. For example, poly (alkyl cyanoacrylate) nanocapsules are obtained by emulsion polymerisation, whereas reservoir type nylon microcapsules are usually prepared by interfacial polymerisation. Similarly albumin microcapsules are prepared by suspension crosslinking, polylactide microcapsules by solvent evaporation/solvent extraction and gelatin and related products by coacervation.

The most common microencapsulation techniques are detailed below.

Polymerization Techniques [24]: The conventionally used polymerization techniques are,

- Normal polymerization
- Interfacial polymerization

Normal Polymerization:
Carried out using different techniques.

- Bulk polymerization
- Suspension polymerization
- Emulsion polymerization

Bulk Polymerization: A monomer or a mixture of monomer along with the initiator is usually heated to initiate polymerization. The initiator is added to the reaction mixture to facilitate or accelerate the rate of reaction. The polymer obtained may be moulded or fragmented as microcapsules. Loading of drug is by adsorptive drug loading or adding drug during the process of polymerization.

Suspension Polymerization: It is also called as bead or pearl polymerization. Monomer is heated with active principles as droplets dispersion in continuous phase. The droplets may contain an initiator and other additives.

Emulsion Polymerization: In this polymerization, the presence of the initiator in the aqueous phase, which later on diffuses to the surface of micelles or the emulsion globules. Suspension and emulsion polymerization can be carried out at a lower temperature. The two process also lead to the formation of the higher molecular weight polymer at relatively faster rate. The major disadvantage of suspension and emulsion polymerization is association of polymer with the unreacted monomer and other additives.

Interfacial Polymerization: It is essentially proceeds involving reaction of various monomers at the interface between two immiscible liquid phases to form a film of polymer that essentially envelops the dispersed phase. Two reacting monomers are employed in this one of which dissolved in continuous phase while the other being dispersed in continuous phase. The continuous phase is generally aqueous in nature throughout which the second monomer is emulsified. The monomer present in the either phase diffuses rapidly and polymerize rapidly at the interface. Two conditions arise depending upon the solubility of formed monomer in the emulsion droplet. If the polymer is soluble in the droplet it will lead to the formation of the monolithic type of carrier on the other hand. If the polymer is in soluble in monomer droplet, the formed carrier is of capsular (reservoir) type.

Emulsion Techniques [25]:

Single emulsion technique

The micro particulate carriers of natural polymers, i.e. those of proteins and carbohydrates are prepared by single emulsion technique. The natural polymers are dissolved or dispersed in aqueous medium followed by dispersion in non-aqueous medium E.g. oil. Cross-linking of the dispersed globule is carried out.

- By heat cross linking
- By chemical cross linkers

Cross linking by heat is done by adding the dispersion to previously heated oil. Heat denaturation is not suitable for thermo labile drug.

Double Emulsion Technique: This method involves the formation of microcapsules from multiple emulsions or the double emulsion of type w/o/w.

This method is best suited for

- Water soluble drugs, peptides, proteins and vaccines.
- Both natural and synthetic polymer

Interfacial Polycondensation [26]: This technique involves the polycondensation (condensation polymerization) of two complementary monomers at the interface of a two phase system. For the preparation of microcapsules, this two-phase system is mixed under controlled conditions to form small droplets of one phase (dispersed phase) in the other one (continuous phase/suspension medium). The material to be encapsulated must be chosen in such a way as to be present (dissolved or dispersed) in the droplets. It is also necessary to use a small amount of a suitable stabilizer to prevent droplet coalescence or particle coagulation during the polycondensation process and capsule formation.

Interfacial polycondensation can be utilized to produce both monocore type or matrix type microcapsules, depending on the solubility of the polycondensate in the droplet phase. Thus if the polymer is soluble in the droplets, matrix type microcapsules are formed. On the other hand, if the polymer is not soluble, it precipitates around the droplets and leads to the formation of monocore type microcapsules. Preparation of microcapsules takes by interfacial polycondensation is applicable to a large number of polymers including polyamides, polyureas, polyurethanes and polyesters. Polyurea microcapsules encapsulating osmium tetroxide have been synthesised by using this technique.

Suspension Crosslinking [27]: Suspension crosslinking is the method of choice for the preparation of protein and polysaccharide micro-capsules. This technique involves

dispersion of an aqueous solution of the polymer containing core material in an immiscible organic solvent (suspension/dispersion medium) in the form of small droplets. The suspension medium contains a suitable stabilizer to maintain the individuality of the droplet/microcapsules. The droplets are subsequently hardened by covalent crosslinking and are directly converted to the corresponding microcapsules. The crosslinking process is accomplished either thermally (at >500º C) or by the use of a crosslinking agent (formaldehyde, terephthaloyl chloride, etc). Suspension crosslinking is a versatile method and can be adopted for microencapsulation of soluble, insoluble, liquid or solid materials and for the production of both micro and nanocapsules. Albumin nanocapsules containing doxorubicin and magnetite particles have been synthesized by using this technique.

Solvent Evaporation/Solvent Extraction [28, 29]: Microcapsule formation by solvent evaporation/solvent extraction is very similar to suspension crosslinking, but in this case the polymer is usually hydrophobic polyester. The polymer is dissolved in a water immiscible volatile organic solvent like dichloromethane or chloroform, into which the core material is also dissolved or dispersed. The resulting solution is added dropwise to a stirring aqueous solution having a suitable stabilizer like poly (vinyl alcohol) or polyvinyl pyrrolidone, etc. to form small polymer droplets containing encapsulated material. With time, the droplets are hardened to produce the corresponding polymer microcapsules. This hardening process is accomplished by the removal of the solvent from the polymer droplets either by solvent evaporation (by heat or reduced pressure), or by solvent extraction (with a third liquid which is a precipitant for the polymer and miscible with both water and solvent). Solvent extraction produces microcapsules with higher porosities than those obtained by solvent evaporation. Solvent evaporation/extraction processes is suitable for the preparation of drug loaded microcapsules based on the biodegradable polyesters such as polylactide, poly (lactideco- glycolide) and polyhydroxybutyrate.

Coacervation/Phase Separation [29]: Coacervation (or phase separation) is widely employed for the preparation of gelatin and gelatin-acacia microcapsules, as well as for a large number of products based on cellulose derivatives and synthetic polymers. Phase separation processes are divided into simple and complex coacervation.

Simple coacervation involves the use of a single polymer such as gelatin or ethyl cellulose, in aqueous or organic media, respectively. Complex coacervation involves two oppositely charged polymeric materials such as gelatin and acacia, both of which are soluble in aqueous media. In both the cases, coacervation is brought about by gradual desolvation of the fully solvated polymer molecules.

Microencapsulation by coacervation is carried out by preparing an aqueous polymer solution (1-10 %) at 40-50°C into which the core material (hydrophobic) is also dispersed. A suitable stabilizer may also be added to the mixture to maintain the individuality of the final microcapsules. A suitable desolvating agent (coacervating agent) is gradually introduced to the mixture, which leads to the formation of partially desolvated polymer molecules and hence their precipitation on the surface of the core particles. The coacervation mixture is cooled to about 5-20°C, followed by the addition of a crosslinking agent to harden the microcapsule wall formed around the core particles. Gelatin microcapsules loaded with carboquone as well as gelatin acacia microcapsules loaded with sulfamethoxazole have been produced by coacervation.

This method is specially designed for preparing the reservoir type of the system, i.e. to encapsulate water soluble drugs e.g. peptides, proteins, however, some of the preparations are of matrix type particularly, when the drug is hydrophobic in nature e.g. steroids. In matrix type device, the drug or the protein is soluble in the polymer phase. The process is based on the principle of decreasing the solubility of the polymer in the organic phase to affect the formation of the polymer rich phase called coacervates. The coacervation can be brought about by addition of the third component to the system which results in the formation of the two phases, one rich in the polymer, while the other one, i.e. Supernatant depleted of the polymer.

Spray Drying and Spray Congealing [30]: Spray drying and spray congealing methods are based on the drying of mist of the polymer and drug in the air. Depending upon the removal of the solvent or the cooling of the solution, the two processes are named spray drying and spray congealing respectively. The polymer is first dissolved in a suitable volatile organic solvent such as dichloromethane, acetone, etc. The drug in the solid form is then dispersed in the polymer solution under high-speed homogenization. This dispersion is then atomized in a stream of hot air. The atomization leads to the

formation of the small droplets or the fine mist from which the solvent evaporates instantaneously leading the formation of the microcapsules in a size range 1-100µm. Micro particles are separated from the hot air by means of the cyclone separator while the traces of solvent are removed by vacuum drying.

Other Techniques of Microencapsulation [31-33]: In addition to the techniques described above, microencapsulation can also be carried out by fluidised bed coating, melt solidification, polymer precipitation, co-extrusion, layer-by-layer deposition, supercritical fluid expansion and spinning disk.

- Fluidised bed coating is used for encapsulation of solid core materials including liquids absorbed into porous solids. This technique is used extensively to encapsulate pharmaceuticals. Ascorbic acid has been microencapsulated in polymethacrylate as well as ethyl cellulose by using this technique.
- Biodegradable microcapsules are also produced by the solidification of molten polymer droplets or by polymer precipitation. Insulin has been microencapsulated in polyanhydride by using this technique.
- In the polymer precipitation process, an aqueous solution of the polymer containing the drug is dropped into a stirred solution, which acts as the precipitating medium. Here, the polymer droplets precipitate immediately and are thus converted into the drug loaded microcapsules. Enzymes have been encapsulated in conjugated phenolic polymers by using this technique.
- The co-extrusion process also possesses a number of commercial applications. In this process a dual fluid stream of liquid core and shell materials is pumped through concentric tubes and forms droplets under the influence of vibration. The shell is then hardened by chemical crosslinking, cooling or solvent evaporation. Hepatocytes encapsulated in polyacrylonitrile were prepared by this technique.
- In layer by- layer deposition, polyelectrolyte multilayers are prepared by sequentially immersing a substrate in positively and negatively charged polyelectrolyte solutions in a cyclic procedure. Core shell particles with tailored size and properties are prepared using colloidal particles as the core material that serves as a template onto which multilayers are fabricated. Hollow capsules of organic, inorganic or hybrid particles can be obtained by dissolving the core material. Glucose oxidase has been microencapsulated by alternate deposition of polyallylamine and polystyrene sulfonate layers.
- Microencapsulation has also been carried out by rapid expansion of supercritical fluid. Supercritical fluids are highly compressed gases that possess several advantageous properties of both liquids and gases. Most widely used ones are supercritical CO_2, alkanes and nitrous oxide (N_2O). Different core materials such as pesticides, pigments, pharmaceutical ingredients, vitamins, flavours and dyes have been encapsulated by using this method.
- In the spinning disc method the microencapsulation of suspended core materials is carried out by using a rotating disc. Suspensions of core particles in liquid shell material are poured into a rotating disc and due to the spinning action of the disc, the core particles become coated with the shell material. The coated particles along with the excess shell material are then cast from the edge of the disc by centrifugal force, after which the shell material is solidified by external means (usually cooling). This technology is rapid, cost effective, simple and has high production efficiencies. Paraffin micro beads have been synthesized by using this technique.

Evaluation of Microcapsules [34,35]: A variety of analytical and physical methods is used to characterize particles and encapsulated ingredients.

- Particle size
- Payload
- Content uniformity and stability
- Active ingredient release profiles and activity
- Colloid stability
- Particle stability

Particles:

- Sizing down to 3 nm
- Zeta potential

Particle Morphology:

- SEM/EDX (scanning electron microscope/energy-dispersive X-ray spectroscopy)
- Environmental SEM/STEM [scanning electron microscope (SEM)/scanning-transmission electron microscope (STEM)]
- Optical microscopy

Thermal Analysis:

- Differential scanning calorimetry
- Thermal gravimetric analysis
- Dynamic mechanical analysis

Rheology:

- Low viscosity fluids, gelation and curing profiles, reinforced solid mechanical properties
- Large dynamic shear range, sub-ambient to >600°C temperature range
- Multiple frequency waveform generation

Payload/Content:

- HPLC (high performance liquid chromatography)
- IC, GC (gas chromatography), GC/MS (gas chromatography/mass spectrometry)
- Fluorescent
- Thermal gravimetric analysis

Release:

- Dissolution (pH, solvent)
- Simulated body fluids
- Cell culture
- Tissue culture

Stability:

- Controlled environment such as:
- Time
- Temperature
- Relative humidity
- Ultraviolet
- Simulated fluids
- Thermal and pressure
- By products

Release Mechanisms of Microencapsulation [36, 37]: The aim of a microencapsulation application is the isolation of the core from its surrounding; the wall must be ruptured at the time of use. Many walls are ruptured easily by pressure or shear stress, as in the case of breaking dye particles during writing to form a copy. Capsule contents may be released by melting the wall, or dissolving it under particular conditions. In other systems, the wall is broken by solvent action, enzyme attack, chemical reaction or slow disintegration.

Microencapsulation can also be used to control or slow the release of a drug into the body. This may permit one controlled release dose to substitute for several doses of non-encapsulated drug and also may decrease toxic side effects for drugs by preventing high initial concentrations in the blood. There is usually a certain desired release pattern. In some cases, it is zero-order, i.e. the release rate is constant. In this case, the microcapsules deliver a fixed amount of drug per minute or hour during the period of their effectiveness. This can occur as long as a solid reservoir or dissolving drug is maintained in the microcapsule.

The other typical release pattern is first-order in which the rate decreases exponentially with time until the drug source is exhausted. In this situation, a fixed amount of drug is in solution inside the microcapsule. The concentration difference between the inside and the outside of the capsule decreases continually as the drug diffuses.

The other mechanisms that may take place in the liberation of the encapsulated material include biodegradation, osmotic pressure, diffusion, etc. Each one will depend on the composition of the capsule made and the environment it is in. Therefore, the liberation of the material may be affected with various mechanisms that act simultaneously.

The release mechanism depends on the nature of application, for example, carbonless copy paper, scratch and sniff perfumes and self-healing structures rely on mechanical rupture of shell to release the core contents. The rupture may be caused by pressure as in case of carbonless copy paper and scratch and sniff perfumes or due to propagation of cracks as for self-healing structures.

In the self-healing structures microcapsules act as means of storing and delivering an *in situ* glue, to prevent the spread of cracks. Thus a microencapsulated healing agent and a catalyst known to trigger polymerization in the chosen agent are embedded in a composite matrix. Rupture of any microcapsules by an approaching crack defect releases the healing agent into the crack plane by capillary action. When the released healing agent comes in contact with the catalyst, the resulting polymerization bonds the crack face closed, stopping the defect in its track. For example urea formaldehyde microencapsulated dicyclopentadiene (DCPD) healing agent and Grubb's catalyst have been incorporated into an epoxy matrix to produce a polymer composite capable of self-healing.

Detergent industry utilises dissolution of shell wall of powder detergents for release of encapsulated protease enzyme in order to remove bloodstains from the clothing.

In food industry baking mixes encapsulated in fat are released after shell melting (when proper temperature is reached) to react with food acid to produce leavening agents, which gives baked goods their volume and lightness of texture.

In food industry some ingredients such as nutrients are encapsulated to mask taste and flavourings are encapsulated due to their volatile nature, that would otherwise evaporate out and be lost as in chewing gum.

Pesticides are microencapsulated to be released over time, allowing farmers to apply the pesticides less often rather than requiring very highly concentrated and toxic initial applications.

Similarly, in pharmaceutical industry microencapsulated products are designed for sustained/ controlled release by either biodegradation of the shell, or by diffusion through the shell. Aspirin, for example provides effective relief from fever, inflammation and arthritis, but direct doses of aspirin can cause peptic ulcers and bleeding. The drug is, therefore, encapsulated in ethyl cellulose or hydroxypropylmethyl cellulose and starch. In this way the aspirin diffuses through the shell in a slow, sustained dose rather than being released all at once. Insulin has also been encapsulated in biodegradable polylactic acid microcapsules for its controlled release into the body.

One of the important diffusion controlled defence application is novel clothing fabric, which contains microcapsules composed of chemical decontaminants encapsulated within semipermeable polymers. The polymer being selectively permeable to toxic chemical agents but impermeable to the decontaminating agents, thereby allowing the toxic chemicals to diffuse into the microcapsules where they undergo irreversible detoxifying chemical reactions.

Applications of Microencapsulation [38- 40]: Agriculture One of the most important applications of microencapsulated products is in the area of crop protection. Polymer microcapsules, polyurea, gelatin and gum Arabic serve as efficient delivery vehicles to deliver the pheromone by spraying the capsule dispersion. Further, encapsulation protects the pheromone from oxidation and light during storage and release.

Food Industry: Microencapsulation provide viable texture blending, appealing aroma release and taste, odour and colour masking in nutraceuticals. The technology enables food companies to incorporate minerals, vitamins, flavours and essential oils. In addition, microencapsulation can simplify the food manufacturing process by converting liquids to solid powder, decreasing production costs by allowing batch processing using low cost, powder handling equipment. Microcapsules also help fragile and sensitive materials survive processing and packaging conditions and stabilize the shelf life of the active ingredient.

Pharmaceutics: One of the major applications areas of encapsulation technique is pharmaceutical/ biomedical for controlled/sustained drug delivery. Potential applications of this drug delivery system are replacement of therapeutic agents (not taken orally today like insulin), gene therapy and in use of vaccines for treating AIDS, tumours, cancer and diabetes. Protein such as insulin, growth hormone and erythropoietin (used to treat anemia) are example of drugs that would benefit from this new form of oral delivery.

Microencapsulation forms tiny liquid-filled, biodegradable micro-balloons containing various drug solutions that can provide better drug delivery and new medical treatments for solid tumors and resistant infections. Microcapsules containing antitumor treatments and visualization markers, the treatment can be directed right to the tumor, which has several benefits over systemic treatment such as chemotherapy. The microcapsules also contain a contrast agent that enables C-T, X-ray or ultrasound imaging to monitor the distribution within the tissues to ensure that the entire tumor is treated when the microcapsules.

Microencapsulation Electrostatic Processing System-II experiment, or MEPS-II, led by Dennis Morrison at NASA Johnson Space Center, was performed on the station in 2002 and included innovative encapsulation of several different anti-cancer drugs, magnetic triggering particles and encapsulation of genetically engineered DNA..

With more than 60 years of encapsulation research and development experience, Southwest Research Institute (SwRI) is a leader in the field and have expertise in diverse technical fields such as pharmaceuticals, food and nutrition, polymer and materials science and process engineering, SwRI's encapsulation specialists solve product stability, release and application problems in a wide range of industries. SwRI has conducted more than 1,000 encapsulation research programs for commercial and government clients.

CONCLUSION

Microcapsule is one of the versatile drug delivery system of either oral or parenteral route of administration

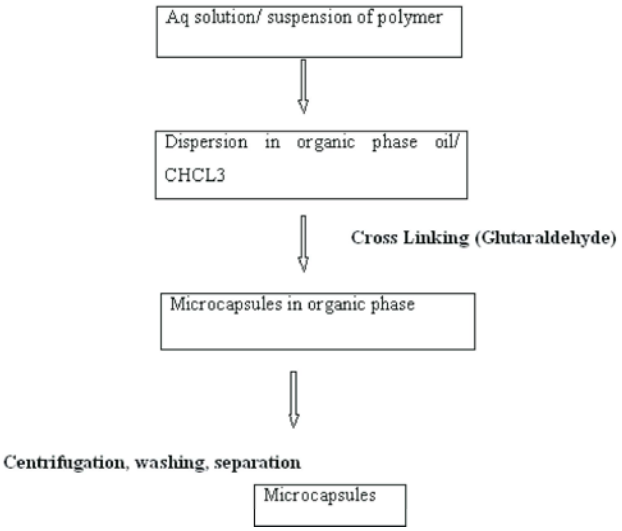

Fig. 1: Single Emulsion based method of microcapsules preparation

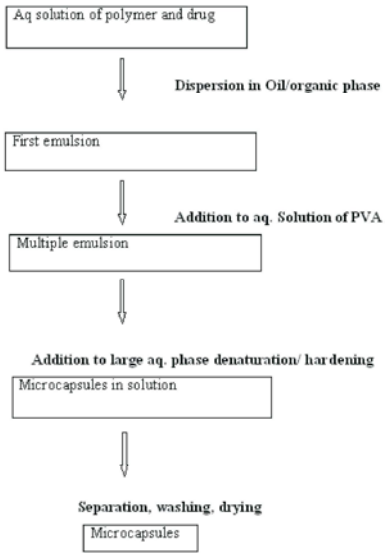

Fig. 2: Double Emulsion Method of Microcapsules Preparation

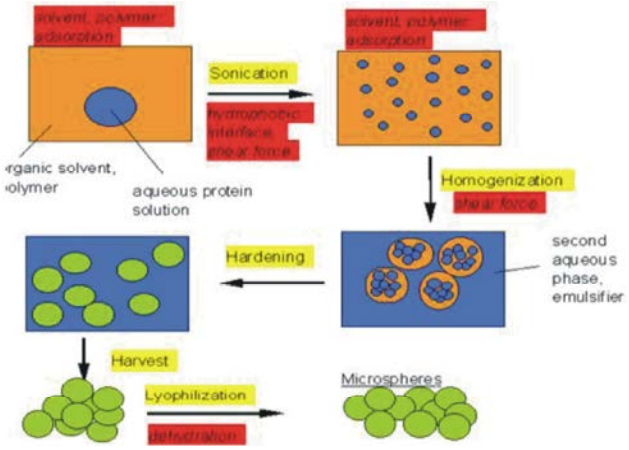

Fig. 3: Solvent evaporation method for the preparation of microcapsules [28, 29]

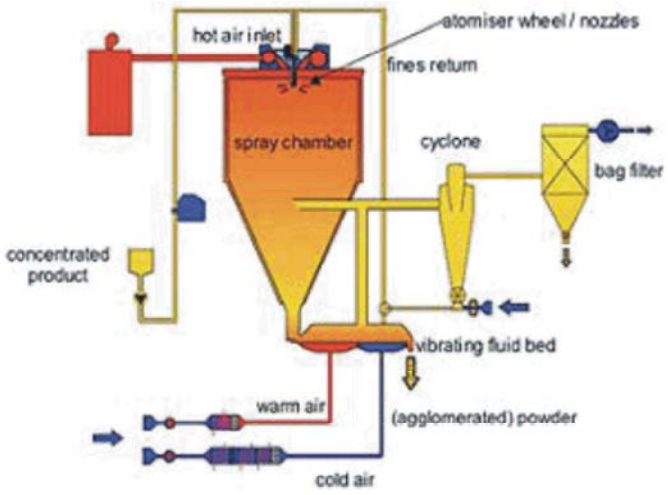

Fig. 4: Spray drying method for the preparation of microcapsules [30]

Table 1: Microencapsulation Processes & their approximate particle size [8]

Microencapsulation process	Applicable core material	Approximate particle size (μm)
Air suspension	Solids	35-5000
Coacervation-phase separation	Solids & liquids	2-5000
Multiorifice centrifugal	Solids & liquids	1-5000
Pan coating	Solids	600-5000
Solvent evaporation	Solids & liquids	5-5000
Spray drying and congealing	Solids & liquids	600

Table 2: List of micro capsulated drugs

S.No	Drug	Polymers used	Method
1.	Captopril	Carbopol,Chitosan	Emulsion Ionic Gelation[41]
2.	Verapamil	Ethyl cellulose, Cellulose Acetate	Hotmelttechnique,Ionic Gelation[42]
3.	Tetracycline	Ethyl Cellulose	Solvent evaporation[43]
4.	5-Flurouracil	Sodium Alginate/Chitosan	Suspension crosslinking[44]
5.	Propranolol	Eudragit	Solvent Evaporation[45]
6.	Metoprolol Succinate	SCMC, HPMC, Sodium alginate	Ionic Gelation[46]
7.	Cefotaxime	Ethylcellulose	Solvent Evaporation[47]
8.	Diclofenac Sodium	Ethylcellulose	Emulsion Solvent Evaporation[48]
9.	Norfloxacin	Gelatin	Coacervation, Complex emulsion [49]
10.	Salbutamol	SCMC,MC	Ionotropic Gelation[50]

of a medication and should ideally produce the required plasma level and maintain a steady level for a prolonged period of time and overcome problems associated with the conventional therapy and enhance the therapeutic efficacy of a given drug. The techniques of developing microacpsules through microencapsulation process pioneered the researchers to develop colloidal and nano drug delivery system for innumerable drugs.

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