ABSTRACT

Microencapsulation is a process in which tiny particles or droplets are surrounded by a coating to give small capsules with various useful properties. A microcapsule is a tiny sphere with a uniform wall around it. The inside material in microcapsule is referred to as the core, internal phase or fill, whereas the wall is sometimes called a shell, coating or membrane. This process produces small particles ranging in size from 1 to 1000 μm. It is a one of the most fascinating filed in the area of drug delivery system. Microencapsulation includes bioencapsulation which is more restricted to entrapment to the entrapment of a biologically active substance (from DNA to entire cell or groups of cells) generally to improve its performance & enhance its shelf life. The microencapsulation study would be encouraged with the motto “Small is better”\(^1\). There are several pharmaceutical applications of microencapsulation as discussed below.

**INTRODUCTION**

Microencapsulation is a process in which tiny particles or droplets are surrounded by a coating to give small capsules with various useful properties. A microcapsule is a tiny sphere with a uniform wall around it. The inside material in microcapsule is referred to as the core, internal phase or fill, whereas the wall is sometimes called a shell, coating or membrane. This process produces small particles ranging in size from 1 to 1000 μm. It is one of the most fascinating fields in the area of drug delivery systems. Microencapsulation includes bioencapsulation which is more restricted to entrapment to the entrapment of a biologically active substance (from DNA to entire cell or groups of cells) generally to improve its performance & enhance its shelf life. The microencapsulation study would be encouraged with the motto “Small is better”\(^1\). There are several pharmaceutical applications of microencapsulation as discussed below.

**TASTE MASKING OF DRUG BY MICROENCAPSULATION**

Taste that’s not desired, one of the main problems encountered with certain drugs. The problem of bitter and obnoxious taste is a challenge to the pharmacist in the present scenario. Various oral preparations and bulking agents have unpleasant, bitter-tasting components. The need to improved palatability in these products has prompted the development of numerous formulations with improved performance and acceptability. Taste masking by coating, solid dispersion system and ion exchange resin are the popular approaches. With respect to OTC preparations, such as cough and cold syrups, the impalatability of the preparation causes lack of patient compliance. To overcome the problem of bitter and obnoxious taste for pediatric and geriatric formulations are the challenge to the pharmacist in the present scenario. Two main approaches are utilized to overcome such problems. The first includes reduction of drug solubility in saliva, where a balance between reduced solubility and bioavailability must be achieved. Another approach is to alter the ability of the drug to interact with taste receptor.

Malik et al, 2011 describe that Ofloxacin is a synthetic chemotherapeutic antibiotic used for treatment of a variety of bacterial infections, but therapy suffers from low patients’ compliance due to its unpleasant taste. The taste masked microspheres of ofloxacin using Eudragit and to prepare orodispersible tablets of the formulated microspheres using natural superdisintegrant. Taste masking Eudragit E100 microspheres were prepared by solvent evaporation technique. The microcapsules of ofloxacin was prepared and the taste of the drug was masked by this method by using eudragit polymers.\(^2\)

Sushant and Satheesh, 2009 describe Masking of bitter taste of clarithromycin by microencapsulation in this technique alginate microcapsules were prepared by employing the sodium alginate in combination with the two hydrophilic, polymers-methyl cellulose and hydroxypropyl methyl cellulose. These polymers are suitable for taste masking as a coat material that is used for the preparation of the alginate microcapsules. The taste masked microcapsules by this technique was made and the taste was masked.\(^3\)

**DELIVERY OF DNA VACCINES**

Erodible hydrophobic polyanhydrides \([e.g.,\ poly(\text{fumaric-co-sebacic anhydride})]\) exhibited strong bioadhesiveness and microparticles made of such polymers have been investigated as potential oral drug delivery systems. The bioadhesiveness occurs due to the hydrogen bonding interactions between mucin and carboxylic acid groups formed during the polymer erosion. Furthermore, the small size of microparticles provides additional assistance by promoting cellular uptake of the formulation. Thus owing to the small size of...
microparticles and the chemical attributes of the polymeric system, the bioadhesive microparticles have shown enhanced oral bioavailability of dicumarol, insulin, and DNA. Mohamed and Walle 2006 described the fabrication of DNA-loaded poly (lactic-co-glycolic acid) (PLGA) microcapsules with novel surface morphologies that will be of use in pulmonary delivery. A water-in-oil-in-water (w/o/w) double emulsion–solvent evaporation technique was used for the preparation of microcapsule. The approach was to examine surface morphology and DNA encapsulation efficiency as a function of primary emulsion stability; using two surfactant series based on hydrophile–lipophile balance and hydrophobe molecular weight. The depth and definition of the dimples was greatest for triblock copolymers with high MW hydrophobe blocks. By cascade impaction, the geometric mean weight diameter of the microcapsules was 3.43μm, suggesting that they will be of interest as biodegradable pulmonary delivery vehicles.

Polymeric microspheres have been used for delivery of DNA vaccines, which enable prolonged immune responses through sustained release of DNA encoding a protein antigen. It has been known that <10mm particles are preferentially internalized through phagocytosis by macrophages and antigen-presenting cells. Poly(lactic-co-glycolic acid) (PLGA) was used as an encapsulating polymer in the initial research with promising results. On the other hand, disadvantages of PLGA particles in delivering DNA vaccines were acidification of microenvironment, which can inactivate encapsulated DNA, and slow release rate, which does not catch up with the life span of the target cells such as dendritic cells. In order to provide rapid and tunable release and to avoid internal acidification, pH-triggered biodegradable polymers based on poly(ortho esters) and polyb-amino esters are preferred. These microspheres loaded with DNA successfully internalized into the antigen presenting cells, enhanced immune response and suppressed in vivo tumor challenges significantly.

PRO DRUG APPROACH

The ester pro drug contained in biodegradable polymeric microparticle system prepared using the o/w emulsion solvent evaporation methods prepared a composition in the form of thin film or strip composed of microspheres containing antibiotic such as minocycline HCl. It was made using a biodegradable polymer, prepared by a modified o/w emulsification technique followed by solvent evaporation. Water-soluble polysaccharide polymers such as pectin was used for making thin film or strip containing microspheres intended for local sustained release administration into the periodontal pocket. The thin film or strip is coated by spray-coating with cation salt aqueous solution of calcium or barium chlorides. In one embodiment, Traynor et al. used the o/w emulsion to produce sol-gel microcapsules (containing sunscreens) that are highly positively charged using non-ionizing cationic additives which can include cationic polymers.

BIODEGRADABLE AND BIOCOMPATIBLE MICROPARTICLES

A novel method for the preparation of biodegradable and biocompatible microparticles containing a biologically active agent such as risperidone or testosterone. The method involve dissolution of biologically active agent in a blend of at least two substantially non-toxic solvents, free of halogenated hydrocarbons such as benzyl alcohol and ethyl acetate. The blend was dispersed in an aqueous solution to form droplets. The resulting emulsion is added to an aqueous extraction medium. One of the solvents in the solvent blend would be extracted in the quench step (aqueous solution) more quickly than the other solvent. Owing to the high boiling point of the left solvent (benzyl alcohol) which is not easily removed by evaporation in air or other conventional evaporative means, some of the more rapidly extracted solvent can be added to the quench extraction medium prior to addition of the emulsion. Thus, when the emulsion is added to the quench liquid, extraction of the more rapidly extracted solvent is retarded and more of the second, more slowly extracted solvent is removed. A method for encapsulating vitamins, food supplements, oil soluble substances at high loading (70 wt %) by the solvent o/w emulsion extraction technique. Since evaporating the solvent from the dispersion is not applicable for delicate and sensitive compounds and it is not effective, because diffusion of solvent through a hard polymer wall is very slow, water at 10-30 times higher than the whole quantity of the organic solvent is added to the emulsion for extracting the solvent. Makadia and Siegel et al. describe poly lactic-co-glycolic acid (PLGA) has been among the most attractive polymeric candidates used to fabricate devices for drug delivery and tissue engineering applications. PLGA is biocompatible and biodegradable, exhibits a wide range of erosion times, has tunable mechanical properties and most importantly, is a FDA approved polymer. In particular, PLGA has been extensively studied for the development of devices for controlled delivery of small molecule drugs, proteins and other macromolecules in commercial use and in research. The various fabrication techniques for these devices and the factors affecting their degradation and drug release.7

OTHER PHARMACEUTICAL APPLICATION

An injectable slow-release partial opioid agonist or opioid antagonist in a poly (D, L-lactide) microspheres with a small amount of residual ethyl acetate was provided by where an o/w emulsion is first prepared from an organic phase made of ethyl acetate and an aqueous phase comprised an aqueous ethyl acetate containing solution of polyvinyl alcohol. Microspheres are recovered by extraction with water. Prepared single wall biodegradable microspheres by extracting an o/w emulsion containing steroidal and non-steroidal anti-inflammatory agents. Otherwise, double wall microspheres were prepared. Microspheres containing the active ingredient were then immobilized on a substrate surface in a polymeric matrix that is an implantable medical article or an in situ formed matrix. Solidification method of the hydrophilic capsule materials such as gelatin can be through rapidly lowering the temperature and subsequent dehydration. While such method achieved some significant commercial success, difficulties have sometimes been encountered in rapidly inducing solidification of the microencapsulating material. The use of various gel forming proteins (collagen and gelatin) and polysaccharides (agar, calcium alginate, and carrageenan) introduced a milder, biocompatible immobilization or isolation system employed a one step method for the preparation of microspheres having enteric and controlled release characteristics in one embodiment and swelling and controlled properties in another using the nonaqueous solvent evaporation method. Microspheres were especially useful for delivery of moderately non-polar active ingredients but can be formulated to deliver very soluble polar compounds. Single o/w or double w/o/w emulsion solvent evaporation method was utilized to prepare microspheres with improved
Encapsulation of probiotics in a biodegradable polymer matrix has a number of advantages shown in table 1. Once entrapped/encapsulated in matrix beads or in microcapsules, the cells are easier to handle than in a suspension or in slurry. The number of cells in beads or microparticles can be quantified, allowing the dosage to be readily controlled. Cryo & osmoprotective components can be incorporated into the matrix, enhancing the survival of cells during processing and storage. Finally, once the matrix beads/microcapsules have been dried, a further surface coating can be applied. This outer layer can be used to alter the aesthetic and sensory properties of the product and may also be functional, providing an extra level of protection to the cells. In addition, the coating layer can have desirable dissolution properties, which permit delayed release of the cells or release upon, for example, a change in pH.

Various polymer systems have been used to encapsulate probiotic microorganisms to protect against low pH and high bile concentrations and to enhance physical stability during downstream processing. Microcapsule or bead systems using various biopolymers are very easy to prepare on a lab-scale, and any ingredients can be encapsulated, whether it is hydrophilic, hydrophobic, liquid, or viscous oil, a solid etc. However, the scaling up of the process is very difficult and processing costs are very high. Moreover, most of the conventionally produced microcapsules (e.g. calcium alginate beads/microcapsules), tend to be very porous which allows fast and easy diffusion of water and other fluids in and out of the matrix.

Spherical polymer beads with diameters ranging from 0.3 to 3.0 mm and immobilizing active biomass are produced using extrusion or emulsification techniques, by thermal (k-carrageenan, gellan, agarose, gelatin) or ionotropic (alginate, chitosan) gelation of the droplets.

Mortazavian et al 2007 describe probiotic microorganisms and their products on the one hand, and their general weak viability in food products (especially fermented types) as well as gastrointestinal conditions on the other hand, has encouraged researchers to innovate different methods of probiotics viability improvement. Microencapsulation of the probiotic cells is one of the newest and highly efficient methods, which is now under the special attention and is being developed by various researchers and describe the principles and methods of probiotic cell microencapsulation.

**Pesticide Microencapsulation**

It is having the Controlled release with improved residual activity and higher persistence. They are also higher specificity in toxicity and volatility reduction. They are Easy to handle. The choice of polymer wall is to suit the required purpose. Such microcapsules are flexible in controlling release rate. Eg- Isocyanate Microcapsules, having the thin outer layer which is diffusion resistant to the flow of pesticide. Thicker spongy layer provide the mechanical support and have unusually low microcapsule wall to core ratio. Eg Isocyanate Microcapsules as shown in figure 1.

![Figure 1- Isocyanate Microcapsules](Image)

**Table 1: Applications of Micro-Encapsulation of Probiotic Bacteria**

<table>
<thead>
<tr>
<th>Culture</th>
<th>Product</th>
<th>Technique/Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. bifidum, B. infantis &amp; B. longum</td>
<td>Cresenza cheese</td>
<td>Calcium alginate gels</td>
</tr>
<tr>
<td>L. paracasei</td>
<td>Cheddar cheese</td>
<td>Milk fat</td>
</tr>
<tr>
<td>L. casei</td>
<td>Yoghurt</td>
<td>k-Carrageenan and locust bean gum</td>
</tr>
<tr>
<td>B. bifidum, B. adolescens</td>
<td>White brined cheese</td>
<td>Cream</td>
</tr>
<tr>
<td>L. lactis subsp. Lactis</td>
<td>Fresh cheese</td>
<td>k-Carrageenan and locust bean gum</td>
</tr>
<tr>
<td>L. casei</td>
<td>Lactic acid</td>
<td>Liquid core alginate capule</td>
</tr>
<tr>
<td>Lactobacilli</td>
<td>Frozen dessert</td>
<td>Calcium alginate</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>Cheddar cheese</td>
<td>Milk fat</td>
</tr>
<tr>
<td>Lactococci</td>
<td>Cream</td>
<td>Calcium alginate</td>
</tr>
<tr>
<td>B. bifidum, B. infantis</td>
<td>Mayonnaise</td>
<td>Calcium alginate</td>
</tr>
</tbody>
</table>

B. = Bacillus, L. = Lactobacillus
Its improve the delivery of bioactive compounds eg probiotics, vitamins and minerals, fatty acids, antioxidants.  

Another example is Milk fat microcapsules. It should protect flavor, the enzymes and give low fat cheese as well as texture of full fat cheeses shown in fig 3.

IMMOBILIZATION AND ENCAPSULATION (CELL IMMOBILIZATION)-
Cell Entrapment in a gel matrix of alginites is the most popular system of immobilization reported. The terms immobilization and encapsulation were used interchangeably in most reported literature. While encapsulation is the process of forming a continuous coating around an inner matrix that is wholly contained within the capsule wall as a core of encapsulated material, immobilization refers to the trapping of material within or throughout a matrix. A small percentage of immobilized material may be exposed at the surface, while this is not the case for encapsulated material. Encapsulation occurs naturally when bacterial cells grow and produce exo-polysaccharides. The microbial cells are entrapped within their own secretions that act as a protective structure or a capsule, reducing the permeability of material through the capsule and therefore less exposed to adverse environmental factors. Many lactic acid bacteria synthesize exo-polysaccharides, but they produce insufficient exo-polysaccharides to be able to encapsulate themselves fully.

PROTECTION OF MOLECULES FROM OTHER COMPOUNDS
Protection of the chemicals, very dangerous for our body, is required. This problem can be solved by micro encapsulation like the difficulty to handle chemicals (detergents dangerous if directly exposed to human skin) as well as many other molecules inactive or incompatible if mixed in any formulation.

DEVELOPMENT OF MATERIALS FOR SMART SYSTEMS
New applications of the microencapsulated additives as functional materials or smart system were found in the recent past time. Intelligent sealants contain spherules with a moisture soluble shell. Following shell dissolution the core material swells and reaches a multiple of the initial volume. Screws are immediately glued together during tightening if the threads are coated with glue containing microcapsules. Applying the microencapsulation technology it is possible to associate apparent contradictory properties in one material. After microencapsulation water-soluble fertilizers, insecticides or herbicides withstand even heavy rain and function over the complete season. Possible application areas are:
- Plastics industry (incorporation of active agents or additives)
- Plating (incorporation of lubricants or corrosion inhibitors)
- Building industry (heat accumulators, pesticides)
- Painting industry (pigments, antifouling agents)
- Textile industry

CURRENT AND FUTURE DEVELOPMENTS
Micro encapsulation formulations have many advantages over normal formulations. With this formulation, less frequent drug administration is possible, lower plasma peak concentration can be obtained to avoid adverse effects. This technology to ensure time controlled pulsatile release of bioactive compounds has been developed. Micro-encapsulated products increase the stability, bioavailability, and dissolution of the drug properties. This is also useful in the other fields like biotechnology for the cell immobilization, in food industry, in drug delivery etc. The pulsatile delivery of bioactive compound is possible. In pharmaceuticals micro encapsulation could bring improvement of existing approaches to treatment of various diseases. Still, numerous studies of micro encapsulation techniques are believed to result in the development of new and effective clinical protocols in near future. Various type of micro encapsulated drug delivery system have been studied in the recent years these system releases the drug in respond to various physiological stimuli according to need of body. Thus it shows broad potential opportunities in using various strategies of drug targeting for resolving important clinical problems.

CONCLUSION
The microencapsulation technology, which started as a way of encapsulating dyes and flavors, has now become one of the most intriguing fields in the area of controlled drug delivery systems. The encapsulation techniques have been advanced to such a level that not only small molecular weight drugs but also macromolecules, such as proteins and genes, can be delivered via microparticle carriers. Although the technological advances have led to commercialization of several microparticulate products in recent years, many technical problems are to be overcome yet. Examples of such hurdles are maintaining the stability of encapsulated drugs throughout the lifetime of the products, manipulating release rates according to the applications, and transferring bench scale processes to the manufacturing scale. Some of the answers to those problems have been provided by advances in polymer chemistry, formulation efforts, and recent progresses in new microencapsulation techniques. The microencapsulation technology will remain as one of the most important areas in drug delivery and various other applications.

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