REVIEW ON MICROENCAPSULATION OF BIOPHARMAEUTICAL CLASSIFICATION SYSTEM CLASS II DRUGS

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Abstract

Microencapsulation is a process in which minor particles or beads are layered with several useful properties to give small containers, of numerous helpful properties. In general it is used to join dietary fixations, proteins, cells or different materials on a smaller metric scale. It can also be used to enclose solids, fluids or gases in a micrometric splitter made of hard or delicate dissolvable film to minimize recurrence of dosage and avoid pharmaceutical corruption. The strategy of microencapsulation plays the vital role in enhancing the solubility of BCS class second and fourth remedy. This strategy is also implemented in to increasing the bioavailability. The objective of this periodical study is to review the state of art microencapsulation strategy of food ingredients through different process and to provide the relevant theoretical and practical knowledge on these process.

Key words- *Core materials, Coating materials, Microencapsulation*

INTRODUCTION

The term microencapsulation is well-defined as the method of integrating remedy or any other material or active agent within the core. In this process small particles of any nature whether it is solid or liquid are coated by the polymers of appropriate nature. in order to protect the inner material from environmental conditions or conditions inside the body. These micro-encapsules are available in various particle size range varying from microns to millimeters. The purpose of microcapsule was to alter the release of drug from any formulation. The material which is present in the capsule is called as core material and the material which is used to coat it is known as coating material. The material inside the capsule release by several mechanisms. The release rate of drug from capsule is modified which will help in attaining optimum level of drug inside the body of long duration which is quite difficult in case of conventional dosage form.[1,2]

S.NO.	CLASSIFICATION	PERMEABILITY	SOLUBILITY	EXAMPLE
1.	First Class Drugs	HIGH	HIGH	Metoprolol
2.	Second Class Drugs	HIGH	LOW	Aceclofenac
3.	Third Class Drugs	LOW	HIGH	Cimetidine
4.	Fourth Class Drugs	LOW	LOW	Bifonazole

BCS CLASSISICATION OF DRUGS

BCS classification is a method which differentiates or distinguished the drugs on the behalf of their solubility and permeability. According to this system drugs are classified into 4 classes on the basis of solubility and permeability:-As clear from above table BCS class drugs are having low solubility and high permeability. If soluble is low it will also lead to dissolution problem. Due to low solubility dissolution will also get hindered which cause problem with release of drug. It leads to fluctuation of dose of drug inside body. So in order to improve solubility various techniques are used out of which microencapsulation is one. By forming microencapsulate dosage form its solubility can be improved which will improve its dissolution which leads to resolve the problem of dose fluctuation inside body.[3,4,5]

EXAMPLES OF BCS CLASS 2 DRUGS

Sr.No.	Drugs
1	Amiodarone
2	Atorvastatin
3	Azithromycin
4	Carbamazepine
5	Carvedilol
6	Chlorpromazine
7	Dapsone

8	Diclofenac
9	Glipizide
10	Indomethacin
11	Naproxen
12	Phenytoin
13	Warfarin
14	Tacrolimus
15	Ofloxacin

Reasons for microencapsulation [6]:-

- For improving the drug release.
- For making the salty medicines taste better.
- To deliver shelter from environmental conditions.
- To avoid incompatibilities between drugs.
- To prevent loss of various volatile components.
- To deliver the drug at target site.
- To increase the availability of drugs.
- To improve the handling properties of sticky materials.
- To convert liquid drugs in free flowing powders.

FORMULATION CONSIDERATION FOR MICROENCAPSULATION

For microencapsulation of any drug several consideration need to be taken. The requirement for microencapsulation of drugs following things are required.

i. ***Core materials:***- Core material is classified as the material that is either solid or liquid that will be integrated into the polymer shell, in other words we may assume that the core material is the material that is filled inside the polymer coating that will release certain mechanism from the formulation. If core material is liquefied in environment it may be available in the dispersed form, if core material is solid in the material of nature, diluent, stabilizer or excipient may be available.[7]

ii. ***Coating materials:***- The coating material is well-defined as the material which is used to provide protection to core material from harsh conditions. It should be capable of forming a film around the core material. It should be chemical compatible with core material and non-reactive as well as stable enough to withhold the core material. The coating material should provide the desired coating properties such as strength, flexibility, impermeability.[8]

Types of coating material

a. **Water miscible resins: -** Gelatin, Gum arabica, Polyvinyl pyrrolidine, Carboxymethyl-cellulose.
b. **Water immiscible resins: -** Ethyl cellulose, Cellulose nitrate, Silicones.
c. **Waxes and lipids: -** Paraffin, Carnauba, Stearic acid, Stearyl alcohol.
d. **Enteric resins: -** Shellac, Zein

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Properties of coating material

- It must be capable of providing stability to core ingredients.
- It should be inert with core materials.
- It should be stable and tasteless.
- It should be easily soluble in water or in aqueous media.
- It should be flexible, brittle and hard.

TECHNIQUES OF MICROENCAPSULATION

1. Physical technquies:-

a. Air susupension
b. Centrifugal extrusion
c. Pan coating
d. Spray drying[17]

2. Physico-Chemical techniques:-

a. Ionotropic gelation
b. Coacervation

3. Chemical techniques:-

a. Solvent evaporation
b. Polymerization

1.Physical techniques:-

a) ***Air-suspension coating:-***The air suspension covering allows for better control and durability with specific solutions or melts. The particles are immersed in a current of upward moving air when suspended. The cylindrical is insert is covered by a perforated plate with various holes in and out of patterns. Only ample air will flow through the outside ring region to fluidise the settling particles. There is an upward air flow (usually heated) within the tube that allows the particles to increase quickly. The air flow differs and slows down to repeat the cycle, and settles on the outer bed on the edge. The air suspension system features a wide range of microencapsulation coating materials. The strategy may apply covering in equipment varying from one pound to 990 pounds in size in the form of solvent solutions, aqueous solutions, emulsions, dispersions or heat melts. The air suspension strategy can effectively encapsulate the core materials composed of microns or submicron particles, but natural particle aggregation is accomplished to a greater extent[8]

b) ***Centrifugal extrusion:-***A rotating extrusion head with fixed nozzles trappes the liquids. In this process a sheath of a wall solution is encircled or melt by a central fluid pump. As the jet passes by the water it spreads into droplets of the heart, covered with a wall solution that leads to Rayleigh's instability. A molten surface can be hardened by flight of droplets, and a solvent evaporated from the solution of the wall. Because most droplets have a mean diameter of ± 10 %, they fall around the spray powder in small circle. Therefore the containers can be solidified by picking them in a ring formed solidifying shower if necessary.[1]

c) ***Pan coating:-*** It is the one of the oldest industrial process for making small, coated particles or tablets products that are widely used in pharmaceutical industry. Particles are tumbled in a bowl or in a different device whilst gradually applying the coating material. In the pharmaceutical industry the large scale pan coating process is one of the oldest industrial process small scale, coated particles or tablets. In a pot or other tool solid particles over 600 microns of solid particles are generally considered appropriate for effective covering whereas the coated content must be slowly added with regard micro capsulation.[9]

d) ***Spray Drying:-***It is used as a microencapsulation process when the active substance is dissolved or suspended in a melt or polymer solution, and trapped in a dried component. Because of their less contact time in the dryer the main benefits are the ability to handle liable materials, and the operation is economical. The viscosity of the products to be sprayed can be up to 300m Pa for conventional spray dryers. Spray drying and spray congealing procedure are similar in that either the spray or injection into a liquefied coating product into some environmental conditions of the core material and thus influence the relatively faster solidification and formation of the covers. The method for congealing and spray are the same. The main difference between two strategies is how the covering is solidified with spray drying, the covering solidifies through a direct evaporation of the solvent in which the covering content is dissolved. The laying is never the less solidified by thermally congealing a molten surface or by solidifying a liquid

layer by injecting the base of the sheet into a non-solvent. The non-solvent and water are then removed from the coated surface by the process of sorption, extraction or evaporation.[10]

1. **Physico-chemical techniques:-**

a) ***Coacervation:-***The approach will have its key material added. The core material must not be reacted or dissolved in water (2% maximum solubility). In the solution the key element is dispersed. The particle size shall be described as stirring velocity, stirring shape, surface tension and viscosity by its dispersion parameter cooperation from 2 micrometer to 1200 meter begins with a dispersal ph change e.g by adding sulphuric acids and hydrochloric acid. The consequence is a loss of the miscibility of the distributed process .

a) The shell content continue to precipitate from the solution.

b) The shell substance produce a continuous core droplet covering.[11]

2. ***Chemical process:-***

i. ***Solvent evaporation:-***The strategy has been used by industries such as NCR industry, Gavaert Photo production NV, Fuji Photo film Co limited in the manufacture of microcapsules. Processes are conducted in a system containing liquids. A poisonous liquid which can't be combined with the engines fluids output process dissolves the microcapsule surface. In the polymer coating solution a core substance to be microencapsulated is dissolved or dispersed. During a liquid manufacturing machines process the core material mixing is agitated in order to achieve the microcapsule size. The mixture is then heated to evaporate the polymer solvent if necessary. Polymers shrink around the heart in the event that the base material is dispersed in the polymer solution. In the case where the core material is dissolved a matrix type microcapsule is formed in the coating polymer solution, when all the polymer solvent has evaporated the temperature of the fluid vehicle will be reduced to the ambient temperature if necessary with continuous agitation. At this level microcapsules can be used as a solution, wrapped or isolated on substrates as powders. The solvent development process for microcapsule formation require a wide range of fluid and solid core materials.[12]

ii. Polymerization [13,19]

A. ***Interfacial polymerization:-***In interfacial polymerization, the two polycondensed reactants meet and react quickly at an interface. The product of this process is the classic Schotten Baumann reaction between acid chloride and an active hydrogen atom which produces compounds like amine or ethanol, polyesters, polyurethane. Lightly thin elastic walls at the interface in the right conditions. Chloride is emulsified in water and the amine and polyfunctional isocyanate containing aqueous solution added. The base in formed neutralizing acid is present in the reaction.

B. In-situ polymerization:-

Direct polymerization of a single monomer occurs on the particle surface in a few microencapsulation processes. In one process for example during immersion in dry toluene the

cellulose fiber is encapsulated in polyethylene. The normal deposition rate is around 0.5 micron per min. Coating thickness ranging between 0.2-75 microns. Even with sharp projections the covering is uniform.

C. Matrix polymer:-

During particle formation a base product is incorporated into a polymer matrix in several processes. Spray drying is an easy approach whereby the particle is formed by means of solvent evaporation from the matrix material. Nonetheless, matrix solidification may also be the result of a chemical modification's. With this approach Chang manufactures microcapsules that contain protein solution by adding protein aqueous diamine cycle. Chang showed that the enzymes stays in the microcapsules perm selectively when it is incorporated through its ability to transformed blood urea to ammonia extracorporeal shunt cycle.

APPLICATIONS OF MICROENCAPSULATION TECHNIQUES [14,15,16,18]

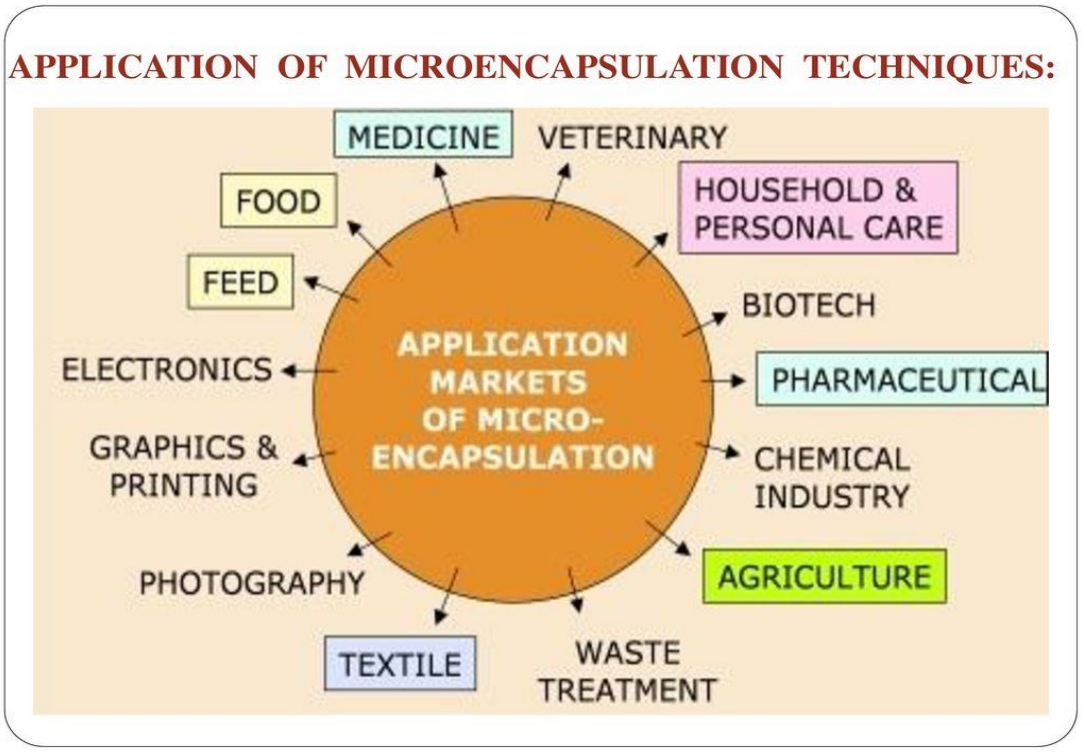

Figure 1 Application of Microencapsulation

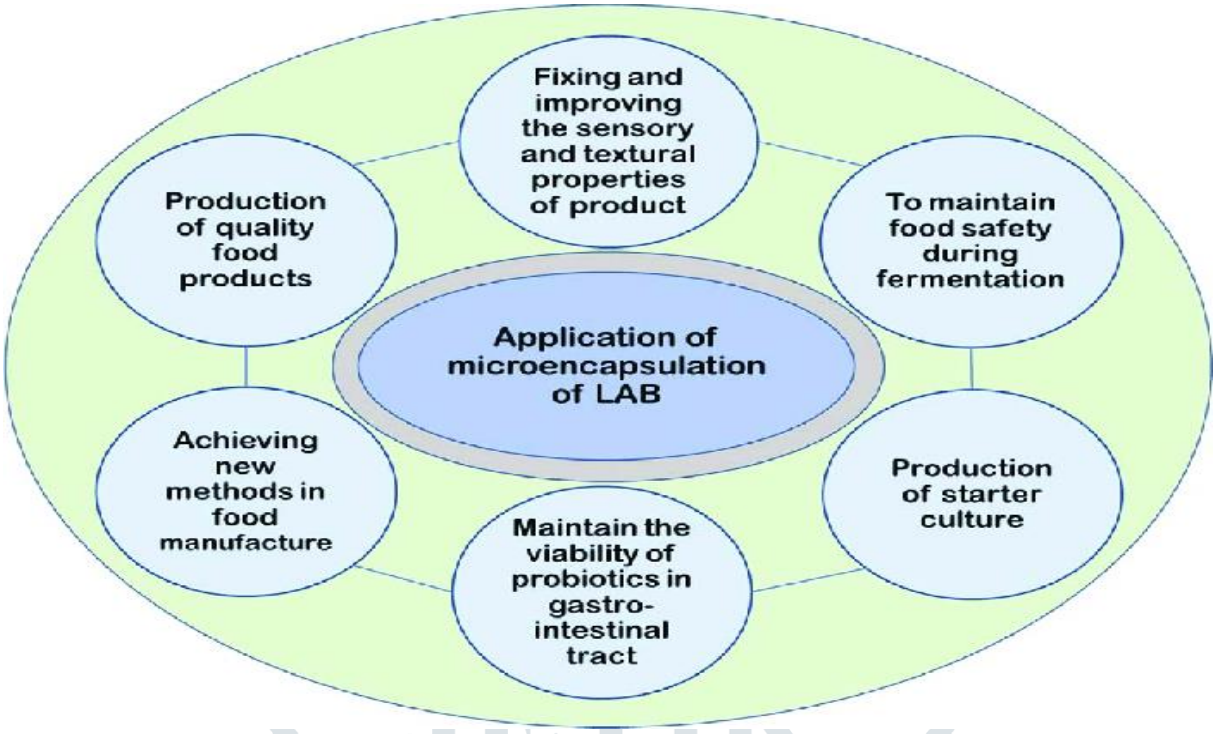

Figure 2 Application of Microencapsulation of LAB

1. It provides prolong release of dose from formulation.
2. The drug microencapsulated is administrable as the preparation of tablets, capsules or forms of parenteral dosage may be most useful when microencapsulating.
3. It can be used to prepare formulations of enteric-coated treatment in order to selectively absorb the drug in the intestine rather than the stomach.
4. To overcome the bitter taste of drugs.
5. Microencapsulation has been used from a mechanical point of view to help add oily drugs to solid dosage forms. This was used to overcome problems inherent in tablet output from otherwise tacky granulations and direct tablet compression.
6. This technique also helps in provide protection to drugs from heat, moisture, light or oxygen..

CONCLUSION:-

Microencapsulation is a technique in which drugs particles are coated with some polymer material in order to enhance the release pattern of drugs. In case of BCS class 2 drugs which are having low solubility their solubility can be improved, which ultimately results in improvement of dissolution rate of drugs. Apart from all these formulation consideration the bitter taste of drugs can be masked which helps in delivery of bitter taste drugs Example:- Castor oil. It also helps in improving flow properties of drugs. Example:-Thiamine. It also helps in improving stability of drugs Example:- Vitamins. In case of conventional dosage forms such as tablets the release

of drug is not uniform which will lead to fluctuation of dose inside the body. But this problem can be overcome by designing microencapsule of that drug by preventing drug from gastric fluid or other factors which will improve release pattern of drug inside the body. Example Aspirin Sustained Release tablets are produced which provide better release profile as well as reduction in gastric irritation has been achieved. Capsule of Isosorbide dinitrate has been produced in microencapsulation to improve the release characteristics. Menthol is having problem of volatility which leads to loss in content in some time, if we use menthol as such it leads to loss from formulation, but this problem can be overcome by microencapsulation of menthol. By knowing all these parameters we can easily say that microencapsulation is a better technique which helps in protection of drugs as well their release can be modified.

FUTURE TRENDS

Microencapsulation was invented in early 1930s by chemist Barry green. He produced the first carbon free paper by microencapsulation technique. For this Barry green received patent in 1950. The latest invention which is going on in this technique is prevention of iron from corrosion. Research is going on related to this but industries have not accepted this technique for corrosion prevention but the day is not far when this technique is going to be used for prevention. Microencapsulation is also having applications in field of waste treatment, food industry, Pharma industries. By considering all these aspects we can say this microencapsulation is promising technique in future in many fields. [8,20]

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