

TECHNOLOGICAL DEVELOPMENTS IN MICROENCAPSULATION: THE FUTURE OF SUSTAINABLE PRODUCT CREATION

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ABSTRACT

Through the use of microencapsulation technology, a substance can be contained within a microsphere, also known as a microcapsule, which is a tiny sphere with an average diameter ranging from one micrometre to several hundred micrometres. Based on their size and shape, microcapsules can be divided into two categories: (1) micro/nano-capsules, or (2) morphological microcapsules. The technique of encasing micron-sized particles in a polymeric shell is known as microencapsulation. A variety of methods are available for encapsulating medicinal molecules. A number of variables, such as the polymer's content, solubility in solvent, rate of solvent removal, solubility of organic solvent in water, etc., affect how well a microparticle, microsphere, or microcapsule encapsulates. Numerous industries, including printing, cosmetics, food, pharmaceuticals, agriculture, textiles, and defence, have made use of this technology. The main justifications for microencapsulation, significant methods for microencapsulation, and uses of microencapsulated products in many scientific and technological fields are highlighted in this review study.

Keywords: Pharmaceuticals, Polymers, Stabilisers, Emulsions, Microencapsulation Technology, Microcapsules, And Release Mechanisms.

I. INTRODUCTION

The technique of encasing micron-sized solid particles or liquid or gas droplets in an inert shell, which isolates and shields them from the outside world, is known as microencapsulation (Ghosh 2006). Microparticles, microcapsules, and microspheres are the end products of this procedure, and they differ in their internal structure and morphology. According to Remunan and Alonso (1997), particles with a diameter of 3–800 nm are referred to as micro particles, microcapsules, or microspheres, while those with a diameter of less than 1 μm are called nanoparticles, nanocapsules, or nanospheres, respectively. According to Thies (1996), macroparticles are particles that are larger than 1000 nm. It was reported in the 1960s that a thermosensitive display material might be created by microencapsulating cholesteric liquid crystal through the complicated coacervation of gelatin and acacia. By microencapsulating nematic liquid crystal, J.L. Ferguson created the nematic curvilinear aligned phase (NCAP), a liquid crystal display technology. Encapsulation technology has made it possible to increase viewing angles and display areas.

A. Microparticles :-

The term "microparticles" describes particles with a diameter between one and a thousand micrometres, regardless of their exact internal and/or external features.

B. Microspheres :-

Within the general category of microparticles, "microspheres" specifically refers to the spherical-shaped microparticles.

C. Microcapsules :-

The term "microcapsules" describes microparticles with a core encased in a coat or wall material (or materials) that are significantly different from the core, payload, or nucleus, which can be solid, liquid, or gas.

❖ Three types of microcapsules can be distinguished (Fig. 1) :-

- 1) Mononuclear:- Encloses the core in a shell.
- 2) Polynuclear :- Consisting of several cores encased in a shell.
- 3) Matrix :- Evenly distributed throughout the shell components.

II. CLASSIFICATION OF MICROCAPSULES

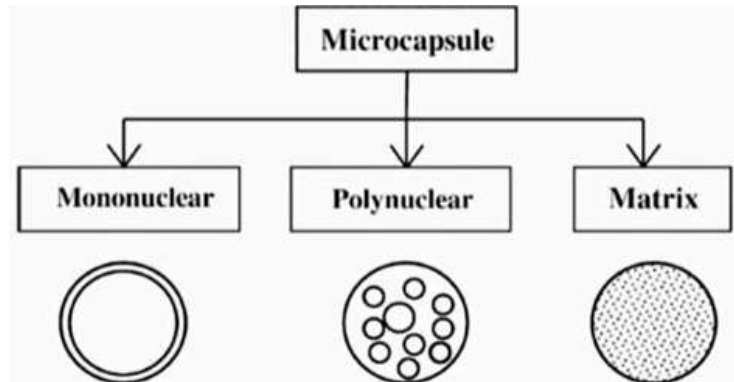


Fig 1: Classification of Microcapsules.

Classification:

Microcapsules can be categorised according to their shape or size :-

- 1) Nano/microcapsules.
- 2) Microcapsules with morphology.

A. Nano/microcapsules :-

The size of microcapsules varies from a micron (one thousandth of a millimetre) to a few millimetres. To highlight their tiny size, some microcapsules with a diameter in the nanometre range are called nano-capsules.

B. Microcapsules with Morphology :-

As illustrated in Fig. 2, microcapsules can be divided into three fundamental categories: matrix, polycored, and monochord. A single hollow chamber is present in monocored microcapsules. The shell of the polycore microcapsules has several chambers of varying sizes. The active components of the matrix type microcapsule are integrated into the shell material's matrix.



Fig 2: Different types of Microcapsules.

Microencapsulation Techniques:

Core materials can be encapsulated using a variety of methods. In general, the approaches can be separated into three categories. The following are examples of several microencapsulation techniques :-

- Physical Approach :-
 - a) Air suspension technique.
 - b) The pan coating technique.
 - c) The spray drying technique.
- The Physico-chemical Approach :-
 - a) Inotropic method.
 - b) Coacervation method.
- Chemical Method :-
 - a) Evaporation of the solvent.
 - b) Polymerisation.

1. Air Suspension Method:

The air suspension method of microencapsulation involves spray coating the air-suspended particles and spreading solids and particulate core materials in a supporting air stream (Fig. 3). Particulate core materials are suspended on an upward-moving air stream inside the coating chamber. A recirculating flow of the particles through the coating-zone section of the coating chamber, where a coating material is sprayed to the moving particles, is influenced by the chamber's design and operational characteristics. Depending on the goal of microencapsulation, the core material is coated during each pass through the coating zone, and this cycle is repeated. During the encapsulation process, the product is also dried by the supporting air stream. The temperature of the supporting air stream employed has a direct impact on the drying rate.

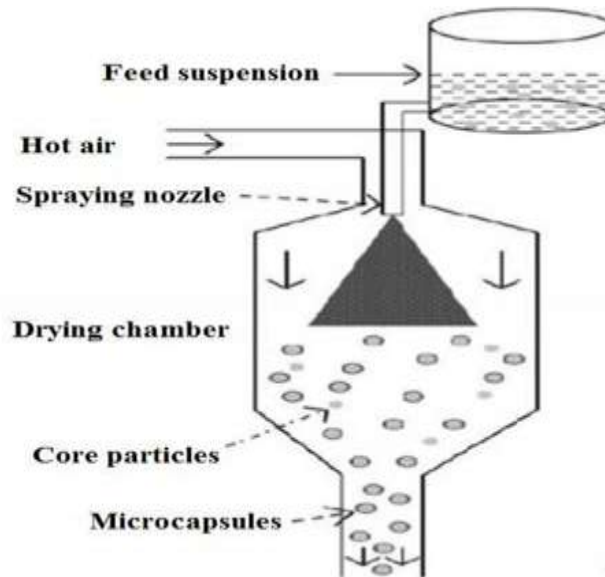


Fig 3: Air suspension method for microencapsulation.

2. Pan coating method:

The pan coating procedure, which is frequently employed in the pharmaceutical sector to prepare controlled release particulates, can be used to microencapsulate rather big particles, larger than 600 micrometres. This technique involves coating different spherical core materials, including nonpareil sugar seeds, with different polymers (Fig. 4). The coating is actually sprayed to the chosen solid core material in the coating pan either as an atomised spray or as a solution. To remove the coating solvent, heated air is typically circulated over the coated materials as the coatings are being applied in the coating pans. In certain instances, the drying oven is used to complete the final solvent removal procedure.

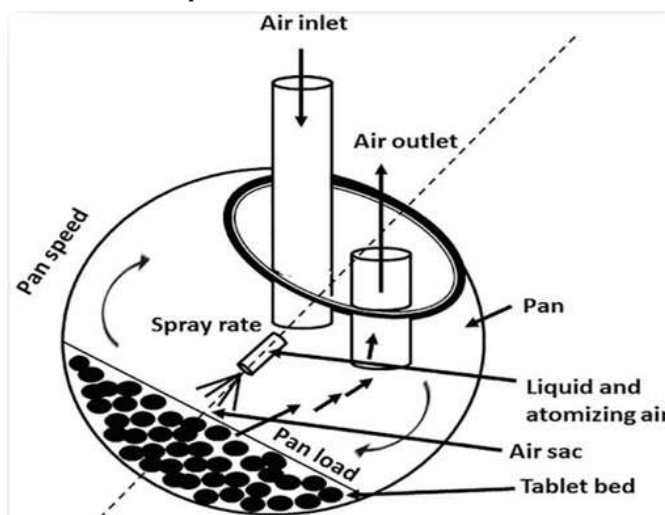


Fig 4: Pan coating method for microencapsulation.

3. Coacervation method:

Gelatin and gelatin-acacia microcapsules, as well as other products based on cellulose derivatives and synthetic polymers, are prepared by coacervation (also known as phase separation) (Fig. 5). There are two types of phase separation processes: simple and complex coacervation. A single polymer, such as gelatin or ethyl cellulose, is used in aqueous or organic mediums for simple coacervation. Gelatin and acacia, two oppositely charged polymeric molecules that are both soluble in aqueous conditions, are examples of complex coacervation. The progressive desolvation of the completely solvated polymer molecules causes coacervation in both situations. The process of microencapsulation by coacervation involves making an aqueous polymer solution (1–10%) at 40–50 °C and dispersing the hydrophobic core material into it. To keep the finished microcapsules unique, an appropriate stabiliser can also be added to the mixture. Gradually adding an appropriate desolvating agent (coacervating agent) to the mixture causes partially desolvated polymer molecules to form and precipitate on the surface of the core particles. After cooling the coacervation mixture to between 5 and 20 °C, a crosslinking agent is added to solidify the microcapsule wall that forms around the core particles. Coacervation has been used to create gelatin microcapsules filled with sulfamethoxazole and carboquone.

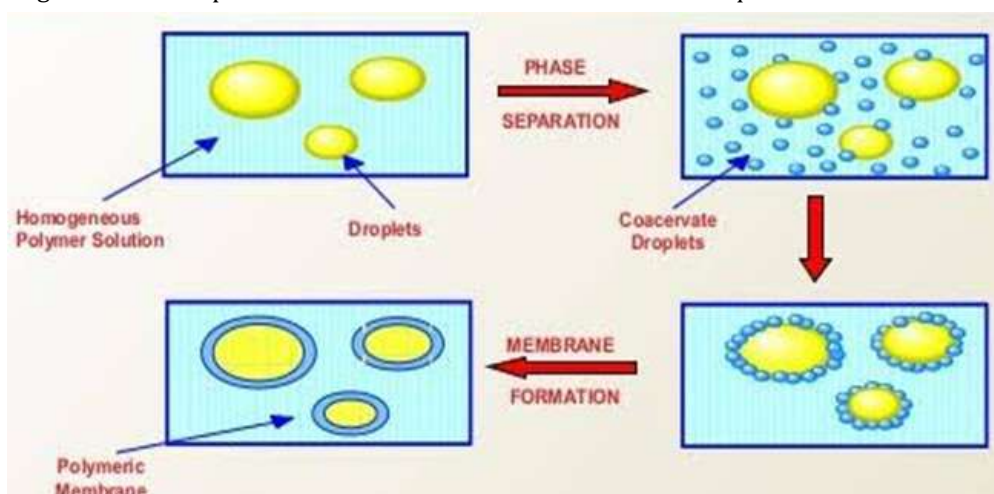


Fig 5: Coacervation phase separation method for microencapsulation.

4. Solvent evaporation:

There are three stages in the solvent evaporation process. They are liquid manufacturing vehicle (LMV), core, and coat material. A volatile solvent that is insoluble in the LMV phase will be used to dissolve the initial cost material. The coating polymer solution will dissolve or disperse the core substance that will be enclosed. After being stirred into the liquid production vehicle phase, this combination is heated to cause the solvent for the polymer to evaporate. In this case, the covering material surrounds the core material by shrinking around it. Using three grades of ethyl cellulose as wall-forming materials and a solvent evaporation process, 5-fluorouracil microspheres have been created in ambient settings. Liquid paraffin containing 33.3% n-heptane was used to disperse an alcoholic solution of 5-fluorouracil and polymer. In two distinct mediums, the impact of drug loading, polymer grade, stirring rate, and stirring duration on drug release was assessed. The drug-loaded particles could be incorporated into a gel base since they were spherical in shape and ranged in diameter from 25 to 200 mm. Acidic media provide a faster release rate than neutral media, according to studies on drug release in aqueous media. The formulation of a gel-microsphere product for the treatment of skin lesions was found to be promising based on the drug release investigation from an aqueous gel base preparation at pH 7.0 via a synthetic membrane (Ghorab et al. 1990). The extremely water-soluble medication pseudoephedrine HCl was trapped in poly (methyl methacrylate) microspheres using a solvent evaporation technique combined with water/oil/water emulsification. To create a water/oil/water emulsion, an aqueous drug solution was emulsified into a polymer solution in methylene chloride, and then this main emulsion was emulsified into an exterior aqueous phase. The continuous phase and the internal drug-containing aqueous phase were separated by the middle organic phase. Following solvent evaporation and polymer precipitation, microspheres were created. The microspheres' drug content rose as theoretical drug loading, organic solvent, polymer, and polymeric

stabiliser levels increased, and it decreased as stirring time, continuous phase pH, and internal and external aqueous phase volume increased (Rainer and Bodmeier 1990).

Factors influencing encapsulation efficiency:

Several factors will influence the microparticle, microcapsule, or microsphere's encapsulation efficiency. (Fig. 6). shows the variables affecting the effectiveness of encapsulation.

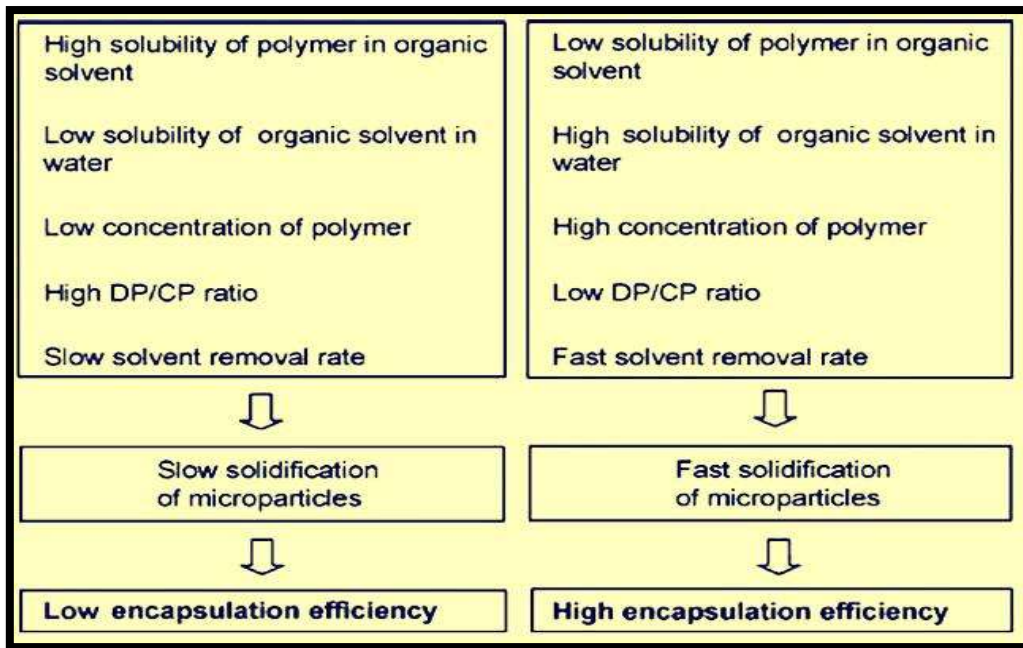


Fig 6: Factors influencing encapsulation efficiency. (Redrawn from Yeo and Park 2004)

III. APPLICATIONS

1. Agriculture:

Crop protection is one of the most significant uses of microencapsulated products. Insect pheromones are now showing promise as a biorational substitute for traditional harsh insecticides. In particular, by interfering with the mating process, sex-attractant pheromones can lower insect populations. As a result, during mating season, trace amounts of species-specific pheromone are released, increasing the background pheromone level to the point where it obscures the pheromone plume released by its female mate. By spraying the capsule dispersion, polymer microcapsules, polyurea, gelatin, and gum arabic act as effective delivery systems for the pheromone. Additionally, during storage and release, encapsulation shields the pheromone from light and oxidation.

2. Energy Generation:

Nuclear fusion is harnessed to generate electrical energy using hollow plastic microspheres filled with gaseous deuterium, a fusion fuel. There are several layers to the capsules. A three micrometer-thick polystyrene shell makes up the inner layer, which compresses the fuel. A layer of poly (vinyl alcohol) that is roughly three micrometres thick comes next, which prevents deuterium from diffusing out of the capsule. The ablator, or outer layer, is composed of a highly cross-linked polymer derived from 2-butene and is roughly 50 micrometres thick. The surface of the microcapsule shell absorbs energy from powerful laser beams during the fusion operations. The reaction force drives the remainder of the shell inward as the ablator, the shell's outermost portion, burns off, compressing and heating the deuterium inside. High temperatures and densities in the middle of the capsule cause deuterium nuclei to fuse, producing tritium, helium, and other particles while releasing a tremendous amount of energy. We call this process inertial confinement fusion (ICF). Since the 1980s, these organic microcapsule-based ICF targets have been in use.

3. Pharmaceuticals:

Pharmaceutical and biomedical industries use encapsulation techniques extensively for regulated and sustained medication delivery. Potential uses for this drug delivery system include gene therapy, the replacement of

therapeutic medicines (such as insulin, which are currently not taken orally), and the use of vaccinations to treat AIDS, tumours, cancer, and diabetes. Examples of medications that would profit from this novel oral delivery method include proteins like insulin, growth hormone, and erythropoietin, which is used to treat anaemia. Corrective gene sequences delivered using plasmid DNA may offer practical treatment for a variety of hereditary illnesses, including haemophilia and cystic fibrosis. Before gradually releasing their contents into the circulatory system, the spheres are designed to adhere firmly to and even pierce the linings of the gastrointestinal tract. Lupin has previously introduced the world's first Cephalexin (Ceff-ER) and Cefadroxil (Odoxil OD) antibiotic tablets for the treatment of bacterial infections, based on this innovative medication delivery method. ZORprin CR tablets, a controlled release form of aspirin, are used to treat arthritis symptoms. Tablets containing quinidine gluconate CR are used to treat and prevent irregular heartbeats. By lowering cholesterol, the NiaspanCR pill lowers the chance of having a heart attack. Glucotrol, also known as Glipizide SR, is an anti-diabetic medication used to manage hypertension.

4. Catalysis:

The agrochemical, fine chemical, and pharmaceutical industries depend heavily on transition metal-based catalytic processes. Operational handling may be risky because a large percentage of these catalytic metal species are frequently costly and toxic. Recently, microencapsulation has been acknowledged as a practical substitute approach that facilitates safe handling, simple recovery, reuse, and disposal at a reasonable cost. Different catalysts have been encapsulated in polyurea microcapsules because of their resistance to degradation and insolubility in organic and aqueous solvents. Palladium (II) acetate and osmium tetroxide are two examples of metal species that have been successfully employed as recoverable and reusable catalysts without undergoing considerable leaching or activity loss when encapsulated in polyurea microcapsules. It is believed that the metal species are ligated and retained inside the polymeric matrix by the urea functionality, which forms the polymer's backbone. In order to investigate rate enhancement in such reactions, the next trend is to explore different polymers for encapsulating and incorporate additional chelating and ligating functional groups into the polyurea framework.

5. Defence:

Self-healing polymers and composites are among the significant defensive uses of microencapsulation technology. They have the ability to provide long-lasting structural materials and have microencapsulated healing agents integrated inside the matrix. When damage occurs in the host material and the capsules burst, the self-healing process is mechanically triggered by the microcapsules in self-healing polymers, which also store the healing agent during quiescent phases. The microcapsules are strong enough to hold together while the host polymer is being processed, but they burst when the polymer is harmed. It is necessary to have a moderately strong microcapsule shell and a high binding strength to the host polymer. The capsules must be resistant to the encapsulated healing agent's diffusion and leakage for a significant amount of time in order to have a lengthy shelf life. A technique based on the in situ polymerisation of urea-formaldehyde microcapsules encasing dicyclopentadiene healing agent is used to accomplish these combination properties. These microcapsules give the composite system a special toughening mechanism when added to an epoxy matrix. In the aerospace industry, these microcapsules are used extensively to create self-repairing spacecraft. By extending a spacecraft's lifespan, these self-healing spacecraft make longer-duration missions possible. Additionally, unique materials for military personnel are designed using microencapsulation to improve their chemical protection against chemical warfare. Special reactive microcapsules have been created for this purpose, and they can be put to textiles or completed clothing to give reactive sites for chemical reagent neutralisation. This entails the formulation of the microcapsules in a resin finish that can be uniformly applied to fabric substrates, as well as the microencapsulation of conventional decontamination chemicals that are currently effective for deactivating toxic nerve agents known conventionally as G agents, such as isopropylmethylphosphonofluoridate (GB, sarin), and toxic mustard blistering agents (H agents). Ethyl cellulose microcapsules with a solid decontamination agent made of sym-bis (N-chloro-2,4,6-trichlorophenyl) urea and ZnO were separated organically to produce the preferred microcapsules with a decontaminating agent. After that, an acrylic binder emulsion was used to adhere the microcapsules to the fabric. The wearer is shielded from

harmful chemical agents by the extremely thin walls of the microcapsule (1 to 10 microns), which provide quick agent penetration for optimal cleaning.

6. Food Industry:

Consumers are becoming more conscious of what they eat and the advantages that particular substances offer for preserving good health as part of the current movement towards a healthier way of living. A distinctive selection of cutting-edge so-called "functional foods," many of which are enhanced with components to support health, is available for preventing disease through diet. However, food products' flavour, colour, texture, and aroma can all be negatively impacted by merely adding substances to increase their nutritional worth. They can occasionally deteriorate gradually and lose their activity, or oxidation processes can make them dangerous. Additionally, components in the food system may react with ingredients, limiting bioavailability. By offering feasible texture blending, enticing scent release, and taste, odour, and colour masking, microencapsulation helps to solve all of these difficulties. Food manufacturers can use the technique to add vitamins, minerals, flavours, and essential oils. Additionally, by turning liquids into solid powder, microencapsulation can streamline the food manufacturing process and lower production costs by enabling batch processing with inexpensive powder handling equipment. Additionally, microcapsules stabilise the shelf life of the active component and help delicate and delicate products withstand packaging and processing conditions. By offering feasible texture blending, enticing scent release, and taste, odour, and colour masking, microencapsulation helps to solve all of these difficulties. Food manufacturers can use the technique to add vitamins, minerals, flavours, and essential oils. Additionally, by turning liquids into solid powder, microencapsulation can streamline the food manufacturing process and lower production costs by enabling batch processing with inexpensive powder handling equipment. Additionally, microcapsules stabilise the shelf life of the active component and help delicate and delicate products withstand packaging and processing conditions.

IV. QUALITY CONTROL TESTS FOR CAPSULES

Numerous quality control tests are carried out throughout the formulation and filling of capsules to guarantee that the final product satisfies the standards set forth in official compendiums and industry-standard requirements accumulated over time. Quality control tests for capsules are the following :-

1. Permeability and sealing :-

Visual inspection is used to check the physical integrity (lack of leaking) of soft gelatin capsules. In a similar manner, hard gelatin capsules are examined for any physical integrity violations, such as cracking or an open cap and body.

2. Potency and impurity content :-

The medication content (potency, expressed as a percentage of the label claim) of each capsule is examined. The majority of pharmaceutical items are also examined for contaminants or related compounds. For a batch to be deemed acceptable, these must fulfil certain requirements.

3. Weight variation test :-

Weight variation or content uniformity can be used to show how uniform the dose units are. The Weight variation method is as follows :-

- a) Weight variation test for hard gelatin capsules.
- b) Weight variation test for soft gelatin capsules.

4. Uniformity of content :-

Only when the content is mentioned in the individual monographs and when the capsules fail the weight fluctuation test is this test carried out. This test is not necessary if the weight of the capsules is fully filled. The amount of drug substance, as determined by assay, falls between 85.0% and 115.0% of the label claim for nine (9) of ten (10) dosage units assayed, with no unit falling outside of the range of 75.0% to 125.0% of the labelled drug content, unless the monograph for a specific capsule specifies otherwise. When two or three dose units fall beyond the target range but fall within the specified extremes, more testing are recommended.

5. Disintegration time test for capsules :-

To make sure the medication substance is completely available for dissolving and absorption from the gastrointestinal tract, the disintegration of both hard and soft gelatin capsules is assessed. The same protocol and equipment are used in the compendial disintegration test for both soft and hard gelatin capsules as detailed in the article "Quality Control Tests for Tablets." For the duration specified in the specific monograph, the capsules are positioned in the basket-rack assembly, which is repeatedly lowered 30 times per minute into a fluid bath that is thermostatically controlled at 37 ± 2 °C.

6. Dissolution test for capsules :-

The drug material must be dissolved at the site of drug absorption in order for it to be absorbed and become physiologically available. A dissolution test determines the pace and degree of medication disintegration from the capsule dosage form. This test serves as a quality control tool to make sure that various medication product batches have comparable drug release properties and that a particular batch of capsules dissolves similarly to the batch that was first demonstrated to be clinically efficacious.

7. Moisture content :-

In order to correlate water content with the degradation profile or drug-release features of capsules, Karl Fisher titrimetry is used to determine the water content of the entire capsule or of the contents of the capsule.

8. Moisture permeation test :-

To ensure that single-unit and unit dose containers are suitable for packaging capsules, the USP mandates that their moisture-permeation properties be determined. By packing the dosage unit with a color-revealing desiccant pellet, exposing it to known relative humidity for a predetermined amount of time, watching for a change in colour (indicating moisture absorption), and comparing the weight of the packaged unit before and after the test, the degree and rate of moisture penetration are ascertained.

9. Microbial content :-

Microbiological tests are performed on the capsules to make sure that no germs or mould are growing. The capsule contents are often incubated in a growth medium for these tests, and the colonies that form after a predetermined amount of time are counted. A successful assessment of microbial contamination with this method depends on the choice of growth medium, test duration, and aseptic conditions maintained during the test.

10. Shelf-life test :-

These tests are often conducted under specified settings and following specified storage times. They aid in determining and confirming the drug product's usability and shelf life.

11. Stability testing of capsules:-

To ascertain the physicochemical stability of the drug substance in the final drug product under the recommended storage conditions and the specified package, as well as the intrinsic stability of the active drug molecule and the impact of environmental factors (such as temperature, humidity, and light) on formulation components, the container, and the closure system, stability testing of capsules is carried out. The product's expected shelf life and suitable storage conditions are ascertained with the aid of a battery of stress-testing, long-term stability, and accelerated stability tests.

12. Packaging and storage of capsules :-

There are two types of packaging and storage of capsules, it is the following :-

- a) Packaging and storage of hard gelatin capsules.
- b) Packaging and storage of soft gelatin capsules.

Recent Research/Advance :-**New Technology/Recent Developments :-**

These days, a lot of technologies are being developed, and some are being considered. The following are these :-

1. A new method of protein microencapsulation that uses a high-voltage electrostatic field.
2. Byliposome-encapsulated aminoglycosides.

3. In vitro :-

(a) Hydrophilic core material such as,

(i) Cisplatin

(ii) Doxorubicin

(iii) 5- Fluorouracil

(b) Hydrophobic core material like,

(i) Taxol

(ii) Comptotheicin (CPT)

4. Release in vivo.

5. The Technology of Dispersal.

6. New Techniques for Solution Gel Microparticulate Development.

7. Microcapsules that biodegrade Formulation,

(i) Microencapsules of calcium alginate

(ii) Microencapsules of chitosan

(iii) Microencapsules of albumin

8. Method for solvent emulsion evaporation using surface reaction analysis

9. A novel method that uses a combination of poloxamer I Plga as a toxoid delivery system fortetanus,

(i) Continuous oral release system design

(ii) Direct compression matrix preparation

(iii) Liquid granulation matrix preparation

Reasons for microencapsulation :-

Microencapsulation is used in pharmaceutical formulations for a number of reasons :-

1. Extended or sustained drug release :-

A common method for achieving prolonged or sustained drug release that enhances patient compliance and therapeutic results is microencapsulation.

2. Taste and odor masking :-

By encapsulating medications with disagreeable tastes or odours, microencapsulation can improve patient acceptance and a Conclusion.

3. Conversion of liquids into free-flowing powders :-

By converting liquid medications into freely flowing powders, microencapsulation makes handling and processing easier.

4. Stabilization of light, moisture, or oxygen-sensitive drugs :-

Drugs that are susceptible to environmental influences can be stabilised by the protective coating that microencapsulation offers, increasing their shelf life and guaranteeing their effectiveness.

5. Avoidance of drug incompatibility :-

By preventing interactions between incompatible medications or excipients, microencapsulation can improve the stability of formulations.

6. Modification of absorption site :-

Through modification of the release profile and targeting of particular absorption sites, microencapsulation can increase the bioavailability and effectiveness of medications.

7. Protection against potential sensitization :-

Toxic compounds, including insecticides, can be encapsulated to reduce the possibility of sensitisation or negative reactions.

V. CONCLUSION

Research in the field of microencapsulation holds great promise for improving raw materials and producing better products. New products have occasionally been produced as a result of advancements in this field; for example, the first noteworthy product was carbonless copy paper, and the second was controlled release medication. Currently, there is a lot of interest in chemically decontaminating textiles, self-healing structures, and paper-like displays.

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