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MICROENCAPSULATION: AN UPDATED REVIEW ARTICLE

Sahil Bhardwaj*, Ritu Rani, Rajesh Kumar, Ajeet Pal Singh & Amar Pal Singh

Department of Pharmaceutics, St. Soldier institute of pharmacy, Lidhran Campus, Behind NIT (R.E.C.), Jalandhar –Amritsar by pass, NH-1, Jalandhar -144011, Punjab, India.

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Abstract

This overview covers microencapsulation classification, process, drug release mechanism, methods& applications as they are applied n medicines and other field applications. Microencapsulation is essentially an interaction or approach that allows thin coatings to be applied reproducibly on small particles of solids, droplets of liquids, and dispersion, so forming microcapsules. The reason for this is that microcapsules are not a finished product, but rather a process to overcome measurement restrictions.

Keywords: Microencapsulation, Classification of Microcapsule, Terminology, Method, Field Application.

***Corresponding Author**

Sahil Bhardwaj

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Introduction

Microencapsulationis a physical or chemical process in which every minute droplets or particles of fluid and strong fabric are encompassed or coated with a nonstop film of polymeric fabric to deliver particles within the micrometer to millimeter run, for assurance and/or afterward discharge. Pharmaceutical microencapsulation was originally investigated in 1931 using a coacervation process using a tiny gelatin sphere [1].

It includes bio encapsulation, which is more limited to the trapping of an organically dynamic substance (from DNA to whole cells and groups of cells generally to enhance its functionality and/or lengthen its shelf life [2].

Microencapsulation gives the implies of changing over fluids to solids, of modifying colloidal and surface properties, of giving natural security and of controlling the discharge characteristics or accessibility of coated materials. Be that as it may, the uniqueness of microencapsulation is the littleness of the coated particles and their ensuing utilizes and adjustment to a wide assortment of measurement shapes [3].

Microcapsules are made up of a solid or liquid core substance that contains one or more medications and is encased in a covering material. The core is also known as the nucleus, and the coating as the wall or sheet [4].

Microcapsules made of biodegradable and non-biodegradable polymers have been studied for longterm and controlled release. The word "microcapsule" refers to a spherical particle with a core portion material that ranges in size from 50 nm to 2 mm. While the word capsule implies a core and shell structure, the term microcapsules admits not only membrane enclosed particles or droplets but also dispersion in solid matrix lacking a characteristic exterior wall phase as well as intermediate types. The size range (2 to 2000µm approximately) distinguishes them from the smaller nano particles or nanocapsules. The walled prototype may be mononuclear or may have multiple core structure. Also double or multiple concentric coating may be present. Although micro-structure of both membrane and interior can be detected by SEM (scanning electron microscopy) of surfaces or sections, their physical quality, involving porosity, tortuousity and crystalinity, is difficult to be characterized quantitatively in microcapsules [4].

A solid envelope encapsulating a solid, liquid, or pale substance is what the French Pharmacopeia defines as a microcapsule.

However, the tiny size of the coated particles is what makes microencapsulation unique [5-7].

Classification of Microcapsule [6, 8]

The Microcapsule is mainly classified into three categories mentioned below.

1. **Mononuclear (Core shell):** This keeps the shell around the core in place.

2. **Poly nuclear:** This capsule's shell conceals a number of cores.
3. **Matrix encapsulation:** In this process core material is distributed homogeneously into shell material.

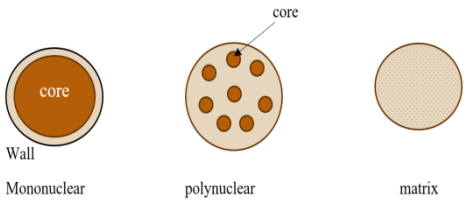

Fig. 1. Microcapsulation types

Microcapsulation Materials [8-12]

Core Material

- ❖ It may beliquidor solid
- ❖ Fluid center may be broken up or scattered material
- ❖ Solid core is combination of
  - Active ingredients
  - Stabilizers Excipients (diluents etc.)

Coating Material

- ❖ Compatible with the core material
- ❖ Inerttowardactive ingredients.
- ❖ Controlled release under defined criteria.
- ❖ Stabilization of core material.
- ❖ Composition of coating
  - Inert polymer
  - Plasticizer
  - Colour in agent
- ❖ E.g.Coatingmaterials:
  - Gums: Gumarabic, sodiumalginate.
  - Celluloses: methylcellulose.
  - Carbohydrates:Starch,sucrose
  - Lipids:stearicacid,phospholipids
  - Proteins:Gelatin.

Vehicle

Vehicle used for dissolving coating material.

- Aqueous vehicle: - Water
- Non- aqueous vehicle: - Alcohol, Poly vinyl pyrrolidine, Isopropyl alcohol [8].

Release Mechanisms of Microencapsulation

This study aims to isolate core material from its surrounding by rupturing the wall during use. The release of capsule contents can be processed through melting or dissolving the wall, solvent pressure, enzymatic attack, chemical reaction, or slow disintegration. Microencapsulation can control drug release into the body, allowing one controlled dose to substitute for several doses and reducing toxic side effects. The release pattern depends on the capsule's composition and environment, with mechanisms such as biodegradation, osmotic pressure, and diffusion. The release mechanism depends on the nature of the application, such as carbonless copy paper, scratch and sniff perfumes, and self-healing structures. Microcapsules act as means of storing and delivering in situ glue to prevent crack spread, and their rupture can be caused by pressure or crack propagation. In the detergent industry, dissolution of shell walls of powder detergents is used to release encapsulated protease enzyme for blood stain removal [4].

1. Dissolution control system

Disintegration rate of polymer coat decides the discharge rate of medicate from the microcapsule when the coat is dissolvable within the disintegration liquid. Thickness of coat and its dissolvability within the dissolution fluid impact the discharge rate [3]. Disintegration could be a rate controlling step in disintegration control framework. The sedate is coating with moderate dissolving substances. There are two sorts of dissolving substance they are as take after:

- **Encapsulation:** Microencapsulation techniques are utilized to coat or encapsulate medication particles using cellulose, a slow-dissolving substance. The solubility and coating thickness affect the rate of dissolution [8].
- **Matrix(Monoliths):** Hydrogenated castor oil is used in matrix waxes, such as bees wax, to regulate drug dissolution by regulating the rate of dissolution fluid penetration into matrix [8].

2. Diffusion control system

Drug diffusion via an inert, water insoluble membrane barrier is a rate- limiting phase in this system [8]. Diffusion is the most commonly involved mechanism wherein the dissolution fluid penetrates the shell, **breaks down** the **center** and **spill** out through the interstitial channels or pores.

The pace at which the dissolution fluid penetrates the microcapsule wall, the rate at which the drug dissolves in the dissolution fluid, and the rate at which the dissolved drug leaks out and disperses from the surface, all affect the overall release [3].

As seen below, the kinetics of drug release follows Higuchi's equation.

$$Q = [D/J\ (2A - \varepsilon\ CS)\ CS\ t]1/2$$

Where,

- Q represents the amount of medication released per square inch of exposed surface over the course of time t, D represents the solute's diffusion coefficient, and J represents the tortuosity of the capillary system in the wall. Q = vt, where v represents the apparent release rate, can be used to represent the preceding equation more easily.
- A represents the total amount of medication per unit volume; CS represents the drug's solubility in permeating dissolving fluid; and represents the porosity of the microcapsule wall. (3)

  (3)Following are the two different types of diffusion control systems:

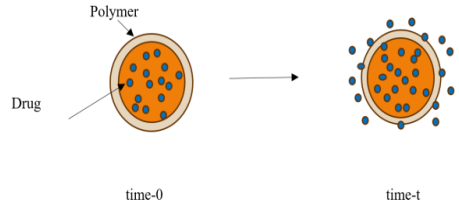

Fig. 2.Reservoir Diffusion System

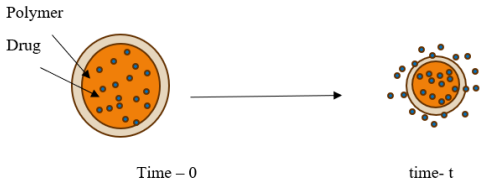

Fig.3 :Matrix Diffusion System

3. Water penetration control system

Water penetration is the phase in this system that controls rate. It comes in two different varieties.

- **Swelling control system**:
  These kinds of systems, which are implanted in the body and are essentially dry, absorb water and cause swelling. As the size of the polymer mesh is increased in the formulation, the aqueous solvent that causes swelling also increases [8].
- **Osmotically control system**
  A semi-permeable arrier consisting of a biocompatible polymer, such as cellulose acetate, surrounds the combination of an osmotically inert medication and an osmogene in this type of system.(8). By acting as a semi-permeable membrane, the microcapsule's polymer coat induces an osmotic pressure difference between its interior and exterior, which forces the drug solution through the coat's tiny pores and out of the microcapsule [3].

4. Chemically control system

In this technique, polymers are broken down into smaller, physiologically harmless components through hydrolysis. There are two categories in this system, and they are as follows [8].

Pendent:

A linear or homo copolymer linked to the medication is called a pendent. The medication is liberated from the polymer by hydrolysis or enzymatic breakdown of the bond [8].

Hydrogels

- A 3-D structure that is swollen by water called a hydrogel is made mostly of hydrophilic polymers.
- Physical or chemical cross connections make crystallites insoluble because they involve weak associations like hydrogen bonds in their structure [8].

5. Erosion [3]

Certain coat components, such as glyceryl monostearate, beeswax, and stearyl alcohol, promote medication release via causing coat erosion due to pH and/or enzymatic hydrolysis.

The rate of drug release from microcapsules that fit the reservoir type is zero order.

For the first half of the total drug release, the release rates of monolithic microcapsules carrying dissolved drug are t1/2 dependent, and after that, they fall exponentially.

The release rate, however, is virtually t1/2 dependent during almost the whole drug release if a monolithic microcapsule has a considerable surplus of dissolved drug.

4. Methods of Microencapsulation

Methods of microencapsulation are as follow:

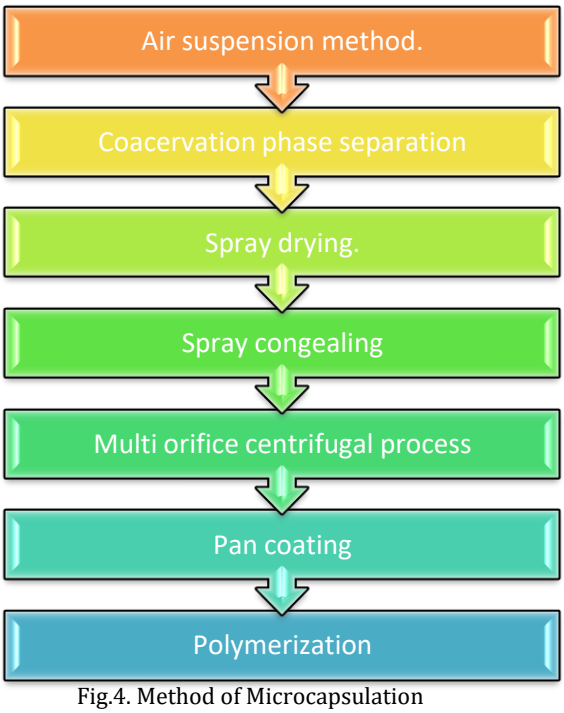

Fig.4. Method of Microcapsulation

1. Air Suspension Technique

Principle: "DALE E. WURESTER" gave the opening remarks. In most cases, it entails dispersing a solid core material in an air stream that is suspending particles and covering those particles with a spray. (8The air stream temperature directly affects the drying rate, which must be repeated until the appropriate thickness is reached. During the formulation process, numerous process variables are taken into account, including the concentration, solubility, melting point, surface area, density, and volatility of the core material as well as the air stream temperature and the amount of fluidization [3].

Process [8]:1. Within the air suspension channel, vaporized air stream delivered from the air distribution plate suspends the core material above.

2. A nozzle transfers the coating material, which is then evenly distributed across the core material.'

3. The procedure is repeated until the desired thickness is achieved.

Process variables [8]: 1. The core material's density, surface area, melting temperature, solubility, friability, crystallinity, and flow capacity. 2. The amount of coating substance. 3. The speed at which the coating is applied. 4. Air volume is necessary for fluidization and support. 5. The quantity of coating material needed.

Benefits: 1. The materials can be coated in hot melt, emulsion, solution, or aqueous solution form. 2. Suitable for both micro and macro encapsulation due to the tiny particle size. 3. More adaptability and control than pan coating [8].

Disadvantages: 1. just applicable to solids. 2. Calls for extensive expertise.

3. Particles of solid matter may band together [8].

2. Coacervation Phase Separation

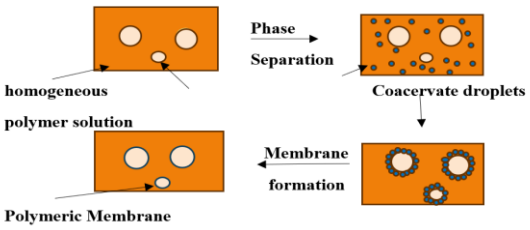

Fig.5 Coacervation Phase Separation

Principle: The core material is dispersed in a coating solution, causing coacervation when pH changes are made. This decreases the solubility of the shell material, forming a precipitate. The shell forms a continuous coating, hardening and forming a microcapsule, which can be dried [3].

Process [8]:- There are three steps in the separation process during the coacervation phase.

1. The emergence of three irreducible phases
2. Coating material deposition
3. The stiffening of microcapsules

Step 1: In a coating polymer solution, three phases of core material are disseminated; liquid solvent is used as a polymer in the production of the vehicle phase. These methods are used to modify the temperature of polymeric solution in order to make the coating material phase immiscible with the solvent: Coating material separates from polymeric solution and creates coacervates as a result of the temperature shift [8].

Step 2: The liquid polymer is deposited on the base material. If the polymer is adsorbed at the contact between the core and the coating material, the coating material is applied to the core material. Step 3 entails rigidizing the coating via heating, cross-linking, or desolvation processes to create a self-sustaining microcapsule [8].

Benefit: 1. Flexible procedure. 2. Coating that is uniform can be obtained 3. The process is simple and quick. 4. The capsules can be produced in a uniform size.

Disadvantages: 1. scaling up is challenging. 2. Agglomeration could happen. 3. Spray drying is only appropriate for medications that are heat sensitive [8].

3. Spray Drying and Congealing Method

Due of its affordability and shorter contact time in the dryer, this approach is appropriate for labile pharmaceuticals. Active substance is dissolved or suspended in the polymer solution during this procedure, then trapped in the dried particle. While the processes for dispersing the coating and core materials are comparable in both approaches, the rate at which the coating solidifies varies [3].

Spray drying involves the quick evaporation of the solvent used to dissolve the coating material, whereas spray congealing involves the introduction of a non-solvent to solidify the coating. Sorption, extraction, and evaporation are used to remove non-solvent materials [3].

Solvent evaporation method

This process is frequently used to create solid and liquid core materials from water soluble and water insoluble components. It is possible to use a range of polymers or film-forming agents. In this procedure, a volatile solvent that is immiscible with the liquid vehicle phase is used to dissolve the coating material (polymer). Either continuous agitation or the use of an external heat source causes the solvent to evaporate [3].

4. Multi-Orifice Centrifugal Process

The method throws the core material into the covering material using centrifugal force to create microcapsules [3].

Process: 1. the coating material is introduced through the coating material intake, which is routed through grooves 1 and 3. 2. The coating material is pumped so that it should spill over the sides of the intermediate grooves and into the grooves themselves. 3. The coating substance enters the countersunk area and creates a film all the way around the orifice. 4. Each core particle is propelled toward the aperture by the counter spinning disc. 5. When the core material reaches the orifice, it comes into contact with the membrane of the coating material [8].

Advantages

- Able to encase both solid and liquid core materials.
- A variety of coating materials are available [8].

Disadvantages

1. Coating material waste could occur.
2. Microcapsules must be dried at a high temperature [8].

5. Pan Coating:

It is one of the earliest techniques still in use in the pharmaceutical industry. In this technique, the coating substance is slowly applied as the particles are tumbling in a pan. Hot air is passed to remove the coating solvent after the solution has been sprayed on the core material using an atomized spray. For pan coating, particles larger than 600 m are essentially effective [3].

6. Polymerisation

- In the process known as interfacial polymerization, the reactants connect at the interphase and react quickly. An acid chloride and a substance like amine, alcohol, polyester, or polyuria that contains an active hydrogen atom are involved in the process. As a result, thin flexible walls are quickly generated at the contact; the reaction's base also serves to neutralize the acid that is produced [3].
- Interfacial cross-linking: In this procedure, a polymer, such as a protein, takes the place of the monomer containing active hydrogen [3].

Advantages of Microencapsulation [4, 13]

- ❖ This method is more successful at masking the taste and odor of different substances.
- ❖ Administering other dosage forms, including macro-sized implants, is simple.
- ❖ Drug release profiles can be offered to patients based on their therapeutic need.
- ❖ The microencapsulation allows access to the site of absorption.
- ❖ Additionally, it lessens drug incompatibility.
- ❖ A number of medications lessen toxicity in this way.
- ❖ Treating liquids like solids
- ❖ Preventing a harsh environment (pH) from damaging sensitive drugs
- ❖ Better processing, better texture and reduced ingredient waste.
  - Dust free powder
  - Enhance flow ability and dispersibility
  - Hygroscopicity control
  - Increase solubility

Disadvantages of microencapsulation [3, 22]

- ❖ Potential cross reactions between the core and wall materials that could happen.
- ❖ Customers with allergies may not be aware they have them due to foreign components in foods, and hygroscopic pharmaceuticals have a shorter shelf life.
- ❖ Due to foreign ingredients in foods, customers with allergies may not be aware.
- ❖ Production cost

Terminology of microencapsulation [22]

Terminology	Description	Size range
Microcapsules	Mono or multinuclear materials enclosed by a coat or membrane	µ m
Nanocapsules	Similar to microcapsules in structure, but smaller.	µ m
Micro spheresor Microparticles	Walls and cores both have a solid structure. The thick solid wall serves as a porous matrix that allows active chemicals to be embedded, therefore there is frequently no obvious difference between them.	µ m
Nano spheresor Nano particles	Similar to microspheres in structure, but smaller.	nm

Methods of Microencapsulation [14-15]

Technique	Particle size range [µm]	Methods used
Coacervation	2– 1200	Physico–chemical
Polymer-polymer in compatibility	0.5–1000	Physico–chemical
Encapsulation by supercritical Fluid Encapsulation by Poly electrolyte multilayer	0.02 –20	Physico–chemical
Phase Inversion	0.5—5.0	Physico–chemical
Hot Melt	1—1000	Physico–chemical
Spray-drying	5– 5000	Physico–mechanical
Fluidized-bed technology	20 –1500	Physico–mechanical
Pan coating	600 –5000	Physico–mechanical
Spinningdisc	5– 1500	Physico–mechanical
Co-extrusion	250 –2500	Physico–mechanical
Inter facial polymerization	0.5–1000	Physico–mechanical
In situ polymerization (0.5 –1100um)	0.5–1100	Physico–mechanical
Layer-by-layer(LBL)assembly	0.02–20	Physico–chemical
Sol-gel encapsulation	2–20	Physico–chemical

Application

1. in preparation of different dosage form

Microencapsulation is a method used for preparing prolonged release dosage forms, enteric-coated dosage forms, masking bitter drugs, adding oily medicines to tableted dosage forms, protecting drugs from environmental hazards, separating incompatible substances, decreasing volatility, and reducing potential dangers of handling toxic substances. It is also used to reduce gastric irritation, prepare intrauterine contraceptive devices, and fabricate multilayered tablet formulations for controlled release. Microencapsulation protects drugs sensitive to moisture, light, and oxygen, prevents incompatibility between drugs, and prevents volatile drugs from vaporizing at room temperature. It is used for sustained release or prolonged action of drugs, in manufacturing powders and suspensions, immobilizing microbes and microorganisms to prevent oxidative degradation, separating incompatible substances,

protecting the gastro intestinal tract, and in genetic engineering [8].

Microencapsulation is a method for creating delayed release dosage formulations for tablets, capsules, or parenteral dosage forms. It allows enteric-coated dosage forms, selective absorption, and masking bitter medications. It protects drugs from environmental hazards, separates incompatible substances, and reduces volatility. Applications include plant cell cultures, human tissue, fermentation processes, food drinks production, and handling chemicals [4].

2. Food Industry

All of these challenges are overcome by the food industry thanks to microencapsulation's efficient texture mixing, alluring aroma release, and taste, odor, and color masking. Microcapsules also help the fragile. These methods allow food producers to incorporate tastes, vitamins, minerals, and essential oils. Microencapsulation allows for batch processing with low-cost powder handling equipment, streamlining the food manufacturing process and lowering production costs [22].

3. Beverage Production:

Today, immobilization is used in the manufacturing of food and beverages like beer, wine, and vinegar. Technologies that change smells, boost output, and improve quality [22].

4. Agriculture

The application of microencapsulated chemicals is mostly in crop protection. Nowadays, insect pheromones are proving to be a more biologically sound substitute for harsh conventional insecticides. Particularly sex attractant pheromones can reduce insect populations by interfering with their reproductive cycle. The production of pheromone during mating season raises the foundation level to the point that it conceals the pheromone crest produced by the male's female mate [16-18].

5. Pharmaceutics

Biomedical is the pharmaceutical application field of the encapsulation technique for controlled and sustained drug delivery [19].

- Gene therapy, the replacement of medicinal drugs, and the use of vaccinations to treat AIDS, cancer, tumors, and diabetes are possible uses [20].
- Growth hormone, insulin, and erythropoietin are examples of proteins that are exploited as innovative oral drug delivery systems to treat anemia.
- plasmid DNA delivery of gene sequences, which would offer a practical treatment for hemophilia [21,22].
- The spheres are designed to adhere firmly and even pierce the linings of the digestive tract [22].

6. Catalysis

Applications in the fields of fine chemistry, agriculture, and pharmaceutics all depend on reactant forms based on transition metals. Operational care could be perilous because a lot of these synergist metal species are frequently costly and hazardous [23].

7. Biotechnology

By simulating the natural environment of the cell in plant cell cultures, microencapsulation increases the productivity of many metabolites utilized for pharmaceutical, pharmacological, and cosmetic applications. Immobilization is utilized in continuous fermentation operations to boost cell density and productivity and prevent the washout of biological catalysts from the reactor. This has already been used in the manufacturing of ethanol and solvents, the conversion of sugar, or the treatment of wastewater [4].

Conclusion

The most pleasant way of assurance and covering, microencapsulation slows the rate of dissolution and aids in maintenance. It is a capsule with a range of sizes that shields the main active excipients from the immediate area until the proper time is not released. This method is helpful for medications that the stomach is unable to break down.

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Conflicts of Interests

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Authors Contributions

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Conflict of Interests

Declares none

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