IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

An Overview On Microencapsulation

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ABSTRACT

The horizon of pharmaceutical development can be expanded by creating novel controlled and delayed release oral formulations with the use of microparticulate drug delivery devices. Numerous industries, including pharmaceutical, agricultural, food, printing, cosmetic, textile, and defence, have adopted this technique. Microencapsulation is used to modify and delayed drug release form Pharmaceutical dosage form. Microencapsulation is one of the most efficient methods. Microencapsulation is a well-established dedicated to the preparation properties and uses of individually encapsulated novel small particles, as well as significant improvements to tired and-tested techniques relevant to micro and nano particles and their use in wide variety of industrial engineering, Pharmaceutical, biotechnology and Research applications. The technique of encasing micron-sized particles in a polymeric shell is known as Microencapsulation. Various techniques can be employed to form microcapsules, including spray drying, spray chilling or spray cooling, extrusion coating, fluidized-bed coating, liposomal entrapment, lyophilization, coacervation, centrifugal suspension separation, cocrystallization and inclusion complexation.

KEYWORDS

Core material, coating material, mononuclear, polynuclear, microencapsulation, morphology

INTRODUCTION

It was Green and Scheicher who invented microencapsulation technology in the 1950, Burg de Jon and Kan came up with the microencapsulation procedure.

In microencapsulation, continuous film of polymeric material surrounds or coats the small drop or particle of solid, liquid,

Gas.

There is a size range of 1 - 1000 μm in diameter for microencapsulated products.

Size of the nanoparticles is <1μm and size of microcapsule is >800μm. Contain 10-90w/w core.

The main aim of microencapsulation is to protect the core material from environmental factors (such as light, moisture, temperature, and oxygen), to extend shelf-life , and to improve the release properties of compounds.

DEFINITION:

Microencapsulation is the process by which individual particles or droplets of solid or liquid material (the core) are surrounded or coated with a continuous film of polymeric material (the shell) to produce capsules in the micrometer to millimeter range, known as microcapsulation. .

MATERIAL INVOLVED IN MICROENCAPSULATIONS

1. Core Material:

a. The material to be coated

b. It may be liquid or solid

c. Liquid core may be dissolved or dispersed material

Composition of coating material:

Drug or active constituent, Additive likes diluents, Stabilizers, Release rate enhancers.

2. Coating Material:

a. Inert substance which coats on core with desired thickness

b. Compatible with the core material Stabilization of core material.

c. Inert toward active ingredients.

d. Controlled release under specific conditions.

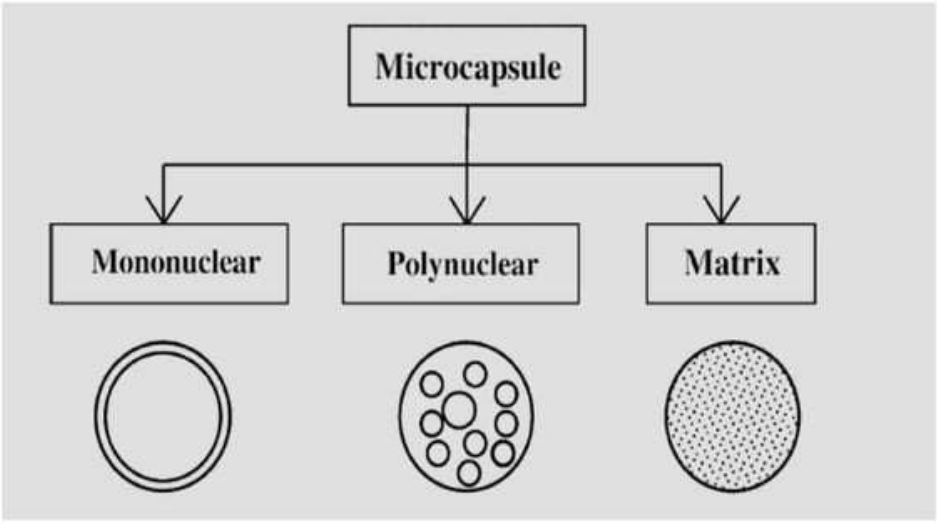
e. The coating can be flexible, brittle, hard, thin etc.

f. Abundantly and cheaply available

g. Composition of coating

- Inert polymer
- Plasticizer
- Colouring agent
- E.g. Coating materials:
- Gums: Gum arabic, sodium alginate, carragenan
- Carbohydrates: Starch, dextran, sucrose
- Celluloses: Carboxymethylcellulose, methylcellulose.
- Lipids: Bees wax, stearic acid, phospholipids.
- Proteins: Gelatin, albumin

Morphology of Microencapsulation:



Microcapsule morphology is mostly determined by the shell's deposition mechanism and core substance monomers.

1) **Mononuclear**: The shell of mononuclear (core-shell) microcapsules surrounds the core.
2) **Polynuclear**: The shell of a polynuclear capsule encloses several cores.
3) **Matrix encapsulation**: where the shell material and core material are uniformly distributed. As Apart from these three fundamental morphologies, microcapsules can also form clusters of microcapsules or be mononuclear with multiple shells.

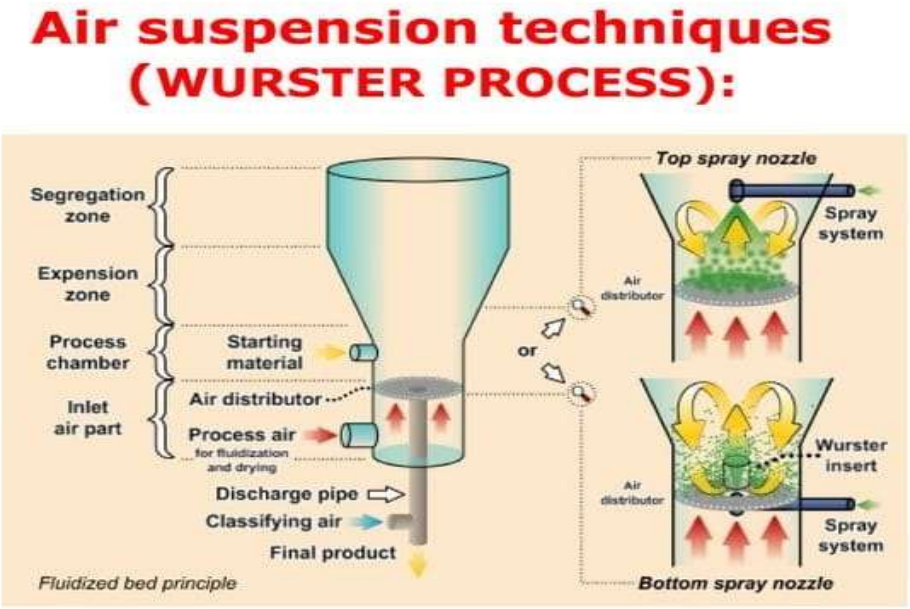
Structure of Microcapsule:

The majority of microcapsules are tiny spheres that range in diameter from a few micrometers to a few millimeters. But many of these microcapsules are not much like these basic spheres. In actuality, the substances and techniques utilised to create the microparticles affect both their size and shape. A variety of wall materials, such as monomers and/or polymers, are used to create the various forms of microcapsules and microspheres (King, 1995; Shahidi and Han, 1993). Different types of particles can be generated depending on the wall composition, the microencapsulation process, and the physico-chemical properties of the core (Fig. 1): a straightforward sphere encircled by a layer of consistent thickness; a particle with a centre of irregular form; many central particles contained within an ongoing matrix of wall material; multiwalled microcapsules; multiple unique cores inside a single capsule.

Methods of Microencapsulation:

1. Air suspension method
2. Multi orifice centrifugal process
3. Pan coating
4. Spray drying
5. Coacervation phase separation
6. Solvent evaporation method
7. Polymerization

1] Air Suspension Method :



Microencapsulation by air suspension technique involves scattering solid, particulate core materials in a supporting air stream and spray coating the air suspended particles. Within the coating chamber, particles are suspended in an upward-moving air stream. The chamber's design and operational characteristics influence the recirculating flow of particles through the coating zone portion of the chamber, where a coating material, often a polymer solution, is sprayed onto the moving particles. During each pass through the coating zone, the core material receives an additional coating material. The cyclic process is repeated, maybe several hundred times during processing, depending on the aim of microencapsulation and the coating thickness.

This method, which is sometimes referred to as Wurster coating or fluidized bed coating, entails suspending particles in an air stream that is traveling upward .The Fluid bed coater has solid, non-volatile cores at the bottom that are bigger than 50 micrometers. A high-velocity, non-turbulent air stream is injected as the coating solution is sprayed, which fluidizes the solid cores and propels them upward. The particles climb quickly because the cylinder is filled with the majority of the rising air, which is typically hot. The solvent evaporates and the coating substance is applied to the ascending cores. By the time they get to the upper chamber, the air has expanded, lost pressure, and is unable to support the heavier cores. It only takes ten seconds to complete this operation, and With every passing, the coating is continually accumulated by the cores. The coating material is applied and dried onto fluidized cores simultaneously in this method. Particles coated with melts or solutions by air suspension provide more control and flexibility. Numerous coating materials are available as potential candidates for microencapsulation by the air suspension technique. Until the appropriate thickness of the capsule walls is achieved, the operations of suspending, spraying, and chilling are repeated. This technique is called the Wurster process when the spray nozzle is placed at the bottom of the fluidized bed of particles. The pan coating technique has two variations: the Wurster process and the fluidized bed coating. The airstream's temperature directly affects the rate of drying, and this temperature can be changed to the properties of the coating.

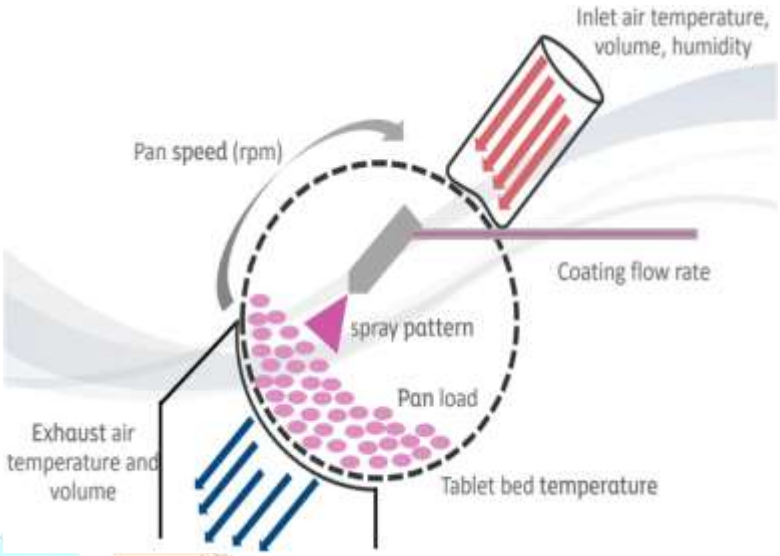
2] Multi orifice centrifugal process :

The centrifugal extrusion procedure is only applicable for liquids and slurries. This procedure encapsulates employing a revolving extrusion head with concentric nozzles. The jet of core liquid is enveloped by a sheath of solution. As the jet passes through the air, it separates into core droplets that are each coated with wall solution. While the droplets are fluidized or in flight, the molten wall hardens and the solvent may evaporate from the wall solution .Droplets having a mean diameter of ±10% settle in a small ring around the spray nozzle. Thus, capsules can be hardened after formation by immersing them in a ring-shaped hardening bath. This method produces particles ranging from 400 to 2000 µm.

Larger-sized capsules are typically produced via centrifugal extrusion techniques. Materials that should be immiscible with one another, the core and shell, are forced via a rotating two-fluid nozzle. This motion creates a

continuous rope that, as soon as it passes the nozzle, spontaneously breaks into round droplets. Depending on the makeup and characteristics of the coating substance, these droplets' continuous walls can be cemented by chilling or by a gelling bath.

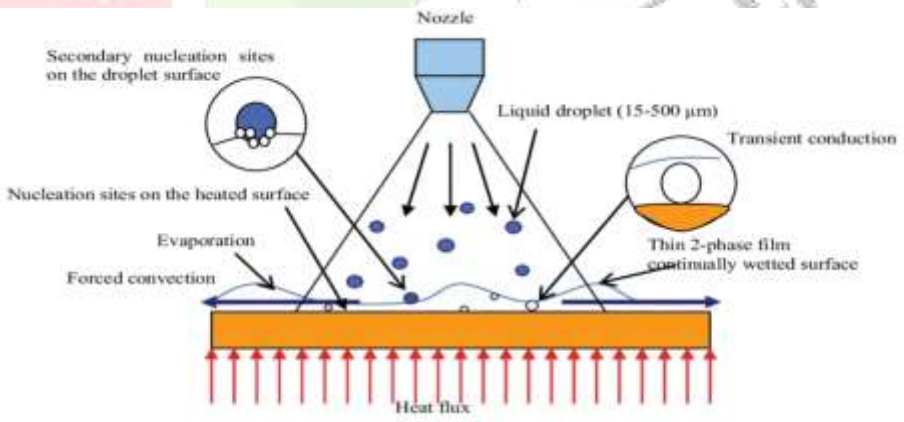
3] Pan coating:



The pan coating technique, widely employed in the pharmaceutical sector, is one of the oldest industrial procedures for producing small coated particles or tablets. The particles are tossed in a pan or other device while the coating material is applied gradually. The pan coating technique, widely employed in the pharmaceutical sector, is one of the earliest industrial procedures for creating small, coated particles or tablets.

The particles are tumbled in a pan or other device while the coating material is slowly applied. In terms of microencapsulation, solid particles larger than 600 microns in size are generally considered necessary for effective coating, and the process has been widely used to prepare controlled-release beads. Medicaments are often coated onto spherical substrates, such as nonpareil sugar seeds, and then protected with layers of different polymers. In practice, the coating is sprayed as a solution or atomized spray on the required solid core material in coating pans. Warm air is typically circulated over coated surfaces as coatings are applied in coating pans to remove the coating solvent.

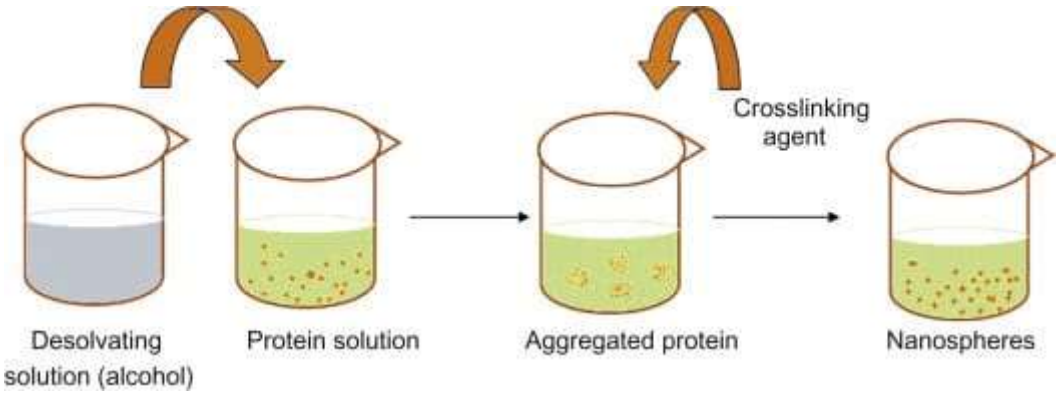
4] Spray drying :



This method entails the creation of structures such as emulsions, suspensions, arrangements, and dividers that are then nebulized in a sightseeing circulation chamber. The water instantly evaporated when it came into contact with the heated air, and the material enveloped the heart. Compared to other techniques, atomization has the following advantages: a large number of facilities are available, a variety of microencapsulating agents may be used, large-scale production may be possible, simple machinery, reasonable performance, lower transportation and storage costs, and cost-effective manufacture. The creation of unevenly made items is the main disadvantage of atomized. One of the most widely utilized microcapsulation techniques; spray drying has been around for ten years and is mostly used to microencapsulate flavors, lipids, and pigmenting chemicals.

Spray drying/congealing this process involves solubilizing, dispersing, or emulsifying the core material with a solution of coating material. It is the continual conversion of liquid to solid particle matter via spraying feed into a hot drying medium. This process produces microcapsules ranging from 5 to 5000 μm.

5] coacervation phase separation :



In this procedure, the coating material's solution disperses the core material, preventing it from dissolving or reacting with the solvent. Coacervation happens when the dispersion's pH changes. This can be accomplished by adding sulfuric acid, hydrogen chloride, or organic acids. As a result, the solubility of the dispersed phase (shell material) is reduced, and precipitate begins to form from the solution. Around the core, the shell material continuously coats the core, cooling to solidify and create a microcapsule. It is possible to add hardening chemicals like formaldehyde to the procedure. The suspension was a fluidized bed dryer or dried in spray drier.

This process consists of three Steps-

- Formation of three immiscible phases; a liquid manufacturing phase, a core material phase and a coating material phase
- Deposition of the liquid polymer coating on the core material
- Rigidizing of the coating material

Step-1: The first step of coacervation phase separation involves the formation of three immiscible chemical phases: a liquid vehicle phase, a coating material phase and a core material phase. The three phases are formed by dispersing the core material in a solution of coating polymer, the vehicle phase is used as a solvent for polymer. The coating material phase consists of a polymer in a liquid phase, is formed by using one of the of phase separation- coacervation method, i.e. .by changing the temperature of the polymer solution, by adding a solution, or by inducing a polymer- polymer interaction.

Step-2: It involves the deposition of the liquid polymer coating upon the core material. This is done by controlled mixing of liquid coating material and the core material in the manufacturing vehicle. The liquid coating polymer deposited on the core material if the polymer is adsorbed at the interface formed between the core material and liquid phase. The reduction in the total free interfacial energy of the system help to promote the deposition of the coating material, brought by the decrease of the coating material surface area during coalescence of the liquid polymer droplets.

Step-3: In the last step rigidizing of the coating material done by the thermal, cross linking desolvation techniques, to forms a self-supporting microcapsule.

6] Solvent evaporation:

In the pharmaceutical industry, the solvent evaporation method of microencapsulation is frequently employed. It makes a drug's regulated release possible, which has numerous therapeutic advantages. This method uses water-insoluble polymers as the encapsulating matrix. Poly (lactic-co-glycolic acid), a biodegradable polymer, is widely utilised as an encapsulating material.16 Many medications have been effectively encapsulated, including

hydrophilic medications like insulin, proteins, peptides, and vaccines, as well as hydrophobic medications like cisplatin, lidocaine, naltrexone, and progesterone. Extensive research has been done on both the selection of encapsulating materials and drug release tests. Process-engineering components of this technique are still not well documented, nevertheless. Studying the latter is crucial for the successful production of microspheres under control.

Process involves:

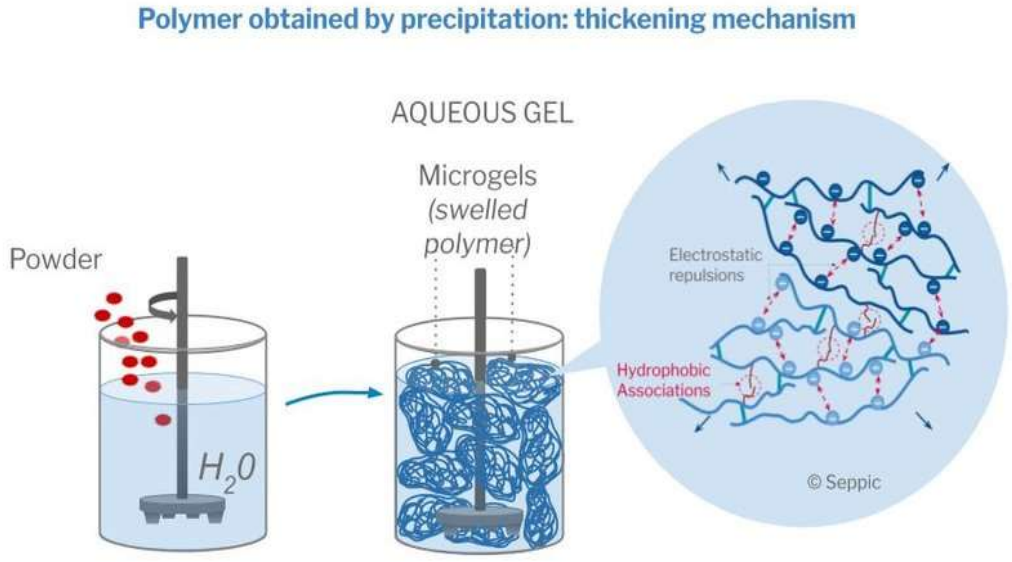
1. Prepare an aqueous solution of the drug (which may include a stabilising or viscosity-building agent).
2. Add the aqueous solution to an organic phase that consists of the polymer solution in solvents such as dichloromethane or chloroform, stirring vigorously to form the primary water in oil emulsion.
3. After this emulsion is added, a large volume of water that contains an emulsifier such as PVA or PVP is added to form the multiple emulsions (w/o/w). After churning the double emulsion until the majority of the organic solvent evaporates, solid microspheres are left behind, which can then be dried and cleaned.

The operations are performed within a liquid production apparatus. A volatile solvent that is immiscible with the liquid production vehicle phase is used to dissolve the microcapsule coating. In the coating polymer solution, a core material to be microencapsulated is dissolved or distributed. To create the right size microcapsule, the liquid production vehicle phase's core coating material mixture is stirred and distributed. The solvent for the polymer is then evaporated by heating the mixture, if needed. The polymer shrinks around the core when the core material is distributed throughout the polymer solution. A matrix-type microcapsule is created when the core material dissolves in the covering polymer solution. After all of the polymer's solvent has been dissolved, the liquid vehicle's temperature is steadily agitated down to room temperature. The microcapsules can now be isolated as powders, coated on surfaces, or employed in suspension form. There are several different liquid and solid core materials that can be used with the solvent evaporation method to create microcapsules. Either water soluble or water insoluble compounds could make up the core components. Coatings can be made from a wide range of film-forming polymers.

Example: Using the solvent evaporation method to assess sucrose esters as substitute surfactants for protein microencapsulation.

7] Polymerization:

Monomers In this technique the capsule shell will be formed at or on the surface of the droplet or particle by polymerization of the reactive monomers. The substances used are multifunctional monomers.



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Multifunctional isocyanates and multifunctional acid chlorides are examples of commonly used monomers. They will be applied alone or in combination. The liquid core material dissolves the multifunctional monomer, which is then dispersed in an aqueous phase with a dispersion agent. We will incorporate a multifunctional amine coreactant into the combination. This causes the contact to polymerize quickly, resulting in the creation of the capsule shell. A poly urea shell will be created when amine and isocyanate combine, and when amine and acid chloride combine, a polynylon or polyamide shell will be produced. Polyurethane shell is created when isocyanate combines with hydroxyl-containing monomer. Similar to IFP, the addition of polymerization monomers to the encapsulation reactor causes the development of the capsule shell. Reactive agents are not added to the core material during this process; instead, polymerization only takes place in the continuous phase and on the side of the interface that is created by the continuous phase and distributed core material. A low molecular weight prepolymer will first form, and as it matures, it will deposit onto the surface of the dispersed core material to form a solid capsule shell.

An illustration would be the encapsulation of different water-impermeable liquids in shells made from the reaction of formaldehyde and urea in aqueous conditions at an acidic pH.

- **Reason for microencapsulation:**

1. The primary reason for microencapsulation is found to be either for sustained or prolonged drug release.
2. Separation of incompatible components.
3. Conversion of liquids to free flowing solids.
4. This technique has been widely used for masking the organoleptic properties like taste and odour of many drugs and thus improve patient compliance.
5. The drugs, which are sensitive to oxygen, moisture or light, can be stabilized by microencapsulation.
6. Increased stability (protection of the encapsulated materials against oxidation or deactivation due to reaction in the environment).
7. Microencapsulation technique also help to prevent the incompatibility between the drugs.
8. Vaporization of many volatile drugs e.g. Methyl salicylate and peppermint oil can be prevented by microencapsulation.
9. Targeted release of encapsulated materials.
10. Controlled release of active compounds (sustained or delayed release)

Advantages:

1. To provide environmental protection of the core material from moisture, light, and oxygen. E.g., Nifedipine
2. To prevent the physical and chemical incompatibilities between drugs and to avoid volatilization of medicines like aspirin at room temperature.
3. To formulate sustained or prolonged release dosage forms that continuously release the drugs at a constant rate for a set period.
4. It enhances the solubility of poorly soluble drugs and the safe handling of toxic medications.
5. For the targeted release of the encapsulated material at the desired site.
6. To alter the physical and surface properties of certain drugs. E.g., Reducing the hygroscopicity of sodium chloride.
7. It Masks the taste of bitter drugs to make them more palatable and improving patient compliance. Eudragit E100 is the most commonly used coating material for this purpose. The microencapsulated drugs do not interact with the taste receptors as it insoluble in the mouth. E.g., Ofloxacin
8. Conversion of a liquid dosage form to pseudo solid or free-flowing powder. E.g., Eprazinone

Disadvantages:

1. The cost of the materials used and the formulation process might be higher than standard formulations.
2. Reproducibility is less.
3. The effect of the polymer matrix, polymer additives, and their degradation products on the environment in response to heat, hydrolysis, or biological agents vary significantly.
4. The core particle's stability is affected by the change in the process conditions like change in temperature, pH, solvent addition, or evaporation of the solvent.

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