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Review Article

Microencapsulation Technology For Novel Pharmaceutical Formulations

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ABSTRACT

Microencapsulation is essentially a method or process that forms microcapsules by applying thin coatings to dispersions, small solid particles, or liquid droplets in a repeatable manner. Its particle size ranges from several tenths of a micron to 5000µ, which makes it easily distinguishable from other coating techniques. The microencapsulation process offers solutions for a number of issues, including how to make prolonged-action dosage forms, mask the taste of bitter medications, separate incompatible materials, shield chemicals from oxidation or moisture, and change a material's physical properties to make them easier to handle during formulation and manufacturing. Compared to traditional multiple dose therapy, novel drug delivery systems offer a number of benefits. Currently, significant efforts are being made to administer the medication in a way that will get maximum advantages. Pharmaceutical dosage forms with delayed drug release can be altered by using microencapsulation.

INTRODUCTION

The process of creating thin wall material coatings around solids, liquids, or even gases is known as microencapsulation. The process started in the late 1930s when the business machines industry was looking for a cleaner alternative to carbon paper and carbon ribbons[1]. The 1950s saw the pinnacle of reproduction paper development, and Ribbons with dyes in tiny gelatine capsules that were released when a typewriter key or pen or pencil pressure was applied were the encouragement for the creation of various materials in microencapsulation, such as pharmaceuticals[1-2]. In order to protect the active ingredient from the environment, solid, liquid, or gaseous active ingredients can be packaged inside another material using a process called microencapsulation1. As a result, the active component is referred to as the core material, and the surrounding material as the shell[2]. This method has been used in many different industries, including printing, chemicals, and

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pharmaceuticals. For this reason, microencapsulation technology has become very popular. The process of creating microcapsules began in the 1950s when Green and Schleicher 2,3 combined gum Arabic and gelatine to create microencapsulated dyes that were used to make carbonless copying paper. One of the most important products to use microencapsulation technology is carbonless copy paper, which is still manufactured on a commercial basis. The technologies created for carbonless copy paper have subsequently led to the creation of a number of microcapsule products[2-3]. The process of "micro-encapsulation" involves coating minuscule particles or droplets to create tiny capsules with a variety of beneficial characteristics. To lower dosage frequency and stop medication deterioration, microencapsulation can also be used to enclose solids, liquids, or gases inside a micrometric wall composed of hard or soft soluble film. A microcapsule is a small sphere with a uniform wall surrounding it in its most basic form. While the wall of the microcapsule is sometimes referred to as a shell, coating, or membrane, the material inside is known as the core, internal phase, or fill[3]. A combination of lipids and polymers, like alginate, may be utilised to ensnare the target material inside.

Importance of Microencapsulation:-

The product being encapsulated has more stability and shelf life thanks to microencapsulation. This method works well for turning liquid solutions into powder. By using the encapsulation technique, bioactive components that are sensitive to light, pH, oxygen, and moisture can be stabilised[3-4]. It is possible to avoid incompatibility between the various bioactive ingredients and the food matrix. At room temperature, microencapsulation stops the volatile food ingredients from vaporising. The release of active ingredients is regulated. As a result, it presents food producers with a fantastic opportunity to create affordable, wholesome food for consumers across all market segments[4]. The most important characteristic of microcapsules is their tiny size, which permits a large surface area[4-5]. For instance, it has been reported that the total surface area of 1 mm hollow microcapsules with a 0.1 mm diameter is roughly 60 m2. The diameter and total surface area have an inverse relationship. This huge surface area can be used for light scattering, chemical reactions, adsorption and desorption sites, and other processes. In-depth descriptions of microcapsule characteristics[5].

Novel Pharmaceutical Formulation

Innovative combinations can mask the flavour and aroma of their constituents. To enhance the uptake of nanoparticles within cells: Because of their enhanced permeability and retention characteristics, cancer cells primarily absorb nanoparticles passively (EPR effect).

NANOPARTICLE.

Particulate dispersions or solid particles with a size range of 10–1000 nm is referred to as nanoparticles. The medication was encapsulated, dissolved, or attached to a matrix of nanoparticles. One can obtain nanoparticles, nanospheres, or nano capsules depending on the preparation technique used[5-6]. Nanospheres are matrix systems where the drug is uniformly and physically dispersed, whereas nano capsules are systems where the drug is contained within a cavity surrounded by a special polymer membrane. Biodegradable polymeric nanoparticles, especially those coated with hydrophilic polymers like poly (ethylene glycol) (PEG), also referred to as long-circulating particles, have been explored as possible drug delivery vehicles in recent years due to their capacity to circulate for an extended amount of time, target a specific organ, and function as carriers of DNA in genes[6]. The creation of an

extensive range of nanoscale technologies is starting to shift basis for diagnosing and treating diseases, as well as defence. These days, technology breakthroughs, dubbed "nanomedicines" by National Institutes of Health could possibly transform the molecular findings that come from proteomics and genomics into broad advantage for the sick[6-7]. Nanomedicines is a broad field and contains acting nanoparticles as biologically inspired (functionalized carbon, for example "Nanoachics" (such as those made of from DNA and replaceable DNA components scaffolds (stick cube and octahedron, for example), polymeric nano constructs and nanofibers as biomaterials (such as molecules assembling themselves and (Peptide nanofibers and peptide amphiphiles shape memory for tissue engineering) Polymers as nanoporous and (molecular switches membranes) and microfabrication at the nanoscale based devices, such as drug-delivery silicon microchips[7]. Many studies' main objective is to evaluate the way in which manufactured. The skin and nanoparticles: cutaneous toxicity, dermal absorption, and the capacity to transfer to the skin following systemic exposure. One of the main pathways of possible exposure to harmful substances, such as new tiny particles[7-8]. But no information is available about whether or not particles are taken in across the barrier of the stratum corneum or whether systemically applied particles may build up in the skin tissue. A well has been developed in our lab. Verified a different, humane animal model that is indicative of human dermal absorption in vivo that is most appropriate for evaluating both the dermal the assimilation of nanoparticles and their possible buildup in the skin following systemic exposure. These investigations will make use of iron oxide tiny crystals[8].

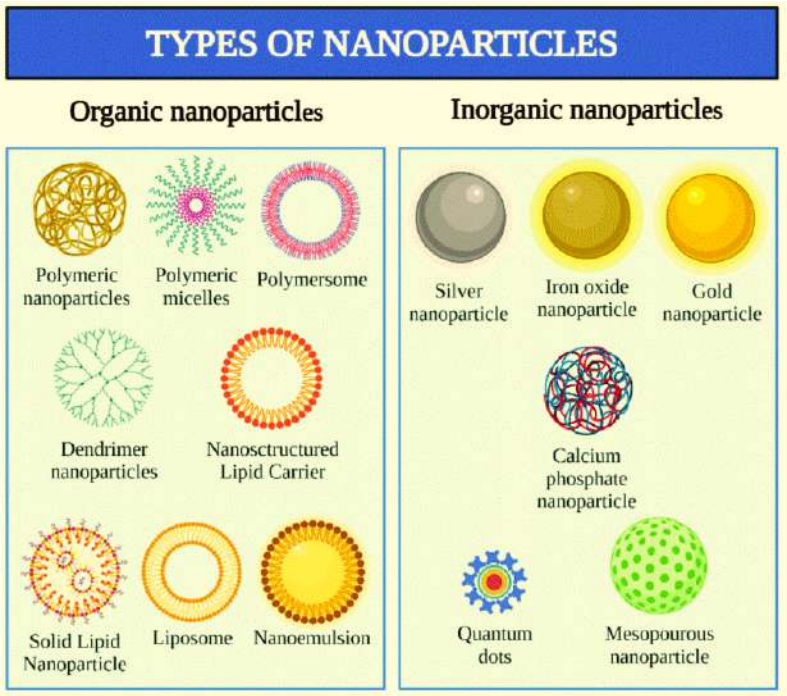

Fig.no. 1 Types of Nanoparticles.

Applications of Nanoparticles

Antimicrobial Properties

Due to their large surface area, aluminium nanoparticles have a strong antibacterial effect. Sadiq M. et al. (2009) confirmed the antimicrobial effect of Al nanoparticles against Escherchia coli (E. coli)[8-9].

Cancer Therapy

3-methyladenine, an autophagy inhibitor, was given in conjunction with Al oxide nanoparticle

nanotubes containing Thapsigarin to aim the signalling of human normal and malignant cells both exhibit autophagy (Evdokiou et al. 2015).

Biosensing

Aluminium oxide nanoparticles are being considered as cutting-edge instruments for detection of different chemical compounds. The Al oxide nanoparticles are being used to find the bovine serum BSA, or albumin (Ito et al. 2017)[9].

Drug Delivery

As a low water-soluble amalgam, Al nanoparticles, such as mesoporous Al oxides, are being used for improved oral administration of the hypertension medication Telmisartan (Borbane et al. 2015).

Effective for Treating Other Illnesses

Intestinal peptide, a vasoactive substance, has been combined with alpha nanoparticles to treat allergic asthma in a mouse model. In a mouse model of asthma, alpha Al nanoparticles were used to stabilise intestinal vasoactive peptides against enzymatic degradation in the pulmonary system. Compared to non-conjoined beclomethasone and intestinal vasoactive peptides, it demonstrated significant efficacy against asthma (Shamsadin et al. 2016)[9-10].

Stabilisation and Preservation of Biomolecules

Protein molecules can be folded back into shape by using aluminium nanoparticles as a nanoplatform. Al nanoparticles interact electrostatically with the negatively charged remoulded proteins to prevent misfolding and aggregation (Volodina et al. 2017)

Immunotherapy

It has been discovered that Al nanoparticles can trigger autophagy. The primary goal of immunotherapy and vaccines for the next generation is to induce autophagy because autophagy plays a major role in introducing antigens to T cell's. In order to induce autophagy in macrophage cells, aluminium nanoparticles conjugated to cysteine peptidase A and B were used as a leishmania vaccination. Al nanoparticles in their conjugated form showed quick internalisation.

Biological Applications

SiNPs are used in biomedicine as nanocarriers, diagnostic tools, and cancer treatment because of their non-toxic, biocompatible, and other special qualities (Min-Dianey et al. 2018).

Medication Delivery

When altered, mesoporous silica nanoparticles (MSNs) can be used as a multipurpose drug delivery system. MSNs have a multifunctional, porous, less cytotoxic structure, among other characteristics. Because MSNs have morphologies and pores that can be altered, they can transport drug molecules of different sizes. Additionally, MSNs can add different functional groups to the surfaces of compounds to modify their solubility and bioavailability (Watermann and Brieger 2017). As a result, the delivery system for MSNs offers great promise for cancer treatment and tumour diagnosis[10].

Regeneration of Tissues

MSNs have applications in bone tissue engineering because they can produce nanosized apatite of carbon when they react with the physiological environment of the bone. This is achieved by using silanol groups on their surface. (Rosenholm et al. 2016). MSNs' unique characteristics enable them to support the development of an imaging material for focused bioimaging. Thus, MSNs' characteristics make them appropriate for long-term, high-speed laser bioimaging that occurs in real time (Cha and Kim 2019).

Applications for Energetic Materials

It is possible to create and alter silicon quantum dots so that they retain the porous silicon properties, which allows for the manifestation of highly energetic material reactions. They can therefore be applied to the use of energetic material.

Applications in Agriculture

SiNPs can be used as biopesticides, as a vehicle for fertilisers and herbicides, as a target delivery system for proteins, nucleotides, and other chemicals into plants, as a part of nano zeolites to retain more water, and as nano sensors. SiNPs therefore have a chance to transform agriculture[11].

Enhancement of Solar Cells

The performance of perovskite solar cells has been enhanced by scientists through the use of SiNPs, which have the ability to absorb a wide range of light wavelengths without interacting with other battery components. Because SiNPs are readily and cheaply produced, Perovskite solar cells of this type are cost-effective.

Protein Adsorption and Separation

MSNs have the capacity to serve as protein carriers for both in vitro and in vivo administration. They are also the best options for the adsorption and separation of particular protein molecules. This is because of its physiochemical characteristics, affordability, structure, and ability to have distinct surface functionalization (Lui and Xu 2019). Bio-separation, immunoassays, enzyme immobilisation, and biosensors are therefore beneficial[12].

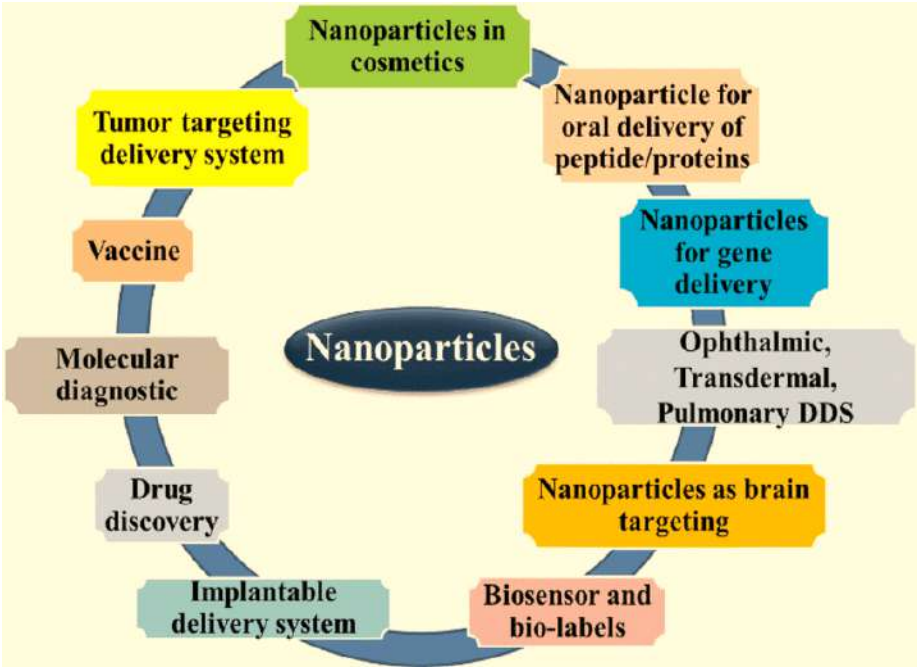

Fig.no.2 Applications of nanoparticles

Microsphere

Microspheres are materials or compounds that have the ability to flow freely; these are known as powder' s. The components of microspheres are of synthetic polymers or biodegradable proteins in nature, with the ideal particle size falling between 1 and 1000 µm. Another name for microspheres is micro particle' s[12-13]. There are several ways to produce microspheres materials like ceramics, polymers, and glass microbes. These find usage in various contexts. Their material and particle size depend on how they are used during building. There are two kinds of microspheres: microcapsules. and micrometrics, also referred to as micro-capsules are those where the material that is trapped is clearly distinct capsule wall encircling it. Moreover, micrometrics in which material is trapped and scattered across the matrix. Microsphere is significant to enhance bioavailability[13].

Advantages of Microspheres

1. The poorly soluble drug becomes more soluble when the particle size is reduced.
2. The microsphere offers consistent and extended therapeutic outcome.
3. Maintain a steady drug concentration in the blood, so boosting adherence to patents.
4. Reduce toxicity and dosage.
5. Guard the medication from photolytic and enzymatic and It was discovered that cleavage works best for drug delivery.

Disadvantages of Microspheres

1. Compared to standard formulations, the costs of the materials and processing for the controlled release preparation are significantly higher.
2. What happens to polymer matrix and how does it affect the environment?
3. What happens to polymer additives like fillers, stabilisers, plasticizers, and antioxidants?
4. There is less reproducibility.
5. Process variables including agitation/evaporation, pH changes, solvent addition, and temperature changes may have an impact on how stable the core particles are to be encapsulated.

Applications of Microspheres

Localised drug delivery

By delivering the product directly to the site where it is needed or required, systemic exposure to the drug can be minimised. This becomes critical when it comes to toxic medications that have a number of systemic side effects (like chemotherapeutic medications).

Sustained delivery of drugs

Tablets that are encapsulated release their contents over time, minimising the need for repeated injections. This feature can help increase patient compliance, particularly with medications for long-term conditions that call for frequent injections (like a protein deficiency).

Drug stabilisation

The polymer helps shield the medication from the physiological environment, which increases the medication's stability in vivo. This specific attribute

Microcapsule

Making a thin membrane coating of one material over another containing an active agent is known as microencapsulation. The coating material's percentage to the active material is minuscule. The size of the microcapsules ranges from 1 micron to about 100 microns[14]. Typically, the coating is referred to as a coating membrane, cover, shell, or film. Furthermore, the coating's active ingredient may also be referred to as the internal fill, core material, core element, etc. The gas, liquid, and solid phases of the core material can all be processed using the microencapsulation technique. This makes handling and processing liquid and gaseous materials as solids simpler. With few adverse effects, microcapsules increase dosage efficiency[14-15].

Advantages of Microcapsule

1. It improves patient compliance by masking the taste of bitter medications to make them more palatable. The most popular coating material for this use is Eudragit E100. Since the medications in microencapsulation are insoluble in the mouth, they do not interact with taste receptors. For instance, ofloxacin.
2. Transformation of a liquid dosage form into a free-flowing powder or pseudo-solid. For instance, eprazinone
3. It improves the safe handling of toxic medications as well as the solubility of poorly soluble drugs.
4. For the material that has been encapsulated to be released at the intended location.
5. To change some drugs' surface qualities and physical characteristics. Reducing sodium chloride's hygroscopicity, for instance.

Disadvantages of Microcapsule

1. Compared to standard formulations, the cost of the ingredients and the formulation process may be higher.
2. There's less reproducibility.
3. Significant differences exist in how the polymer matrix, additives, and degradation products react with heat, hydrolysis, and biological agents.
4. Changes in process parameters, such as temperature, pH, solvent addition, or solvent evaporation, have an impact on the stability of the core particle.

Like other drug delivery methods, microcapsules frequently aid in increasing dosage efficacy while lowering the likelihood of adverse effects. Pharmaceutical companies can create release profiles that are best suited for a specific therapeutic by using active pharmaceutical ingredient (API) encapsulation. Examples include delayed release, targeted release, prolonged release, and fast release formulas. For bitter compounds, microencapsulation processing also necessitates oral administration without water and flavour masking in chewable tablets[16].

Applications of Microcapsule

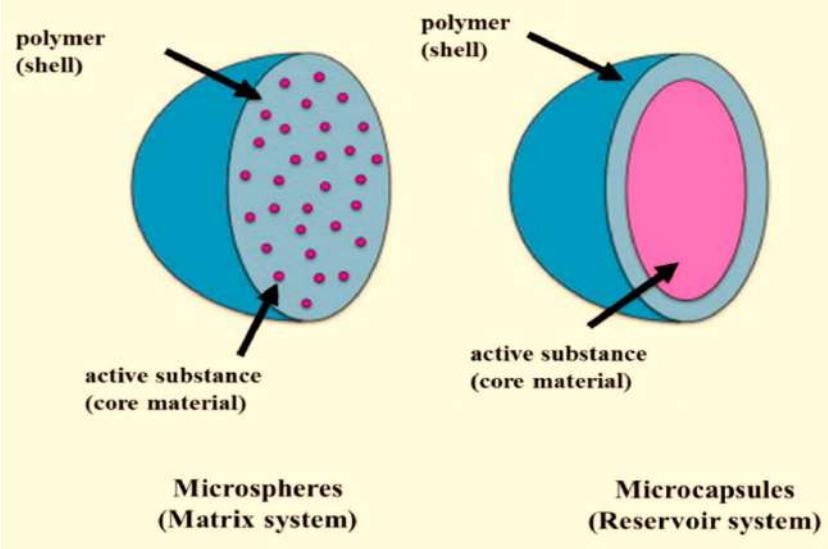

Fig.no. 3 Shell of Microsphere and Microcapsules.

Classification of Microencapsulation

A. Mononuclear-

Mononuclear (core-shell) microcapsules contain the shell around the core.

B. Polynuclear-

While poly nuclear capsules have many cores enclosed within the shell.

C. Matrix types-

In matrix encapsulation, the core material is distributed homogeneously into the shell material.

Materials for Microencapsulation

Core Materials

The particular material to be coated, known as the core material, can have a liquid or solid composition. Since the liquid core can contain materials that are dissolved or dispersed, the composition of the core material can vary[16-17]. Active ingredients, stabilisers, diluents, excipients, and accelerators or retardants of release rates make up the solid core.

Coating Materials

The coating material should have the necessary coating properties, such as strength, flexibility, impermeability, stability, and optical qualities, and it should be able to form a film that is cohesive with the core material and both chemically and nonreactively compatible. The coating materials that are utilised in microencapsulation techniques can be modified in situ to some extent[17].

Examples of Coating Materials

1. **Water soluble resin–**
   Gelatine, Gum Arabic, Starch, Polyvinylpyrrolidone, Carboxymethylcellulose, Hydroxyethyl cellulose, Methylcellulose, Arabinogalactan, Polyvinyl alcohol, Polyacrylic acid.
2. **Water insoluble resins –**
   Ethyl cellulose, Polyethylene, Polymethacrylate, Polyamide (Nylon), Poly (Ethylene- Vinyl acetate),cellulose nitrate, Silicones, Poly(lactideco- glycolide).
3. **Waxes and lipids –**
   Paraffin, Carnauba, Spermaceti, Beeswax, Stearic acid, Stearyl alcohol, Glyceryl stearates.
4. **Enteric resins –**
   Shellac, Cellulose acetate phthalate, Zein.

Methods of Microencapsulation

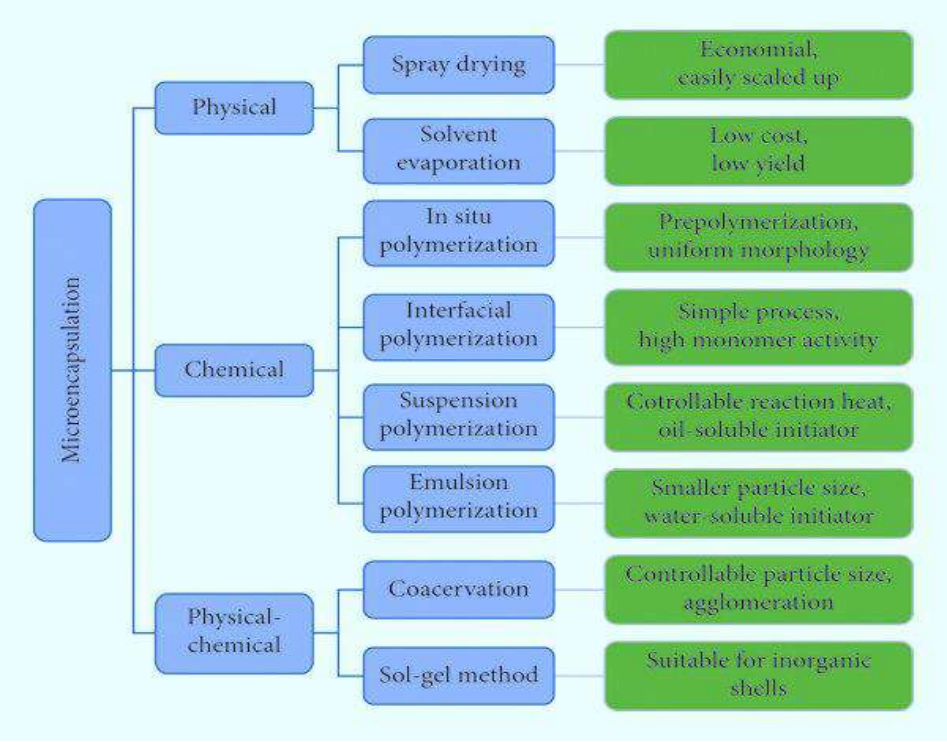

Fig.no. 4 Various methods of microencapsulation

Physical Method:-

Spray drying

Spray-drying is among the earliest methods for encapsulating active ingredients. When it comes to foods, it's not always thought of as an encapsulation—for example, aroma in a spray-dried form. Spray-drying of the active agent is typically accomplished by dissolving, emulsifying, or dispersing the active ingredient in an aqueous solution of carrier material, then atomizing and spraying the mixture into a heated chamber. [18]. The larger active molecules are delayed during this process by a film that forms at the droplet surface, causing the smaller water molecules to evaporate. Spray drying is another option for the active ingredient in organic solutions such as acetone or ethanol; however, it is much less common due to safety and environmental concerns (which also raise the expense). In order to minimise particle overheating, spray-dryers in the food industry typically atomize the infeed using a high-pressure nozzle or centrifugal wheel, also known as a rotary atomizer. They also run on a co-current air and particle flow. This latter is important if any contents are volatile in any way or are heat

sensitive (as is the case with aromas). While the co-currently dried particles are probably more porous, the counter-currently prepared particles are less porous[18-19]. The liquid's viscosity and surface tension, the spray's velocity, and the pressure drop across the nozzle are some of the variables that affect the size of the atomizing droplets. The size of the atomizing droplets also affects the drying time and particle size. In typical spray-drying circumstances, the temperature of the wet bulb is approximately 50°C. The larger the spray-dryer, the longer the particle will reside in the dryer (usually 5–100 s), and thus the larger the maximum size of the droplets that can be dried. Additionally, atomizing nozzles can be installed to spray upward, much like a fountain[19]. This allows for the drying of relatively larger droplets because of the longer droplet residence time. Atomizing nozzles, however, are often installed to spray downward.

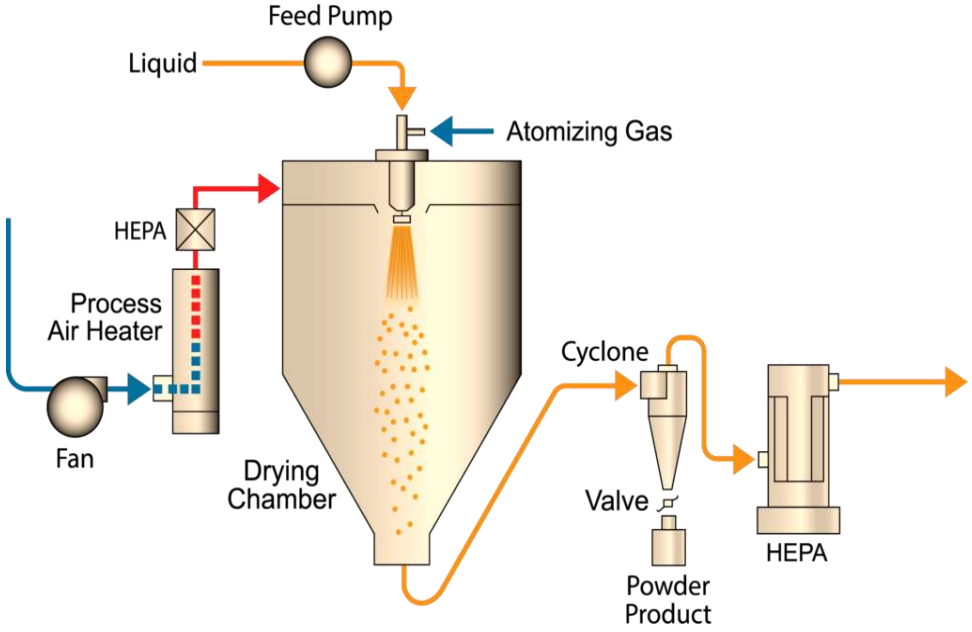

Fig.no. 5 Spray drying.

Solvent Evaporation

The O/W emulsion, a liquid manufactured vehicle created by stirring together two immiscible liquids, is a suitable application for the solvent evaporation method. A volatile solvent that is immiscible with the liquid manufacturing vehicle phase is used to dissolve the microcapsule coating (polymer) in the solvent evaporation method[19]. In the coating polymer solution, a core material (drug) to be microencapsulated is dissolved or dispersed. The core-coating material mixture is agitated in the liquid manufacturing vehicle phase to produce microcapsules of the right size. System agitation is maintained until the solvent evaporates and partitions into the aqueous phase. The microcapsules produced by this process are hardened. Dispersion of the oil phase in the continuous phase can be accomplished through a variety of methods[19-20]. The most popular approach involves mounting a variable speed motor to a propeller-style blade. The rate of solvent evaporation for the coating polymer(s), temperature cycles, and agitation rates are some of the process variables that affect how dispersions are formed. The selection of the vehicle phase and solvent for the polymer coating, as well as solvent recovery systems, are the most crucial elements to take into account when preparing microcapsules using the solvent evaporation method. Many different liquid and solid core materials can be microencapsulated using the solvent evaporation method. Either water soluble or water insoluble

materials could make up the core components. As coatings, a range of film-forming polymers are available.

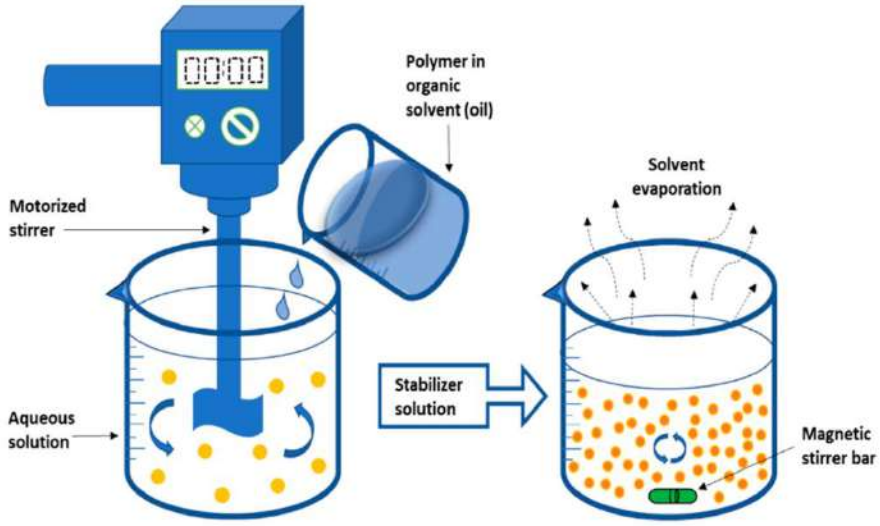

Fig.no. 6 Solvent Evaporation

Air Suspension Method

The process of microencapsulation via air suspension involves spray coating the air suspended particle and dispersing a solid, particulate core material in a supporting air stream. Particles are suspended in an upward-moving air stream inside the coating chamber. The way the chamber is constructed and how it operates affects how the particles circulate through the coating zone, which is where a. The moving particles receive a spray application of coating material, typically a polymer solution[20]. More control and flexibility are provided by air suspension coating of particles with solutions or melts. While suspended in an upward-moving air stream, the particles get coated. A perforated plate with holes of varying patterns both inside and outside of a cylindrical insert supports them. The amount of air that can rise through the outer annular space is just enough to cause the setting particles to become fluid. Particles rise quickly as a result of the cylinder's rising air flow. A large range of coating material candidates for microencapsulation are available through the air suspension process. The procedure can apply coating in the form of hot melts, emulsions, dispersions, solvent solutions, or aqueous solutions to equipment with capacities ranging from 1 to 990 pounds

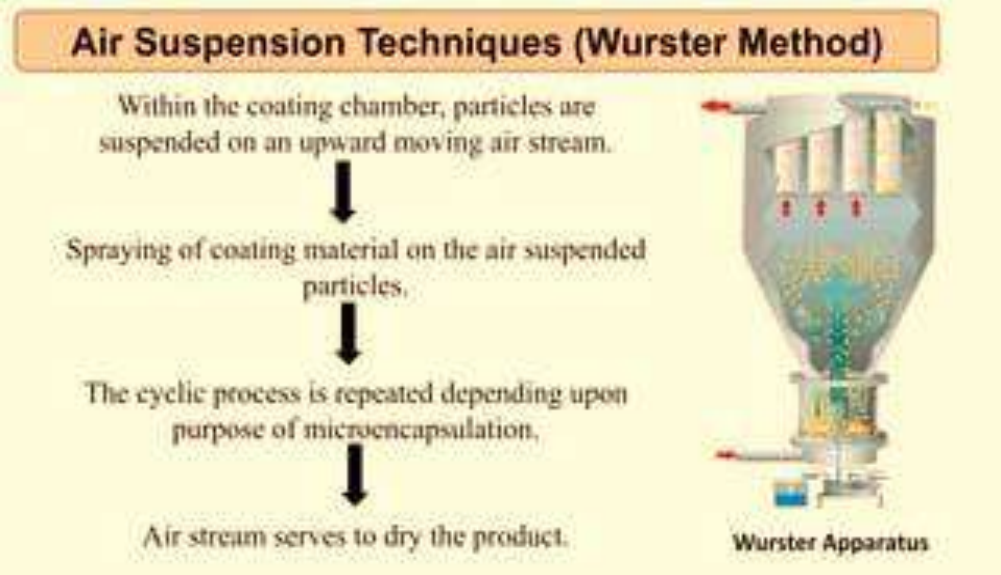

Fig.no. 7 Air suspension techniques.

Pan Coating

One of the earliest industrial processes for creating tiny, coated particles or tablets is the pan coating method, which is extensively employed in the pharmaceutical sector. The coating material is applied slowly while the particles are tumbling in a pan or other apparatus[20-21]. One of the earliest industrial processes for creating tiny, coated particles or tablets is the pan coating method, which is extensively employed in the pharmaceutical sector. Solid particles larger than 600 microns are generally regarded as essential for effective coating, and the process has been widely used for the preparation of controlled-release beads. The particles are tumbled in a pan or other device while the coating material is applied slowly with respect to microencapsulation. Typically, medications are applied to a variety of spherical surfaces, like nonpareil sugar seeds, and then covered in layers of different polymers for protection

Fig.no. 8 Pan coating.

Fluidized Bed Coating

Encapsulating solid core materials, including liquids absorbed into porous solids, is the usual use for fluidized bed coating. Although this technique is commonly used to encapsulate medications, its application in the food processing sector has grown recently. A spray of liquid coating material is applied after the solid particles to be encapsulated are suspended in a jet of air (Naveena and Nagaraju, 2020). The capsules are then transported to the solidification area, where the solvent vaporisation or cooling processes are used to solidify the capsules' shells[21]. The procedure of suspending, misting, and chilling is iterated until the desired thickness of the capsule walls is achieved. This method has been used to microencapsulate ascorbic acid in ethyl cellulose and polymethacrylate.

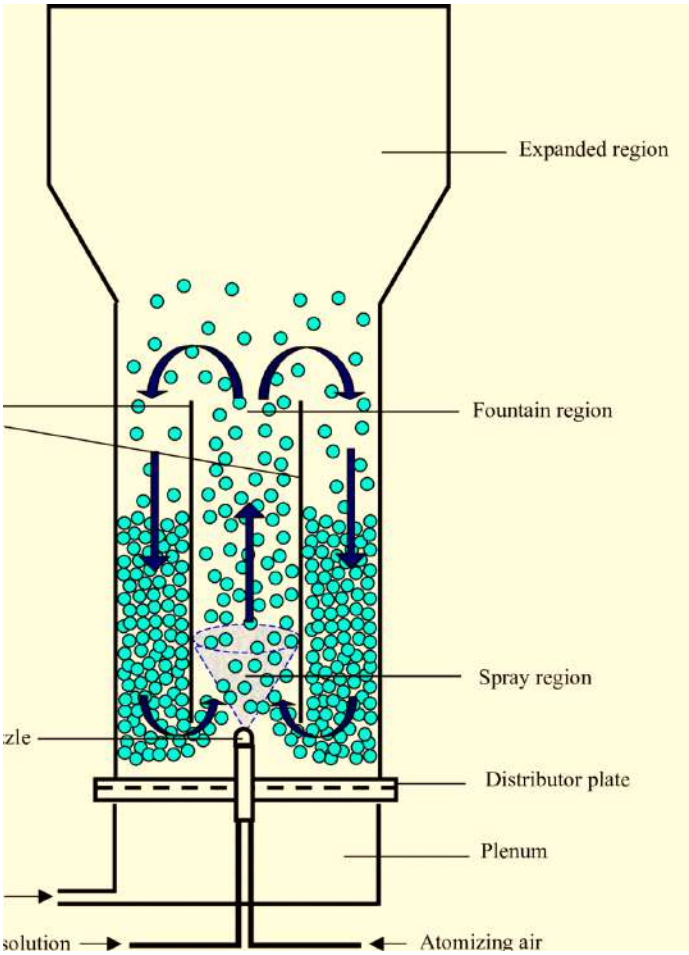

Fig.no.9 Fluidized bed coating.

Multi-orfice Centrifugal method

A mechanical method for creating microcapsules has been developed by the Southwest Research Institute (SWRI). It uses centrifugal forces to propel a core material particle through an enclosing microencapsulation membrane, resulting in mechanical microencapsulation[21-22]. The cylinder's rotational speed, the coating and core materials' flow rates, the concentration, viscosity, and surface tension of the core material are examples of processing variables. A variety of coating materials can be used to microencapsulate liquids and solids with varying size ranges using the multi-orifice centrifugal process (as illustrated in figure 9). The encapsulated product may be provided as a dry powder or as a slurry in the hardening mediator. With the process, production

rates of 50 to 75 pounds per hour have been attained.

B. Chemical Method:-

Polymerization

The polymerization method of microencapsulation is used to from protective microcapsule coatings, in situ. The method involves the reaction of monomeric units positioned at the interface existing in-between a core material and a continuous phase, wherein the core material is dispersed. The continuous or core material supporting phase is usually a liquid or gas, and therefore, the polymerization reaction occurs at the interfaces of liquid-liquid, liquid-gas, solid-liquid, or solid-gas[22]. Similar to IFP, the polymerization of monomers introduced to the encapsulation reactor results in the formation of the pill shell. No reactive retailers are introduced to the core material using this method. With the help of the dispersed core material and non-stop segment, polymerization occurs entirely inside the continuous segment and at the non-stop segment side of the interface formed. A low molecular weight prepolymer will first take shape, but as time passes, it will enlarge in size. It uses the process of creating a robust pill shell to deposit at the floor of the distributed middle material there[22-23]

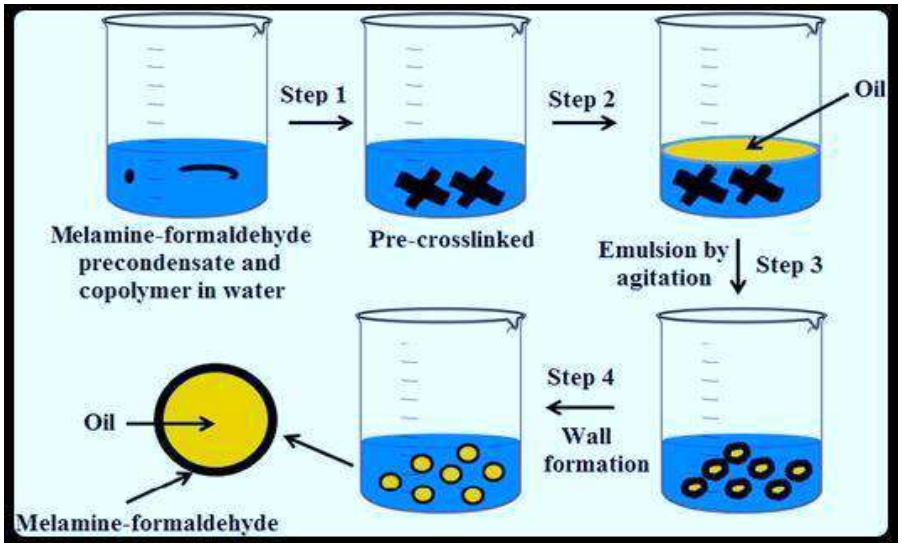

Fig.no.10 Polymerization.

Interfacial Polymerization

Multifunctional monomers, such as multifunctional isocyanates and multifunctional acid chlorides, are the materials utilised.You can use these separately or in combination.The liquid centre material dissolves the multifunctional monomer.It is possible to add a coreactant multifunctional amine to the mixture[23-24]. Delivered to neutralise the acid created throughout the reaction is base.This results in rapid polymerization at the interface and the formation of the pill shell.As isocyanate and amine react, a polyurea shell can be created.A polyamide or nylon shell can be created as an amine and acid chloride react.

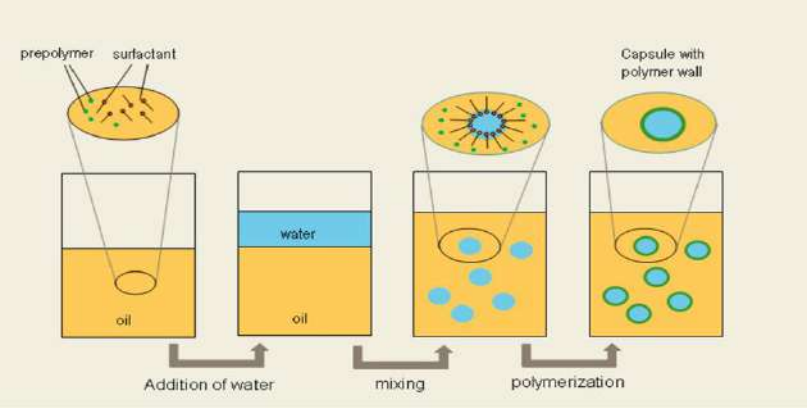

Fig.no. 11 Interfacial polymerizations.

Matrix Polymerization

A core material is embedded in a polymeric matrix during the formation of the particles in several processes (Figure 11). Spray-drying is a straightforward technique of this kind where the particle is created by the solvent evaporating from the matrix material. Nevertheless, a chemical alteration may also be the reason for the matrix's solidification. Using this method, the material to be encapsulated (core) is mixed with a stirred aqueous polymerization medium and drops of monomer (alkyl acrylate) are added substance) and an appropriate emulsifier. The process of polymerization starts and creates the first polymer molecules precipitate to create primary in the aqueous medium cores[24].

C. Physio-chemical Methods:-

Coacervation

Coacervation are created when an aqueous solution separates into a polymer-rich phase (also referred to as a coacervate) and a polymer-poor phase via a liquid–liquid phase separation mechanism. Depending on the number of polymer types present, the process of coacervation can be identified as either (simple) coacervation, in which only one type of polymer is involved, or complex coacervation, in which two or more types of polymers of opposite ionic charges are present. The active agent is typically encapsulated using complex coacervates. Gelatin and gum arabic typically make up their shell[24-25]. To prepare complex coecervates, an o/w emulsion containing gelatin and gum arabic at a 1:1 w/w ratio and at a 2-4% w/w of each polymer dissolved in the water phase is typically used. This is achieved by adjusting the pH from neutral to about 4 under turbulent conditions in a stirred vessel at >35°C, a temperature above to which gelatin gels. Three immiscible phases are created as a result: the oil, polymer-rich, and polymer-poor phases. The polymer-rich phase droplets settle on the emulsion surfaces as a result of interfacial sorption. On the other hand, dilution can cause complex coacervation in place of pH adjustment. To do this, emulsify the oil in an 8–11% (w/w) gelatin solution, then add gum arabic and dilute the water. Many coating materials were tested for coacervation microencapsulation; however, the gelatin/gum Acacia device is the most thoroughly researched and understood coating device[25].

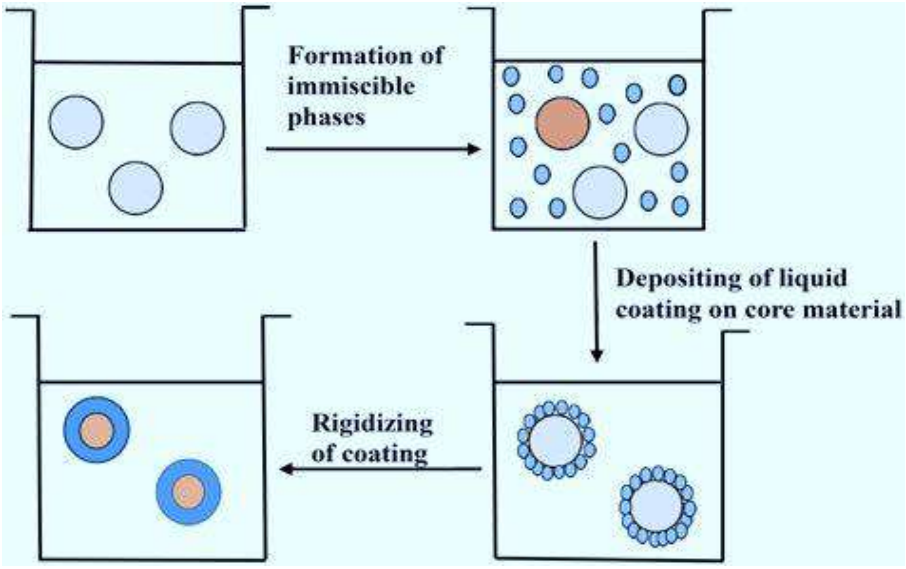

Fig.no. 12 Coacervation

Applications of Microencapsulation

1. By altering or delaying the release of encapsulated active agents or core materials, microencapsulation can be utilised to formulate different sustained controlled release dosage forms.
2. **Enteric-**
   Coated dosage forms, which allow the medication to be absorbed in the intestine rather than the stomach, can also be created using microencapsulation. 3. To lessen the likelihood of gastric irritation, medications that irritate the stomach are being microencapsulated[26].
3. The use of microencapsulation techniques can mask the taste of bitter drug candidates.
4. Liquids and gases can be transformed into solid particles in the form of microcapsules through the process of microencapsulation[27].
5. To help with greasy medication addition to tableted dosage forms and to get around the issues with tacky granulations and direct compression, microencapsulation can be used[28].
6. One way to reduce volatility is by using microencapsulation. Volatile materials that are microencapsulated can be kept for extended periods of time without experiencing significant evaporation[29].
7. The encapsulated active agents are protected from a variety of environmental factors by microencapsulation, including light, heat, humidity, oxidation, etc.
8. By using microencapsulation, the hygroscopic properties of many core materials can be minimised.
9. Microencapsulation can be used to separate substances that are incompatible. For instance, microencapsulation can be used to separate pharmaceutical eutectics. In this instance, liquid formation results from direct material contact. By microencapsulating the two before mixing, the incompatible aspirin-chlorpheniramine maleate mixture can be stabilised more effectively.

10. Agriculture:-

Crop protection is one of the most significant uses of microencapsulated products. These days Pheromones from insects are starting to work as a biological a substitute for traditional, hard

pesticides. In particular, extractant Pheromones can lower the number of insects by obstructing their reproductive cycle. Thus, modest amounts of Pheromones unique to a species are released during mating season, increasing the pheromone background level to the point at which it conceals the plume of pheromones released by its female partner[30].

11. Food Industry:-

There may be a trend right now towards a healthier way of living, which includes consumers becoming more aware of what they eat and the benefits certain foods have for maintaining good health. Contamination avoidance with a diet plan is an entirely original supply of cutting-edge, so-called "practical Foods," many of which may be enhanced with ingredients to support health. But adding ingredients to food products to increase nutritional value can undoubtedly affect their flavour, colour, texture, and scent. Occasionally they become inactive and gradually deteriorate, or they can become hazardous due to oxidation reactions. Additionally, ingredients may react with additives found in the food system, which may further limit bioavailability[30-31].

12. Catalysis:-

Catalytic processes based on transition metals are essential. significance to the fine chemical, agrochemical, and pharmaceutical industries. A significant fraction of these species of catalytic metals are frequently costly and hazardous, making operational handling possibly dangerous materials. The use of microencapsulation has lately acknowledged as a practical substitute tactic to facilitate simple recovery, safe handling, reuse, and disposal at a reasonable financial expense. Microcapsules of polyurea Because they are insoluble in both organic and aqueous solvents, and resilience to deterioration have been employed for combination of several catalysts in one[31].

13. **Energy Production:-**

Utilising gaseous deuterium, a fusion fuel, inside hollow plastic microspheres, nuclear fusion is harnessed to produce electricity. There are layers to the tablets. A three mm-thick polystyrene shell serves as the internal layer that compresses the fuel. The next layer is a three mm thick layer of poly(vinyl alcohol), which prevents deuterium from diffusing out of the pill. The ablator, or outer layer, is 50 mm thick and contains a beautiful crosslinked polymer derived from 2-butene. Electricity from overly intense laser beams is absorbed through the microcapsule shell's floor during the fusion experiments. The response pressure quickens the shell's inward relaxation as the Ablator, or outer layer, burns off, compressing and heating the deuterium within[32].

Characterization of Microcapsule and Microspheres

Characterising the microparticulate carrier is a significant phenomenon that aids in the creation of an appropriate carrier for the delivery of proteins, medications, or antigens. Different microstructures can be found in these microspheres. The carrier's stability and release are dictated by these microstructures.

Sieve analysis

Using a mechanical sieve shaker (Sieving machine, Retsch, Germany), it is possible to determine how the microspheres are separated into different size fractions. Five common stainless-steel sieves (20, 30, 45, 60, and 80 mesh) are set up in decreasing order of aperture size. On the topmost sieve, five grammes of drug-loaded microspheres are positioned[33]. The particles on the screen are weighed after the sieves are shaken for roughly ten minutes.

Morphology of Microsphere

A scanning electron microscope (XL 30 SEM Philips, Eindhoven, The Netherlands) is used to study the surface morphologies of microspheres. A double-sided adhesive tape is used to mount the microspheres onto a copper cylinder (10 mm in

diameter and 10 mm in height). The samples are coated using an ion sputtering device (JFC-1100E, Jeol, Japan) for 4 minutes at a current of 10 mA[34].

Atomic Force Microscopy

The surface morphology of the microspheres is examined using a Digital Instrument Multimode Atomic Force Microscope. Using double-sided adhesive tapes, the samples are affixed to metal slabs and examined under a microscope in an environment with constant temperature and minimal vibration[34-35].

Particle Size

Scanning electron microscopy, or traditional mild microscopy, is the most widely used method for visualising microcapsules (SEM). The form and shape of microcapsules are studied using each of these approaches. gives more choices than when using light microscopy. It allows for the investigation of double-walled systems in addition to the microsphere surfaces. The non-destructive visualisation method known as confocal laser scanning microscopy (CLSM) provides results not only about surfaces and systems but also about interior particles[35]. After determining the particle size using ultrasound, about 30 mg of microparticles are redispersed in 2-4 ml of distilled water containing 0.1% (m/m) Tween 20 for three minutes. The mixture is then put into a small volume recirculating unit that runs at 60 ml/s. Using a Malvern Masteries X, laser diffractometry can be used to determine the microparticle size.

Carr's Index

The resting attitude was determined using a constant funnel and cone method. Combined microcapsule bulk densities were determined by utilising the Carr's Index or Hausner's Ratio, in conjunction with poured or trapped bulk densities of recognised weight of pattern using a measuring cylinder (Hausner, 1967; Carr, 1965).

Carr's Index=[Bulk Density/Tapped Density - Tapped Density] × 100.

Hausner's ratio=ρT/ρB,

Where,

ρB represents bulk density

ρT is tapped density.

Determination of drug loading, encapsulation performance and microcapsule yield

The drug content was determined by extracting 20 mg of the microcapsule pattern with methanol. After filtering and diluting with methanol, the resulting material was examined using UV spectrophotometry[36].

%loading = drug weight/microcapsule weight

%Encapsulation performance = [actual drug content/%theoretical drug content] ×100

%Yield=M/ M0 ×100 M = Microcapsule weight M0 = Total predicted weight of pharmaceutical and polymer

Drug release kinetics and mechanism

The four main processes by which drugs are released from microcapsules are osmosis, erosion, dissolution, and diffusion.

Diffusion

The most frequent process by which the dissolution fluid enters the shell, dissolves the core, and leaks is diffusion. Therefore, the rate at which the drug dissolves in the dissolution fluid, the rate at which the drug leaks out and disperses from the surface, and the rate at which the dissolution fluid penetrates the wall of the microcapsules all affect the overall release. As shown below, the kinetics of such drug release follow Higuchi's equation[37].

Q = [D/J (2A – ε CS) CS t]½

Dissolution

When the polymer coat dissolves quickly in the dissolution fluid, the drug release rate from the microcapsule is also determined by the coat's dissolution rate. The coat's thickness and solubility in the dissolution fluid affect how quickly the coat releases particles.

Osmosis

The drug solution is forced out of the microcapsule through tiny pores in the polymer coat, which

functions as a semi-permeable membrane and permits the development of an osmotic pressure differential between the interior and exterior of the microcapsule[38].

Erosion

Certain coat materials, such as stearyl alcohol, beeswax, and glyceryl monostearate, cause drug release when their coats are eroded by pH changes and/or enzymatic hydrolysis. The wide variation in the size, shape, and arrangement of the core and coat materials in microcapsules has made attempts to model drug release from them more difficult. Drug release modelling is further complicated by the physiochemical characteristics of coating materials, such as variable thickness, porosity, and inertness, and core materials, such as solubility, infusibility, and partition coefficient[39]. Due to the wide variation in the size, shape, and arrangement of the core and coat materials within microcapsules, the release of drugs from them has become more complex. The physiochemical characteristics of coating materials, such as their variable porosity, thickness, and inertness, and core materials, such as their solubility, infusibility, and partition coefficient, make it challenging to model drug release. But taking into account the different research that has been done on the release characteristics, the following points can be made[40].

i. Microcapsule drug release rates are governed by zero order kinetics.
ii. Monolithic microcapsules exhibit a t1/t2 dependent release rate during the first half of the total drug release before experiencing an exponential decline.
iii. Monolithic microcapsules with a significant amount of dissolved medication; the release rate is t1/2 dependent for nearly the whole drug release.

FUTURE PROSPECTIVES

In the broad field of microencapsulation, a number of methods and techniques have the potential to be helpful in the preparation of polymeric microparticles. The preparation technique affects the ability of the components used in microparticle formulations to interact with one another as well as the type and size of the microparticles. Microparticles are systems with a diameter greater than one micrometre; the term is typically used to refer to both microspheres and microcapsules. Drugs containing microparticles are used for a number of reasons, such as controlled drug delivery, obfuscating the taste and smell of drugs, shielding the drugs from deterioration, and shielding the body from the harmful effects of the drugs. Since polymeric carriers are essentially multidisciplinary, they are frequently used in the fabrication of microparticles and can have either an erodible or nonerodable. A large number of patents and publications have been released recently. In order to treat or prevent a disease or condition that affects mammals, Hughes developed a technique for the continuous delivery of an active medication to the posterior region of the eye. The technique consists of applying a sufficient quantity of an ester prodrug of the active medication subconjunctivally or periocularly, like tazarotene (prodrug of tazarotenic acid), as systemic administration necessitates a high systemic concentration of the prodrug. Utilising o/w emulsion solvent evaporation techniques, a biodegradable polymeric microparticle system containing the ester prodrug is created.

CONCLUSION

An active ingredient is packaged inside a capsule that ranges in size from one micron to several millimetres, a process known as microencapsulation. The active ingredient is shielded from its surroundings by the capsule until the right moment. The material then escapes through the capsule wall through a variety of channels, such as diffusion, dissolution, melting, or rupture. Microencapsulation is a scientific and artistic process. Every new application presents a

different challenge, and there isn't just ONE way to do it. It takes knowledge of numerous technologies, expertise, and experience to solve these puzzles. Research on microencapsulation holds great promise for improving the quality of products by adding desirable properties to raw materials. New products have occasionally resulted from advancements in this field; two notable examples are carbonless copy paper and controlled drug release. Currently, there is a lot of interest in paper-like exhibits, self-healing structures, and chemically decontaminating textiles. Microencapsulation provides a number of benefits, including protection and masking, a lower rate of dissolution, ease of handling, and the ability to target the active ingredient spatially. This strategy can also be used to accurately deliver small amounts of potent drugs, lower drug concentrations at locations other than the target organ or tissue, and protect labile compounds both before and after administration and before they appear at the site of action. In the future, when combined with other strategies, microencapsulation will play a crucial role in innovative drug delivery systems.

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