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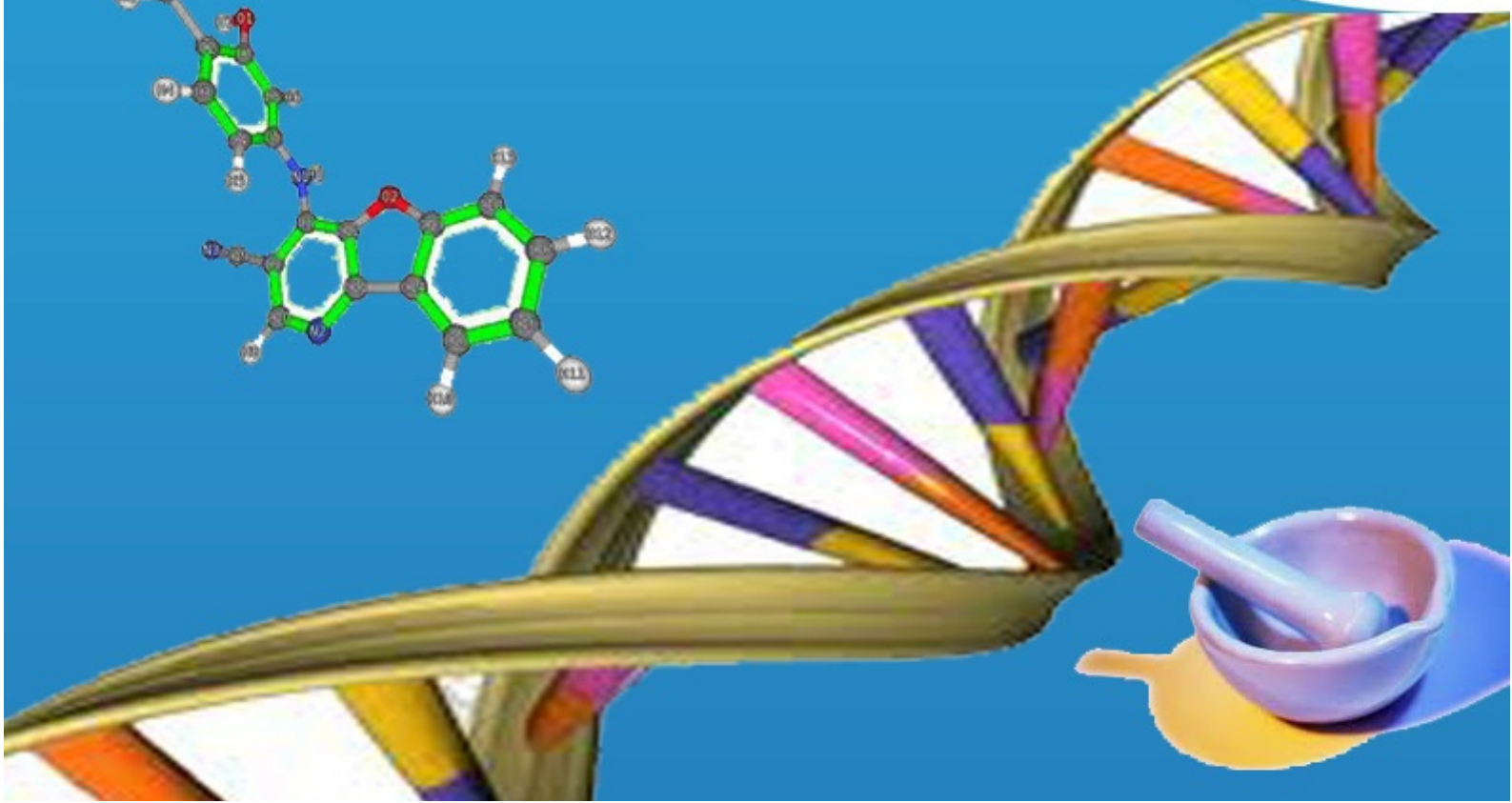
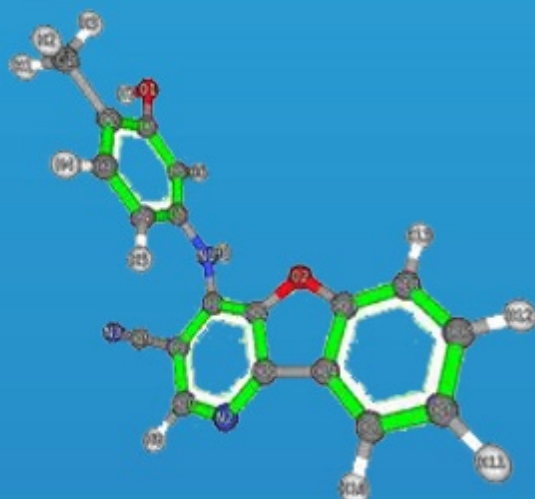
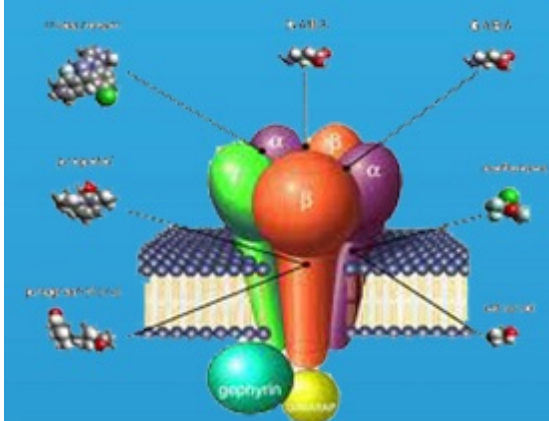
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A REVIEW ON MICROENCAPSULATION: A NEW MULTIUTILITY ADVANCED TECHNOLOGY

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Abstract:

This abstract represents the new advance technology of microencapsulation, its complete study, morphology of microcapsules, reasons for microencapsulation, release mechanism including degradation, osmosis, diffusion, dissolution and erosion. Materials for microencapsulation, different methods of microencapsulation like physical method- air suspension coating, coacervation, spray-drying , pancoating ,centrifugal extrusion, chemical methods- solvent evaporation, polymerization involving interfacial polymer, *in-situ* polymerization and matrix polymer , its general methods of applications in cell immobilization, drug delivery, beverages production ,in textiles ,soil inoculation, quality and safety in food etc and its efficient use in controlled release and sustained release of drug delivery like to mask bitter drugs, separation of incompatible substances, protection to core against atmospheric effects, sieve analysis and etc.

Key words: Microencapsulation, Degradation, Osmosis, Diffusion, Erosion, Dissolution.

Introduction:

MICROENCAPSULATION: A NEW MULTIUTILITY ADVANCE TECHNOLOGY

Microencapsulation is process of enclosing micron sized particles in a polymeric shell¹. A new technology where by small discrete solid particles or small liquid droplets are surrounded and enclosed by an intact shell. Microencapsulation is used to modify and delayed drug release form pharmaceutical dosage forms². In microencapsulation the tiny particles or droplets are surrounded by a coating to give small capsules many useful properties. In a relatively simplistic form, microcapsules are a small sphere with a uniform wall around it³.

Microencapsulation includes Bioencap - sulation which is more restricted to the entrapment of a biologically active substance (from DNA to entire cell or group of cells for example) generally to improve its performance and/or enhance its shelf life⁴.

Microencapsulation provides the means of converting liquids to solids, of altering colloidal and surface properties, of providing environmental protection and of controlling the release characteristics or availability of coated materials. Several of these properties can be attained by macro

packaging techniques; however, the uniqueness of microencapsulation is the smallness of the coated particles and their subsequent use and adaptation to a wide variety of dosage forms and not has been technically feasible⁶.

Firstly the microencapsulation procedure was discovered by Bungen burg de Jon and Kan in 1931 and which were deal with the preparation of gelatine spheres and use of a gelatine coacervation process. The controlled drug delivery system has used to reduce the problems associated with conventional therapy and to improve the therapeutic efficacy of a given drug. The maximum therapeutic efficacy can be achieved by delivering of the active agent in the optimal rate to the target tissue, then causing little toxicity and minimum side effects⁷.

1. REASONS FOR MICROEN - CAPSULATION

- The primary reason for microencapsulation is found to be either for sustained or prolonged drug release.
- This technique has been widely used for masking taste and odour of many drugs to improve patient compliance.

- This technique can be used for converting liquid drugs in a free flowing powder.
- The drugs, which are sensitive to oxygen, moisture or light, can be stabilized by microencapsulation.
- Incompatibility among the drugs can be prevented by microencapsulation.
- Vaporization of many volatile drugs e.g. methyl salicylate and peppermint oil can be prevented by microencapsulation.
- Many drugs have been microencapsulated to reduce toxicity and GI irritation including ferrous sulphate and KCl.
- Alteration in site of absorption can also be achieved by microencapsulation.
- Toxic chemicals such as insecticides may be microencapsulated to reduce the possibility of sensitization of factorial person. Bakan and Anderson reported that microencapsulated vitamin A palmitate had enhanced stability⁸.

2. RELEASE MECHANISMS

Mechanisms of drug release from microspheres are:

2.1. Degradation controlled monolithic system:

-The drug is dissolved in matrix and is distributed uniformly throughout. The drug is strongly attached to the matrix and is released on degradation of the matrix. The diffusion of the drug is slow as compared with degradation of the matrix⁹.

2.2. Diffusion- Diffusion is the most common mechanism of drug release (core material) in which the dissolution fluid penetrates the shell then the core material comes into the contact with the dissolution fluid and leak out through the interstitial channels or pores¹⁰.

Basically, the release of core material depends on (1)the rate of drug dissolution in the dissolution fluid, (2) the rate of penetration of dissolution fluid to the microcapsules and (3) the rate at which the dissolved drug escape from the microcapsule¹¹.

The kinetics of such drug release follows Higuchi's equation¹².

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

Here, Q is the amount of drug released per unit area of exposed surface in time t; J is the tortuosity of the capillary system in the wall; D is the diffusion coefficient of the solute in the solution; A is the total amount of drug per unit volume; ε is the

porosity of the wall of microcapsule; CS is the solubility of drug in permeating dissolution fluid.

2.3. Dissolution- The release rate of drug from the microcapsule depends on the dissolution rate of polymer coat, when the coat is soluble in the dissolution fluid¹³. The solubility in the dissolution fluid and thickness of coat influence the release rate.

2.4. Osmosis- Another method of drug release is through osmosis. The essential requirement of osmosis is semi permeable membrane and in microcapsule polymer coat serve the purpose. As the process progress an osmotic pressure is created between the outside and inside membrane of microcapsule which result in release of drug through small pores.

2.5. Erosion- Erosion of coat generally occur due to pH or enzymatic hydrolysis and causes drug release¹⁴ with certain coat materials like bee's wax, stearyl alcohol and glyceryl monostearate. The drug release from microcapsules has become complicated because of great diversity in physical forms of microcapsules with size, shape and arrangement of the core and coat materials^{15, 16}.

The physiochemical properties of core materials like solubility, diffusibility and

partition coefficient and of coating materials like variable porosity, thickness and inertness which makes difficult to modeling of drug release. However, based on various studies concerning with the release characteristics, the following considerations can be made-

- 1) Drug release rate from microcapsules follow the zero order kinetic.
- 2) Microcapsules of monolithic type have the $t_{1/2}$ dependant release rate for the first half of the total drug release and thereafter turn down exponentially.
- 3) Microcapsules of monolithic type having large excess of dissolved drug, the release rate are $t_{1/2}$ dependant throughout almost the entire drug release.

The path travelled by drug is not constant in monolithic capsules; as the drug at the center travels a large distance than the drug at the surface. Therefore, the release rate in monolithic capsules generally decreases with time.

3. FEATURES AND MORPHOLOGY OF MICROCAPSULE:

Microencapsulation is the packaging of small droplets of liquid or particles with a thin Film¹⁷. Typically, the lowest particle size of microcapsules is $1\mu\text{m}$ and the largest size is

1mm. Microcapsules consist of a core and a wall (or shell). The configuration of the core can be a spherical or irregular particle, liquid-phase suspended solid, solid matrix, dispersed solid and aggregates of solids or liquid forms¹⁸.

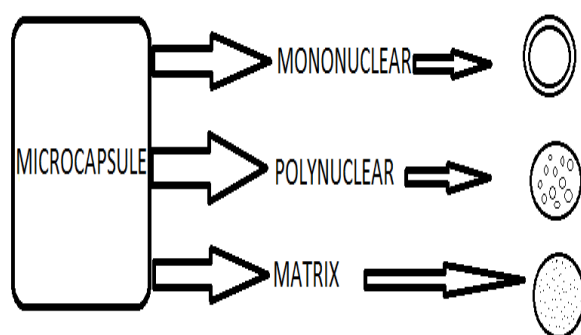
The morphology of microcapsules depends mainly on the core material and the deposition process of the shell.

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

2- Polynuclear capsules have many cores enclosed within the shell.

3- Matrix encapsulation in which the core material is distributed homogeneously into the shell material.

4- In addition to these three basic morphologies, microcapsules can also be mononuclear with multiple shells, or they may form clusters of microcapsules¹⁹.



[Fig.1.different types of microcapsules with structure^{5]}

4. MATERIALS FOR MICROENCAPSULATION

4.1 Core Materials: The specific material to be coated by using the specific coating material can be liquid or solid in nature. The composition of the core material can be varied, as the liquid core can include dispersed and/or dissolved materials. The solid core material can be active constituents, stabilizers, diluents, and release-rate inhibitors or accelerators. This variation in the core material composition provides definite flexibility and utilization of this characteristic then allows effective design and development of the preferred microcapsule properties²⁰.

4.2 Coating Materials: The coating material should be capable of forming a film that is cohesive with the core material; be chemically compatible and nonreactive with the core material; and provide the desired coating properties, such as strength, flexibility, impermeability, optical properties, and stability. The coating materials used in microencapsulation methods are amenable, to some extent, to in situ modification.

5. CRITERIA FOR SELECTION COATING MATERIAL:

The selection of a given coating often can be aided by the review of existing literature and by the study of free or cast films, although

practical use of free-film information often is impeded for the following reasons:

1. Cast or free films prepared by the usual casting techniques yield films that are considerably thicker than those produced by the microencapsulation of small particles; hence, the results obtained from the cast films may not be extrapolate to the thin microcapsule coatings.
2. The particular microencapsulation method employed for the deposition of a given coating produces specific and inherent properties that are difficult to simulate with existing film-casting methods.
3. The coating substrate of core material may have a decisive effect on coating properties. Hence, the selection of a particular coating material involves consideration of both classic free-film data and applied results²⁰.

5.1 Material: That would be depending upon review of existing coating material properties

1. Stabilization of core material.
2. Inert toward active ingredients.
3. Controlled release under specific conditions.

4. Film-forming, pliable, tasteless, stable.

5. Non-hygroscopic, no high viscosity, economical.

6. Soluble in an aqueous media or solvent, or melting.

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

Examples of coating materials:

1. Water soluble resins – Gelatin, Gum Arabic, Starch, Polyvinylpyrrolidone, Carboxymethylcellulose, Hydroxyethylcellulose, Methylcellulose, Arabinogalactan,

Polyvinyl alcohol, Polyacrylic acid.

2. Water insoluble resins – Ethylcellulose, 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, Zein⁶.

6.MICROENCAPSULATION PROCESS SELECTION

The selection of the preferred microencapsulation process for a given application is not always a simple task for there is a large number of processes from which to choose. One must be concerned with such factors as: whether the core is solid or liquid; the solubility characteristics of the core; the reactivity of the core with candidate wall materials and solvents; the size of the desired capsule; the method of attaching the capsule to the desired substrate; the method of core release; and process and product economics²¹.

7. TECHNIQUES TO MANUFACTURE MICROCAPSULES

Manufacturing techniques of micro-capsules:

Microcapsules as bulk materials, in either dry powder or dispersed form, can be processed into final product applications using common equipment such as V-blenders, tablet machines, granulators, homogenizers, kneaders, hard gelatine capsule filling machines, or coating equipment if deposition onto a substrate is desired⁶.

There are many factors to consider when selecting the encapsulation process and also various techniques are available for the encapsulation of core materials. Broadly the methods are divided into two

types, such as physical and chemical methods.

7.1. Physical methods

7.1.a. Air-suspension coating

Air-suspension coating of particles by solutions or melts gives better control and flexibility. The particles are coated while suspended in an upward-moving air stream. They are supported by a perforated plate having different patterns of holes inside and outside a cylindrical insert. Just sufficient air is permitted to rise through the outer annular space to fluidize the settling particles. Most of the rising air (usually heated) flows inside the cylinder, causing the particles to rise rapidly. At the top, as the air stream diverges and slows, they settle back onto the outer bed and move downward to repeat the cycle. The particles pass through the inner cylinder many times in a few minutes methods.

The air suspension process offers a wide variety of coating materials candidates for microencapsulation. The process has the capability of applying coatings in the form of

solvent solutions, aqueous solution, emulsions, dispersions or hot melts in equipment ranging in capacities from one pound to 990 pounds. Core materials comprised of micron or submicron

particles can be effectively encapsulated by air suspension techniques, but agglomeration of the particles to some larger size is normally achieved²².

The process variables that can affect the process-⁶

- 1) Concentration of the coating material or if in solution form then melting point.
- 2) Solubility, surface area, density, melting point volatility, volatility of core material.
- 3) Application rate of coating material.
- 4) Temperature of air stream.
- 5) The amount of air required to fluidize the core material.

7.1.b Non Aqueous phase separation

Non Aqueous phase separation is the inverse of the aqueous phase process in that the continuous wall-containing phase is organic or hydrophobic in nature, and the core material is usually water-immisible (hydrophilic). In the process the core liquid is suspended in droplet form by stirring in polymer solution (wall material). Phasing out and core wrapping of the wall material is caused by the addition of a liquid (non solvent) that is miscible with the organic solvent but immiscible with both the core particle and particle and the polymeric wall material²³.

7.1.c. Coacervation Process

Solution of the shell material in water.

Example: Copolymer coating

Gum arabic solution 20-30%

Gelatin solution 20%

➤ Preparation

- The core material will be added to the solution. The core material should not react or dissolve in water (maximum solubility 2%)

➤ Dispersion

- The core material is dispersed in the solution. The particle size will be defined by dispersion parameter, as stirring speed, stirrer shape, surface tension and viscosity. Size range ca. 2 μ m - 1200 μ m

➤ Coacervation

- Coacervation starts with a change of the pH value of the dispersion, e.g. by adding H₂SO₄, HCl or organic acids. The result is a reduction of the solubility of the dispersed phases (shell material).
- The shell material (coacervate) starts to precipitate from the solution.
- The shell material forms a continuous coating around the core droplets.

➤ Cooling and hardening phase

- The shell material is cooled down to harden and forms the final capsule.
- Hardening agents like formaldehyde can be added to the process.
- The microcapsules are now stable in the suspension and ready to be dried.

➤ **Drying phase**

- The suspension is dried in a spray dryer or in a fluidized bed drier.
- Spray Drying is a suitable method for heat sensitive Products.
- The atomized particles assume a spherical shape. The rapid the coating material keeps the core material below 100°C, even if the temperature in the drying chamber is much greater.
- Microencapsulation makes the spray drying process easier for sticky products like fruit pulp or juice, with a high content of invert sugar²⁴.

7.1.c. (a) Coacervation-Phase Separation

The general outline of the processes consists of three steps carried out under continuous agitation:

- 1. Formation of three immiscible chemical phases** – A liquid manufacturing vehicle phase, a core

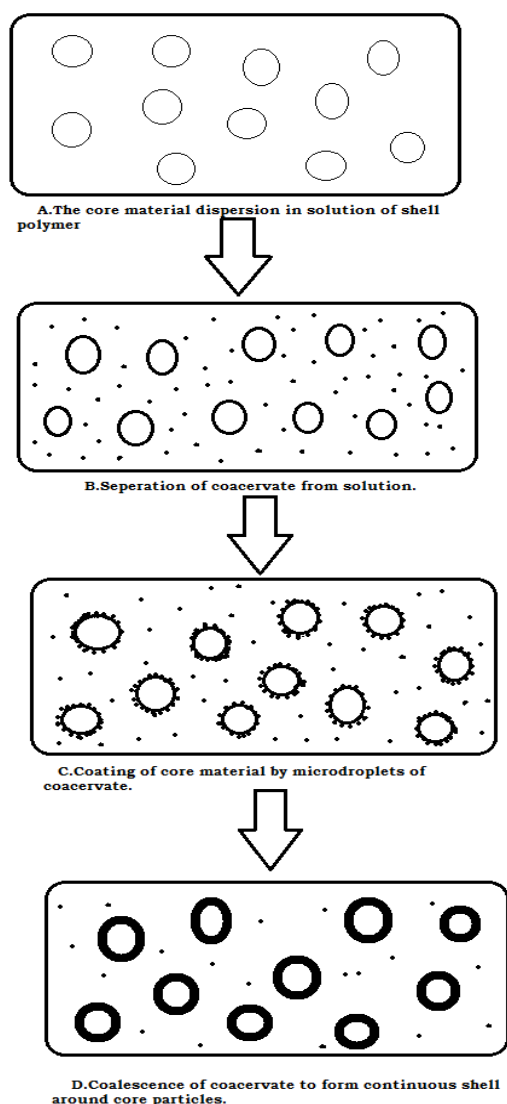
material phase, and a coating material phase. To form the three phases, the core material dispersed in a solution of the coating polymer, the solvent for the polymer being the liquid manufacturing vehicle phase. The coating material phase, an immiscible polymer in a liquid state, is formed by utilizing one of the methods of the methods of phase separation-coacervation, i.e., by changing the temperature of the polymer solution; or by adding a salt, nonsolvent, or incompatible polymer to the polymer solution; or by inducing a polymer-polymer interaction.

2. Deposition of the coating – It consists of depositing the liquid polymer coating upon the core material. This is accomplished by controlled, physical mixing of the material in the manufacturing vehicle.

Deposition if the liquid polymer coating around the core material occurs if the polymer is adsorbed at the interface formed between the core material and the liquid vehicle phase, and this adsorption phenomenon is a prerequisite to effective coating. The continued deposition of the coating material is promoted by a reduction in the total free interfacial energy of the system, brought about by the

decrease of the coating material surface area during coalescence of the liquid polymer droplets.

3. Rigidization of the coating – It involves rigidizing the coating, usually by thermal, cross-linking, or desolvation techniques, to form a self-sustaining microcapsules⁶. *e.g.* Coacervation Microencapsulation of talc particles with Poly (methyl methacrylate) by Pressure-Induced Phase Separation of CO₂-Expanded Ethanol Solutions²⁵.



[Fig.2. Schematic representation of coacervation process⁵.]

7.1.d Centrifugal extrusion

Liquids are encapsulated using a rotating extrusion head containing concentric nozzles. In this process, a jet of core liquid is surrounded by a sheath of wall solution or melt.

As the jet moves through the air it breaks, owing to Rayleigh instability, into droplets of core, each coated with the wall solution. While the droplets are in flight, a molten wall may be hardened or a solvent may be evaporated from the wall solution. Since most of the droplets are within $\pm 10\%$ of the mean diameter, they land in a narrow ring around the spray nozzle. Hence, if needed, the capsules can be hardened after formation by catching them in a ring-shaped hardening bath.

This process is excellent for forming particles 400–2,000 μm (16–79 mils) in diameter. Since the drops are formed by the breakup of a liquid jet, the process is only suitable for liquid or slurry. A high production rate can be achieved, i.e., up to 22.5 kg (50 lb) of microcapsules can be produced per nozzle per hour per head. Heads containing 16 nozzles are available²².

7.1.e Pan coating

The pan coating process, widely used in the pharmaceutical industry, is among the oldest industrial procedures for forming small, coated particles or tablets. The particles are tumbled in a pan or other device while the coating material is applied slowly²².

The pan coating process, widely used in the pharmaceutical industry, is among the oldest industrial procedures for forming small, coated particles or tablets. The particles are tumbled in a pan or other device while the coating material is applied slowly with respect to microencapsulation, solid particles greater than 600 microns in size are generally considered essential for effective coating, and the process has been extensively employed for the preparation of controlled - release beads. Medicaments are usually coated onto various spherical substrates such as nonpareil sugar seeds, and then coated with protective layers of various polymers.

In practice, the coating is applied as a solution, or as an atomized spray, to the desired solid core material in the coating pans. Usually, to remove the coating solvent, warm air is passed over the coated materials as the coatings are being applied in the coating pans. In some

cases, final solvent removal is accomplished in a drying oven⁶.

1.6 Spray-drying

Spray drying serves as a microencapsulation technique when an active material is dissolved or suspended in a melt or polymer solution and becomes trapped in the dried particle. The main advantages is the ability to handle labile materials because of the short contact time in the dryer, in addition, the operation is economical. In modern spray dryers the viscosity of the solutions to be sprayed can be as high as 300mPa.s.

Spray drying and spray congealing processes are similar in that both involve dispersing the core material in a liquefied coating substance and spraying or introducing the core - coating mixture into some environmental condition, whereby, relatively rapid solidification (and formation) of the coating is effected. The principal difference between the two methods is the means by which coating solidification is accomplished. Coating solidification in the case of spray drying is effected by rapid evaporation of a solvent in which the coating material is dissolved.

Coating solidification in spray congealing methods, however, is accomplished by thermally congealing a

molten coating material or by solidifying a dissolved coating by introducing the coating - core material mixture into a nonsolvent. Removal of the nonsolvent or solvent from the coated product is then accomplished by sorption, extraction, or evaporation techniques.

In practice, microencapsulation by spray drying is conducted by dispersing a core material in a coating solution, in which the coating substance is dissolved and in which the core material is insoluble, and then by atomizing the mixture into air stream. The air, usually heated, supplies the latent heat of vaporization required to remove the solvent from the coating material, thus forming the microencapsulated product. The equipment components of a standard spray dryer include an air heater, atomizer, main spray chamber, blower or fan, cyclone and product collector.

Microencapsulation by spray congealing can be accomplished with spray drying equipment when the protective coating is applied as a melt. General process variables and conditions are quite similar to those already described, except that the core material is dispersed in a coating material melt rather than a coating solution.

Coating solidification (and microencapsulation) is accomplished by spraying the hot mixture into a cool air stream. Waxes, fatty acids and alcohols, polymers and sugars, which are solids at room temperature but meltable at reasonable temperatures, are applicable to spray congealing techniques. Typically, the particle size of spray congealed products can be accurately controlled when spray drying equipment is used, and has been found to be a function of the feed rate, the atomizing wheel velocity, dispersion of feed material viscosity, and variables⁶.

Airflow

The initial contact between spray droplets and drying air controls evaporation rates and product temperatures in the dryer. There are three modes of contact:

1.6.1. Co-current

Drying air and particles move through the drying chamber in the same direction. Product temperatures on discharge from the dryer are lower than the exhaust air temperature, and hence this is an ideal mode for drying heat sensitive products. When operating with rotary atomizer, the air disperser creates a high degree of air rotation, giving uniform temperatures throughout the drying chamber. However, an alternative non-rotating airflow is often

used in tower or FILTERMAT®-type spray dryers using nozzle atomizers with equal success.

1.6.2. Counter-current

Drying air and particles move through the drying chamber in opposite directions. This mode is suitable for products which require a degree of heat treatment during drying.

The temperature of the powder leaving the dryer is usually higher than the exhaust air temperature.

1.6.3. Mixed-flow

Particle movement through the drying chamber experiences both co-current and counter-current phases. This mode is suitable for heat stable products where coarse powder requirements necessitate the use of nozzle atomizers, spraying upwards into an incoming airflow, or for heat sensitive products where the atomizer sprays droplets downwards towards an integrated fluid bed and the air inlet and outlet are located at the top of the drying chamber. e.g. Study on microencapsulation of lycopene by spraydrying²⁶.

2. Chemical process

2.1 Solvent Evaporation

This technique has been used by companies including the NCR Company, Gavaert Photo - Production NV, and Fuji Photo Film Co., Ltd. to produce microcapsules. The processes are carried out in a liquid manufacturing vehicle. The microcapsule coating is dissolved in a volatile solvent, which is immiscible with the liquid manufacturing vehicle phase.

A core material to be microencapsulated is dissolved or dispersed in the coating polymer solution. With agitation, the core coating material mixture is dispersed in the liquid manufacturing vehicle phase to obtain the appropriate size microcapsule. The mixture is then heated (if necessary) to evaporate the solvent for the polymer. In the case in which the core material is dispersed in the polymer solution, polymer shrinks around the core. In the case in which core material is dissolved in the coating polymer solution, a matrix - type microcapsule is formed. Once all the solvent for the polymer is evaporated, the liquid vehicle temperature is reduced to ambient temperature (if required) with continued agitation. At this stage, the microcapsules can be used in suspension form, coated on to substrates or isolated as powders.

The solvent evaporation technique to produce microcapsules is applicable to a wide variety of liquid and solid core materials. The core materials may be either water - soluble or water - insoluble materials. A variety of film - forming polymers can be used as coatings ⁶.

eg. Evaluation of Esters as Alternative Surfactants in Microencapsulation of Proteins by the Solvent Evaporation Method²⁷.

2.2. Polymerization

A. Interfacial polymer

In Interfacial polymerization, the two reactants in a polycondensation meet at an interface and react rapidly. The basis of this method is the classical Schotten Baumann reaction between an acid chloride and a compound containing an active hydrogen atom, such as an amine or alcohol, polyesters, polyurea, polyurethane. Under the right conditions, thin flexible walls form rapidly at the interface. A solution of the pesticide and a diacid chloride are emulsified in water and an aqueous solution containing an amine and a polyfunctional isocyanate is added. Base is present to neutralize the acid formed during the reaction. Condensed polymer walls form instantaneously at the interface of the emulsion droplets.

B. *In-situ* polymerization

In a few microencapsulation processes, the direct polymerization of a single monomer is carried out on the particle surface. In one process, e.g. Cellulose fibers are encapsulated in polyethylene while immersed in dry toluene. Usual deposition rates are about 0.5 μ m/min.

Coating thickness ranges 0.2-75 μ m. The coating is uniform, even over sharp projections.

C. Matrix polymer

In a number of processes, a core material is imbedded in a polymeric matrix during formation of the particles. A simple method of this type is spray-drying, in which the particle is formed by evaporation of the solvent from the matrix material. However, the solidification of the matrix also can be caused by a chemical change.

Using this phenomenon, Chang prepares microcapsules containing protein solutions by incorporating the protein in the aqueous diamine phase. Chang has demonstrated the permselectivity, by their ability to convert blood urea to ammonia, the enzyme remaining within the microcapsules when incorporated within an extracorporeal shunt system.

Numerous groups are utilizing polymerization techniques to accomplish microencapsulation. Examples are the National Lead Corporation, Eurand America²².

6. APPLICATIONS

6.1 General Applications

1. Cell immobilization: In plant cell cultures, Humantissue is turned into bio-artificial organs, in continuous fermentation processes.
2. Beverage production.
3. Protection of molecules from other compounds:
4. Drug delivery: Controlled release delivery systems.
5. Quality and safety in food, agricultural & environmental sectors.
6. Soil inoculation.
7. In textiles: means of imparting finishes.
8. Protection of liquid crystals^{28, 29}.
9. Most flavouring is volatile; therefore encapsulation of these components extends the shelf-life of products by retaining within the food flavours that would otherwise evaporate out and be lost. Some

ingredients are encapsulated to mask taste, such as nutrients added to fortify a product without compromising the product's intended taste³⁰.

6.2 Controlled Release And Sustained Release Dosage Forms^{7, 31}.

It includes,

1. To mask the bitter taste of drugs like Paracetamol, Nitrofurantoin etc.
2. To reduce gastric and other gastro intestinal (G.I) tract irritations, e.g., sustained release Aspirin preparations have been reported to cause significantly less G.I. bleeding than conventional preparations.
3. A liquid can be converted to a pseudo-solid for easy handling and storage e.g. eprazinone.
4. Hygroscopic properties of core materials may be reduced by microencapsulation e.g., Sodium chloride.
5. Carbon tetrachloride and a number of other substances have been microencapsulated to reduce their odor and volatility.

6. Microencapsulation has been employed to provide protection to the core materials against atmospheric effects, e.g., Vitamin-A Palmitate.

7. Separation of incompatible substance has been achieved by encapsulation^{7, 31}.

8. Physicochemical evaluation characterization: The characterization of the microparticulate carrier is an important phenomenon, which helps to design a suitable carrier for the proteins, drug or antigen delivery. These microspheres have different microstructures. These microstructures determine the release and the stability of the carrier³².

9. Sieve analysis: Separation of the microspheres into various size fractions can be determined by using a mechanical sieve shaker³³.

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